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Identifying Typologies of Breast Cancer Patients Undergoing Chemotherapy Based on Multiple Indicators of Sleep and Fatigue

A dissertation submitted in partial satisfaction of the requirements for the degree of Doctor of Philosophy

in

Clinical Psychology

by

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The Dissertation of Rina Sobel Fox is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

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DEDICATION

In dedication to my husband, Jason, my parents, Richard and Rachel, my brother, Mark, my grandfather, Martin, and the memory of my grandparents David, Dolores, and Janet. Without your unconditional, unquestioning, and unending love and support I never would have been capable of completing this dissertation. Your encouragement and faith in me fueled my efforts to continue when I doubted that the light at the end of the tunnel could ever be reached. I am more fortunate than I can express to have had you in my corner through every step of this journey, and to know that we will always remain in each other's corners regardless of what the future may hold.

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Chapters 1, 2, 3, 4, and 5 are being prepared for publication. Publications based on this dissertation will be co-authored by Vanessa L. Malcarne, Sonia Ancoli-Israel, Scott C. Roesch, Georgia Robins Sadler, and Kristen Wells. The dissertation author was the primary investigator and author of this material.

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BOOK CHAPTERS

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ABSTRACT OF THE DISSERTATION

Identifying Typologies of Breast Cancer Patients Undergoing Chemotherapy Based on Multiple Indicators of Sleep and Fatigue

by

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Doctor of Philosophy in Clinical Psychology

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Rationale. Secondary to breast cancer and its treatment, fatigue has been identified as one of the most commonly reported symptoms by patients at all stages along the cancer continuum. In addition, sleep disruption has been shown to be notably elevated among cancer patients as compared to the general population. Sleep disruption and cancer-related fatigue have often been evaluated as components of larger symptom clusters, along with other cancer-related medical and psychosocial symptoms. While

many studies have evaluated symptom clusters in breast cancer, few have examined symptom clusters that consider multiple indicators of sleep disruption and fatigue, and most have utilized suboptimal statistical strategies. The present project identified sleep and fatigue symptom cluster groups of breast cancer patients using Latent Profile Analysis (LPA) based on two indicators of objective sleep, one measure of subjective sleep quality, and five dimensions of cancer-related fatigue. Groups were then compared on sociodemographic, medical, and psychosocial characteristics.

Design. Participants were 152 women with newly diagnosed stage I-III breast cancer with no prior exposure to chemotherapy who were scheduled to receive at least four cycles of anthracycline-based chemotherapy. Participants were recruited through two separate studies with identical protocols, recruitment techniques, and inclusion criteria. Across both studies data were collected prior to the initiation of chemotherapy treatment (i.e., T1), and again at the last week of the fourth cycle of chemotherapy (i.e., T2). Exploratory LPA was used to derive categorical latent variables at T1 and T2 representing groups of individuals who scored similarly on percent of the day spent asleep and percent of the night spent asleep based on actigraphy (i.e., objective sleep), the Pittsburgh Sleep Quality Index total score (i.e., subjective sleep quality), and the General fatigue, Physical fatigue, Emotional fatigue, Mental fatigue, and Vigor subscales of the Multidimensional Fatigue Symptom Inventory-Short Form (i.e., five dimensions of cancer-related fatigue). Logistic regression analyses then evaluated if sociodemographic, medical, and psychosocial characteristics at T1 significantly predicted group membership at both time points. Analyses of covariance (ANCOVAs) evaluated if groups identified at both time points had different means on psychosocial variables at T2. The psychosocial

characteristics explored included depression, climacteric symptomatology, and mental, physical, and breast cancer specific health-related quality of life.

Results. At T1 (N = 152) three groups were identified, and at T2 (n = 128) five groups were identified. Bivariate logistic regression analyses demonstrated that T1 values on select sociodemographic, select medical, and all psychosocial variables significantly predicted group membership at T1 and at T2. ANCOVAs identified that, after controlling for covariates, groups identified at T1 did not significantly differ on any psychosocial variables measured at T2. Conversely, after controlling for covariates, groups identified at T2 had different means on all psychosocial variables measured at T2.

Conclusions. Distinct groups with unique sleep and cancer-related fatigue experiences were found among breast cancer patients prior to the initiation of chemotherapy, and again at the last week of the fourth cycle thereof. Results identify T1 sociodemographic, medical, and psychosocial variables that can be used to indicate likely group membership, and clarify which groups may be at heightened risk for poor psychosocial outcomes at T2. These results can inform the development of assessments and interventions to improve breast cancer patients' overall experience of disease.

CHAPTER 1: INTRODUCTION

The present study addressed three primary questions regarding the roles of sleep disruption and cancer-related fatigue in breast cancer. First, this project evaluated the distinguishing characteristics of groups of patients based on their differential experiences of a symptom cluster comprised of objective sleep, subjective sleep quality, and multidimensional cancer-related fatigue prior to the initiation of chemotherapy and again at the last week of the fourth cycle of treatment. Second, this project demonstrated how sociodemographic, medical, and psychosocial variables evaluated prior to the initiation of chemotherapy treatment predicted group membership both prior to the initiation of chemotherapy and at the last week of the fourth cycle of treatment. Finally, the present analysis investigated if group membership had implications for psychosocial well-being at the last week of the fourth cycle of chemotherapy treatment among patients being treated for breast cancer.

The present study evaluated data provided by women undergoing chemotherapy treatment for breast cancer to 1) establish groups of patients using latent profile analysis based on simultaneous consideration of cross-sectional objective sleep (two observed variables), subjective sleep quality (one observed variable), and multiple dimensions of cancer-related fatigue (five observed variables) at pre-treatment (N = 152), and again at the last week of the fourth cycle of chemotherapy (n = 128); 2) evaluate if sociodemographic, medical, and psychosocial variables measured prior to the initiation of chemotherapy treatment could significantly predict group membership; and 3) evaluate psychosocial differences among groups at the last week of the fourth cycle of chemotherapy, after controlling for pre-treatment levels of those psychosocial variables

as well as all other variables found to significantly differ across groups prior to the initiation of chemotherapy treatment. Such an approach can shed light on the specific ways in which different aspects of sleep and cancer-related fatigue are interrelated, how they are associated with pre-treatment sociodemographic, medical, and psychosocial variables, and the implications this may have for psychosocial well-being among women undergoing chemotherapy treatment for breast cancer.

Chapter 1 is being prepared in part for publication. This publication will be co-authored by Vanessa L. Malcarne, Sonia Ancoli-Israel, Scott C. Roesch, Georgia Robins Sadler, and Kristen Wells. The dissertation author was the primary investigator and author of this material.

CHAPTER 2: BACKGROUND AND SIGNIFICANCE

2.1 The Epidemiology of Breast Cancer in the United States

Breast cancer is a highly prevalent disease, particularly among developed nations such as the United States (American Cancer Society [ACS], 2013; 2014a; 2015). Breast cancer is a clinical disease characterized by the uncontrolled division and multiplication of abnormal cells in the mammary lobules, the glands responsible for milk production, or in the ducts connecting the lobules to the nipples (ACS, 2013; National Cancer Institute [NCI], 2013). Breast cancer is most frequently detected during a screening examination in the absence of clinical symptoms, or at a diagnostic appointment following identification of a breast lump (ACS, 2013). It is anticipated that over 200,000 incident cases of invasive breast cancer will be diagnosed among women in the United States in 2015, in addition to nearly 65,000 incident cases of in situ breast cancer (ACS, 2015). Moreover, the anticipated mortality in 2015 is over 40,000 women, making breast cancer the second leading cause of cancer-related death among women in the United States, following cancers of the lung and bronchus (ACS, 2015).

The epidemiological burden of breast cancer has been shown to increase with age and is highest for women between the ages of 50 and 80, with a median diagnostic age of 61 years (ACS 2013; 2014a). The lifetime risk of breast cancer for a woman living in the United States is currently 12.3%, representing a one in eight chance of diagnosis over a woman's entire lifetime (ACS, 2013). Breast cancer rates have been shown to vary across racial/ethnic groups. Non-Hispanic white women have typically been shown to be at higher risk than African Americans, followed by all other racial and ethnic groups; Asian and Pacific Islander women have the lowest breast cancer incidence and mortality rates

(ACS, 2013). Breast cancer risk has also been shown to be heightened among individuals who are overweight or obese, have previously used estrogen replacement therapy, consume alcohol, are long-term heavy smokers, are shift workers, or are physically inactive (ACS, 2014a; 2015). Other risk factors include high breast tissue density, high bone mineral density, type II diabetes, long menstrual history, nulliparity, having one's first child after age 30, recent use of oral contraceptives, family history of breast cancer, personal history of certain benign breast conditions such as atypical hyperplasia, and genetic mutations (e.g., BRCA-1 and BRCA-2 mutations; ACS, 2014a; 2015).

2.2 Sleep and Breast Cancer

Prevalence and severity of disordered sleep in cancer. Sleep disturbance is one of the primary complaints of cancer patients before, during, and after treatment (Liu & Ancoli-Israel, 2008; Palesh et al., 2013). Numerous sleep disorders have been examined in cancer patients, such as sleep disordered breathing and periodic limb movements during sleep; however, the majority of research evaluating sleep in cancer has focused on insomnia (Liu & Ancoli-Israel, 2008). Insomnia disorder is characterized by dissatisfaction with sleep quantity or quality related to difficulty falling asleep, difficulty staying asleep, or experiencing early-morning awakenings and being unable to return to sleep (American Psychiatric Association, 2013). To meet diagnostic criteria these symptoms must occur on at least three nights per week, last at least three months, occur despite adequate opportunity for sleep, and result in clinically significant distress or functional impairment. Research has demonstrated that insomnia risk is elevated among cancer patients as compared to the general population (Fiorentino, Rissling, Liu, & Ancoli-Israel, 2011). Rates of clinical insomnia in cancer have varied across studies, with

reports ranging from 20% to 75% in recent reviews (Fiorentino et al., 2011; Liu & Ancoli-Israel, 2008). Moreover, subclinical symptoms of insomnia have been reported in up to 80% of cancer patients (Palesh et al., 2013), and an estimated 41% of cancer patients experience chronic sleep deprivation (Carter, Mikan, & Patt, 2014). In their systematic review, Fiorentino and Ancoli-Israel (2007) postulated that sleep disturbance among cancer patients may be underestimated, as not all patients who are experiencing sleep disruption report it to their medical providers. Further, insomnia has been shown to be even more highly prevalent among patients with breast cancer as compared to other cancer patients (Davidson, MacLean, Brundage, & Schulze, 2002; Palesh et al., 2010). Comparatively, in the general population insomnia prevalence has been estimated at only 20%, and approximately 30% of adults worldwide have reported experiencing at least one symptom of insomnia (Fiorentino & Ancoli-Israel, 2006; Roth, 2007).

Objective and subjective measurement of disordered sleep. Sleep disruption is typically measured in one of two ways: via objective evaluation tools or via subjective evaluation tools. Prior studies have demonstrated that these two measurement techniques often disagree (Dhruva et al., 2012; Silberfarb, Hauri, Oxman, & Schnurr, 1993). Across both techniques there are a number of indicators of sleep quality that are generally evaluated, including the time it takes to fall asleep (i.e., sleep onset latency; SOL), the amount of time spent awake between sleep onset and final awakening (i.e., wake after sleep onset; WASO), the ratio of time spent asleep to time spent in bed attempting to sleep (i.e., sleep efficiency; SE), and the total amount of time spent sleeping (i.e., total sleep time; TST).

The "gold standard" method for evaluating sleep is laboratory-administered polysomnography, an objective indicator. However, given the high patient burden, difficulty of use, and large demand on clinical resources, this approach is not well suited for fieldwork. In their systematic review, Van de Water, Holmes, and Hurley (2011) listed objective alternatives to polysomnography, including actigraphy, bed actigraphy (i.e., movement/load sensors under bed legs), sensitive bed sensors (i.e., a thin sensor sensitive to changes in pressure, light, and temperature used in addition to actigraphy), eye movement- and non-invasive arm sensors, a sleep switch, and a remote device. Of these, only actigraphy has been widely used and validated among various populations. According to this review, among healthy populations actigraphy and polysomnography had an agreement rate of 72.1% to 96.5%, and the ability of actigraphy to accurately detect sleep (i.e., sensitivity) and wakefulness (i.e., specificity) ranged from 86.5% to 98.7% and 27.7% to 67.1%, respectively (Van de Water et al., 2011). These rates were somewhat lower among clinical populations, and actigraphy demonstrated a tendency to overestimate time spent asleep, particularly among individuals with lower sleep efficiency. This is because inactive stillness, which can be achieved during both wakefulness and sleep, is the criterion used to define sleep in actigraphy (Van de Water et al., 2011). Thus, this overestimation may be more severe among individuals experiencing sleep disruption, who are more likely to spend time lying still and awake while in bed (Sadeh, Hauri, Kripke, & Lavie, 1995). With specific regard to cancer patients, a systematic review by Liu and Ancoli-Israel (2008) found evidence that both polysomnography and actigraphy detect increased levels of sleep disruption as compared to the general population.

Subjective sleep assessments, on the other hand, provide more information about individuals' perceptions of the quantity and quality of their sleep. Commonly used subjective measurements include sleep diaries and self-report questionnaires, such as the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989). Research has demonstrated that subjective estimates of sleep depend greatly on SOL and the frequency and overall duration of WASO (Lewis, 1969), as well as sleep efficiency (Åkerstedt, Hume, Minors, & Waterhouse, 1994). Further, as compared to objective assessments, subjective sleep estimates often overestimate SOL and underestimate WASO (Baker, Maloney, & Driver, 1999), although this may be due to the sensitivity of objective measurement to awakenings that are so superficial and brief that they are not consciously recognized. Interestingly, research has shown that when data provided by actigraphy are supplemented by those provided by subjective measures such as sleep diaries, sleep parameters from actigraphy do not significantly differ from those provided by the gold standard of polysomnography (Kushida et al., 2001). This provides support for the use of both objective and subjective assessments of sleep in a single study when conducting field research that precludes the use of polysomnography. Like objective measurement techniques, subjective ratings of sleep have detected increased rates of sleep disruption among cancer patients as compared to the general population (Liu & Ancoli-Israel, 2008).

Process and correlates of disordered sleep in cancer. A leading theory of insomnia etiology is the four-factor model. This theory was founded in Spielman and colleagues' diathesis-stress based Behavioral Model of Insomnia, in which insomnia is believed to be motivated by predisposing, precipitating, and perpetuating factors (also

known as the "3Ps Model"; Spielman & Glovinsky, 1991; Spielman, Saskin, & Thorpy, 1987). Another leading theory is Bootzin's Stimulus Control perspective, which posits that excessive engagement in non-sleep behaviors in the bedroom serves as a perpetuating factor of chronic insomnia (Bootzin, 1972). This fourth factor, "conditioned arousal," was later added to the model as a target in Cognitive Behavioral Therapy for Insomnia (Perlis, Jungquist, Smith, & Posner, 2005). In their review applying this model to the cancer context, Savard and Morin (2001) identified 1) hyper-arousability, female gender, age, and personal/family history of insomnia as potential predisposing factors, 2) emotional distress, functional loss, and pain secondary to cancer and its treatment as precipitating factors, and 3) poor sleep hygiene and dysfunctional beliefs about sleep as perpetuating factors of insomnia. It has been further hypothesized that the most likely etiology of insomnia in cancer is a detrimental feedback cycle (Fiorentino & Ancoli-Israel, 2007; Fiorentino et al., 2011). In this cycle, the challenges related to cancer's diagnosis and treatment can preempt an acute bout of insomnia, which can in turn worsen health symptoms associated with cancer such as pain, psychiatric disorders, fatigue, use of opioids and stimulants, and napping. These can then in turn perpetuate dysfunctional sleep (Fiorentino et al., 2011). Further supporting this, in their longitudinal study Rumble et al. (2010) identified dysfunctional cognitions about sleep and sleep-disruptive behaviors as antecedents to insomnia in cancer, and pain, fatigue, hot flashes less positive mood, and dysfunctional cognitions about sleep as consequences thereof. Additionally, Flynn et al. (2010) reported that, in addition to causes of sleep disturbance commonly reported by non-cancer populations, cancer patients often identify additional cancer-

specific causes including abnormal dreams, cancer-specific anxiety, night sweats, and difficulty finding a position in which to sleep.

The increased prevalence of sleep disruption within breast cancer is likely due to myriad reasons, including female gender, increased incidence of hot flashes and night sweats secondary to breast cancer treatment, and increased levels of depression and psychological distress (Fiorentino & Ancoli-Israel, 2006). In their cross-sectional study of 2,645 breast cancer patients, Bardwell and colleagues (2008) identified physical health/symptoms and psychosocial factors as the leading correlates of insomnia. Specifically, hierarchical binary logistic regression analysis identified depressive symptoms and vasomotor symptoms, particularly night sweats, as the only significant individual risk factors for insomnia when controlling for cancer-specific variables, patient characteristics, health behaviors, other physical health/symptom variables, and other psychosocial variables.

Disordered sleep has also been shown to have a number of negative functional outcomes, including excessive daytime somnolence, increased risk for automobile accidents, and cognitive impairment (Connor, Whitlock, Norton, & Jackson, 2001; Fulda & Schulz, 2001; Pagel, 2009). Correlates of disordered sleep have also been explored specifically among breast cancer patients. For example, in their study of 63 women, Caplette-Gingras, Savard, Savard, and Ivers (2013) found that insomnia was associated with worse cognitive functioning. Sleep disturbance has also been shown to be associated with general distress in patients with metastatic breast cancer (Mosher & DuHamel, 2012). Furthermore, among long-term breast cancer survivors, correlates of sleep disturbance include hot flashes, worse physical functioning, depressive symptoms, non-

cancer comorbidities, distress, and residual effects of completed cancer treatments (Otte, Carpenter, Russell, Bigatti, & Champion, 2010). Further, among patients with different advanced cancers, sleep disturbance has been shown to be associated with other cancer-related symptoms such as pain, depression, anxiety, and overall subjective well-being (Delgado-Guay, Yennurajalingam, Parsons, Palmer, & Bruera, 2011). A recent study found that, among women with advanced breast cancer, lower sleep efficiency and increased sleep disruption may be associated with overall mortality even after adjusting for known prognostic variables including age, estrogen receptor status, cancer treatment, metastatic spread, cortisol levels, and depression (Palesh et al., 2014).

Interestingly, there is some research suggesting that the correlates of sleep may differ depending upon whether sleep is measured via objective or subjective evaluation tools. Dhruva et al. (2012) evaluated correlates of subjective and objective measurements of sleep disturbance separately using hierarchical linear modeling with a sample of 73 breast cancer patients undergoing radiation therapy. These authors found that pre-treatment objective sleep disturbance was associated with body mass index, while pre-treatment subjective sleep disturbance was associated with comorbidities and other cancer-related symptoms including fatigue and depression. These findings provide additional support for measuring sleep using both objective and subjective assessment techniques in a single study. Additionally, the repeated identification of cancer-related fatigue as a correlate of sleep disruption among cancer patients in studies focusing on sleep (e.g., Dhruva et al., 2012; Rumble et al., 2010) highlights the need for studies that consider the interrelationship of these two constructs within the cancer context.

2.3 Cancer-Related Fatigue

Prevalence and severity of cancer-related fatigue. Cancer-related fatigue has garnered a great deal of research attention and has been the focus of numerous reviews published within the past decade (e.g., Berger, Gerber, & Mayer, 2012; Brown & Kroenke, 2009; Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, & Morrow, 2007; Kangas, Bovbjerg, & Montgomery, 2008; Minton & Stone, 2008, 2009; Seyidova-Khoshknabi, Davis, & Walsh, 2011). It is well established that cancer-related fatigue is one of the most commonly experienced and reported symptoms of the disease and its treatment (Hofman et al., 2007; Morrow, Andrews, Hickok, Roscoe, & Matteson, 2002; National Comprehensive Cancer Network [NCCN], 2012; Stasi, Abriani, Beccaglia, Terzoli, & Amadori, 2003; Stone & Minton, 2008). A panel of fatigue experts convened by the NCCN defined cancer-related fatigue as "an unusual, persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (p. 527, Mock et al., 2000). As compared to typical fatigue experienced by healthy individuals, cancer-related fatigue is relatively more severe, more upsetting, more disabling, more long lasting, and more challenging to relieve (de Jong, Courtens, Abu-Saad, & Schouten, 2002). In fact, cancer-related fatigue has been described as more closely approximating chronic fatigue syndrome than it does normal, healthy fatigue (Bennett, Goldstein, Friedlander, Hickie, & Lloyd, 2007). It involves excessive physical, emotional, and/or cognitive weakness, tiredness, and lack of energy associated with cancer and its treatment (Cella, Peterman, Passik, Jacobsen, & Breitbart, 1998; Portenoy & Itri, 1999). Cancer-related fatigue does not subside with adequate sleep and rest, and is disproportionate to exertion (Cella, Davis, Breitbart, & Curt, 2001; Morrow, Shelke,

Roscoe, Hickok, & Mustian, 2005; NCCN, 2012). Unlike other symptoms and side effects of cancer and its treatment, such as pain, nausea, vomiting, and muscle weakness, cancer-related fatigue often does not diminish in the aftermath of treatment (Curran, Beacham, & Andrykowski, 2004; Stone et al., 2000). Rather, research has indicated that cancer-related fatigue may persist or even increase in severity over time (Bower et al., 2000; Cella et al., 2001; Hofman et al., 2007; Reinersten et al., 2010). Moreover, cancer-related fatigue has been reported as more distressing and having a stronger negative impact on quality of life than other cancer-related symptoms (Hofman et al., 2007).

Specifically within breast cancer, cancer-related fatigue has been shown to be highly prevalent (de Jong et al., 2002; Minton & Stone, 2008). Although there is notable variability across studies, research has shown that 24% to 89% of breast cancer patients report cancer-related fatigue while undergoing treatment, and 22% to 90% continue to do so after completion of chemotherapy (de Jong et al., 2002). Studies have shown that breast cancer patients frequently experience cancer-related fatigue before, during, and after treatment (Fiorentino et al., 2011; Jacobsen & Stein, 1999). A systematic review by Minton and Stone (2008) demonstrated strong evidence for the occurrence of persistent cancer-related fatigue up to five years after the completion of adjuvant treatment among disease-free breast cancer survivors. A separate review by Berger and colleagues (2012) clarified that many women report that their energy never returns to pre-diagnostic levels.

Measurement of cancer-related fatigue. One hypothesized explanation for the inconsistencies observed in the prevalence estimates of cancer-related fatigue is the high variability in the measurement thereof. Multiple reviews have been published identifying different tools used to measure cancer-related fatigue (e.g., Dittner, Wessely, & Brown,

2004; Jacobsen, 2004; Jean-Pierre et al., 2007; Minton & Stone, 2009; Seyidova-Khoshknabi et al., 2011). These reviews demonstrate that cancer-related fatigue has been conceptualized and measured as both a unidimensional and a multidimensional construct. Unidimensional and single-item measures have been shown to be more widely used than their multidimensional counterparts (Minton & Stone, 2009). Examples of such measures are the Brief Fatigue Inventory (Mendoza et al., 1999), the Functional Assessment of Cancer Therapy Fatigue subscale of the FACIT series of quality of life questionnaires (Yellen, Cella, Webster, Blendowski, & Kaplan, 1997), and the fatigue subscale of the Profile of Mood States (McNair & Lorr, 1971). While quick, inexpensive, and simple to administer, unidimensional measures are limited. For example, different researchers have interpreted unidimensional scales as evaluating distinct components of cancer-related fatigue, such as physical fatigue (Minton & Stone, 2009), versus other components such as cognitive or emotional fatigue. By nature fatigue is a subjective experience, and thus the term as presented on self-report scales can be interpreted in myriad ways. For example, if a given patient were to complete a unidimensional fatigue scale on a day characterized by extreme activity, that patient may be likely to interpret and report physical fatigue, as opposed to another patient who has experienced a day requiring a great deal of critical thought, for whom mental fatigue may be more salient. Accordingly, it can be difficult to conclusively determine how fatigue is being conceptualized, and thus rated, by a given respondent (Brunier & Graydon, 1996; Wewers & Lowe, 1990; Youngblut & Casper, 1993).

Conversely, in an effort to be more comprehensive many investigators have conceptualized and assessed cancer-related fatigue as a multidimensional construct.

Examples of measures reflecting this perspective include the Chalder Fatigue Scale (Chalder et al., 1993), the Multidimensional Fatigue Inventory (Smets, Garssen, Bonke, & De Haes, 1995), the Fatigue Symptom Inventory (Hann et al., 1998), the Piper Fatigue Scale (Piper et al., 1998), and the Multidimensional Fatigue Symptom Inventory – Short Form (Stein, Jacobsen, Blanchard, & Thors, 2004; Stein, Martin, Hann, & Jacobsen, 1998). These measures have generally shown good psychometric properties; however, the increased breadth of assessment that they provide generally comes at the expense of brevity and ease of administration. Nonetheless, evaluating multiple dimensions permits for the possibility that different respondents may interpret the term "fatigue" as more reflective of certain subdomains of cancer-related fatigue than others. A recent investigation by Sobel-Fox et al. (2013) provided support for such a conceptualization. In their analysis of 52 survivors of mixed cancer sites, multilevel modeling demonstrated that unidimensional cancer-related fatigue was more strongly related to certain subdomains of cancer-related fatigue than others at different assessment points over the course of one month. Similarly, Banthia and colleagues (2006) reported that unidimensional cancer-related fatigue was more strongly related to general fatigue than other forms of fatigue among 25 breast cancer survivors. These findings support the assertion that cancer-related fatigue is indeed a multidimensional construct, and that unidimensional measures of cancer-related fatigue may only be assessing one portion of the construct, rather than accurately assessing and reflecting all components thereof. Accordingly, despite the increased burden required it has been argued that multidimensional measures may be preferable to unidimensional measures when evaluating cancer-related fatigue, should such measurement be appropriate to the

research question (Banthia et al., 2006; Sobel-Fox et al., 2013).

Process and correlates of cancer-related fatigue. The specific mechanisms underlying cancer-related fatigue remain poorly understood. Hypothesized contributing factors include chronic inflammatory processes, other physiological variables such as pain and neuroendocrine changes, psychosocial factors such as depression, anxiety, education, and cognition, and chronobiological factors such as circadian rhythms (Ancoli-Israel, Moore, & Jones, 2001; Bower, Ganz, Aziz, Fahey, & Cole, 2003; Fiorentino et al., 2011; Jacobsen & Stein, 1999). Despite the lack of understanding of the causal factors, numerous correlates of cancer-related fatigue have been previously explored, including demographic variables, medical comorbidities, treatment factors, and cancer-related symptoms. For example, in their study of 114 breast cancer survivors, Minton and Stone (2012) found that women with cancer-related fatigue had significantly higher rates of insomnia, less daytime activity, and worse cognitive performance on tests of sustained attention, reaction time, and verbal memory. In a related study of 278 disease-free breast cancer survivors it was found that individuals with cancer-related fatigue had significantly lower plasma sodium levels, and significantly higher self-reports of depression, pain, insomnia, and systemic side effects of treatment (Minton, Alexander, & Stone, 2012). Another analysis of 70 breast cancer survivors found that age, staging, mood, and sleep were all cross-sectional predictors of cancer-related fatigue; however, different predictors were found to relate to different domains of cancer-related fatigue (Banthia, Malcarne, Ko, Varni, & Sadler, 2009). Additionally, in their systematic review, Prue, Rankin, Allen, Gracey, and Cramp (2006) found that increased cancer-related fatigue was associated with symptoms of depression, anxiety, pain, nausea, dyspnea, loss

of appetite, diarrhea, hemoglobin levels, cytokine levels, sleep quality, symptom distress, and physical activity levels both during and after treatment.

As has been observed among studies focusing on sleep disruption, studies focusing on cancer-related fatigue have consistently found a relationship between cancer-related fatigue and sleep within the cancer context. In fact, it has specifically been posited that the heightened levels of cancer-related fatigue reported by patients might be directly related to the quantity, quality, and rhythms of nighttime sleep (Ancoli-Israel et al., 2001). Such findings further underscore the need for studies that examine these two constructs concurrently.

2.4 Overview of Select Psychosocial Outcomes in Breast Cancer

Depression. Depression is common among breast cancer patients, with prevalence estimates ranging from 10% to 25% (Fann et al., 2008). Although there is great variability in these estimates, they generally suggest that depression is more common among breast cancer patients than among the general United States female population, in which the 12-month estimated prevalence for a Major Depressive Episode in 2008 was 8.4% (Substance Abuse and Mental Health Services Administration, 2013). Of note, although other studies have contradicted this claim, it has also been argued that depression may be under-diagnosed among breast cancer patients (Fann et al., 2008). In their recent systematic review, Fann and colleagues (2008) reported that patients who undergo chemotherapy have elevated rates of depression as compared to breast cancer patients who do not receive adjuvant therapy. This may be due to direct effects of the medication itself, or due to negative side effects thereof such as diminished fertility and

sexuality. Other risk factors for depression in this study included a personal history of depression, premenopausal status, and being less than 65 years of age (Fann et al., 2008).

The implications of depression comorbid with breast cancer can be severe. As Fiorentino et al. (2011) found in their review, depressed patients may be more likely to receive suboptimal treatment, and may be less likely to be adherent to or engage in treatment recommendations. Depressed patients may also experience more severe physical side effects of cancer and its treatment, as well as associated increases in functional impairment (Fann et al., 2008). This can subsequently be associated with increased risk of mortality and decreased quality of life. Although the specific mechanisms underlying depression within breast cancer remain poorly understood, research has shown that depression often occurs in concert with other psychosocial symptoms, including fatigue, pain, and sleep disruption (Aldridge-Gerry et al., 2013; Fann et al., 2008).

Climacteric Symptomatology. Research has shown that chemotherapy can induce ovarian failure, and subsequent early amenorrhea, in premenopausal breast cancer patients (Loibl, Lintermans, Dieudonné, & Neven, 2011; Zhao et al., 2014). Although this ovarian failure can be temporary, it is often permanent. The type, duration, schedule, and dosage of chemotherapy, as well as patient age, can all impact the likelihood of chemotherapy-induced amenorrhea (Zhao et al., 2014). Associated with these increased rates of amenorrhea, many breast cancer patients report increased rates of climacteric symptoms, most commonly hot flashes and night sweats (Loibl et al., 2011). Hot flashes have been defined as subjective, transient sensations of warmth or heat accompanied by physiological signs of cutaneous vasodilation, and in some cases sweating and elevated

heart rate, among other symptoms (Boekhout, Beijnen, & Schellens, 2006). Climacteric symptoms such as these have been reported to be more severe and more frequent among women who enter amenorrhea secondary to cancer treatment as compared to those who experience the menopausal transition in a developmentally normal fashion (Rosenberg & Partridge, 2013). Of note, while hormone replacement therapy is generally an effective strategy for diminishing climacteric symptoms among healthy menopausal women, such treatment has been associated with increased risk of cancer recurrence among women with a history of breast cancer (Holmberg et al., 2008). Additionally, while other treatments are available, the effectiveness of such treatments among breast cancer patients has been understudied (Boekhout et al., 2006; Rosenberg & Partridge, 2013). It has been postulated that the increased rates of climacteric symptomatology in breast cancer patients may be associated with increases in fatigue and sleep disruption; however, the specifics of these relationships remain poorly understood (Rissling, Liu, Natarajan, He, & Ancoli-Israel; 2011). Furthermore, these symptoms have all been associated with worse quality of life outcomes, underlining the need for further study in an effort to better understand these relationships and their impact on psychosocial and functional outcomes among breast cancer patients (Rosenberg & Partridge, 2013).

Quality of Life. Quality of life has been conceptualized as an umbrella term reflecting information about symptoms, overall functioning, physical well-being, and psychological health, among other outcomes (Thong et al., 2013). It is most effectively assessed with patient reported outcomes, or verbatim patient reports of their experiences (Thong et al., 2013). Quality of life has been identified as an important outcome in cancer research, and has been shown to have good prognostic value (Montazeri, 2008). A review

by Montazeri (2009) presented strong evidence demonstrating that quality of life consistently and independently predicts survival time among cancer patients. Diminished quality of life has been shown to be associated with a number of other adverse cancer-related psychosocial symptoms, such as depression, body image distress, and general stress (Andritsch, Dietmaier, Hofmann, Zloklikovits, & Samonigg, 2007; Lehto, Ojanen, & Kellokumpu-Lehtinen, 2005). The research evaluating the relationship of sociodemographic and medical predictors to quality of life within breast cancer has been mixed, although there is some evidence showing that adjuvant chemotherapy is negatively associated with quality of life outcomes (Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005). A number of treatments have been explored to improve quality of life outcomes in oncology; however, conclusive findings have not been obtained regarding optimal treatment strategies. Better comprehension of the way in which quality of life outcomes relate to other components of the cancer experience is needed to improve general understanding of quality of life in cancer, as well as elucidate who is at high risk for negative outcomes and better understand what treatments may be effective at altering these outcomes.

2.5 Studies of Symptom Clusters in Breast Cancer

A great deal of research has been conducted examining symptom clusters in oncology samples (Fan, Filipczak, & Chow, 2007; Nguyen et al., 2011). Symptom clusters have been defined as a set of interrelated symptoms that occur simultaneously, might share a common etiology or variance, and might contribute to outcomes that are different than those that would result from individual symptoms occurring in isolation (Barsevick, Whitmer, Nail, Beck, & Dudley, 2006; Dodd et al., 2001; Miaskowski, Dodd,

& Lee, 2004). Study of symptom clusters in oncology can contribute to improved comprehension of how a specific set of individual cancer symptoms are interrelated, and how they are associated with outcomes of interest (Barsevick et al., 2006).

A number of theoretical frameworks have been developed to facilitate understanding of symptom clusters in cancer. In a review, Barsevick (2007) identified four leading models of symptoms and symptom clusters. The revised Symptom Management Model postulates that the symptom experience, strategies used for symptom management, and patient outcomes are all interrelated (Dodd et al., 2001). According to this model, any of these three components can be impacted by either of the other two components. The Theory of Unpleasant Symptoms posits that physiological, psychological, and situational antecedents preempt the symptom experience, which in turn preempts consequences to the symptom experience (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). This theory also suggests that symptoms that are experienced simultaneously as part of a cluster are likely to have a multiplicative rather than an additive effect, and that symptoms can serve as both predictors of outcomes as well as mediators of the antecedent to outcome relationship. The Symptom Experience Model builds on these two models, and explicates that the symptom experience is associated with both situational meaning, or the perceived impact of a symptom on daily life, and existential meaning, or one's perceived global place in the world (Armstrong, 2003). Finally, the Symptom Interaction Framework purports that the symptom cluster experience may be due to the combination of multiple underlying mechanisms (e.g., biological, psychological, behavioral, sociocultural; Parker, Kimble, Dunbar, & Clark, 2005).

The majority of studies evaluating symptom clusters in oncology samples have done so using factor analysis or cluster analysis (Barsevick et al., 2006; Fan et al., 2007; Nguyen et al., 2011). For example, Jiménez and colleagues (2011) used principal component analysis, a variant of factor analysis, to identify four clusters of commonly co-experienced symptoms (i.e., confusion, neuropsychological, anorexia-cachexia, and gastrointestinal) among advanced cancer patients. They found that the number and type of clusters experienced by a given patient were associated with cancer site, gender, age, performance status, and survival time. Similarly, Matthews, Schmiege, Cook, and Sousa (2012) used confirmatory factor analysis to identify three distinct symptom clusters (i.e., pain-insomnia-fatigue, cognitive disturbance-outlook, and gastrointestinal) among breast cancer patients undergoing radiation therapy.

Factor analysis, as used by these authors, explains the relationships among theoretically associated variables according to their correlation matrix, or a variant thereof (Meyer, Gamst, & Guarino, 2006). Factor analysis identifies how many domains of symptoms there are, and which specific symptom variables contribute to each domain. The other most commonly used statistical approach in symptom cluster identification is cluster analysis. The primary distinction between factor analysis and cluster analytic techniques is that factor analysis yields factors representing groups of *symptom domains* (i.e., factors) based on which symptom variables are most highly intercorrelated, while cluster analysis yields profiles representing groups of *people* (i.e., clusters) based on respondents' patterns of symptom variable reports (Barsevick et al., 2006). Another crucial distinction between factor analysis and cluster analysis is the scale of the latent variable. In factor analysis the latent variable is continuous and is assumed to have a

normal distribution (Lanza, Flaherty, & Collins, 2003). Conversely, in cluster analysis the latent variable is categorical. Thus it has been argued that cluster analysis may be more clinically relevant, as it enables the identification of groups of patients with distinct profiles of symptoms.

As stated, a number of researchers have used cluster analysis as an alternative to factor analysis when identifying symptom clusters in cancer. For example, Denieffe, Cowman, and Gooney (2013) identified groups of patients based on severity of pain, fatigue, subjective sleep disturbance, and depression. These authors used hierarchical cluster analysis to identify five groups of pre-surgery breast cancer patients: *mild sleep/pain/fatigue* (*n* = 55, 59%)*, moderate sleep disturbance and mild fatigue/pain* (*n* = 15, 16%)*, moderate fatigue, mild pain/sleep disturbance* (*n* = 18, 19%)*, moderate pain and mild fatigue/sleep disturbance* (*n* = 3, 3%)*,* and *moderate for all symptoms except mild depression* (*n* = 3, 3%). It must be noted; however, that these final two clusters were each comprised of less than 5% of the study sample, and thus are likely spurious clusters. Similarly, Trudel-Fitzgerald, Savard, and Ivers (2014) used cluster analysis with a large sample of patients scheduled to undergo surgery for mixed cancers at six distinct time points to identify clusters of patients with comparable levels of anxiety, depression, insomnia, fatigue, pain, nausea, vomiting, night sweats, concentration complaints, and memory complaints. Results yielded between five and eight clusters at different time points, with the *low symptoms* cluster identified as the mostly common, accounting for 25% to 35% of the sample depending upon the time point.

Although cluster analysis is a commonly used statistical approach in symptom cluster research, it is limited in many ways. A stronger alternative that has recently

received increased attention is Latent Profile Analysis (LPA). As a form of cluster analysis, LPA is a statistical technique that interprets patterns of responses to variables and thereby assigns individuals to internally homogenous, orthogonal, mutually exclusive groups (Roesch, Villodas, & Villodas, 2010). Although both cluster analysis and LPA share a common primary aim, there are several notable differences between the two analytic techniques. Stated simply, LPA is considered to be a much stronger statistical approach. For example, while cluster analysis assumes that there is no error, an assumption that has been debated in the literature (Herman, Ostrander, Walkup, Silva, & March, 2007), LPA takes error into account by assigning profile membership based on probabilities. Furthermore, LPA identifies a solution using maximum likelihood estimation while cluster analysis utilizes less sophisticated ad hoc mathematical algorithms. Thus, LPA yields a solution that more accurately reflects the true solution in the population based on the study sample. Additionally, LPA uses conditional response means to identify variables that better define groups, and are thus given more weight when identifying a solution, while cluster analysis gives all variables equal weight. LPA also yields posterior probability values, which represent the statistical degree of certainty that can be applied to a given individual's group assignment, and recognizes that there is intrinsic uncertainty in group membership and the overall solution. Additionally, in LPA, the observed data are used to estimate parameter values for the model (Vermunt & Magidson, 2002), and LPA applies more formal criteria to aid in the identification of groups (Collins & Lanza, 2010), including fit statistics and tests of statistical significance (Herman et al., 2007).

Select studies have used LPA to evaluate symptom clusters among cancer patients. For example, Dirksen, Belyea, and Epstein (2009) used LPA to identify groups among 86 breast cancer survivors with insomnia who were similar to each other based on seven individual items evaluating fatigue. Specifically, these authors used the seven continuous items that comprise the Fatigue/Inertia subscale of the Profile of Mood States to inform the LPA, and identified three groups of women: *Exhausted* (n = 29, 35%), *Tired* (n = 34, 41%), and *Restored* (n = 20, 24%). These groups corresponded to patients who consistently endorsed high, medium, and low levels of fatigue on the seven items administered. Individuals in the *Exhausted* group reported the most severe fatigue on each of the seven items, as well as greater levels of insomnia, state anxiety, trait anxiety, and depression, and worse physical, emotional, functional, and breast cancer quality of life, relative to the other two groups. Interestingly, the groups did not significantly differ on sociodemographic or medical characteristics, including age, education, income, marital status, employment, cancer stage at diagnosis, number of comorbidities, time since diagnosis, type of treatment, or history of hormonal therapy. While this study successfully utilized a more advanced and more appropriate statistical approach than many others, it is not without limitations. Although it initially seems that multiple dimensions of fatigue were considered, as group identification was informed by seven distinct fatigue variables, this was not the case. Further evaluation clarifies that fatigue was actually measured unidimensionally in this study, because the individual items used to identify groups all contribute to a single subscale of a larger measure, and the items have never been validated as individual measurement constructs.

Illi and colleagues (2012) also used LPA to identify groups among 168 breast, prostate, lung, and brain cancer patients and 85 family caregivers. In their analysis, group identification was based on pain, fatigue, sleep disturbance, and depression, four distressing and commonly reported symptoms of the cancer experience (Barsevick, 2007). These authors identified three distinct groups characterized by *low depression/low pain* (*n* = 210, 83%), *high depression/low pain* (*n* = 12, 4.7%), and *high on all four symptoms* (*n* = 31, 12.3%). Of note, as was observed in Denieffe et al.'s (2013) study, one of the identified groups was comprised of less than 5% of the study sample, suggesting that it was likely spurious. Additionally, a major limitation of this study is that groups were based on analysis of data provided by both oncology patients and their family caregivers. Thus, it is unclear if these groups would also have emerged had the authors exclusively considered patient reports.

In two separate recent studies, Miaskowski et al. (2014, 2015) used Latent Class Analysis, a latent variable modeling technique that is equivalent to LPA except that observed variables are categorical rather than continuous (Roesch et al., 2010), to identify groups of cancer patients based on commonly occurring symptoms as measured by the Memorial Symptom Assessment Scale (Portenoy et al., 1994). In the first study, Miaskowski et al. (2014) found three groups among 582 mixed-cancer patients undergoing chemotherapy based on 25 endorsed symptoms: *low* (*n* = 210, 36.1%), *moderate* (*n* = 291, 50.0%) and *all high* (*n* = 81, 13.9%). In the second study, Miaskowski et al. (2015) found four groups among 582 mixed-cancer patients undergoing any form of active treatment: *all low* (*n* = 163, 28.0%), *moderate physical and lower psych* (*n* = 153, 26.3%), *moderate physical and higher psych* (*n* = 148, 25.4%)

and *all high* (*n* = 118, 20.3%). Age and gender distinguished groups in both studies, and education, cancer diagnosis, and presence of metastatic disease differentiated groups of patients from the second study who were undergoing any form of active treatment. Furthermore, in both studies patients in the *all high* group had worse quality of life outcomes as compared to patients in the other groups.

In another study by the same research team, Doong et al. (2015) used LPA to evaluate a symptom cluster comprised of pain, fatigue, sleep disturbance, and depression among 398 breast cancer patients prior to surgical intervention. In this study the authors uncovered three groups of patients: *all low* (*n* = 241, 61%), *low pain and high fatigue* (*n* = 124, 31.6%), and *all high* (*n* = 28, 7.1%). Groups were distinct with regard to age, education, race, income, cohabitation status, comorbidity scores, disease progression, and select cytokine genes. Additionally, as was observed in Miaskowski et al. (2014, 2015), patients in the *all high* group had worse functional outcomes as compared to the other groups. These studies shed preliminary light on demographic and clinical characteristics that may contribute to heightened risk for increased symptom burden and associated poor quality of life among cancer patients undergoing treatment. Additionally, these studies suggest that groups characterized by generally low symptom severity and generally high symptom severity are common. However, while they do advance the literature, there are nonetheless limitations. While difficulty sleeping and lack of energy were both used to identify groups in the LPAs, they were either represented by dichotomous variables indicating whether or not the symptom was experienced (yes/no; Miaskowski et al., 2014, 2015), or by single scale total scores (Doong et al., 2015), and were only two of multiple

symptoms considered. Thus, the unique and multidimensional contributions of these constructs were not explored in these studies.

Dodd and colleagues (2011) used LPA to identify groups among 187 mixed cancer patients undergoing biotherapy based on a symptom cluster also comprised of pain, fatigue, sleep disturbance, and depression. Interestingly, these authors completed two separate LPAs, one evaluating data collected after administration of the first dose of biotherapy, and a second evaluating data collected one month later. At the first time point, the authors identified five groups: *mild fatigue and sleep disturbance* (*n* = 104, 56%), *mild fatigue and moderate pain* (*n* = 20, 11%), *mild pain and sleep disturbance, moderate fatigue, and severe depression* (*n* = 22, 12%), *moderate, fatigue, sleep disturbance, depression, and severe pain* (*n* = 28, 15%), and *high severity scores on all four symptoms* (*n* = 13, 7%). At the second time point, three groups were identified: *mild pain, fatigue, and sleep disturbance, but no depression* (*n* = 64, 56%), *moderate pain, fatigue, sleep disturbance, and depression* (*n* = 38, 33%), and *mild pain, moderate fatigue, sleep disturbance, and depression* (*n* = 12, 11%). Across both data collection time points, the group characterized by the most severe symptoms also reported significantly lower quality of life and functional ability. Unlike the results found by Miaskowski et al. (2014, 2015) and Doong et al. (2015), very few differences were found across groups based on sociodemographic or medical characteristics. At the first time point it was noted that women were more likely to be in the *high severity scores on all four symptoms* group, but no differences were found across groups at time two. A notable strength of this study is the identification of groups at multiple time points across treatment. The authors found that, of the 104 participants in the group characterized by

the mildest symptoms at the first time point (i.e., *mild fatigue and sleep disturbance*), approximately three quarters were in the group characterized by the mildest symptoms at the second time point (i.e., *mild pain, fatigue, and sleep disturbance, but no depression*). By conducting LPAs at multiple time points the authors were able to find preliminary evidence that patients reporting relatively low levels of pain, fatigue, sleep disturbance, and depression maintained group membership over time. Additionally, this study demonstrated that LPA can be used to identify symptom clusters indicated by multiple different constructs. However, notable limitations of this study must also be considered. To facilitate the naming of groups identified by the LPAs, the authors used *a priori* selected cut-points for mild, moderate, and severe symptomatology for pain and fatigue symptoms. They also dichotomized the sleep disturbance and depression variables to indicate absence or presence of clinically relevant symptoms, once more based on *a priori* selected cut-points. The use of such cut-points prohibits the characterization of groups relative to the other patients in the analysis. Additionally, while the authors thoughtfully selected four of the most commonly explored variables to inform symptom cluster identification, each of these variables was operationalized as a single score on a unidimensional measure. Thus, important dimensions of these multidimensional constructs were likely not captured by this analysis.

Kim, Malone, and Barsevick (2014) used LPA to investigate the interrelationship of pain and fatigue among 276 patients with a variety of cancers undergoing chemotherapy. Like Dodd et al. (2011), Kim and colleagues were particularly innovative in conducting LPA at two time points throughout treatment, once on Day 4 after the first treatment and once more within three days following the third, fifth, or seventh treatment,

depending upon the chemotherapy regimen. Three groups were identified at the first time point: *high pain/high fatigue* (*n* = 114, 41%), *low pain/high fatigue* (*n* = 90, 34%), and *low pain/low fatigue* (*n* = 68, 25%). Two groups were identified at the second time point: *high pain/high fatigue* (*n* = 101, 37%) and *low pain/low fatigue* (*n* = 175, 63%). As was observed by Dodd et al. (2011), but discrepant from Miaskowski et al.'s (2014, 2015) and Doong et al.'s (2015) findings, groups did not differ on sociodemographic variables at either time point. However, differences were noted with regard to depressed mood, in that greater depressive symptomatology was associated with increased likelihood of being in the *high pain/high fatigue* group as opposed to the *low pain/low fatigue* group at both time points. Additionally, at the second time point comorbid hypertension was found to significantly indicate a greater likelihood of being in the *high pain/high fatigue* group. Finally, being in the *high pain/high fatigue group* was associated with increased functional limitations at both time points. Like Dodd et al. (2011), the identification of symptom clusters at multiple time points enabled Kim et al. (2014) to evaluate the stability of identified clusters throughout treatment. Further, unlike prior studies, Kim et al. (2014) examined only two components of the cancer experience, which enabled them to better understand how just pain and fatigue contribute to symptom cluster identification in oncology. However, once more these authors only used single indicators for each of these two variables, rather than considering the full multidimensional nature of each construct.

Although a number of studies have evaluated symptom clusters focusing on the experiences of breast cancer patients, including the roles of sleep disruption and cancer-related fatigue, many of these studies have employed limited statistical approaches.

Additionally, these studies have often evaluated a variety of symptoms in a variety of different combinations, and little consensus has been established. While studies have examined sleep disruption and cancer-related fatigue as part of a larger symptom cluster among breast cancer patients, few studies, if any, have examined how subjective versus objective assessments of sleep, and different dimensions of cancer-related fatigue, contribute to cluster identification. Interestingly, in a separate analysis based on the same sample they explored in their LPA, Kim et al. (2014) reported that they collected both objective (i.e., actigraphy) and subjective (i.e., PSQI) sleep data in addition to the cancer-related fatigue and pain data on which they based their analysis (Barsevick et al., 2010). Thus, even though these authors had the opportunity to evaluate how multiple assessments of sleep and cancer-related fatigue can contribute to oncology symptom clusters, to date this question nonetheless remains unexplored. Furthermore, among known studies that have considered sleep and cancer-related fatigue in the same analysis, these complex constructs have generally been evaluated with unidimensional, single-item, or single-subscale scores. At this time, advanced analyses that consider different dimensions and measurement approaches to sleep and cancer-related fatigue are needed to better understand how these symptoms may synergistically impact the cancer experience.

2.6 Summary and Limitations of Prior Research

Breast cancer is the most commonly diagnosed non basal- or squamous-skin cell cancer among women living in the United States, currently accounting for 29% of incident cases of cancer in this population (ACS, 2013; 2014a; 2015). The incidence rate for breast cancer in the United States has remained relatively stable since 2003; however,

the mortality rate has been steadily decreasing, dropping by 34% from 1990 to 2010 (ACS, 2013; 2014b; 2015). This reduction in mortality has been attributed to improvements in breast cancer early detection and treatment techniques (ACS, 2013; 2014a; 2015). Such techniques include surgical intervention, radiation therapy, and systematic therapy such as chemotherapy, hormone therapy, and targeted therapy (ACS, 2013; 2014a; 2015). However, secondary to these treatments, as well as the disease itself, sleep disruption has been shown to be notably elevated among cancer patients as compared to the general population (Otte et al., 2010; Palesh et al., 2010). Additionally, cancer-related fatigue is one of the most commonly reported symptoms among cancer patients and survivors (Hofman et al., 2007; Morrow et al., 2002; NCCN, 2012; Stasi et al., 2003; Stone & Minton, 2008). Cancer-related fatigue has been shown to be highly prevalent among long-term breast cancer survivors (Minton & Stone, 2008), and among patients undergoing treatment (de Jong et al., 2002).

Sleep disruption and cancer-related fatigue have often been evaluated as components of symptom clusters, along with other cancer-related symptoms such as pain and depression (Fan et al., 2007; Fiorentino et al., 2011; Nguyen et al., 2011). While these studies have shed light on the nature of the cancer experience, many of them have used suboptimal statistical approaches, such as factor analysis and cluster analysis (Barsevick et al., 2006). A select few studies have used LPA, a notably superior statistical approach, for the identification of symptom clusters in cancer. However, even these studies have generally examined either subjective or objective indicators of sleep but not both, have failed to consider cancer-related fatigue as a multidimensional construct, and have used other variables to indicate group membership in addition to sleep disruption

and cancer-related fatigue, thus compromising understanding of sleep disruption and cancer-related fatigue, as it is possible that groups may be uncovered as a function of the other symptoms being considered rather than just as a function of these symptoms of interest.

2.7 Specific Aims and Hypotheses of the Present Study

The present study aimed to identify groups of breast cancer patients based on their experiences of sleep disruption and cancer-related fatigue symptoms at pre-treatment and again during treatment to determine if group membership can be predicted by pre-treatment sociodemographic, medical, and psychosocial variables; and evaluate the impact of group membership on psychosocial variables at the last week of the fourth cycle of chemotherapy treatment.

Specific Aim 1. The first study aim was to establish typologies of breast cancer patients 1) prior to the initiation of chemotherapy treatment and 2) at the last week of the fourth cycle of chemotherapy, based on two objective indicators of sleep, one subjective indicator of sleep quality, and reports of five dimensions of cancer-related fatigue. As LPA is an inherently exploratory approach, no specific hypotheses could be made regarding the number or defining characteristics of typologies that would be uncovered. However, it was anticipated that multiple groups of patients would be identified based on the simultaneous consideration of two indicators of objective sleep, one indicator of subjective sleep quality, and five dimensions of cancer-related fatigue. Further, it was anticipated that different groups would be identified at the two data collection time points, as has been seen in prior studies (Dodd et al., 2011; Kim et al., 2014).

Specific Aim 2. The second study aim was to empirically examine if pre-treatment sociodemographic variables (i.e., age, ethnicity, education, and marital status); medical variables (i.e., body mass index, cancer stage at diagnosis, type of surgical intervention, chemotherapy formulation, current medications, and medical comorbidities); and psychosocial variables (i.e., depression, climacteric symptomatology, and mental, physical, and breast cancer specific health-related quality of life) predicted categorical profile membership 1) prior to the initiation of chemotherapy treatment, and 2) at the last week of the fourth cycle of chemotherapy. It was hypothesized that some sociodemographic, medical, and psychosocial variables would predict profile membership, based on prior LPA-based symptom cluster research (Dodd et al., 2011; Doong et al., 2015; Kim et al., 2014; Miaskowski et al., 2014, 2015). However, due to a lack of sufficient research on groups indicated by sleep and fatigue variables, it was not possible to make any explicit *a priori* predictions.

Specific Aim 3. The third study aim was to empirically examine how individuals in different groups 1) identified prior to the initiation of chemotherapy treatment, and 2) identified at the last week of the fourth cycle of chemotherapy, differed at the last week of the fourth cycle of chemotherapy on continuous indicators of psychological distress including depression, climacteric symptomatology, and mental, physical, and breast cancer specific health-related quality of life. Based on prior LPA-based symptom cluster research, it was hypothesized that groups would differ at the last week of the fourth cycle of chemotherapy with regard to these outcomes (Dodd et al., 2011; Doong et al., 2015; Kim et al., 2014; Miaskowski et al., 2014, 2015). Once more, due to insufficient existing

research on groups indicated by sleep and fatigue variables, it was not possible to make any explicit *a priori* predictions.

Chapter 2 is being prepared in part for publication. This publication will be co-authored by Vanessa L. Malcarne, Sonia Ancoli-Israel, Scott C. Roesch, Georgia Robins Sadler, and Kristen Wells. The dissertation author was the primary investigator and author of this material.

CHAPTER 3: METHODS

3.1 Participants

The present study used data provided by 152 patients with newly diagnosed stage I-III breast cancer who were scheduled to receive at least four cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy. Participants were recruited through two separate studies with identical protocols, recruitment techniques, and inclusion criteria. Oncologists at the University of California, San Diego (UC San Diego) Moores Cancer Center and oncologists in the greater San Diego, California area referred participants to study personnel. Of note, during the first study one oncologist in the greater Yakama, Washington area also recruited participants using procedures identical to those implemented in California, and a few individuals living in that area were enrolled. Across both studies pre-treatment data were collected prior to initiation of chemotherapy treatment.

Women were considered ineligible for participation if they were pregnant, were undergoing bone marrow transplant, had received radiotherapy, had metastatic or stage IIIB (including inflammatory) breast cancer, had confounding underlying medical comorbidities, had a pre-existing diagnosis of severe anemia, or had any other physical or psychological impairment that could confound study results. All men were considered ineligible. Human subjects research approval was obtained from the University of California Committee on Protection of Human Subjects as well as the UC San Diego Moores Cancer Center Protocol Review and Monitoring Committee prior to enrollment. Across both studies each participant provided informed consent at the initiation of her participation.

3.2 Measures

Sociodemographic and medical variables. Age, ethnicity, education, and marital status were assessed by self-report. Body mass index, cancer stage at diagnosis, type of surgical intervention, chemotherapy formulation, current medications, and medical comorbidities were extracted from medical records.

In the present analysis, medications that were evaluated included analgesics, antacids, anticonvulsants, antidepressants, antihistamines, antihypertensives, antiparkinson medications, cardiac medications, diuretics, insulins, laxatives, major tranquilizers, minor tranquilizers, over-the-counter hypnotics, oxygens, sedative hypnotics, stimulants, vasodilators, vitamins, and "other" medications. Comorbidities that were evaluated included cardiovascular diseases, pulmonary diseases, central nervous system diseases, gastroenterological diseases, renal diseases, endocrine diseases, connective tissue diseases, infections, dementia, arthritis, diabetes, ulcers, hiatal hernia, esophageal diseases, neck or back diseases, epilepsy, headaches, high blood pressure, kidney diseases, stroke, asthma, emphysema, edema, thyroid diseases, and "other" diseases.

Objective sleep. ***Wrist activity.*** Sleep was objectively assessed with actigraphy, which has been previously validated and shown to be a reliable method for estimating sleep and wake (Ancoli-Israel et al., 2003; Lichstein et al., 2006). All participants in Study 1 and 14 participants in Study 2 wore an Actillume-II (Ambulatory Monitoring Inc., Ardsley, NY), while the remaining participants in Study 2 wore an Actiwatch-Light (Actiwatch-L; Philips Respironics Mini Mitter, Bend, OR). The Actillume-II is approximately 1x3x6 centimeters in size and contains a log-linear photometric transducer

that is sensitive from < .01 to > 100,000 lux, representing less than moonlight to noon on the brightest summer day. It additionally contains a piezoelectric linear accelerometer, which is sensitive to movements 0.003g and above, as well as a microprocessor, 32K RAM memory, and associated circuitry. The sampling rate is 20Hz to assess and record wrist movement. Prior research has demonstrated that the log lux measurements at the wrist and forehead as recorded by the Actillume-II are strongly correlated (r = .93), providing support for wrist placement as an accurate reflection of light exposure near the eyes (Cole, Kripke, Gruen, & Nava, 1990). The Actiwatch-L is slightly smaller than the Actillume-II (1x2.5x5 cm) and contains a luminance sensor with a spectral sensitivity from 0.1 to 150,000 lux, similar to that of the human eye. It also contains a piezoelectric linear accelerometer, which is sensitive to movements < .01g and above, as well as a 64K on-board memory and associated circuitry. The sampling rate is 32Hz to assess and record wrist movement. The change in device was made mid-study as the newer Actiwatch-Light is smaller and less cumbersome for the patient than the older Actillume-II, which was becoming obsolete.

To establish the equivalency of the two devices a validation study was completed in which eight volunteers wore both devices concurrently and on the same wrist for 72 hours. The activity count data derived from both devices, as well as the software-scored sleep/wake data, were highly correlated (rs > 0.85), providing support for the equivalency of the data provided by the Actillume-II and the Actiwatch-L.

For both devices a one-minute epoch setting was utilized, and epoch-by-epoch data were downloaded onto a desktop computer for analysis. Data were manually edited based on additional information extracted from sleep diaries that participants completed

while wearing the actigraphs. Diary data included information about time to bed, time up in the morning, and napping, among other variables. Sleep and wake times were scored with the Action-4 software package for data from the Actillume-II devices, and the Actiware 5 software package for data from the Actiwatch-L. For analysis in the present study, Percent Nighttime Sleep, an estimate of sleep efficiency, and Percent Daytime Sleep, an estimate of daytime napping, were calculated.

Subjective sleep quality. ***Pittsburgh Sleep Quality Index.*** The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) is a 19-item self-report assessment of sleep quality and sleep disturbances over the prior month. These 19 items are grouped into seven theoretically-derived component scores representing areas typically assessed in clinical interviews with patients complaining of sleep disruption: Subjective Sleep Quality, Sleep Latency, Sleep Duration, Habitual Sleep Efficiency, Sleep Disturbances, Use of Sleeping Medications, and Daytime Dysfunction. Items reflecting each of these areas are recoded into component scores, which are indicated by one to nine items. Component scores can range from 0 (*no difficulty*) to 3 (*severe difficulty*), wherein higher scores indicate worse subjective sleep quality. The component scores can also be summed to yield a single global score ranging from 0 (*no difficulties*) to 21 (*severe difficulties in all areas*); higher scores again indicate worse subjective sleep quality. A global score of 5 or higher is considered indicative of clinically significant poor sleep quality.

The PSQI was developed among a sample of 52 “good sleepers” and 116 “poor sleepers,” and was found to have strong internal consistency reliability ($\alpha = 0.83$), test-retest reliability, and concurrent discriminative criterion validity (Buysse et al., 1989).

The measure has also specifically been validated for use among cancer patients (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004). Among this population it has demonstrated strong internal consistency reliability (αs ranged from 0.77 to 0.81). It also demonstrated construct validity as evidenced by clinically significant differences in global sleep quality between patients with low and high fatigue scores on the Schwartz Cancer Fatigue Scale (Schwartz, 1998).

While the PSQI yields both a total score and seven component scores, the component scores were derived from theory rather than factor-analytic methods. Additionally, the factor structure of the measure has been debated in the literature. While there is preliminary evidence supporting a multifactor structure, there is insufficient research available to conclusively support changes to the scoring algorithm, and it remains unclear if sleep dysfunction should be analyzed as a polychotomous or continuous construct (Mollayeva et al., 2015; Otte, Rand, Carpenter, Russell, & Champion, 2013). Given this, and the limitations presented by the current study's sample size, the originally published total global severity score was used in the present analysis.

Cancer-related fatigue. ***Multidimensional Fatigue Symptom Inventory – Short Form*****.** The Multidimensional Fatigue Symptom Inventory – Short Form (MFSI-SF; Stein et al., 1998, 2004) is a 30-item self-report assessment of cancer-related fatigue over the prior week. It is composed of five factor analytically-derived subscales that evaluate General fatigue, Physical fatigue, Emotional fatigue, Mental fatigue, and Vigor. Participants rank the applicability of each statement to their life along a continuum ranging from 0 (*not at all*) to 4 (*extremely*). Subscale scores are computed by summing responses to relevant individual items, and can range from 0 to 24. For the four Fatigue

subscales, higher scores indicate more cancer-related fatigue; for the Vigor subscale, higher scores indicate less cancer-related fatigue. A total score can be computed by summing the four Fatigue subscale scores, and then subtracting the Vigor score from that value. The MFSI-SF has been validated and has shown strong psychometric properties in multiple community-based and cancer populations for use in the assessment of cancer-related fatigue (Asvat, Malcarne, Sadler, & Jacobsen, 2014; Donovan et al., 2015; Stein et al., 1998, 2004). It was originally developed among a mixed sample comprised of women undergoing breast cancer treatment, women who had completed breast cancer treatment, and women with no history of cancer. Internal consistency reliability was strong among the development sample (αs for the subscales ranged from .85 to .96), as was test-retest reliability (*r*s ranged from .51 to .70, all *p*s < .05) and sensitivity (Stein et al., 1998). Evidence was additionally provided for the concurrent, convergent, and discriminative validity of scores from the measure (Stein et al., 1998). The MFSI-SF was later cross-validated among 304 mixed-cancer patients undergoing chemotherapy, and further support for its psychometric properties was found (Stein et al., 2004). To allow for a more nuanced examination of cancer-related fatigue than has previously been achieved by symptom cluster LPAs, the five subscales of the MFSI-SF were used in the present analysis.

Psychosocial variables. ***Center for Epidemiological Studies – Depression.*** The Center for Epidemiological Studies – Depression (CES-D; Radloff, 1977) is a 20-item measure of depressive symptoms as experienced over the prior week. Items were originally written to reflect the major components of depressive symptomatology as identified from the clinical literature and previously conducted factor analyses: depressed

mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. The frequency with which each item has been experienced is rated on a four-point scale ranging from 0 (*rarely or none of the time*) to 3 (*most or all of the time).* Principal component analysis identified four factors (i.e., Depressed Affect, Positive Affect, Somatic and Retarded Activity, and Interpersonal), although due to the high internal consistency of the scale a single total score has been recommended as an alternative to the four subscale scores (Radloff, 1977). Thus, item responses are summed to yield a total score ranging from 0 to 60, with higher scores indicating more depressive symptomatology. A score of 16 or higher is considered to reflect clinically significant distress related to depressive symptoms (Radloff, 1977).

The measure was developed via a series of household interview surveys and surveys in psychiatric settings in an effort to identify individuals who may be at risk for depression (Radloff, 1977). Internal consistency reliability was strong in both the general population (αs ranged from .84 to .85) and a psychiatric patient sample (α = .90), as was test-retest reliability (general population: *r*s ranged from .32 to .67, no *p*s provided; patient sample: $r = .53$, no *p* provided). Evidence was also provided for the concurrent discriminative criterion validity, construct validity, and discriminant validity of the measure (Radloff, 1977). The psychometric properties of the CES-D have also been specifically evaluated in an oncologic sample (Hann, Winter, & Jacobsen, 1999). Among a group of women undergoing treatment for breast cancer, both the internal consistency reliability (α = .89) and test-retest reliability ($r = .57$, $p < .01$) were strong. Additionally, concurrent discriminative criterion validity was evidenced by significant differences in

CES-D scores for breast cancer patients as compared to healthy controls. Support was also found for the measure's construct and discriminant validity. As recommended by Radloff (1977), the total score was used in the present analysis.

Greene Climacteric Scale. The Greene Climacteric Scale (Greene, 1998) was used to assess climacteric symptomatology. This 21-item self-report questionnaire was theoretically constructed based on seven previous factor analytic studies of climacteric symptoms. All components of the Greene Climacteric Scale, including the number of factors, the number of items/symptoms evaluated, and the standardization of the wording of items, were selected based on the consensus of findings from these seven previous studies. Factors that were present in at least three of the seven analyses were retained, including a vasomotor symptom factor, a somatic factor, and a psychological factor that sub-divides into anxiety and depressed mood. With regard to the symptoms assessed, Greene elected to retain only those symptoms that had a factor loading > 0.35 in at least three of the seven studies. Twenty symptoms met these criteria. In instances where different studies used similar but non-identical wording to query a symptom (e.g., "nervousness" and "nervous tension"), Greene used a single phrase to reflect the idea (e.g., "feeling tense or nervous"). An additional item assessing loss of sexual interest was also added to indicate if more detailed assessment of this construct might be warranted.

The final measure that was developed is comprised of three subscales evaluating Psychological (i.e., anxiety and depression), Somatic, and Vasomotor symptoms associated with the transition to menopause. Respondents rate the severity with which they experience each symptom at the time of data collection along a four-point scale ranging from 0 (*not at all*) to 3 (*extremely*). The three subscales are computed by

summing the responses to relevant items, with higher scores indicating more severe symptomatology. Scores on the 11-item Psychological subscale can range from 0 to 33, scores on the 7-item Somatic subscale can range from 0 to 21, and scores on the 2-item Vasomotor subscale can range from 0 to 6. Item #21 can serve as a single-item evaluation of loss of interest in sex ranging from 0 to 3, and this item can be summed along with the three subscales to create a total score, ranging from 0 to 63. Although a specific, comprehensive analysis of the psychometric properties of the Greene Climacteric Scale is not available, it has been reported to have good test-retest reliability and construct validity among women between the ages of 40 and 55 who had been referred to a hormone replacement therapy clinic (Zöllner, Acquadro, & Schaefer, 2005). For the present analysis, the three subscales of the Greene Climacteric Scale, evaluating psychological, somatic, and vasomotor symptoms, were evaluated.

Quality of Life: Medical Outcomes Study Short Form. The Medical Outcomes Study Short Form (SF-36; Ware, Kosinski, & Gandek, 2002) is a 36-item assessment of health-related quality of life. There are no items on the SF-36 that specifically query sleep or fatigue. The SF-36 evaluates eight domains of functioning: Bodily pain, Physical functioning, Role limitations due to physical health problems, General health perceptions, Mental health, Role limitations due to emotional problems, Vitality, and Social functioning. Each of these subscales is scored on a scale ranging from 0 to 100, with higher scores indicating better health and quality of life. The first four subscales contribute to the Physical Component Summary (PCS) score, and the latter four subscales contribute to the Mental Component Summary (MCS) score. The PCS and MCS are both norm-based, indicating that they have a mean of 50 and a standard deviation of 10. The

reliability and validity of the SF-36 has been well documented among myriad populations (Coons, Rao, Keininger, & Hays, 2000). Data from the Medical Outcomes Study demonstrated good internal consistency reliability for each subscale (αs range from .62 to .96) as well as strong test-retest reliability (McHorney, Ware, Lu, & Sherbourne, 1994). Concurrent discriminative criterion validity has also been demonstrated in multiple chronic illness populations (Coons et al., 2000). Of note, the SF-36 has specifically been recommended for use when a generic assessment of quality of life is needed (Davies, Gibbons, Mackintosh, & Fitzpatrick, 2009).

Functional Assessment of Cancer Therapy – Breast. The Functional Assessment of Cancer Therapy – Breast (FACT-B; Brady et al., 1997) is a 44-item self-report assessment of breast cancer specific health-related quality of life. It is comprised of the 35-item FACT-General scale plus the 9-item Breast Cancer Subscale. The FACT-General scale is comprised of five subscales assessing Physical Well-Being, Emotional Well-Being, Social Well-Being, Functional Well-Being, and Relationship with Doctor. Participants rank the degree to which they have experienced symptoms during the prior week on a scale ranging from 0 (*not at all*) to 4 (*very much*). Subscale scores can be summed to yield a total score, with higher scores indicating better health-related quality of life. Items for the Breast Cancer Subscale were originally developed based on combined input from breast cancer patients and experts in the field. The FACT-B has been specifically developed and validated for use with breast cancer patients, and has shown strong psychometric properties among this population. Among a sample of 295 breast cancer patients, internal consistency reliability was shown to be good (α = .90), as was test-retest reliability (r = .85, no p provided; Brady et al., 1997). Construct validity

has also been evidenced by significant correlations with other measures of quality of life, and concurrent discriminative criterion validity has been demonstrated by the measure's ability to distinguish among groups with varying levels of disease severity and other known differences (Brady et al., 1997). Furthermore, among a sample of 47 breast cancer patients, the FACT-B was shown to be sensitive to change (Brady et al., 1997). Of note, the FACT-B has specifically been recommended for use when a breast cancer specific assessment of health-related quality of life is needed (Davies et al., 2009). The total score was used for the present analysis, in accordance with the developers' recommendations, because the subscales contributing to the FACT-B have been shown to be intercorrelated and, unlike the total score, certain subscales have not evidenced reliability and validity when considered in isolation (Brady et al., 1997).

3.3 Procedure

The first study (Study 1) was prospective in design and focused on fatigue, sleep, and circadian activity rhythms in patients with breast cancer. A total of 132 women were referred by their oncologists for evaluation of eligibility; of these, 83 were included in the present analysis. See Figure 1 for a flowchart of study screening and enrollment. Data for Study 1 were collected between 2000 and 2005, and all women received three-week chemotherapy cycles, as was standard medical practice at that time. Participants in Study 1 provided data at eight time points: prior to the start of the first cycle of chemotherapy, once during each of the three weeks of cycle 1 (week 1 = chemotherapy administration, week 2 = at the point of nadir of blood count, week 3 = recovery), prior to the start of the fourth cycle of chemotherapy (note: this was often during the third week of cycle 3), and once during each of the three weeks of cycle 4. The present analysis will only consider

data provided prior to the start of the first cycle of chemotherapy, and during the last week of the fourth cycle of chemotherapy. Although there was some minor variability, for each cycle the first round of data were generally collected the week before chemotherapy began, the second collection took place the morning after chemotherapy administration, and subsequent data were collected during weeks 2 and 3 on the same day of the week as was done at week 1. Additionally, at each of the eight data collection time points participants wore an actigraph for three consecutive 24-hour periods (i.e., 72 hours), completed a written sleep diary on which they recorded their bedtime, wake time, and naps for the duration of the 72 hours, and completed study questionnaires once during those 72 hours. Of note, this procedure does deviate from the ideal recording duration of one week; however, the American Academy of Sleep Medicine's practice parameters for actigraphy suggest that a minimum of three days' worth of data should be sufficient in studies where subject burden is a potential concern (Ancoli-Israel et al., 2003).

The second study (Study 2) was also prospective in design and focused on cognitive impairments secondary to chemotherapy treatment among breast cancer patients. A total of 107 women were referred by their oncologists for evaluation of eligibility; of these 69 were included in the present analysis. See Figure 1 for a flowchart of study screening and enrollment. Data for Study 2 were collected between 2005 and 2010. During this time the recommended treatment protocol shifted from a three-week chemotherapy cycle to a two-week cycle. As a result, approximately two thirds of the women in Study 2 received a two-week cycle regimen, while the remaining one third received a three-week cycle regimen of chemotherapy. Participants in Study 2 provided

data at three time points: prior to the start of the first cycle of chemotherapy, at the last week of the fourth cycle of chemotherapy (regardless of whether a given participant received a two-week cycle regimen or a three-week cycle regimen), and one year after the start of chemotherapy. As was done with data provided by participants in Study 1, the present analysis only considered data provided prior to the start of the first cycle of chemotherapy, and at the last week of the fourth cycle of chemotherapy. Although there was some minor variability regarding the timing of pre-treatment data collection, all data were provided at least three days prior to chemotherapy administration. Additionally, at each of the three data collection time points, participants wore an actigraph for three consecutive 24-hour periods (i.e., 72 hours), and completed a written sleep diary on which they recorded their bedtime and wake time for the duration of the 72 hours. Actigraphy recording began for each participant on the same day at each of the three time points, and was based on the day of chemotherapy administration.

There is evidence that supports the combination of data from Study 1 and Study 2. Not only did the two studies follow identical protocols, but data provided by these two protocols have been previously combined for analysis and publication (e.g., Liu et al., 2013a; Liu et al., 2013b). In these previous studies, which used samples highly similar to the one analyzed in present study, no significant differences were found across participants from Study 1 versus Study 2 with regard to age, race, body mass index, education level, marital status, annual household income, menopausal status, use of other medications, cancer stage, surgery type, chemotherapy regimen, health-related quality of life, subjective sleep quality, and objective sleep (Liu et al., 2013a). The sample explored by Liu and colleagues (2013a) evaluated 166 women, 152 (91.75%) of whom were

included in the present analysis. The sample explored by Liu and colleagues (2013b) evaluated 148 (97.37%) of the 152 participants included in the present analysis. The very slight discrepancies in sample sizes were due to missing data, as the present study attempted to answer a different research question than these two prior analyses and thus explored different primary variables of interest. Differences between individuals included in the present analysis who participated in Study 1 versus those who participated in Study 2 are presented below.

3.4 Data Analytic Plan

Analysis for Specific Aim 1. Exploratory Latent Profile Analysis (LPA) was used to derive categorical latent variables representing groups of individuals who scored similarly on two measures of objective sleep, one measure of subjective sleep quality, and five dimensions of cancer-related fatigue. Two separate LPAs were conducted, one informed by data from 152 participants provided prior to the initiation of chemotherapy treatment (i.e., T1) and the second informed by data from 128 of those participants provided at the last week of the fourth cycle of chemotherapy (i.e., T2). The difference in the number of patients included in each analysis was due to study attrition. In LPA the probability that an individual is properly classified, which enables each person to be categorized into the best-fitting class, is estimated simultaneously within the overall model (Hill, Degnan, Calkins, & Keane, 2006). Models are estimated with classes added iteratively to determine which model best fits the data. For this study, LPA was conducted using MPlus 7.2, and the maximum likelihood robust (MLR) estimation procedure was used to estimate model parameters (Muthén & Muthén, 1998-2012). MLR estimation allows even those cases with missing data on one or more study variables to

be included in analyses. This is because MLR, as implemented in MPlus, is considered a full-information maximum likelihood approach to missing data. Accordingly, model parameters and standard errors are estimated using all observed data, and therefore data from both complete cases and partial cases are used to estimate target model parameters. Prior research has demonstrated that this estimation technique produces unbiased parameter estimates and standard errors under various missing data conditions (Enders, 2010).

To determine the optimal number of groups for the sample, each iterative model was evaluated using the Akaike information criterion (AIC; Akaike, 1974), the sample size-adjusted Bayesian information criterion (sBIC; Schwarz, 1978), the Bootstrapped Likelihood Ratio Test (BLRT; Arminger, Stein, & Wittenberg, 1999; McLachlan & Peel, 2000), and Entropy (Ramaswamy, DeSarbo, Reibstein, & Robinson, 1993). The AIC and sBIC are descriptive fit indices wherein smaller values indicate better model fit. The BLRT compares the fit of a target model (e.g., a two-profile model) to a comparison model that specifies one less profile (e.g., a one-profile model). The *p*-values generated for the BLRT indicate whether the solution with more profiles ($p < .05$) or fewer profiles ($p > .05$) is a superior fit to the data. Entropy is a measure of how well profiles can be distinguished, and demonstrates the percentage of individuals in the sample who are correctly classified given the specific model.

In addition to these indices, each model was evaluated on interpretability to ensure that different profiles truly represented distinct groups of participants, rather than representing an artifact of a non-normal distribution. Finally, the sample size of each profile was also evaluated, as small profiles containing less than 5% of the sample are

typically considered spurious, a result which is often found when too many profiles have been extracted (Hipp & Bauer, 2006; Roesch et al., 2010). LPA assumes that the residual correlations between observed variables should be zero within a given profile (Vermunt & Magidson, 2002); however, in instances in which this does not occur spurious profiles may arise as a way of reconciling the data with these assumptions (Bauer, 2007). Given that the LPAs in the present study were indicated by non-redundant but nonetheless theoretically interrelated variables (e.g., multiple dimensions of cancer-related fatigue, multiple assessments of sleep), solutions containing profiles comprised of less than 5% of the sample were rejected in favor of a solution with one fewer profile.

Analysis for Specific Aim 2. After the best-fitting models were determined, logistic regression analyses were conducted to evaluate if sociodemographic, medical, and psychosocial characteristics measured at T1 predicted profile membership at T1 and T2. Due to sample size constraints, a series of bivariate logistic regression models were evaluated in which a single sociodemographic, medical, or psychosocial variable was the predictor and group membership was the outcome. Half of these models evaluated groups identified at T1 and the other half evaluated groups identified at T2.

Analysis for Specific Aim 3. A series of analyses of covariance (ANCOVAs) were conducted to evaluate if the means of psychosocial variables measured at T2 differed across groups identified at T1, and across groups identified at T2. These analyses controlled for T1 values on the psychosocial variables being evaluated, as well as all sociodemographic and medical variables that differed across groups at T1. One T2 psychosocial variable (i.e., CES-D total score, Greene psychological score, Greene somatic score, Greene vasomotor score, SF-36 MCS score, SF-36 PCS score, or FACT-B

total score) was the outcome in each of these ANCOVAs. Relevant post-hoc comparisons were conducted, and effect sizes were examined.

Chapter 3 is being prepared in part for publication. This publication will be co-authored by Vanessa L. Malcarne, Sonia Ancoli-Israel, Scott C. Roesch, Georgia Robins Sadler, and Kristen Wells. The dissertation author was the primary investigator and author of this material.

CHAPTER 4: RESULTS

4.1 Participant Characteristics and Preliminary Analysis

Details outlining the study sample's characteristics can be found in Table 1. Preliminary analysis identified few differences between individuals who participated in Study 1 versus those who participated in Study 2. Study participants differed with regard to the type of chemotherapy received, $\chi^2(3) = 22.02$, $p < .01$, in that a larger proportion of participants in Study 1 received an AC and Taxotere formulation, 32.00% vs. 9.00%, while a smaller proportion of participants in Study 1 received an AC and Taxol formulation, 17.33% vs. 47.76%. Additionally, at T1 participants in Study 1 had significantly lower nighttime sleep percent values than did participants in Study 2, $t(119.51) = -4.40$, $p < .01$; M (SD) = 74.78% (13.88) vs. 82.63% (7.11), and smaller proportions of participants in Study 1 were using analgesics, $\chi^2(1) = 6.95$, $p = .01$, 59.26% vs. 79.41%, and laxatives, $\chi^2(1) = 6.50$, $p = .01$, 12.50% vs. 29.41%, and had been previously diagnosed with an endocrine disease, $\chi^2(1) = 6.26$, $p = .01$, 0.00% vs. 7.46%, as compared to participants in Study 2. Finally participants in Study 1 had significantly lower Greene psychological subscale scores than did participants in Study 2, $t(149) = -1.98$, $p = .05$; M (SD) = 6.50 (4.78) vs. 8.16 (5.55). No other significant differences were found across study participants at T1.

At T2 participants in Study 1 had significantly lower nighttime sleep percent values, $t(84.80) = -4.72$, $p < .01$; M (SD) = 74.54 (12.21) vs. 83.43 (6.92), significantly higher daytime sleep percent values, $t(109) = 2.02$, $p = .05$; M (SD) = 10.21 (9.29) vs. 7.06 (6.96), and significantly lower PSQI total scores, $t(124) = -2.06$, $p = .04$; M (SD) = 7.37 (3.79) vs. 8.78 (3.87), than did participants in Study 2. Study participants again

differed with regard to the type of chemotherapy received, $\chi^2(3) = 20.98$, $p < .01$, in that a larger proportion of participants in Study 1 received an AC and Taxotere formulation, 30.56% vs. 8.47%, while a smaller proportion of participants in Study 1 received an AC and Taxol formulation, 18.06% vs. 52.54%, as compared to participants in Study 2. Additionally, smaller proportions of participants in Study 1 were using analgesics, $\chi^2(1) = 6.62$, $p = .01$; 27.27% vs. 50.85%, and were experiencing edema, $\chi^2(1) = 4.00$, $p = .05$; 0.00% vs. 5.08%, as compared to participants in Study 2. Finally participants in Study 1 had significantly lower Greene somatic subscale scores than did participants in Study 2, $t(108.18) = -2.66$, $p = .01$; M (SD) = 2.49 (2.60) vs. 3.95 (3.41). No other significant differences were found across study participants at T2.

There were 152 participants with sufficient data to be included in the LPA at T1, and 128 participants with sufficient data to be included in the LPA at T2. Very few differences were found between participants who had data at T1 but did not have data at T2 and those who had data at both time points. A larger proportion of participants who were only included at T1 reported using minor tranquilizers at T1 as compared to participants who provided data at both time points, $\chi^2(1) = 3.95$, $p = .05$; 40.91% vs. 21.26%, and a smaller proportion of participants who were only included at T1 reported having headaches at T1 as compared to participants who provided data at both time points, $\chi^2(1) = 3.87$, $p = .05$; 4.76% vs. 23.62%. No other significant differences were found at either data collection time point between participants who had complete data at both T1 and T2 and those who were only included in the analysis at T1.

4.2 Sleep and Fatigue Groups

Groups at T1. Models containing one, two, three, and four profiles were fit to the data. The fit indices for each of these models are presented in Table 2a. All indicators of model fit suggested that the two-profile solution fit better than the one-profile solution. Although entropy suggested that the two-profile solution fit better than the three-profile solution, the AIC, sBIC, and BLRT all indicated that the three-profile solution fit better than the two-profile solution. Furthermore, although all indicators of model fit suggested that the four-profile solution was superior to the three-profile solution, the analysis indicated that the standard errors of model parameter estimates might not have been trustworthy for all parameters, indicating possible model nonidentification for the four-profile solution. Additionally, the fourth profile was comprised of only 2.0% of the sample (n = 3), suggesting that it was a spurious group that was too small to be of substantive value (Merz & Roesch, 2011). Given these findings, and concerns related to the likelihood of finding spurious groups in the present analysis given that the LPA was informed by theoretically interrelated observed variables, the three-profile solution was ultimately considered the best fit to the data.

The overall sample means and conditional response means used to substantively interpret the three-profile model are presented in Table 3a and Figure 2. Profile 1 comprised 19.1% of the sample (n = 29), Profile 2 comprised 50.6% of the sample (n = 77), and Profile 3 comprised 30.3% of the sample (n = 46). Based on relative scores on measures of sleep and fatigue, groups were labeled: *Distressed* (Profile 1), *Elevated* (Profile 2), and *Energetic* (Profile 3). The *Distressed* group represented individuals for whom average scores on the four MFSI-SF fatigue subscales were relatively higher than

the overall sample means, the MFSI-SF Vigor subscale score was relatively lower than the overall sample mean, night sleep percent and day sleep percent were somewhat higher than the overall sample means, and the PSQI total score was relatively higher than the overall sample mean. The *Elevated* group represented individuals for whom average scores on all five MFSI-SF subscales were similar to the overall sample means, night sleep percent was relatively lower than the overall sample mean, day sleep percent was similar to the overall sample mean, and the PSQI total score was slightly higher than the overall sample mean. The *Energetic* group represented individuals for whom average scores on the four MFSI-SF fatigue subscales were relatively lower than the overall sample means, the MFSI-SF Vigor subscale score was relatively higher than the overall sample mean, night sleep percent was somewhat higher than the overall sample mean, day sleep percent was similar to the overall sample mean, and the PSQI total score was relatively lower than the overall sample mean.

The total sample included in the LPA at T1 was divided into sub-samples of participants who came from Study 1 versus Study 2, and chi-square analysis compared the proportions of participants in each group across the two sub-samples. Results demonstrated that the proportions of participants in a given group at T1 did not statistically differ across the sub-samples derived from Study 1 versus Study 2, $\chi^2(2) = 0.67$, $p = .72$. Of participants in the Study 1 sample, 16.9% were in the *Distressed* group, 53.0% were in the *Elevated* group, and 30.1% were in the *Energetic* group at T1. Of participants in the Study 2 sample, 21.7% were in the *Distressed* group, 47.8% were in the *Elevated* group, and 30.4% were in the *Energetic* group at T1.

The total sample included in the LPA at T1 was next divided into sub-samples of participants who had sufficient data to be included in the analysis at both T1 and T2 versus those who were lost to follow-up, and therefore only included at T1. Chi-square analysis once again compared the proportions of participants in each group across these two new sub-samples. Results demonstrated that the proportions of participants in a given group at T1 did not statistically vary as a function of whether or not a participant was included at T2, $\chi^2(2) = 0.79$, $p = .68$. Of those who were included in the analysis at both time points, 18.0% were in the *Distressed* group, 50.8% were in the *Elevated* group, and 31.3% were in the *Energetic* group at T1. Of those who were lost to follow-up, 25.0% were in the *Distressed* group, 50.0% were in the *Elevated* group, and 25.0% were in the *Energetic* group at T1.

Groups at T2. Models containing one, two, three, four, and five profiles were fit to the data. The fit indices for each of these models are presented in Table 2b. All indicators of model fit suggested that the two-profile solution fit better than the one-profile solution, and that the three-profile solution fit better than the two-profile solution. Although entropy suggested that the three-profile solution fit better than the four-profile solution, the AIC, sBIC, and BLRT all indicated that the four-profile solution fit better than the three-profile solution. Similarly, although entropy suggested that the four-profile solution fit better than the five-profile solution, the AIC, sBIC, and BLRT all indicated that the five-profile solution fit better than the four-profile solution. A six-profile solution was attempted; however, the -2 log likelihood was unable to be replicated, indicating that the solution was unstable. Therefore, the five-profile solution was considered the best fit

to the data. No models with additional profiles were explored because the six-profile solution did not converge.

The overall sample means and conditional response means used to substantively interpret the five-profile model are presented in Table 3b and Figure 3. Profile 1 comprised 8.6% of the sample (n = 11), Profile 2 comprised 11.7% of the sample (n = 15), Profile 3 comprised 13.3% of the sample (n = 17), Profile 4 comprised 24.2% of the sample (n = 31), and Profile 5 comprised 42.2% of the sample (n = 54). Based on relative scores on measures of sleep and fatigue, groups were labeled *Highly distressed* (Profile 1), *Emotionally fatigued* (Profile 2), *Physically fatigued (*Profile 3), *Elevated* (Profile 4), and *Energetic* (Profile 5). The *Highly distressed* group represented individuals for whom average scores on all four MFSI-SF fatigue subscales were notably higher than the overall sample means, the MFSI-SF Vigor subscale score was notably lower than the overall sample mean, night sleep percent was slightly lower than the overall sample mean, day sleep percent was notably higher than the overall sample mean, and the PSQI total score was notably higher than the overall sample mean. The *Emotionally fatigued* group represented individuals for whom average scores on the MFSI-SF General, Emotional, and Mental fatigue subscales were notably higher than the overall sample means, the MFSI-SF Physical fatigue subscale score was similar to the overall sample mean, the MFSI-SF Vigor subscale score was notably lower than the overall sample mean, night sleep percent was similar to the overall sample mean, day sleep percent was somewhat higher than the overall sample mean, and the PSQI score was somewhat higher than the overall sample mean. The *Physically fatigued* group represented individuals for whom average scores on the MFSI-SF General and Physical fatigue subscales were

higher than the overall sample means, the MFSI-SF Emotional and Mental fatigue subscales scores were similar to the overall sample means, the MFSI-SF Vigor subscale score was somewhat lower than the overall sample mean, night sleep percent was notably lower than the overall sample mean, day sleep percent was slightly lower than the overall sample mean, and the PSQI total score was somewhat higher than the overall sample mean. The *Elevated* group represented individuals for whom average scores on the MFSI-SF General, Emotional, and Mental fatigue subscales were similar to the overall sample means, the MFSI-SF Physical fatigue and Vigor subscale scores were relatively lower than the overall sample means, night sleep percent was similar to the overall sample mean, day sleep percent was somewhat lower than the overall sample mean, and the PSQI total score was similar to the overall sample mean. Finally, the *Energetic* group represented individuals for whom average scores on all four MFSI-SF fatigue subscales were relatively lower than the overall sample means, the MFSI-SF Vigor subscale score was relatively higher than the overall sample mean, night sleep percent and day sleep percent were similar to the overall sample means, and the PSQI total score was relatively lower than the overall sample mean.

For T2, the total sample included in the LPA was again divided into sub-samples of participants who came from Study 1 versus Study 2, and chi-square analysis compared the proportion of participants in each group across the two sub-samples. Results demonstrated that the proportions of participants in a given group at T2 did not statistically differ across the sub-samples derived from Study 1 versus Study 2. Of those who participated in Study 1, 8.7% were in the *Highly distressed* group, 8.7% were in the *Emotionally fatigued* group, 15.9% were in the *Physically fatigued* group, 26.1% were in

the *Elevated* group, and 40.6% were in the *Energetic* group at T2. Of those who participated in Study 2, 8.5% were in the *Highly distressed* group, 15.3% were in the *Emotionally fatigued* group, 10.2% were in the *Physically fatigued* group, 22.0% were in the *Elevated* group, and 44.1% were in the *Energetic* group at T2.

Stability of group membership from T1 to T2. Of the 23 participants who were classified into the *Distressed* group at T1 who also had data at T2, 14 (60.87%) remained in one of the two groups characterized by the most severe symptoms (i.e., *Highly distressed* or *Emotionally fatigued*) at T2, while the remainder were classified into a group indicating less severe sleep and fatigue symptoms at T2. Of the 65 participants who were classified into the *Elevated* group at T1 who also had data at T2, 30 (46.15%) remained in one of the two groups characterized by more moderate symptoms (i.e., *Physically fatigued* or *Elevated*), 10 (15.38%) were classified into a group indicating more severe sleep and fatigue symptoms (i.e., *Highly distressed* or *Emotionally fatigued*), and 25 (38.46%) were classified into a group indicating less severe sleep and fatigue symptoms (i.e., *Energetic*) at T2. Finally, of the 40 participants who were classified into the *Energetic* group at T1 who also had data at T2, 29 (72.5%) remained in the *Energetic* group, while the remainder was classified into a group indicating more severe sleep and fatigue symptoms at T2.

4.3 Associations of Sleep and Fatigue Groups with T1 Levels of Sociodemographic, Medical, and Psychosocial Variables

Sociodemographic variables. For groups identified at T1, the only significant associations found were between group membership and age, and group membership and marital status (see Table 4a). Specifically, younger participants were more likely to be in

the *Distressed* group as opposed to the *Energetic* group. Younger participants were also more likely to be in the *Elevated* group as opposed to the *Energetic* group. Unmarried participants, as compared to married participants, were more likely to be in the *Distressed* group as opposed to the *Elevated* group.

For groups identified at T2, there was a statistically significant association found between group membership and education, as well as between group membership and marital status (see Table 4b). Specifically, participants who had completed some college but had not graduated from college were significantly more likely to be in the *Highly distressed* group as opposed to the *Energetic* group, as compared to participants who had graduated from college. Participants who were not married were significantly more likely to be in the *Highly distressed* or the *Emotionally fatigued* group versus the *Elevated* group, as compared to participants who were married.

Medical variables. For groups identified at T1, the only medical variables significantly associated with group membership were analgesic use, a diagnosis of asthma, and a diagnosis of an "other" (i.e., not specifically queried) disease at T1, as well as stage of cancer at diagnosis, chemotherapy formulation, and type of surgical intervention (see Table 5a). The following variables had insufficient variability to enable analysis: antiparkinson medications, cardiac medications, cardiovascular diseases, central nervous system diseases, connective tissue diseases, dementia, edema, emphysema, endocrine diseases, epilepsy, esophageal diseases, hiatal hernias, kidney diseases, major tranquilizers, over-the-counter hypnotics, oxygens, pulmonary diseases, renal diseases, sedative hypnotics, stimulants, stroke, ulcers, and vasodilators.

For groups identified at T1, participants who were not using analgesics at T1 were significantly less likely to be in the *Distressed* group as opposed to the *Energetic* group at T1. Similarly, participants without diagnoses of asthma or diseases not specifically queried at T1 were significantly less likely to be in the *Distressed* group as opposed to the *Energetic* group at T1. Participants whose cancer was Stage II at diagnosis, as compared to participants whose cancer was Stage III at diagnosis, were significantly more likely to be in the *Elevated* group as opposed to the *Energetic* group at T1. Participants receiving a chemotherapy formulation comprised of AC + Taxol were significantly more likely to be in the *Distressed* group as opposed to the *Elevated* group at T1, as compared to participants receiving a chemotherapy formulation comprised of something other than AC, AC + Taxotere, or AC + Taxol. Finally, participants who had received a lumpectomy or a single mastectomy were significantly more likely to be in the *Elevated* group as opposed to the *Energetic* group at T1, as compared to participants who had a double mastectomy or were receiving chemotherapy treatment prior to surgical intervention.

For groups identified at T2, the only T1 medical variables significantly associated with group membership were body mass index, use of antidepressants, use of minor tranquilizers, a diagnosis of asthma, a diagnosis of arthritis, and a diagnosis of an "other" disease (see Table 5b). As was the case for analyses examining groups identified at T1, a number of variables had insufficient variability to enable analysis, including: anticonvulsants, antiparkinson medications, cardiac medications, cardiovascular diseases, central nervous system diseases, connective tissue diseases, dementia, diabetes, diuretics, edema, emphysema, endocrine diseases, epilepsy, esophageal diseases,

gastroenterological diseases, hiatal hernias, infections, insulins, kidney diseases, major tranquilizers, over-the-counter hypnotics, oxygens, pulmonary diseases, renal diseases, sedative hypnotics, stimulants, stroke, thyroid diseases, ulcers, and vasodilators.

For groups identified at T2, participants with a higher body mass index at T1 were significantly more likely to be in the *Highly distressed* group as opposed to the *Physically fatigued* group at T2. Participants who were not using antidepressants at T1 were significantly less likely to be in the *Emotionally fatigued* group as opposed to the *Energetic* group at T2. Participants who were not using minor tranquilizers at T1 were significantly less likely to be in the *Emotionally fatigued* group as opposed to the *Elevated* group or the *Energetic* group at T2. Additionally, participants without a diagnosis of asthma at T1 were significantly less likely to be in the *Highly distressed* group, the *Emotionally fatigued* group, or the *Physically fatigued* group as opposed to the *Energetic* group at T2, and participants without a diagnosis of arthritis at T1 were significantly less likely to be in the *Physically fatigued* group as opposed to the *Elevated* group or the *Energetic* group at T2. Finally, participants without a diagnosis of an "other" (i.e., not specifically queried) disease at T1 were significantly less likely to be in the *Highly distressed* group or the *Physically fatigued* group as opposed to the *Elevated* group at T2.

Psychosocial variables. For groups identified at T1, all psychosocial variables explored were significantly associated with group membership (see Table 6a). Specifically, participants with higher T1 CES-D total scores, higher Greene psychological, somatic, and vasomotor scores, lower SF-36 MCS and PCS scores, and lower FACT-B total scores, were significantly more likely to be in the *Distressed* group

as compared to the *Elevated* group or the *Energetic* group at T1. Additionally, participants with higher T1 CES-D total scores, Greene psychological and somatic scores, lower SF-36 MCS, and lower FACT-B total scores, were significantly more likely to be in the *Elevated* group as compared to the *Energetic* group at T1. No significant differences in T1 Greene vasomotor scores or SF-36 PCS scores were found between the *Elevated* and *Energetic* groups at T1.

For groups identified at T2, all psychosocial variables explored were again significantly associated with group membership (see Table 6b). Specifically, participants with higher T1 CES-D and Greene psychological scores were significantly less likely to be in the *Energetic* group as opposed to any of the other four groups, and significantly more likely to be in the *Highly distressed* group or the *Emotionally fatigued* group as opposed to the *Elevated* group at T2. Participants with higher T1 Greene somatic scores were significantly less likely to be in the *Energetic group* as opposed to the *Highly distressed* group*, Emotionally fatigued* group*, or Physically fatigued* group at T2. These individuals were also significantly less likely to be in the *Elevated* group as opposed to the *Highly distressed* group at T2. Participants with higher T1 Greene vasomotor scores were more likely to be in the *Physically fatigued* group as opposed to the *Energetic* group at T2. Participants with higher T1 SF-36 MCS scores were significantly less likely to be in the *Emotionally fatigued* group as opposed to the *Physically fatigued* group, the *Elevated* group, or the *Energetic* group at T2. These participants were also significantly less likely to be in the *Highly distressed* group or the *Elevated* group as opposed to the *Energetic* group at T2. Participants with higher T1 SF-36 PCS scores were also significantly less likely to be in the *Highly distressed* group as opposed to the *Energetic*

group at T2. Finally, participants with higher T1 FACT-B total scores were significantly less likely to be in the *Highly distressed* group or the *Emotionally fatigued* group as opposed to the *Energetic* group or the *Elevated* group at T2. These participants with higher T1 FACT-B total scores were also significantly less likely to be in the *Physically fatigued* group or the *Elevated* group as opposed to the *Energetic* group at T2.

4.4 Differences in Psychosocial Outcomes at T2 Across Sleep and Fatigue Groups

A series of ANCOVAs were conducted to evaluate differences in psychosocial outcomes at T2 based on sleep and fatigue groups identified at both time points. With regard to differences across the three groups identified at T1, all analyses controlled for age, marital status, use of analgesics, diagnosis of asthma, diagnosis of an "other" (i.e., not specifically queried) disease, and score on outcome measure at T1, as well as stage of cancer at diagnosis, chemotherapy formulation, and type of surgical intervention. The homogeneity of regression assumption was met, and Levene's test indicated equality of variances. No differences were found among T1 groups for any of the psychosocial variables explored, though a trend toward significance was observed for T2 SF-36 MCS scores (p = .06; see Table 7a).

With regard to differences across the five groups identified at T2, all analyses controlled for use of antidepressants, use of minor tranquilizers, diagnosis of asthma, diagnosis of arthritis, diagnosis of an "other" (i.e., not specifically queried) disease, body mass index, marital status, and score of outcome measure at T1, as well as highest level of education attained. The homogeneity of regression assumption was met, and Levene's test indicated equality of variances. For all outcomes evaluated, scores from T2 were found to significantly differ across sleep and fatigue groups identified at T2 (see Table

7b). Follow-up analyses were conducting using simple contrast coding and a Bonferroni-adjusted alpha level of .010.

With regard to CES-D total scores and Greene psychological scores, the *Highly distressed* group and the *Emotionally fatigued* group both had significantly higher scores than the *Physically fatigued* group, the *Elevated* group, and the *Energetic* group. Additionally, the *Physically fatigued* group and the *Elevated* group both had significantly higher scores than the *Energetic* group.

With regard to Greene somatic scores, the *Highly distressed* group had significantly higher scores than all other groups, and the *Energetic* group had significantly lower scores than all other groups. With regard to Greene vasomotor scores, the *Highly distressed* group had significantly higher scores than the *Elevated* and *Energetic* groups. Additionally the *Physically fatigued* group had significantly higher scores than the *Energetic* group.

With regard to SF-36 MCS scores, the *Highly distressed* group and the *Emotionally fatigued* group both had significantly lower scores, indicating worse mental health-related quality of life, as compared to the *Physically fatigued* group, the *Elevated* group, and the *Energetic* group. Additionally, the *Physically fatigued* group and the *Elevated* group both had significantly lower scores than the *Energetic* group.

With regard to SF-36 PCS scores, the *Highly distressed* group had significantly lower scores, indicating worse physical health-related quality of life, as compared to the *Emotionally fatigued* group, the *Elevated* group, and the *Energetic* group. The *Physically fatigued* group also had significantly lower scores than the *Emotionally fatigued* group, the *Elevated* group, and the *Energetic* group.

Finally, with regard to FACT-B total scores, the *Highly distressed* group had significantly lower scores, indicating worse breast cancer specific health-related quality of life, as compared to the *Physically fatigued* group, the *Elevated* group, and the *Energetic* group. The *Emotionally fatigued* group had significantly lower scores than the *Physically fatigued* group and the *Energetic* group. Additionally, the *Physically fatigued* group and the *Elevated* group both had significantly lower scores than the *Energetic* group.

Chapter 4 is being prepared in part for publication. This publication will be co-authored by Vanessa L. Malcarne, Sonia Ancoli-Israel, Scott C. Roesch, Georgia Robins Sadler, and Kristen Wells. The dissertation author was the primary investigator and author of this material.

CHAPTER 5: DISCUSSION

The present study proposed to address three primary aims regarding sleep and cancer-related fatigue among breast cancer patients undergoing chemotherapy. First, this project aimed to identify typologies of breast cancer patients based on their differential experiences of a symptom cluster including objective sleep, subjective sleep quality, and multidimensional cancer-related fatigue. These symptom cluster groups were identified prior to the initiation of chemotherapy and again at the last week of the fourth cycle of treatment. Second, this project aimed to evaluate if sociodemographic, medical, and psychosocial variables measured prior to the initiation of chemotherapy statistically predicted group membership. Finally, the present analysis investigated if group membership had implications for psychosocial well-being at the last week of the fourth cycle of chemotherapy among patients being treated for breast cancer.

Overall, the present sample demonstrated elevated levels of fatigue, sleep disruption, and poor sleep quality. Although there are no known published cutoff scores on the MFSI-SF subscales indicating clinical fatigue, the present sample had the highest mean value on the Vigor subscale, followed by the General fatigue, Emotional fatigue, Mental fatigue, and Physical fatigue subscales, respectively, at T1. Conversely, at T2 the highest mean value was reported for the General fatigue subscale, followed by the Vigor, Mental fatigue, Emotional fatigue, and Physical fatigue subscales, respectively. Thus, in general the present sample reported more problems with general fatigue and vigor than for other domains of fatigue at both time points evaluated.

The present sample was generally similar to prior samples of cancer patients with regard to reported sleep and fatigue symptoms. Although it was not possible to

statistically compare symptom reports across studies, examination of the MFSI-SF subscale means clarified that the present sample reported similar levels of fatigue at T1 as the MFSI-SF validation sample of 275 breast cancer patients (Stein et al., 1998). Specifically, the present sample reported slightly less general and physical fatigue, slightly more emotional and mental fatigue, and comparable vigor to Stein et al.'s breast cancer patient sample. Additionally, at T1 the present sample demonstrated more general, emotional, and mental fatigue, less vigor, and comparable physical fatigue, compared to the non-cancer comparison sample examined by Stein et al. At T2, the present sample reported more general, physical, emotional, and mental fatigue, and less vigor, than did the MFSI-SF validation breast cancer patient sample and non-cancer comparison sample (Stein et al.).

At both T1 and T2, the mean PSQI total score for the present study was greater than five, which is the generally accepted cutoff used to indicate clinically significant poor sleep quality (Buysse et al., 1989). The mean PSQI total scores observed in the present sample at both T1 and T2 were similar to the mean scores reported by Beck and colleagues (2004) in their evaluation of the PSQI's psychometric properties in a sample of 473 oncology patients. Thus the present sample, like a prior sample of mixed-cancer patients, reported clinically relevant subjectively evaluated poor sleep quality.

At both T1 and T2, the present sample had average nighttime sleep percentages less than 85%, which is the commonly accepted cutoff for "normal" sleep in the greater insomnia literature (Edinger et al., 2004). This indicates that the present sample evidenced clinically relevant sleep disruption both before and during chemotherapy treatment. Additionally, as compared to a sample of 130 breast cancer patients about to

receive adjuvant anthracycline-based chemotherapy (Berger, Farr, Kuhn, Fischer, & Agrawal, 2007), the present sample had lower average nighttime sleep percent values at T1 and at T2. This demonstrates that the present sample was experiencing more disrupted nighttime sleep at both time points. Additionally, although there are no published norms regarding daytime sleep percentage, Berger and colleagues reported that the average daytime sleep percent observed among their sample was 7.49%. The average daytime sleep percent observed in the present study at T1 was lower than this, while the average observed at T2 was higher. This suggests that at T1 the sample was experiencing less daytime sleepiness than Berger et al.'s sample; however, at T2 the present sample was likely experiencing more daytime sleepiness than Berger and colleagues' sample of cancer patients who had not yet received chemotherapy.

5.1 Sleep and Fatigue Groups

This study's first primary aim was to identify sleep and fatigue groups of breast cancer patients prior to chemotherapy initiation and at the last week of the fourth cycle of chemotherapy.

Groups at T1. Three groups were found prior to chemotherapy initiation reflecting participants who, as compared to the overall sample means at T1, had 1) the worst subjective sleep quality, the most severe ratings of five dimensions of fatigue, moderate objectively indicated nighttime sleep disruption, and the most objectively indicated daytime sleepiness (*Distressed*); 2) moderate subjective sleep quality, moderately severe ratings of five dimensions of fatigue, the most objectively indicated nighttime sleep disruption, and less objectively indicated daytime sleepiness (*Elevated*); and 3) the best subjective sleep quality, the least severe ratings of five dimensions of

fatigue, the least objectively indicated nighttime sleep disruption, and less objectively indicated daytime sleepiness (*Energetic*).

At T1, the five dimensions of fatigue assessed by the MFSI-SF followed an identifiable pattern across the three identified groups. Specifically, the Vigor subscale had the lowest raw score of the five subscales in the *Distressed* group, and the highest raw score of the five subscales in the *Elevated* and *Energetic* groups. Moreover, of the four fatigue subscales measured, Physical fatigue had the lowest raw score in all three groups. This suggests that the cancer experience may have taken a large toll emotionally, overall, and mentally, but less so physically, prior to the initiation of chemotherapy treatment. Additionally, vigor was only significantly diminished for patients in the *Distressed* group, who reported more severe concerns across other domains of fatigue. Interestingly, nighttime sleep percent was notably lower for the *Elevated* group as opposed to the *Distressed* group, for which the mean value was very similar to that observed among the *Energetic* group. This indicates that the *Distressed* group actually experienced less disrupted sleep than the *Elevated* group, despite reporting more severe cancer-related fatigue and worse subjective sleep quality. Additionally, while daytime sleep percent was slightly elevated for the *Distressed* group, it was similar for the *Elevated* and *Energetic* groups. This suggests that worse objective sleep was not a direct reflection of the severity of other sleep and fatigue symptoms reported. Conversely, subjective sleep quality as measured by the PSQI did reflect group membership, as sleep quality was reported to be worst among the *Distressed* group, moderate among the *Elevated* group, and best among the *Energetic* group.

Compared to the sample of breast cancer patients Stein and colleagues (1998) examined when developing the MFSI-SF, the *Distressed* group was characterized by notably higher scores on the four fatigue subscales and a notably lower score on the Vigor subscale, indicating more severe cancer-related fatigue across all dimensions measured. Additionally, this profile group was characterized by a notably higher score on the PSQI, indicating worse subjective sleep quality, than the sample of cancer patients examined by Beck et al. (2004) when they cross-validated the PSQI in an oncology sample. Finally, the *Distressed* group also demonstrated more sleep disruption evidenced by lower nighttime sleep percent values, and more daytime sleepiness evidenced by higher daytime sleep percent values, than Berger et al.'s (2007) sample of breast cancer patients about to receive chemotherapy. Thus the *Distressed* group represented patients who were experiencing more severe sleep and fatigue symptoms than other breast cancer patients, across all variables measured.

Compared to Stein et al.'s (1998) sample of breast cancer patients, the *Elevated* group had lower General and Physical fatigue and Vigor scores, higher Emotional fatigue scores, and similar Mental fatigue scores, indicating less severe cancer-related fatigue in some domains, equivalent cancer-related fatigue in some domains, and more severe cancer-related fatigue in some domains. This group also had a slightly higher PSQI total score than Beck et al.'s (2004) oncology cross-validation sample, suggesting that this group had slightly worse subjective sleep quality. Like the *Distressed* group, the *Elevated* group reported more sleep disruption evidenced by lower nighttime sleep percent values, and less daytime sleepiness evidenced by lower daytime sleep percent values, than the sample of breast cancer patients evaluated by Berger and colleagues (2007).

Finally, compared to the sample of breast cancer patients Stein et al. (1998) evaluated, the *Energetic* group reported less severe cancer-related fatigue across all domains evaluated. In fact, the mean MFSI-SF fatigue subscale scores observed among this group were lower, and the Vigor subscale score was higher, than the mean of the 70 non-cancer comparison participants analyzed by Stein and colleagues when developing the MFSI-SF. Additionally, the *Energetic* group's mean PSQI total score was not only lower than the mean observed among Beck et al.'s (2004) cancer patient sample, but it was also lower than the generally accepted cutoff of five. This suggests that this group was not reporting clinically poor sleep quality at T1, unlike the *Distressed* and *Elevated* groups. The average nighttime sleep percent value observed among this group was lower than the generally accepted cutoff of 85%, and was lower than the mean observed in Berger and colleagues' (2007) sample of breast cancer patients. Thus the *Energetic* group found in the present sample reflected a group of cancer patients who were even less fatigued than individuals with no history of cancer, and who reported better sleep quality and demonstrated less daytime sleepiness than prior samples of cancer patients, despite experiencing mildly increased sleep disruption.

Groups at T2. Five groups were found at the last week of the fourth cycle of chemotherapy, reflecting patients who, as compared to the overall sample means at T2, had 1) the worst subjective sleep quality, the most severe ratings of five dimensions of fatigue, somewhat worse objectively indicated nighttime sleep disruption, and the most objectively indicated daytime sleepiness (*Highly distressed*); 2) somewhat worse subjective sleep quality, more severe ratings on General, Emotional, and Mental fatigue and Vigor but not on Physical fatigue, minimal objectively indicated nighttime sleep

disruption, and elevated objectively indicated daytime sleepiness (*Emotionally fatigued*); 3) somewhat worse subjective sleep quality, more severe ratings on General and Physical fatigue but not on Emotional and Mental fatigue or Vigor, the most severe objectively indicated nighttime sleep disruption, and slightly elevated objectively indicated daytime sleepiness (*Physically fatigued*); 4) slightly worse subjective sleep quality, slightly worse General fatigue but moderate Physical, Emotional, and Mental fatigue and Vigor, moderate objectively indicated nighttime sleep disruption, and the least objectively indicated daytime sleepiness (*Elevated*); and 5) the least severe subjective sleep quality, the least severe ratings of five dimensions of fatigue, the least objectively indicated nighttime sleep disruption, and slightly elevated objectively indicated daytime sleepiness (*Energetic*).

The patterns of MFSI-SF scores that were observed among groups identified at T1 were not sustained through four cycles of chemotherapy treatment. While the Vigor subscale was the highest raw MFSI-SF subscale score for two of the three groups uncovered at T1, it shifted in a manner reflective of the overall severity of symptoms characterizing a given group at T2. Of the five MFSI-SF subscales it was the lowest raw score in the *Highly distressed* group, the second lowest raw score in the *Emotionally fatigued* group, the third lowest raw score in the *Physically fatigued* group, the second highest raw score in the *Elevated* group, and the highest raw score in the *Energetic* group. Furthermore, while all groups had similar elevations of General and Mental fatigue, the *Highly distressed* and *Physically fatigued* groups were characterized by notable physical fatigue but relatively lower emotional fatigue, while the *Emotionally fatigued* and

Elevated groups were characterized by more emotional fatigue but relatively lower physical fatigue.

As was observed among groups identified at T1, measures of objective sleep were not a direct reflection of the severity of other symptom reports. Nighttime sleep percent was lower in the *Highly distressed* and *Physically fatigued* groups as compared to the *Emotionally fatigued, Elevated,* and *Energetic* groups, for which the mean values were similar, suggesting a relationship between physical fatigue and nighttime sleep disruption. Interestingly, the *Physical fatigue* group had the lowest average nighttime sleep percentage value of any group identified at T1 or at T2, indicating that participants in this profile experienced the most sleep disruption in the present study despite not having the most severe cancer-related fatigue or the worst subjective sleep quality. The *Energetic* group had a higher mean nighttime sleep percent value than any of the other groups identified at T2. Thus, once more, in addition to being the least fatigued group, the *Energetic* group was also experiencing the least nighttime sleep disruption at T2. Daytime sleep percent was elevated for the *Highly distressed* and *Emotionally fatigued* groups, but not as much for the *Physically fatigued, Elevated,* or *Energetic* groups, suggesting a relationship between overall fatigue severity and daytime sleepiness. Finally, as was observed among groups identified at T1, subjective sleep quality as measured by the PSQI was reflective of group membership at T2.

Compared to the MFSI-SF development sample of breast cancer patients (Stein et al., 1998), the *Highly distressed* and *Emotionally fatigued* groups were characterized by notably higher scores on the General, Emotional, and Mental fatigue subscales and a notably lower score on the Vigor subscale. Additionally, while both of these groups

evidenced higher scores on the Physical fatigue subscale than those observed by Stein et al., the difference between prior research and the mean for the *Highly distressed* group was rather large while the *Emotional fatigue* group had only a very slightly higher mean score. The participants in these two groups also demonstrated higher mean PSQI total scores, indicating worse subjective sleep quality, than Beck et al.'s (2004) PSQI cross-validation sample of cancer patients. Moreover, the *Highly distressed* and *Emotionally fatigued* groups had lower average nighttime sleep percent values and higher average daytime sleep percent values, indicating increased nighttime sleep disruption and daytime sleepiness, than did the sample of breast cancer patients evaluated by Berger et al. (2007). However, as was observed with physical fatigue, the discrepancies between prior research and the *Highly distressed* group were much greater than those between prior research and the *Emotionally fatigued* group. This suggests that the *Highly distressed* group represented cancer patients who were experiencing notably more severe sleep and fatigue symptoms than prior samples of cancer patients across all variables measured. Conversely, the *Emotionally fatigued* group represented patients who were experiencing notably more severe symptoms in some areas, but not with regard to physical fatigue or nighttime sleep disruption, for which symptoms were only slightly elevated.

The *Physically fatigued* group reported more severe fatigue symptoms on all MFSI-SF subscales except for the Emotional fatigue subscale as compared to the MFSI-SF validation sample of breast cancer patients (Stein et al., 1998). For this subscale the mean was similar to that of the measure's validation sample. The discrepancies between reports of fatigue observed in Stein et al.'s study and the present study were generally smaller for the *Physically fatigued* group than for the *Highly distressed* or *Emotionally*

fatigued groups, suggesting that the increased fatigue was less severe for this group. The *Physically fatigued* group also demonstrated worse subjective sleep quality based on a higher average PSQI total score than the sample of cancer patients Beck et al. (2004) evaluated when cross-validating the PSQI for use in oncology settings. Finally, this group had notably worse nighttime sleep disruption indicated by a lower average nighttime sleep percent value, but similar daytime sleepiness indicated by the average daytime sleep percent value, as compared to Berger et al.'s (2007) sample of breast cancer patients.

The *Elevated* group reported more severe fatigue symptoms on all MFSI-SF subscales except for the Physical fatigue subscale, for which the mean was slightly lower than that of the MFSI-SF validation sample (Stein et al., 1998). Similar to the pattern observed with the above mentioned groups, the discrepancies between reports of fatigue observed in Stein et al.'s study and the present study were generally smaller for the *Elevated* group than for the *Physically fatigued* group, suggesting that the increased fatigue was less severe for this group. Participants in the *Elevated* group also demonstrated similar subjective sleep quality, indicated by the average PSQI total score, as compared to Beck et al.'s sample (2004). This group also had more nighttime sleep disruption and less daytime sleepiness, evidenced by lower average nighttime and daytime sleep percent values, than Berger et al.'s (2007) sample of breast cancer patients.

Finally, as was observed at T1, compared to the sample of breast cancer patients Stein et al. (1998) evaluated, the *Energetic* group reported less severe cancer-related fatigue across all domains evaluated. Moreover, the average Physical, Emotional, and Mental fatigue subscale scores were lower, the average General fatigue score was similar,

and the average Vigor score was higher, than the mean of the 70 non-cancer comparison participants Stein et al. evaluated when developing the MFSI-SF. Additionally, although the *Energetic* group's average PSQI total score was above the clinical cutoff of five, it was less elevated than the mean observed in Beck et al.'s (2004) cancer patient sample. As was observed at T1, the average nighttime sleep percent value observed among this group was lower than the generally accepted cutoff of 85%, and was lower than the mean observed in Berger et al.'s (2007) sample of breast cancer patients. The average daytime sleep percent was similar to that observed in Berger et al.'s study. These results suggest that the *Energetic* groups identified at both time points in the present study reflected cancer patients who were less physically, emotionally, and mentally fatigued, and who had more vigor, than individuals with no history of cancer. At T2 these participants also reported better sleep quality and demonstrated similar daytime sleepiness as compared to prior samples of cancer patients, despite experiencing mildly increased sleep disruption.

Stability of group membership from T1 to T2. Consistent with the results of Dodd and colleagues (2011), approximately three quarters of the present sample remained in the group characterized by the least severe subjective and objective symptoms relative to the overall sample means at both time points (i.e., *Energetic*). Additionally, the majority of the sample categorized into the group characterized by the most severe subjective, but less severe objective, symptoms at T1 (i.e., *Distressed*) remained in the groups reflecting more severe subjective symptoms at T2 (i.e., *Highly distressed* or *Emotionally fatigued*). This suggests stability in group membership across four cycles of chemotherapy treatment for those participants categorized in the *Energetic* and *Distressed* groups at T1.

While the largest portion (46.16%) of participants categorized in the *Elevated* group at T1 remained in one of the two groups reflecting moderate symptoms at T2 (i.e., *Physically fatigued* or *Elevated*), more than half of the participants in this group shifted into a group reflecting a different level of symptom severity at T2. Interestingly, over one-third (38.46%) shifted into a group reflecting less severe symptoms at T2 (i.e., *Energetic*), while a smaller portion (15.38%) shifted into a group generally reflecting more severe symptoms (i.e., *Highly distressed* or *Emotionally fatigued*). This suggests that the *Elevated* group was less stable than the other two T1 groups, and that many participants actually improved with regard to sleep and fatigue concerns across four cycles of chemotherapy treatment.

These findings are consistent with a prior examination of a subset of the participants examined in this analysis. Liu and colleagues (2009) analyzed data from 76 of the women who participated in Study 1, and classified participants into groups based on pre-treatment experiences (i.e., clinically relevant or sub-threshold) of zero, one to two, or three of the following symptoms: subjective sleep quality operationalized as PSQI total scores (≥ 5: clinically relevant), fatigue operationalized as MFSI-SF total scores (≥ 0.85: clinically relevant), and depression operationalized as CES-D total scores (≥ 16: clinically relevant). These authors found that women who experienced more of these symptoms at a clinically relevant level prior to the initiation of chemotherapy treatment continued to experience more severe symptoms throughout treatment, as compared to women who experienced fewer symptoms at T1. In the present analysis, the *Distressed* group remained relatively stable throughout the study period. That is to say that over 60% of the participants who had severe subjectively reported symptoms at T1 continued to

report severe symptoms throughout chemotherapy. These are the same participants who would have been classified as having a higher symptom cluster score in Liu and colleagues' (2009) analysis, in which symptom clusters were identified based exclusively on subjective reports. However, the participants who were categorized as *Elevated* at T1 in the present analysis did not conform to the patterns observed by Liu and colleagues. Based on the cutoffs used by Liu et al. to indicate clinical relevance, the average participant in the *Elevated* profile would have been classified as having a higher symptom cluster; however, many of these patients actually experienced improved sleep and fatigue symptoms throughout the course of chemotherapy. By using LPA to identify symptom clusters rather than categorizing participants according to less advanced statistical processes, this separate group of participants who were at lower risk for worse symptom experiences was identified. Liu and colleagues argued that specific interventions should be developed targeting participants who experience more severe pre-treatment symptoms to improve quality of life throughout treatment. The present results support this argument, providing evidence that interventions should be developed for patients who report more severe subjectively assessed sleep and fatigue symptoms. However, a subset of these patients who report moderately elevated symptoms that are above clinical cutoffs, but are not quite as elevated as symptoms reported by the *Distressed* group, independent of objectively measured sleep, may end up with less severe sleep and fatigue concerns during chemotherapy.

5.2 Associations of Sleep and Fatigue Groups with T1 Levels of Sociodemographic, Medical, and Psychosocial Variables

This study's second primary aim was to evaluate if sociodemographic, medical, and psychosocial characteristics evaluated at T1 significantly predicted profile membership at T1 and T2.

Sociodemographic variables. The present results demonstrated that group membership was associated with select sociodemographic variables at both time points. Age and marital status significantly predicted group membership at T1, and education and marital status significantly predicted group membership at T2. It is interesting to note that there were differences in the statistically significant sociodemographic predictors at the two time points. This provides evidence supporting the conceptualization of the groups at T1 and T2 as related, but non-identical, groups of patients. Additionally, these findings identify participants who may be at increased risk for being classified into certain groups based on easily identifiable characteristics.

In the present study younger participants were more likely to be classified into the *Distressed* or *Elevated* group as opposed to the *Energetic* group at T1. Prior symptom cluster latent class analyses/LPAs have demonstrated mixed findings regarding the relationship between age and group membership (Dodd et al., 2011; Doong et al., 2015; Kim et al., 2014; Miaskowski et al., 2014, 2015). However, the association found in the present study is consistent with the larger literature evaluating the relationships of age to sleep disruption in cancer, and to cancer-related fatigue. For example, Dhruva et al. (2010) found that younger age was significantly correlated with higher prevalence of morning fatigue among 73 breast cancer patients preparing to undergo radiation therapy.

Similarly, in their cross-sectional survey of 982 cancer patients, Davidson et al. (2002) found an inverse relationship between age and odds of insomnia. Additionally, although they did not find a significant result in their LPA, Dodd et al. (2011) did observe that the relationship between age and group membership at their first data collection time point trended toward significance ($p = .09$), with younger participants more often in groups representing more severe symptom experiences. This is consistent with what was observed at a statistically significant level in the present analysis, and in some prior LPAs of symptom clusters in cancer (Doong et al., 2015; Miaskowski et al., 2014, 2015). Additionally, in their growth mixture model analysis evaluating scores on the General Sleep Disturbance Scale (Lee, 1992), Van Onselen and colleagues (2012) found that older patients were more likely to be in a class characterized by maintained low sleep disturbance across the study period as opposed to maintained high sleep disturbance. However, despite the statistically significant finding in the present study, it must be noted that the effect sizes for the relationship between age and group membership at T1 were very small, suggesting that age was not an extremely influential predictor of profile membership at T1.

Marital status significantly predicted profile membership at both T1 and T2. At T1 unmarried participants were three times more likely to be classified into the *Distressed* group versus the *Elevated* group, as compared to married participants. At T2 unmarried participants were over six times more likely to be in the *Elevated* group as opposed to the *Highly distressed* group, and over four times more likely to be in the *Elevated* group as opposed to the *Emotionally fatigued* group. Although discrepant from prior LPAs, this finding is consistent with those of Miaskowski et al. (2006), who

reported that married patients were more likely to be classified into a cluster analytically derived group reporting less severe symptoms as opposed to a group reporting more severe symptoms. Research has previously demonstrated that married patients often have better cancer outcomes, including lower mortality rates and less severe self-reported psychosocial symptoms, as compared to their unmarried counterparts (Aizer et al., 2013). It has been postulated that this may be a manifestation of increased perceived social support among married participants (Miaskowski et al., 2006). Although social support was not measured directly in the present analysis, the potential proxy measurement via marital status corroborates this hypothesis. Future research would benefit from directly examining the ability of social support to distinguish sleep and fatigue groups among breast cancer patients, particularly given the moderate to large effect sizes observed.

Finally, graduating from college as opposed to starting but not completing college-level coursework appeared to be protective against sleep and fatigues symptoms. Participants who had completed a college education or above were more likely to be in the *Energetic* group as opposed to the *Highly distressed* group at T2, as opposed to those who had completed some college. As with age, the relationship between education and group membership has received mixed evidence in prior oncology symptom cluster LPAs (Dodd et al., 2011; Doong et al., 2015; Miaskowski et al., 2015; Van Onselen et al., 2012). However, this may be a reflection of differing measurement techniques. For example, Van Onselen et al. (2012) measured education as a continuous variable, finding no difference in the mean number of years of education across groups. Had these authors measured education categorically, as was done in the present analysis, their results may have been different. Dodd and colleagues (2011) did use a categorical approach to

measuring education, categorizing participants' highest level of educational attainment as high school or more than high school. In the present analysis, all participants who completed some college or had graduated from college would have been classified as "more than high school" according to these guidelines. Had the broad education categories used by Dodd et al. been used in the present analysis, the significant relationship between education and group membership that was found would not have been detected. Participants in the present study who started college but did not graduate from college, as opposed to those who graduated from college, were five times more likely to be in the *Highly distressed* group as opposed to the *Energetic* group. Thus, knowledge of patients' education levels, like knowledge of marital status, may help identify participants who could experience and report more severe sleep and fatigue concerns at the last week of the fourth cycle of chemotherapy.

Medical variables. As was found with sociodemographic variables, the present results demonstrated that group membership was associated with select medical variables at both time points. Group membership at T1 was significantly predicted by analgesic use, a diagnosis of asthma, and a diagnosis of an "other" (i.e., not specifically queried) disease at T1, as well as stage of cancer at diagnosis, chemotherapy formulation, and type of surgical intervention. Group membership at T2 was significantly predicted by body mass index, use of antidepressants, use of minor tranquilizers, a diagnosis of asthma, a diagnosis of arthritis, and a diagnosis of an "other" (i.e., not specifically queried) disease, all at T1. Once more, the non-redundant nature of the significant predictors at each time point further supports the interpretation of the groups as associated, but non-identical. Additionally, these findings further identify participants who may be at increased risk for

being classified into a group reflecting more severe sleep and fatigue symptoms based on medical characteristics.

Prior LPAs have found mixed results regarding relationships between medical variables and group membership. In general the medical variables that significantly predicted group membership in the present study have not been significantly associated with group membership in the past; however, this may be due to differences between the present study and prior research. Variables found to significantly relate to LPA-derived groups in prior studies include cancer site, presence of more advanced or metastatic disease, and level of comorbidity (Doong et al., 2015; Miaskowski et al., 2014, 2015), none of which were evaluated in the present study. Furthermore, many of the medical variables examined in the present study have not been previously evaluated as they relate to group membership. Additionally, it should be noted that many prior LPAs in cancer have evaluated patients with different types of cancer, and groups have been derived based on variables different from those used in the present study.

In the present study, participants' use of analgesics at T1 moderately increased the likelihood for being classified into the *Distressed* group as opposed to the *Energetic* group at T1. Specifically, participants who were using analgesics at T1 were more than four times as likely to be in the *Distressed* group. Consistent with this, pain has been shown to be associated with sleep disruption and fatigue in cancer (Bardwell et al., 2008). In the present sample patients reporting more severe sleep and fatigue symptoms may also have been experiencing sufficient pain symptoms to necessitate analgesics, contributing to this moderate effect. Similarly, patients who received a lumpectomy or single mastectomy in addition to adjuvant chemotherapy were more than three times

more likely to be classified into the *Elevated* group as opposed to the *Energetic* group as compared to patients who had a double mastectomy or were receiving neoadjuvant chemotherapy prior to surgical intervention. It is interesting to note that receiving less invasive surgical intervention or receiving surgical intervention prior to undergoing chemotherapy moderately increased likelihood for being classified into the group characterized by more severe objective sleep concerns, but only somewhat heightened subjective sleep and fatigue concerns, as opposed to the group with the least severe symptoms. Although a double mastectomy is a more invasive procedure than a single mastectomy or a lumpectomy, and thus more severe symptoms may be expected, this was not found in the present study. This may be due to the relatively small number of participants who received this treatment ($n = 7$), and the fact that these participants were grouped together for analysis with those who were receiving neoadjuvant chemotherapy as a result of small sample size.

Participants whose cancer was Stage II at diagnosis were also nearly three times more likely to be in the *Elevated* group as opposed to the *Energetic* group at T1 as compared to participants whose cancer was Stage III. Kim et al. (2014) did not find any differences among groups with regard to cancer stage at diagnosis; however, this might also be a result of measurement differences. Unlike in the present study, in which a small to moderate effect was found, Kim and colleagues dichotomized stage of cancer at diagnosis, grouping together stages I and II, and stages III and IV. Van Onselen et al. (2012) observed a trend toward significance with regard to cancer stage ($p = .07$), and Doong et al. (2015) found that more advanced disease was associated with being in a group characterized by more severe symptoms. However, both of these research teams

included patients with stage IIIB, IIIC, and IV cancer at diagnosis, making it difficult to compare the present sample with their two study samples.

Additionally, in the present study participants receiving a chemotherapy formulation comprised of AC + Taxol, as opposed to a chemotherapy formulation comprised of something other than AC, AC + Taxotere, or AC + Taxol, were more likely to be classified into the *Distressed* group as opposed to the *Elevated* group at T1. Specifically, these participants were nearly four times more likely to be in the *Distressed* group, reflecting a moderate effect. Future research can clarify why a prescription for this particular chemotherapy formulation was associated with increased likelihood of being classified into a more symptomatic group prior to the initiation of chemotherapy treatment.

Interestingly, at both T1 and T2 comorbid diagnoses of asthma or diseases not specifically queried at T1 increased likelihood for being classified into a group characterized by less severe rather than more severe symptomatology. Participants without a comorbid diagnosis of asthma were over six times more likely to be classified into the *Energetic* group rather than the *Distressed* group at T1, reflecting a moderate to large effect. Participants without a diagnosis of an "other" disease not specifically queried were five times more likely to be classified in this way at T1, reflecting a moderate yet still notable effect. The effect sizes observed at T2 ranged from just over 11 to nearly 20, demonstrating much larger effects, although the wide confidence intervals indicated low precision. Despite the fact that these specific comorbidities have not been examined in isolation, prior research has demonstrated that individuals with a higher number of and/or more severe medical comorbidities, when measured continuously, are

more likely to be in a group characterized by more severe symptoms (Doong et al., 2015; Miaskowski et al., 2014; Van Onselen et al., 2012). Medical comorbidities were not measured continuously in the present study because doing so would force the examination of all potential comorbidities simultaneously, rather than enabling the individual examination of concerns that may have greater implications for sleep disruption or cancer-related fatigue (e.g., thyroid diseases, headaches). That said, it must be noted that one of the comorbidities explored in the present study was "other" diseases. Moreover, this variable was one of only three out of 25 comorbidities that significantly differentiated groups. This suggests that there may be some still unexplored medical diagnoses that increase the risk of being classified into a group reflecting increased symptom reports. Future research may benefit from exploring additional diagnoses that were not evaluated independently in the present study.

Participants without a diagnosis of arthritis at T1 were five times more likely to be in the *Elevated* group as opposed to the *Physically fatigued* group, and over three times more likely to be in the *Energetic* group as opposed to the *Physically fatigued* group, at T2. Both of these values indicated a moderately decreased likelihood of being in the *Physically fatigued* group in the absence of comorbid arthritis. This is inconsistent with Kim et al. (2014), one of the few studies to specifically evaluate arthritis, who found no significant relationship between comorbid arthritis and group membership. However, Kim and colleagues derived groups from patients with multiple types of cancer, including breast, lung, colorectal, prostate, gynecologic, bladder, or testicular cancer, or lymphoma. Thus, this discrepant finding may be a function of the multiple cancer types experienced by their sample.

In the present study participants with a higher body mass index at T1 were slightly more likely to be in the *Highly distressed* group as opposed to the *Physically fatigued* group at T2. This is inconsistent with Doong and colleagues' (2015) and Van Onselen and colleagues' (2012) findings that body mass index did not significantly differ across groups. Doong et al. did not provide additional information beyond reporting that the relationship between body mass index and group membership was not significant; however, Van Onselen and colleagues observed a trend toward significance ($p = .12$). Specifically, participants in a group characterized by consistent, more severe symptoms had a higher average body mass index than did participants in the other identified groups. The present finding is also consistent with the large body of research demonstrating a relationship between higher body mass index and shorter sleep duration (Cappuccio et al., 2008). Based on the present results, higher body mass index prior to the initiation of chemotherapy may indicate worse overall sleep and fatigue symptoms at the last week of the fourth cycle of chemotherapy. However, it should be noted that the observed effect size was small.

Finally, participants who were not using antidepressants at T1 were over four times more likely to be in the *Energetic* group as opposed to the *Emotionally fatigued* group at T2, a moderate effect. Participants who were not using minor tranquilizers at T1 were nearly six times more likely to be in the *Elevated* group as opposed to the *Emotionally fatigued* group, and nearly nine times more likely to be in the *Energetic* group as opposed to the *Emotionally fatigued* group, both of which reflect large effects. Although this has not been explored in prior LPAs of oncology symptom clusters, minor tranquilizers and many antidepressants are sedative medications that can increase reports

of fatigue, and decrease reports of sleep disruption, while increasing overall sleep time. This finding suggests that participants who were experiencing concerns regarding sleep or mood at T1 to such a degree that they were treating these concerns pharmacologically were at increased risk for being in a group characterized by increased symptom reports, particularly increased emotional fatigue, at the last week of the fourth cycle of chemotherapy. However, it is worth noting that these participants were not at increased risk of being classified into the group representing the most severe symptom experiences, as compared to the other groups.

Psychosocial variables. As has been observed in prior studies of oncology symptom clusters using LPA and cluster analytic techniques (Dodd et al., 2011; Kim et al., 2014; Miaskowski et al., 2006, 2015; Trudel-Fitzgerald et al., 2014; Van Onselen et al., 2012), group membership was cross-sectionally associated with all psychosocial variables evaluated. At T1, higher reports of depression and psychological, somatic, and vasomotor climacteric symptoms, as well as lower reports of physical health-related, mental health-related, and breast cancer specific health-related quality of life, all significantly predicted increased likelihood of being in the *Distressed* group as opposed to either of the other two groups identified at T1. It should be noted; however, that all of these effects were small in magnitude. The same pattern predicted increased likelihood of being in the *Elevated* group as opposed to the *Energetic* group for all variables except for vasomotor climacteric symptoms and physical health-related quality of life. Thus, participants reporting increased depression and psychological and somatic climacteric symptoms, as well as worse mental and breast cancer specific health-related quality of life, at T1 were generally reporting more severe sleep disruption and cancer-related

fatigue symptoms at T1, although the effect sizes were once again small. This suggests that these symptoms do all occur in combination, further supporting the notion of oncology symptom clusters in general. Interestingly, physical health-related quality of life and vasomotor climacteric symptoms were not found to differentiate participants in the *Elevated* group from those in the *Energetic* group at T1. This may be a reflection of the less severe subjective reports of sleep disruption and cancer-related fatigue symptoms, relative to objective recordings of sleep symptoms, observed among participants in the *Elevated* group. Of note, of the groups identified at T1, only the *Distressed* group had a mean T1 CES-D score above the commonly accepted clinical cutoff of 16, indicating clinically relevant depression symptoms in this group.

A similar trend was observed for profiles identified at T2, in that participants who reported more depression and climacteric symptoms and worse quality of life at T1 were generally more likely to be classified into a group reflecting reports of more severe sleep and fatigue symptoms at T2. As was observed at T1, the statistically significant effects that were found were small in magnitude, and, interestingly, not all pairwise differences were statistically significant. For example, none of the T1 psychosocial variables statistically significantly predicted likely membership is the *Highly distressed* group as opposed to the *Emotionally fatigued* or *Physically fatigued* groups identified at T2. Similarly, none statistically significantly predicted likely membership in the *Physically fatigued* group as opposed to the *Elevated* group at T2, suggesting that at a certain level of severity differences in T1 symptoms did not significantly predict T2 groups. Of note, T1 mental health-related quality of life was found to be higher, and T1 depression and psychological climacteric symptoms were found to be lower, among the *Elevated* group

as opposed to the *Emotionally fatigued* group identified at T2. The *Emotionally fatigued* and *Elevated* groups were those characterized by relatively higher levels of emotional fatigue, while the *Highly distressed* and *Physically fatigued* groups were characterized by relatively higher levels of physical fatigue. It is interesting to note that the differing levels of emotional fatigue at T2 were significantly predicted by T1 mental health-related quality of life, psychological climacteric symptoms, and depressive symptoms, but differing levels of physical fatigue at T2 were not predicted by T1 physical health-related quality of life or vasomotor climacteric symptoms. In fact, the only T2 groups with significantly different T1 physical health-related quality of life symptoms were the *Highly distressed* group and the *Energetic* group, the groups representing the most and least severe symptom reports. The only T2 groups with significantly different T1 vasomotor climacteric symptoms were the *Physically fatigued* group and the *Energetic* group. This suggests that mental health symptoms at T1 may have more nuanced implications for sleep and fatigue outcomes later in chemotherapy treatment than physical health symptoms at T1.

As was observed for groups identified at T1, T1 CES-D scores were above the generally accepted clinical cutoff of 16 for certain groups identified at T2, but not for others. Specifically, scores were clinically relevant for the *Highly distressed* and *Emotionally fatigued* groups but not for the *Physically fatigued, Elevated,* or *Energetic* groups. As stated, the *Highly distressed* and *Physically fatigued* groups were both characterized by relatively higher physical fatigue, and the *Emotionally fatigued* and *Elevated* groups were characterized by relatively higher emotional fatigue. Thus the solution identified a group of participants based on T2 sleep and fatigue variables that

was more severely physically fatigued and had been experiencing clinically relevant depression at T1, a group that was more severely emotionally fatigued and had been experiencing clinically relevant depression at T1, a group that was physically fatigued but had not been experiencing clinically relevant depression at T1, a group that was emotionally fatigued but had not been experiencing clinically relevant depression at T1, and a group that was experiencing low levels of all dimensions of fatigue assessed and had not been experiencing clinically relevant depression at T1.

The group with the most severe fatigue and sleep scores at T1 (i.e., *Distressed*) had higher T1 CES-D and Greene psychological, somatic, and vasomotor scores, and lower T1 SF-36 PCS and SF-36 MCS scores, than did the two groups representing the most severe sleep and fatigue scores at T2 (i.e., *Highly distressed* and *Emotionally fatigued*). The finding that, for some patients, psychosocial symptom morbidity was higher prior to the initiation of chemotherapy treatment suggests that these symptoms are likely due to a combination of treatment side effects and preexisting concerns. However, the portion of symptom reports due to each of these influencing variables cannot be discerned from the present analysis. Further investigation is warranted to determine the extent to which each of these components contributed to these reports of psychosocial symptoms. Interestingly, T1 levels of these psychosocial variables did not differ across patients who provided complete data at both time points and those who were lost to follow-up, suggesting that something other than psychosocial symptom experiences at T1 prevented participants from completing study participation.

With regard to quality of life, it has been argued that differences of 0.2 to 0.5 standard deviation units in scores on standardized assessments are clinically meaningful

(Guyatt, Osoba, Wu, Wyrwich, & Norman, 2002; Norman, Sloan, & Wyrwich, 2003). Standard deviation units are calculated as the difference between the means of two groups, divided by the standard deviation of the total sample (Miaskowski et al., 2006). In the present study, statistically significant pairwise differences in T1 SF-36 PCS scores, SF-36 MCS scores, and FACT-B total scores among groups identified at T1 ranged from 0.73 to 2.05 standard deviation units. Statistically significant pairwise differences in T1 SF-36 PCS scores, SF-36 MCS scores, and FACT-B total scores among groups identified at T2 ranged from 0.64 to 1.78 standard deviation units. This is consistent with prior studies evaluating quality of life across cluster analytically derived groups, which have shown differences ranging from 0.50 to 3.53 standard deviation units (Miaskowski et al., 2006, 2014; Pud et al., 2008).

Though a minimal clinically important difference has not been identified for the CES-D or the Greene Climacteric Scale, the standard of 0.20 to 0.50 standard deviation units has previously been applied to other psychosocial variables in addition to quality of life (Andrykowski et al., 2005; Miaskowski et al., 2014, 2015). In the present analysis statistically significant pairwise differences in T1 CES-D total scores and Greene subscale scores among groups identified at T1 ranged from 0.44 to 2.11 standard deviation units, and differences in T1 scores on these measures among groups identified at T2 ranged from 0.56 to 1.54. These values suggest that the differences in T1 depression, climacteric symptomatology, and quality of life scores across groups identified at both T1 and T2 were not only statistically significant, but were clinically relevant as well.

5.3 Differences in Psychosocial Outcomes at T2 Across Sleep and Fatigue Groups

The present study's third aim was to investigate if group membership had implications for psychosocial well-being at the last week of the fourth cycle of chemotherapy among patients being treated for breast cancer. Distinct results were found for ANCOVAs evaluating T2 differences in psychosocial outcomes across sleep and fatigue groups identified at T1 as opposed to those identified at T2. After controlling for T1 levels of sociodemographic and medical variables that differed across T1 groups, as well as the T1 value of the psychosocial variable being predicted, none of the psychosocial outcomes evaluated had significantly different means across sleep and fatigue groups identified at T1. Results demonstrated that the majority of the variance in a given psychosocial outcome at T2 was accounted for by the value of that psychosocial variable at T1. Thus, sleep and fatigue groups identified at T1 did not have significantly different mean values on measures of depression, climacteric symptomatology, or quality of life evaluated at T2; rather, T1 levels of depression, climacteric symptomatology, and quality of life were stronger predictors thereof. Of note, of the groups identified at T1 only the *Distressed* group had a mean T2 CES-D score above the commonly accepted clinical cutoff of 16, indicating clinically relevant depression symptoms in this group. However, as previously stated, although the mean was above a clinical cutoff, it did not statistically significantly differ from the average T2 CES-D scores of the other two groups that were identified at T1 (i.e., *Elevated* and *Energetic*).

Conversely, for groups identified at T2, after controlling for T1 levels of sociodemographic, medical, and psychosocial variables that differed across T2 groups, as well as the T1 value of the psychosocial variable being predicted, all T2 psychosocial

outcomes significantly differed across T2 sleep and fatigue groups. Moreover, the omnibus effect sizes for all models were medium to large. This finding is consistent with prior studies of oncology symptom clusters using LPA and cluster analytic techniques (Dodd et al., 2011; Kim et al., 2014; Miaskowski et al., 2006, 2015; Trudel-Fitzgerald et al., 2014; Van Onselen et al., 2012), in which the variables on which profile membership are based and psychosocial outcomes of interest have typically been measured at the same time point. These results also suggest that when sleep and fatigue symptoms and psychosocial outcomes were both measured at T2, a stronger relationship was found as compared to when sleep and fatigue symptoms were measured at T1 and psychosocial outcomes were measured at T2. This further supports the notion that these symptoms do occur in combination, as was observed in the results for Aim 2.

Participants classified into a T2 group reflecting more severe sleep and fatigue symptoms generally reported more T2 depression and climacteric symptoms, and worse quality of life. This finding is similar to what was observed when examining differences in T1 values of psychosocial outcomes across T2 groups in the analysis for Aim 2. However, not all pairwise differences were statistically significant. For example, the *Highly distressed* group reported significantly more depression symptoms than the *Physically fatigued, Elevated,* and *Energetic* groups, but not the *Emotionally fatigued* group. This may be because mean T2 CES-D scores were notably above the generally accepted clinical cutoff of 16 for the *Highly distressed* and *Emotionally fatigued* groups, slightly above the cutoff for the *Physically fatigued* and *Elevated* groups, and below the cutoff for the *Energetic* group identified at T2. The *Highly distressed* and *Emotionally fatigued* groups also had T1 CES-D total scores above 16. Thus, T2 groups comprised of

participants reporting clinically relevant depression symptoms at T1 (i.e., *Highly distressed* and *Emotionally fatigued*) were also reporting clinically relevant depression symptoms at T2.

The two groups characterized by relatively higher physical fatigue (i.e., *Highly distressed* and *Physically fatigued*) significantly differed from each other with regard to all outcomes except for vasomotor climacteric symptoms and physical health-related quality of life, the two psychosocial outcomes that most closely approximated physical health symptoms. Conversely, the two groups characterized by relatively higher emotional fatigue (i.e., *Emotionally fatigued* and *Elevated*) differed from each other with regard to depression, psychological climacteric symptoms, and mental health-related quality of life. That is to say that differing levels of emotional fatigue at T2 reflected significant differences in mental health-related quality of life, depression, and psychological climacteric symptomatology at T2, but differing levels of physical fatigue at T2 did not reflect differences in vasomotor climacteric symptoms and physical health-related quality of life at T2. This extends the results found for Aim 2, and suggests that mental health symptoms across the cancer continuum may have more nuanced implications for sleep and fatigue outcomes at the last week of the fourth cycle of chemotherapy treatment as compared to physical health symptoms.

While not all pairwise comparisons were significantly different, the *Energetic* group had significantly different mean scores on measures of depression, psychological and somatic climacteric symptoms, mental health-related quality of life, and breast cancer specific health-related quality of life as compared to the other four groups identified at T2. These differences were found after controlling for relevant covariates and T1 levels

of these psychosocial outcomes. Future research can elucidate other defining characteristics that may help to identify patients who are likely to be in the *Energetic* group at the last week of the fourth cycle of chemotherapy. Given the rather universal positive influence of membership in this group with regard to psychosocial well-being at T2, identification of these participants and exploration of what distinguishes them from others, above and beyond those variables explored in the present analysis, may identify target variables for future interventions to improve psychosocial outcomes later in chemotherapy treatment.

In the present study, the statistically significant pairwise differences in T2 SF-36 MCS scores, SF-36 PCS scores, and FACT-B total scores among groups identified at T2 ranged from 0.53 to 1.91 standard deviation units. This is again consistent with prior studies evaluating quality of life across LPA and cluster analytically derived groups, as discussed above (Miaskowski et al., 2006, 2014; Pud et al., 2008). There were no statistically significant pairwise differences in T2 CES-D scores or Greene psychological, somatic, and vasomotor scores among groups identified at T1. However, significant differences in T2 scores on these measures among groups identified at T2 ranged from 0.44 to 2.21 standard deviation units. Thus, as was observed for differences in psychosocial variables at T1, these values suggest that the differences in T2 depression, climacteric symptomatology, and quality of life scores across groups identified both at T1 and at T2 were not only statistically significant, but were clinically relevant as well.

5.4 Limitations

The present study must be interpreted within the context of relevant limitations. Due to sample size constraints, each variable evaluated was examined in a separate

model. Thus, all analyses completed for Aim 2 could not control for potential confounders. Additionally, all models involving group membership at T2 could not control for group membership at T1. It is therefore unclear how T1 sleep and fatigue symptoms may have affected the relationships of T2 sleep and fatigue symptoms to the sociodemographic, medical, and psychosocial variables evaluated. Furthermore, due to a combination of sample size constraints and insufficient data collection time points, longitudinal modeling techniques such as growth mixture modeling or latent growth curve analysis could not be used. Such analyses would shed additional light on trajectories of sleep and fatigue experiences over time above and beyond what was illuminated by the parallel cross-sectional analyses completed in the present study. An additional limitation is that there was no measure of pain in the present study, which has been shown to influence sleep and fatigue among cancer patients (Bardwell et al., 2008). Thus, variability in pain reports across sleep and fatigue groups could not be explored. Sleep disordered breathing was also not assessed, which may have impacted symptom reports. Furthermore, a number of the medical variables included in the present analysis did not have sufficient variability to enable analysis, thus limiting the scope of the results.

With regard to the patient sample, participants for the present analysis were drawn from two nearly identical but nonetheless separate study protocols. Additionally, 24 participants were lost to follow-up and did not provide data at T2. Due to sample size constraints, it was not possible to adjust for study participation, nor was it possible to only examine participants from a single study protocol or those who had sufficient data to be included in the analysis at both time points. Although there were very few differences across participants from the two study protocols, and between participants whose data

were analyzed at both T1 and T2 and those who were lost to follow-up, there were some statistically significant differences that may have impacted the study results.

There were also concerns regarding generalizability that should be mentioned. Participants in the present study were generally highly educated with high annual household incomes. Additionally, only women whose cancer was Stage I to III at diagnosis were included in the present study, and thus it was unclear how these results may apply to women with more advanced cancers or men with breast cancer. Finally, participants in these studies were not enrolled via random selection, but rather volunteered to take part. Thus selection bias may have influenced the results, making it challenging to generalize these findings to breast cancer patients who would not elect to participate in a study such as one of the two from which participants for the present analysis were drawn.

5.5 Summary and Conclusions

Regardless of these limitations, the present study extends the existing literature on oncology symptom clusters. The present study proposed to address three primary aims regarding the roles of sleep and cancer-related fatigue in breast cancer. The results demonstrated that latent profile analysis can be used to distinguish patient groups based on their differential experiences of a symptom cluster comprised of objective sleep, subjective sleep quality, and multidimensional cancer-related fatigue prior to the initiation of chemotherapy and again at the last week of the fourth cycle of treatment. This study also provided evidence supporting the existence of distinct groups with unique sleep and cancer-related fatigue experiences among breast cancer patients prior to the initiation of chemotherapy, and again at the last week of the fourth cycle thereof. Results

further identified pre-treatment sociodemographic, medical, and psychosocial variables that statistically predicted group membership at both of these time points, and clarified which groups from both time points were at heightened risk for poor psychosocial outcomes at the last week of the fourth cycle of chemotherapy. These findings can be used to inform future assessments and interventions targeting cancer-related symptoms to improve patients' overall experience of disease.

Chapter 5 is being prepared in part for publication. This publication will be co-authored by Vanessa L. Malcarne, Sonia Ancoli-Israel, Scott C. Roesch, Georgia Robins Sadler, and Kristen Wells. The dissertation author was the primary investigator and author of this material.

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FIGURES

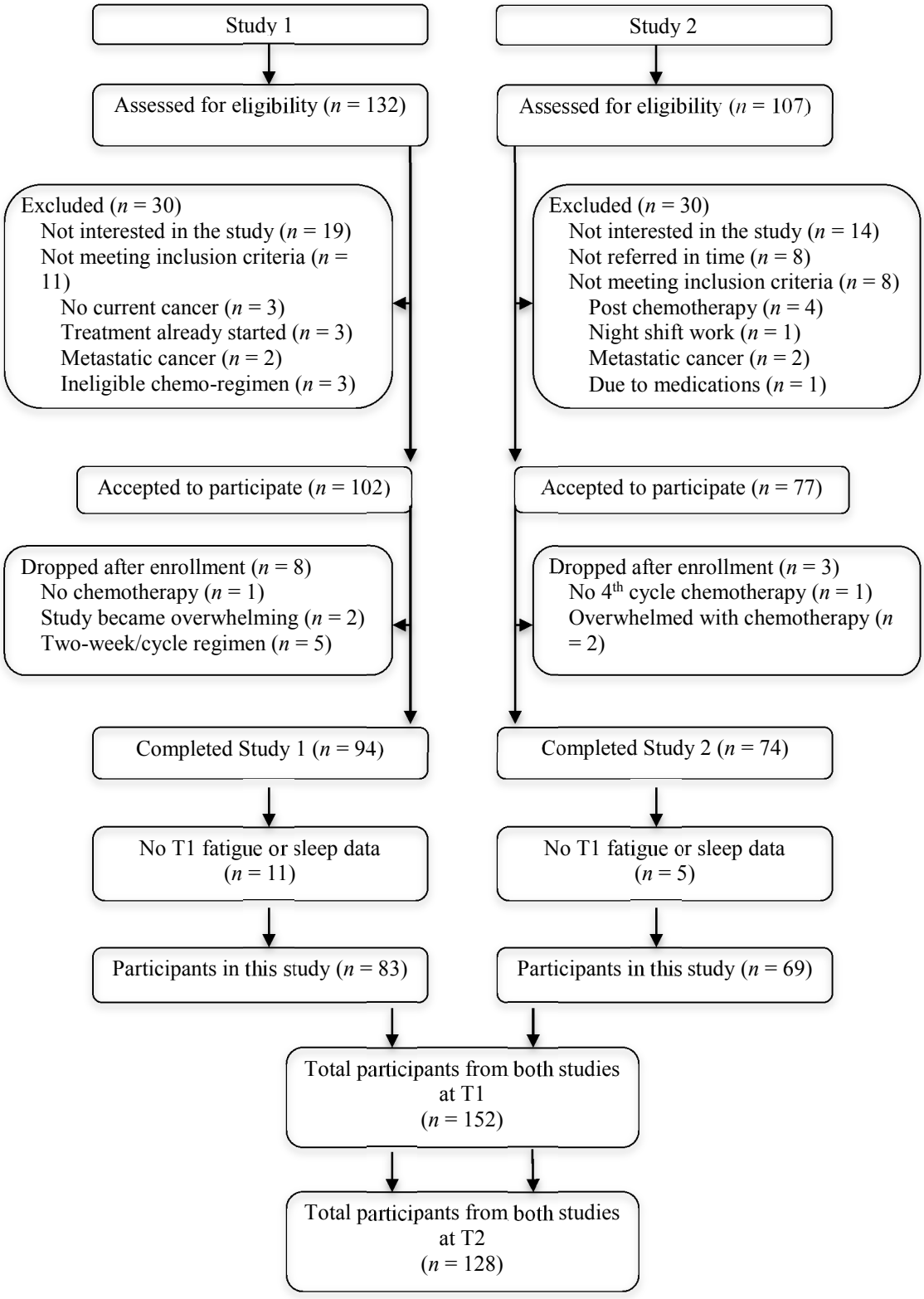

Figure 1. Screening and enrollment flowchart

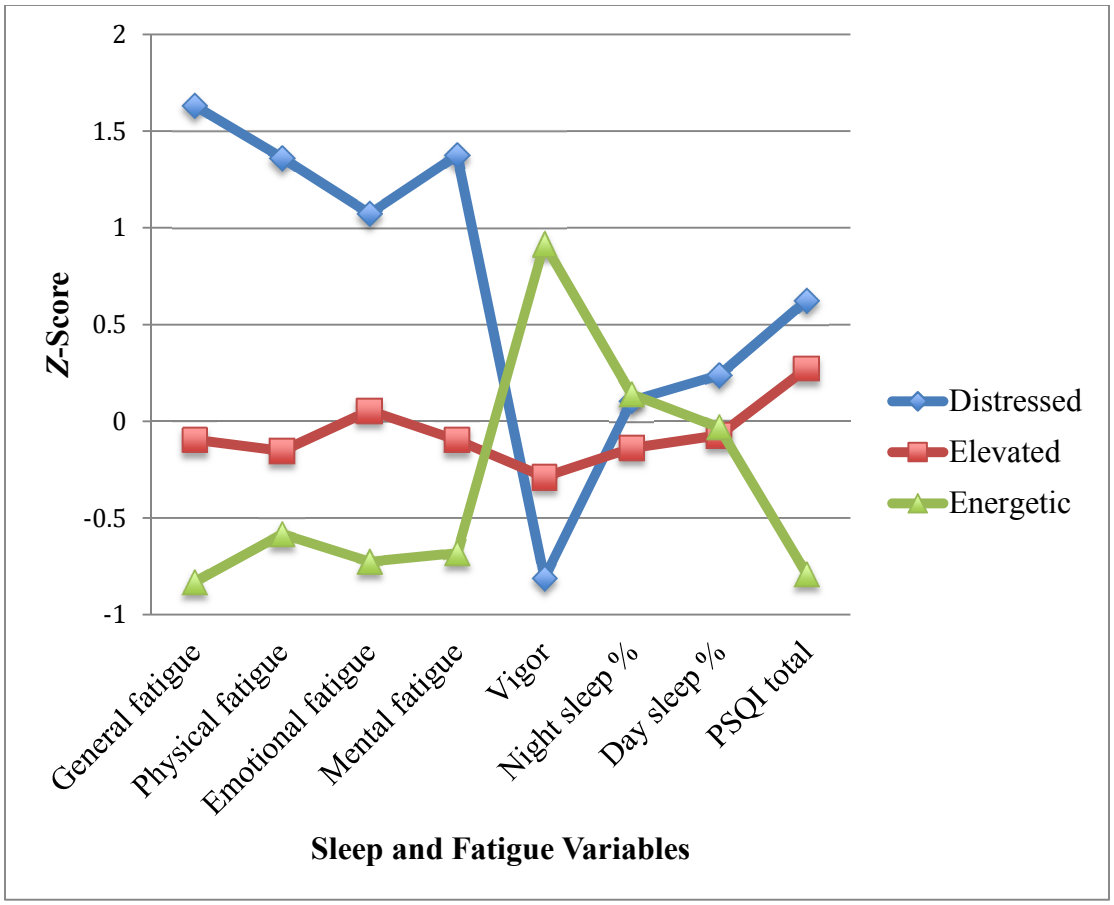

Figure 2. Standardized conditional response means for sleep and fatigue variables by group identified at T1

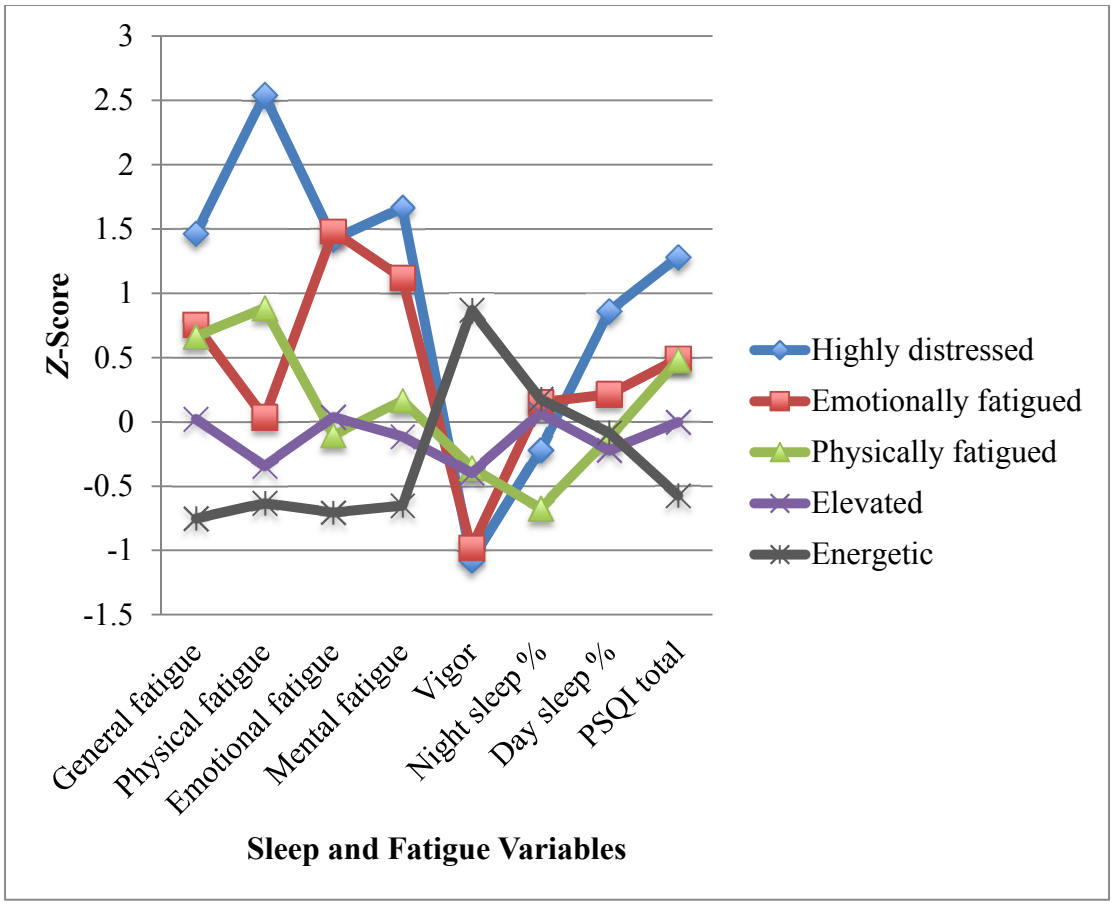

Figure 3. Standardized conditional response means for sleep and fatigue variables by group identified at T2

TABLES

Table 1. Study characteristics

Variable	T1 (N = 152)	T2 (n = 128)
Sociodemographic variables		
Ethnicity[a]		
White	122 (80.3)	100 (78.1)
Not White	30 (19.7)	28 (21.9)
African American	7 (4.6)	6 (4.7)
Asian	9 (5.9)	9 (7.0)
Other	6 (3.9)	6 (4.7)
Missing	8 (5.3)	7 (5.5)
Education[a]		
Completed HS and below	25 (16.5)	22 (17.2)
Some college	49 (32.2)	42 (32.8)
Completed college and above	78 (51.3)	64 (50.0)
Marital status[a]		
Married	105 (69.1)	89 (69.5)
Not married	47 (30.9)	39 (30.5)
Never married	12 (7.9)	10 (7.8)
Divorced	35 (23.0)	29 (22.7)
Age[b]	50.84 (9.39)	50.74 (9.19)

Table 1: Continued

Variable	T1 (N = 152)	T2 (n = 128)
Medical variables		
Cancer stage at diagnosis[a]		
I	42 (27.6)	31 (24.2)
II	66 (43.4)	57 (44.5)
III	35 (23.0)	32 (25.0)
Missing	9 (5.9)	8 (6.3)
Type of chemotherapy received[a]		
AC	35 (23.0)	31 (24.2)
AC + Taxotere	30 (19.7)	23 (18.0)
AC + Taxol	45 (29.6)	41 (32.0)
Other	32 (21.1)	25 (19.5)
Missing	10 (6.6)	8 (6.3)
Type of surgical intervention[a]		
Lumpectomy	62 (40.8)	53 (41.4)
Mastectomy	63 (41.4)	52 (40.6)
Other	19 (12.5)	16 (12.5)
Missing	8 (5.3)	7 (5.5)
Medications taken		
Analgesic	102 (67.1)	45 (35.2)

Table 1: Continued

Variable	T1 (N = 152)	T2 (n = 128)
Antacid	39 (25.7)	51 (39.8)
Anticonvulsant	7 (4.6)	3 (2.3)
Antidepressant	29 (19.1)	21 (16.4)
Antihistamine	34 (22.4)	28 (21.9)
Antihypertensive	16 (10.5)	10 (7.8)
Antiparkinson medications	0 (0.0)	0 (0.0)
Cardiac medications	1 (0.7)	1 (0.8)
Diuretics	11 (7.2)	8 (6.3)
Insulins	7 (4.6)	6 (4.7)
Laxatives	30 (19.7)	28 (21.9)
Major tranquilizers	3 (2.0)	1 (0.8)
Minor tranquilizers	36 (23.7)	32 (25.0)
Over-the-counter hypnotics	0 (0.0)	0 (0.0)
Oxygens	3 (2.0)	0 (0.0)
Sedative hypnotics	2 (1.3)	3 (2.3)
Stimulants	1 (0.7)	1 (0.8)
Vasodilators	0 (0.0)	0 (0.0)
Vitamins	102 (67.1)	67 (52.3)
Other medications	54 (35.5)	30 (23.4)

Table 1: Continued

Variable	T1 (N = 152)	T2 (n = 128)
Medical comorbidities[a]		
Cardiovascular diseases	2 (1.3)	2 (1.6)
Pulmonary diseases	1 (0.7)	2 (1.6)
Central nervous system diseases	2 (1.3)	2 (1.6)
Gastroenterological diseases	6 (3.9)	4 (3.1)
Renal diseases	0 (0.0)	0 (0.0)
Endocrine diseases	5 (3.3)	1 (0.8)
Connective tissue diseases	2 (1.3)	3 (2.3)
Infections	5 (3.3)	3 (2.3)
Dementia	0 (0.0)	0 (0.0)
Arthritis	27 (17.8)	20 (15.6)
Diabetes	8 (5.3)	6 (4.7)
Ulcer	3 (2.0)	1 (0.8)
Hiatal hernia	2 (1.3)	1 (0.8)
Esophageal diseases	3 (2.0)	3 (2.3)
Neck or back diseases	25 (16.4)	24 (18.8)
Epilepsy	1 (0.7)	2 (1.6)
Headache	31 (20.4)	32 (25.0)
High blood pressure	28 (18.4)	21 (16.4)

Table 1: Continued

Variable	T1 (N = 152)	T2 (n = 128)
Kidney diseases	0 (0.0)	0 (0.0)
Stroke	0 (0.0)	1 (0.8)
Asthma	16 (10.5)	14 (10.9)
Emphysema	0 (0.0)	0 (0.0)
Edema	2 (1.3)	3 (2.3)
Thyroid diseases	21 (13.8)	18 (14.1)
Other diseases	21 (13.8)	24 (18.8)
BMI[b]	28.19 (7.11)	28.11 (7.08)
Psychosocial variables		
CES-D total score[b]	11.69 (9.18)	15.04 (12.11)
Greene psychological[b]	7.26 (5.19)	8.21 (6.50)
Greene somatic[b]	2.68 (2.61)	3.18 (3.09)
Greene vasomotor[b]	1.19 (1.55)	2.19 (1.94)
SF-36 MCS[b]	46.52 (10.79)	44.62 (12.41)
SF-36 PCS[b]	43.28 (9.81)	41.17 (8.77)
FACT-B total score[b]	106.03 (16.95)	97.57 (22.74)

Note. [a]*n* (%); [b]*M* (*SD*); HS: High school; BMI: Body Mass Index; CES-D: Center for Epidemiological Studies-Depression; MCS: Mental Component Score; PCS: Physical Component Score; FACT-B: Functional Assessment of Cancer Therapy-Breast

Table 2a. Model fit indices for the 1-, 2-, 3-, & 4-profile solutions at T1

Solution	AIC	sBIC	BLRT *p*-value	Entropy
1 profile	4727.176	4724.918	---	---
2 profile	4447.279	4443.751	< .001	0.946
3 profile	4379.648	4374.851	< .001	0.849
4 profile	4322.862	4316.795	< .001	0.882

Note. AIC: Akaike Information Criterion; sBIC: Sample-size adjusted Bayesian Information Criterion; BLRT: Bootstrapped Likelihood Ratio Test

Table 2b. Model fit indices for the 1-, 2-, 3-, 4-, and 5-profile solutions at T2

Solution	AIC	sBIC	BLRT *p*-value	Entropy
1 profile	4299.324	4294.355	---	---
2 profile	4045.468	4037.705	< .001	0.889
3 profile	3949.544	3938.986	< .001	0.918
4 profile	3920.242	3906.889	< .001	0.916
5 profile	3905.386	3889.239	.013	0.871

Note. AIC: Akaike Information Criterion; sBIC: Sample-size adjusted Bayesian Information Criterion; BLRT: Bootstrapped Likelihood Ratio Test

Table 3a. Sample means and group conditional response means at T1

	M (SE)			
	Full sample (N = 152)	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)
Five dimensions of fatigue: MFSI-SF Subscales				
General fatigue	6.32 (0.46)	15.64 (0.71)	5.77(0.59)	1.56 (0.40)
Physical fatigue	2.66 (0.27)	7.25 (0.79)	2.14 (0.32)	0.69 (0.170
Emotional fatigue	6.06 (0.39)	11.19 (0.99)	6.32 (0.55)	2.60 (0.47)
Mental fatigue	4.28 (0.32)	9.62 (0.74)	3.90 (0.39)	1.63 (0.34)
Vigor	11.08 (0.45)	6.62 (0.74)	9.49 (0.62)	16.12 (1.59)
Objective sleep measures				
Night sleep %	78.44 (0.01)	79.7 (0.02)	76.8 (0.02)	80.1 (0.02)
Day sleep %	6.54 (0.01)	8.3 (0.02)	6.0 (0.01)	6.3 (0.01)
Subjective sleep quality				
PSQI total score	7.31 (0.31)	9.63 (0.69)	8.32 (0.67)	4.37 (0.41)

Note. SE: standard error.

Table 3b. Sample means and group conditional response means at T2

	M (SE)					
	Full sample (n = 128)	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)
Five dimensions of fatigue: MFSI-SF Subscales						
General fatigue	10.35 (0.58)	19.94 (1.02)	15.29 (1.65)	14.72 (1.22)	10.49 (1.71)	5.41 (1.03)
Physical fatigue	4.01 (0.42)	16.12 (0.87)	4.18 (0.51)	8.22 (0.64)	2.39 (0.43)	1.01 (0.28)
Emotional fatigue	5.37 (0.45)	12.63 (1.57)	12.94 (1.86)	4.85 (0.69)	5.56 (1.27)	1.77 (0.44)
Mental fatigue	6.03 (0.47)	14.92 (1.19)	11.99 (2.06)	6.92 (1.00)	5.42 (1.30)	2.55 (0.92)
Vigor	10.23 (0.51)	4.00 (1.17)	4.57 (1.94)	8.17 (0.96)	7.94 (2.61)	15.14 (0.86)
Objective sleep measures						
Night sleep %	78.96 (0.01)	76.6 (0.04)	80.6 (0.02)	71.7 (0.03)	79.7 (0.02)	80.9 (0.02)
Day sleep %	8.62 (0.01)	15.8 (0.04)	10.4 (0.02)	7.6 (0.01)	6.8 (0.02)	7.9 (0.02)

Table 3b: Continued

	M (SE)					
	Full sample (n = 128)	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)
Subjective sleep quality						
PSQI total	8.03 (0.35)	13.00 (0.91)	9.93 (1.21)	9.89 (0.88)	8.02 (0.77)	5.81 (0.61)

Note. SE: standard error.

Table 4a. Differences in T1 sociodemographic characteristics among groups identified at T1

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
Age[a]	49.69 (9.49)	49.06 (8.33)	54.52 (10.13)	**D vs. En**	**0.95**	**0.90, 1.00**
				D vs. El	1.01	0.96, 1.06
				El vs. En	**0.94**	**0.90, 0.98**
Ethnicity[b]						
White	23 (79.3)	61 (79.2)	38 (82.6)	D vs. En	1.06	0.28, 4.02
				D vs. El	1.04	0.30, 3.59
				El vs. En	1.02	0.36, 2.86
Not White	4 (13.7)	11 (14.3)	7 (15.2)	Ethnicity reference		
Education[b]						
Completed HS and below	5 (17.2)	15 (19.5)	5 (10.9)	D vs. En	2.55	0.61, 10.56
				D vs. El	1.18	0.35, 3.98
				El vs. En	2.15	0.70, 6.62
Some college	13 (44.8)	23 (29.9)	13 (28.3)	D vs. En	2.55	0.90, 7.19
				D vs. El	2.00	0.77, 5.20
				El vs. En	1.27	0.55, 2.93
Completed college and above	11 (37.9)	39 (50.6)	28 (60.9)	Education reference		

Table 4a: Continued

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
Marital status[b]						
Not married	14 (48.3)	18 (23.4)	15 (32.6)	D vs. En	1.93	0.74, 5.01
				D vs. El	**3.06**	**1.24, 7.52**
				El vs. En	0.63	0.28, 1.42
Married	15 (51.7)	59 (76.6)	31 (67.4)	Marital status reference		

Note. [a]*M* (*SD*); [b]*n* (%); Comp vs. Ref: Comparison vs. Reference; OR: Odds ratio; 95% CI: 95% Confidence Interval; HS: High school; D: Distressed; El: Elevated; En: Energetic; Bolded statistics are significant at α = .05. The relationship between each sociodemographic variable and group membership was explored in a separate, bivariate logistic regression analysis due to sample size constraints.

Table 4b. Differences in T1 sociodemographic characteristics among groups identified at T2

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Age[a]	49.00 (7.60)	49.93 (8.53)	51.82 (12.25)	48.45 (7.94)	52.30 (9.20)	EF vs. HD	1.01	0.93, 1.11
						PF vs. HD	1.04	0.95, 1.13
						El vs. HD	0.99	0.92, 1.08
						En vs. HD	1.04	0.97, 1.12
						PF vs. EF	1.02	0.95, 1.11
						El vs. EF	0.98	0.91, 1.05
						En vs. EF	1.03	0.97, 1.10
						El vs. PF	0.96	0.90, 1.02
						En vs. PF	1.01	0.95, 1.07
						En vs. El	1.05	1.00, 1.11
Ethnicity[b]								
White	6 (54.5)	13 (86.7)	12 (70.6)	26 (83.9)	43 (79.6)	EF vs. HD	4.33	0.33, 57.65
						PF vs. HD	0.80	0.12, 5.40
						El vs. HD	2.89	0.39, 21.29
						En vs. HD	1.43	0.25, 8.18
						PF vs. EF	0.19	0.02, 1.82
						El vs. EF	0.67	0.06, 7.05
						En vs. EF	0.33	0.04, 2.83
						El vs. PF	3.61	0.74, 17.64
						En vs. PF	1.79	0.51, 6.25
						En vs. El	0.50	0.13, 1.97
Not White	2 (18.2)	1 (6.7)	5 (29.4)	3 (9.7)	10 (18.5)	Ethnicity reference		

Table 4b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Education[b]								
Completed HS and below	1 (9.1)	1 (6.7)	6 (35.3)	4 (12.9)	10 (18.5)	EF vs. HD	0.38	0.02, 8.10
						PF vs. HD	2.25	0.19, 27.37
						El vs. HD	0.80	0.07, 9.92
						En vs. HD	1.00	0.09, 10.74
						PF vs. EF	6.00	0.58, 61.84
						El vs. EF	2.13	0.20, 22.44
						En vs. EF	2.67	0.30, 24.03
						El vs. PF	0.36	0.08, 1.64
						En vs. PF	0.44	0.12, 1.60
						En vs. El	1.25	0.34, 4.66
Some college	7 (63.6)	6 (40.0)	3 (17.6)	12 (38.7)	14 (25.9)	EF vs. HD	0.32	0.06, 1.79
						PF vs. HD	0.16	0.02, 1.07
						El vs. HD	0.34	0.07, 1.62
						En vs. HD	**0.20**	**0.05, 0.89**
						PF vs. EF	0.50	0.09, 2.73
						El vs. EF	1.07	0.29, 3.92
						En vs. EF	0.62	0.18, 2.14
						El vs. PF	2.13	0.46, 9.84
						En vs. PF	1.24	0.29, 5.42
						En vs. El	0.58	0.22, 1.57

Table 4b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Completed college and above	3 (27.3)	8 (53.3)	8 (47.1)	15 (48.4)	30 (55.6)	Education reference		
Marital status[b]								
Not married	6 (54.5)	7 (46.7)	5 (29.4)	5 (16.1)	16 (29.6)	EF vs. HD	0.73	0.15, 3.47
						PF vs. HD	0.35	0.07, 1.69
						El vs. HD	**0.16**	**0.04, 0.74**
						En vs. HD	0.35	0.09, 1.32
						PF vs. EF	0.48	0.11, 2.04
						El vs. EF	**0.22**	**0.05, 0.89**
						En vs. EF	0.48	0.15, 1.55
						El vs. PF	0.46	0.11, 1.90
						En vs. PF	1.01	0.31, 3.34
						En vs. El	2.19	0.71, 6.72
Married	5 (45.5)	8 (53.3)	12 (70.6)	26 (83.9)	38 (70.4)	Marital status reference		

Note. [a]*M* (*SD*); [b]*n* (%); Comp vs. Ref: Comparison vs. Reference; OR: Odds ratio; 95% CI: 95% Confidence Interval; HS: High school; HD: Highly distressed; EF: Emotionally fatigued; PF: Physically fatigued; El: Elevated; En: Energetic; Bolded statistics are significant at α = .05. The relationship between each sociodemographic variable and group membership was explored in a separate, bivariate logistic regression analysis due to sample size constraints.

Table 5a. Differences in T1 medical characteristics among groups identified at T1

Variable	Distressed	Elevated	Energetic	Statistics		
	(*n* = 29)	(*n* = 77)	(*n* = 46)	Comp vs. Ref	*OR*	*95% CI*
BMI[a]	30.03 (9.29)	27.98 (6.12)	27.37 (7.04)	D vs. En	1.05	0.99, 1.12
				D vs. El	1.04	0.98, 1.10
				El vs. En	1.01	0.96, 1.07
Cancer stage at diagnosis[b]						
I	6 (20.7)	23 (29.9)	13 (28.3)	D vs. En	0.99	0.26, 3.70
				D vs. El	0.48	0.13, 1.75
				El vs. En	2.04	0.75, 5.59
II	13 (44.8)	38 (49.4)	15 (32.6)	D vs. En	1.86	0.58, 5.95
				D vs. El	0.64	0.21, 1.94
				El vs. En	**2.92**	**1.13, 7.58**
III	7 (24.1)	13 (16.9)	15 (32.6)	Cancer stage reference		
Type of chemotherapy received[b]						
AC	7 (24.1)	18 (23.4)	10 (21.7)	D vs. En	1.40	0.30, 6.53
				D vs. El	1.94	0.49, 7.76
				El vs. En	0.72	0.23, 2.22

Table 5a: Continued

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
AC + Taxotere	1 (3.4)	18 (23.4)	11 (23.9)	D vs. En	0.18	0.02, 1.95
				D vs. El	0.28	0.03, 2.72
				El vs. En	0.66	0.22, 1.99
AC + Taxol	13 (44.8)	17 (22.1)	15 (32.6)	D vs. En	1.73	0.42, 7.11
				D vs. El	**3.82**	**1.05, 13.94**
				El vs. En	0.45	0.16, 1.33
Other	4 (13.8)	20 (26.0)	8 (17.4)	Chemotherapy reference		
Type of surgical intervention[b]						
Lumpectomy	12 (41.4)	33 (42.9)	17 (37.0)	D vs. En	2.35	0.53, 10.41
				D vs. El	0.73	0.16, 3.38
				El vs. En	**3.24**	**1.01, 10.42**
Mastectomy	11 (37.9)	35 (45.5)	17 (37.0)	D vs. En	2.16	0.48, 9.63
				D vs. El	0.63	0.13, 2.94
				El vs. En	**3.43**	**1.07, 11.01**
Other	3 (10.3)	6 (7.8)	10 (21.7)	Surgical intervention reference		

Table 5a: Continued

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
Medications taken[b,c]						
Analgesic	24 (82.8)	51 (66.2)	27 (58.7)	**D vs. En**	**0.24**	**0.07, 0.80**
				D vs. El	0.35	0.11, 1.14
				El vs. En	0.67	0.31, 1.43
Antacid	9 (31.0)	22 (28.6)	8 (17.4)	D vs. En	0.44	0.15, 1.34
				D vs. El	0.88	0.34, 2.23
				El vs. En	0.51	0.20, 1.26
Anticonvulsant	2 (6.9)	4 (5.2)	1 (2.2)	D vs. En	0.29	0.03, 3.34
				D vs. El	0.73	0.13, 4.24
				El vs. En	0.39	0.04, 3.64
Antidepressant	7 (24.1)	16 (20.8)	6 (13.0)	D vs. En	0.45	0.13, 1.151
				D vs. El	0.81	0.29, 2.25
				El vs. En	0.55	0.20, 1.54
Antihistamine	5 (17.2)	21 (27.3)	8 (17.4)	D vs. En	1.00	0.29, 3.41
				D vs. El	1.82	0.61, 5.43
				El vs. En	0.55	0.22, 1.36

Table 5a: Continued

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
Antihypertensive	5 (17.2)	7 (9.1)	4 (8.7)	D vs. En	0.44	0.11, 1.79
				D vs. El	0.48	0.14, 1.66
				El vs. En	0.91	0.25, 3.30
Diuretics	1 (3.4)	6 (7.8)	4 (8.7)	D vs. En	2.57	0.27, 24.25
				D vs. El	2.38	0.27, 20.73
				El vs. En	1.08	0.29, 4.05
Insulins	2 (6.9)	4 (5.2)	1 (2.2)	D vs. En	0.29	0.03, 3.34
				D vs. El	0.74	0.13, 4.30
				El vs. En	0.39	0.04, 3.59
Laxatives	6 (20.7)	14 (18.2)	10 (21.7)	D vs. En	1.02	0.33, 3.19
				D vs. El	0.86	0.29, 2.50
				El vs. En	1.19	0.48, 2.96
Minor tranquilizers	9 (31.0)	19 (24.7)	8 (17.4)	D vs. En	0.44	0.15, 1.34
				D vs. El	0.72	0.28, 1.85
				El vs. En	0.62	0.25, 1.56
Vitamins	18 (62.1)	53 (68.8)	31 (67.4)	D vs. En	1.15	0.43, 3.09
				D vs. El	1.34	0.53, 3.36
				El vs. En	0.86	0.39, 1.89

Table 5a: Continued

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
Other medications	14 (48.3)	26 (33.8)	14 (30.4)	D vs. En	0.44	0.17, 1.16
				D vs. El	0.53	0.22, 1.28
				El vs. En	0.83	0.38, 1.81
Medical comorbidities[b,c]						
GI diseases	3 (10.3)	2 (2.6)	1 (2.2)	D vs. En	0.18	0.02, 1.85
				D vs. El	0.22	0.03, 1.37
				El vs. En	0.84	0.07, 9.55
Infections	1 (3.4)	3 (3.9)	1 (2.2)	D vs. En	0.59	0.04, 9.85
				D vs. El	1.07	0.11, 10.73
				El vs. En	0.55	0.06, 5.48
Arthritis	8 (27.6)	12 (15.6)	7 (15.2)	D vs. En	0.44	0.14, 1.39
				D vs. El	0.45	0.16, 1.25
				El vs. En	0.98	0.36, 2.71
Diabetes	1 (3.4)	5 (6.5)	2 (4.3)	D vs. En	1.21	0.10, 14.01
				D vs. El	1.83	0.20, 16.42
				El vs. En	0.66	0.12, 3.55

Table 5a: Continued

Variable	Distressed (n = 29)	Elevated (n = 77)	Energetic (n = 46)	Statistics		
				Comp vs. Ref	*OR*	*95% CI*
Neck or back diseases	6 (20.7)	13 (16.9)	6 (13.0)	D vs. En	0.54	0.15, 1.88
				D vs. El	0.72	0.24, 2.14
				El vs. En	0.75	0.26, 2.12
Headache	8 (27.6)	15 (19.5)	8 (17.4)	D vs. En	0.51	0.17, 1.58
				D vs. El	0.58	0.22, 1.59
				El vs. En	0.88	0.34, 2.27
HBP	7 (24.1)	15 (19.5)	6 (13.0)	D vs. En	0.44	0.13, 1.48
				D vs. El	0.70	0.25, 1.97
				El vs. En	0.63	0.22, 1.75
Asthma	6 (20.7)	8 (10.4)	2 (4.3)	**D vs. En**	**0.16**	**0.03, 0.88**
				D vs. El	0.41	0.13, 1.32
				El vs. En	0.40	0.08, 1.96
Thyroid diseases	2 (6.9)	11 (14.3)	8 (17.4)	D vs. En	2.70	0.53, 13.80
				D vs. El	2.12	0.44, 10.23
				El vs. En	1.28	0.47, 3.46
Other diseases	7 (24.1)	11 (14.3)	3 (6.5)	**D vs. En**	**0.20**	**0.05, 0.87**
				D vs. El	0.48	0.17, 1.41
				El vs. En	0.42	0.11, 1.60

Table 5a: Continued

Variable	Distressed	Elevated	Energetic	Statistics		
	(*n* = 29)	(*n* = 77)	(*n* = 46)	Comp vs. Ref	*OR*	*95% CI*

Note. [a]*M* (*SD*); [b]*n* (%); [c]reference is yes; Comp vs. Ref: Comparison vs. Reference; OR: Odds ratio; 95% CI: 95% Confidence Interval; BMI: Body mass index; GI: Gastroenterological; HBP: High blood pressure; D: Distressed; El: Elevated; En: Energetic; Bolded statistics are significant at α = .05. The relationship between each medical variable and group membership was explored in a separate, bivariate logistic regression analysis due to sample size constraints. The following variables had insufficient variability to enable analysis: Antiparkinson medications, Cardiac medications, Cardiovascular diseases, Central nervous system diseases, Connective tissue diseases, Dementia, Edema, Emphysema, Endocrine diseases, Epilepsy, Esophageal diseases, Hiatal hernias, Kidney diseases, Major tranquilizers, Over-the-counter hypnotics, Oxygens, Pulmonary diseases, Renal diseases, Sedative hypnotics, Stimulants, Stroke, Ulcers, and Vasodilators.

Table 5b. Differences in T1 medical characteristics among groups identified at T2

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
BMI[a]	31.49 (7.04)	29.16 (11.13)	25.09 (4.40)	27.28 (6.02)	28.56 (6.73)	EF vs. HD	0.97	0.88, 1.06
						PF vs. HD	**0.86**	**0.75, 0.98**
						El vs. HD	0.93	0.85, 1.02
						En vs. HD	0.96	0.89, 1.03
						PF vs. EF	0.89	0.78, 1.01
						El vs. EF	0.96	0.88, 1.05
						En vs. EF	0.99	0.92, 1.07
						El vs. PF	1.08	0.96, 1.23
						En vs. PF	1.17	0.99, 1.25
						En vs. El	1.03	0.96, 1.10
Stage at diagnosis[b]								
I	1 (9.1)	4 (26.7)	4 (23.5)	5 (16.1)	17 (31.5)	EF vs. HD	3.00	0.21, 42.62
						PF vs. HD	3.00	0.21, 42.62
						El vs. HD	1.88	0.15, 23.40
						En vs. HD	3.92	0.37, 42.20
						PF vs. EF	1.00	0.14, 7.10
						El vs. EF	0.63	0.11, 3.71
						En vs. EF	1.31	0.27, 6.24
						El vs. PF	0.63	0.11, 3.71
						En vs. PF	1.31	0.27, 6.24
						En vs. El	2.09	0.55, 7.91

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
II	6 (54.5)	7 (46.7)	9 (52.9)	15 (48.4)	20 (37.0)	EF vs. HD	0.88	0.14, 5.58
						PF vs. HD	1.13	0.18, 6.94
						El vs. HD	0.94	0.18, 4.79
						En vs. HD	0.77	0.16, 3.63
						PF vs. EF	1.29	0.23, 7.05
						El vs. EF	1.07	0.24, 4.79
						En vs. EF	0.88	0.21, 3.61
						El vs. PF	0.83	0.19, 3.58
						En vs. PF	0.68	0.17, 2.67
						En vs. El	0.82	0.27, 2.48
III	3 (27.3)	4 (26.7)	4 (23.5)	8 (25.8)	13 (24.1)	Cancer stage reference		
Type of chemotherapy received[b]								
AC	1 (9.1)	4 (26.7)	6 (35.3)	8 (25.8)	12 (22.2)	EF vs. HD	6.00	0.35, 101.57
						PF vs. HD	6.00	0.42, 85.25
						El vs. HD	3.43	0.29, 40.95
						En vs. HD	3.60	0.32, 40.23
						PF vs. EF	1.00	0.22, 8.95
						El vs. EF	0.57	0.08, 4.13
						En vs. EF	0.60	0.09, 3.99
						El vs. PF	0.57	0.10, 3.18
						En vs. PF	0.60	0.12, 3.03
						En vs. El	1.05	0.28, 3.92

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
AC + Taxotere	1 (9.1)	1 (6.7)	2 (11.8)	7 (22.6)	12 (22.2)	EF vs. HD	1.50	0.06, 40.63
						PF vs. HD	2.00	0.11, 35.81
						El vs. HD	3.00	0.25, 36.33
						En vs. HD	3.60	0.32, 40.23
						PF vs. EF	1.33	0.07, 26.62
						El vs. EF	2.00	0.15, 27.45
						En vs. EF	2.40	0.19, 30.52
						El vs. PF	1.50	0.19, 11.93
						En vs. PF	1.80	0.25, 12.99
						En vs. El	1.20	0.31, 4.59
AC + Taxol	5 (45.5)	8 (53.3)	6 (35.3)	6 (19.4)	16 (29.6)	EF vs. HD	2.40	0.29, 19.78
						PF vs. HD	1.20	0.16, 8.80
						El vs. HD	0.51	0.09, 3.11
						En vs. HD	0.96	0.19, 4.92
						PF vs. EF	0.50	0.06, 4.00
						El vs. EF	0.21	0.03, 1.43
						En vs. EF	0.40	0.07, 2.28
						El vs. PF	0.43	0.07, 2.50
						En vs. PF	0.80	0.16, 3.94
						En vs. El	1.87	0.49, 7.18
Other	3 (27.3)	2 (13.3)	3 (17.6)	7 (22.6)	10 (18.5)	Chemotherapy reference		

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Type of surgical intervention[b]								
Lumpect	5 (45.5)	7 (46.7)	8 (47.1)	10 (32.3)	23 (42.6)	EF vs. HD	1.40	0.07, 28.12
						PF vs. HD	1.60	0.08, 31.77
						El vs. HD	0.50	0.04, 5.74
						En vs. HD	0.51	0.05, 5.00
						PF vs. EF	1.14	0.06, 21.87
						El vs. EF	0.37	0.03, 3.92
						En vs. EF	0.37	0.04, 3.40
						El vs. PF	0.31	0.03, 3.38
						En vs. PF	0.32	0.04, 2.93
						En vs. El	1.02	0.25, 4.11
Mastect	4 (36.4)	7 (46.7)	8 (47.1)	14 (45.2)	19 (35.2)	EF vs. HD	1.75	0.08, 36.29
						PF vs. HD	2.00	0.10, 41.00
						El vs. HD	0.88	0.08, 10.21
						En vs. HD	0.53	0.05, 5.43
						PF vs. EF	1.14	0.06, 21.87
						El vs. EF	0.50	0.05, 5.36
						En vs. EF	0.30	0.03, 2.83
						El vs. PF	0.44	0.04, 4.62
						En vs. PF	0.26	0.03, 2.44
						En vs. El	0.60	0.15, 2.36

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Other	1 (9.1)	1 (6.7)	1 (5.9)	4 (12.9)	9 (16.7)	Surgical intervention reference		
Medications[b,c]								
Analgesic	9 (81.8)	11 (73.3)	10 (58.8)	22 (71.0)	35 (64.8)	EF vs. HD	1.64	0.24, 11.08
						PF vs. HD	3.15	0.52, 19.27
						El vs. HD	1.84	0.33, 10.25
						En vs. HD	2.31	0.45, 11.86
						PF vs. EF	1.93	0.43, 8.61
						El vs. EF	1.13	0.28, 4.48
						En vs. EF	1.41	0.39, 5.08
						El vs. PF	0.58	0.17, 2.02
						En vs. PF	0.74	0.24, 2.25
						En vs. El	1.26	0.48, 3.29
Antacid	2 (18.2)	2 (13.3)	6 (35.3)	11 (35.5)	12 (22.2)	EF vs. HD	1.44	0.17, 12.23
						PF vs. HD	0.41	0.07, 2.53
						El vs. HD	0.40	0.08, 2.21
						En vs. HD	0.76	0.14, 4.00
						PF vs. EF	0.28	0.05, 1.69
						El vs. EF	0.28	0.05, 1.47
						En vs. EF	0.53	0.10, 2.66
						El vs. PF	0.99	0.29, 3.42
						En vs. PF	1.86	0.57, 6.09
						En vs. El	1.88	0.71, 4.99

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Antidepres	1 (9.1)	6 (40.0)	4 (23.5)	7 (22.6)	7 (13.0)	EF vs. HD	0.15	0.02, 1.50
						PF vs. HD	0.33	0.03, 3.38
						El vs. HD	0.34	0.04, 3.16
						En vs. HD	0.66	0.07, 5.96
						PF vs. EF	2.17	0.47, 9.95
						El vs. EF	2.29	0.60, 8.67
						En vs. EF	**4.38**	**1.19, 16.13**
						El vs. PF	1.06	0.26, 4.29
						En vs. PF	2.02	0.51, 7.99
						En vs. El	1.92	0.60, 6.10
Antihistam	3 (27.3)	1 (6.7)	6 (35.3)	7 (22.6)	13 (24.1)	EF vs. HD	4.88	0.43, 55.29
						PF vs. HD	0.69	0.13, 3.61
						El vs. HD	1.29	0.27, 6.19
						En vs. HD	1.13	0.26, 4.88
						PF vs. EF	0.14	0.02, 1.36
						El vs. EF	0.26	0.03, 2.38
						En vs. EF	0.23	0.03, 1.94
						El vs. PF	1.87	0.51, 6.88
						En vs. PF	1.64	0.51, 5.31
						En vs. El	0.88	0.31, 2.50

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Antihypert	2 (18.2)	2 (13.3)	1 (5.9)	4 (12.9)	4 (7.4)	EF vs. HD	1.33	0.16, 11.36
						PF vs. HD	3.56	0.28, 44.88
						El vs. HD	1.50	0.23, 9.61
						En vs. HD	2.72	0.43, 17.14
						PF vs. EF	2.67	0.22, 32.96
						El vs. EF	1.13	0.18, 7.00
						En vs. EF	2.04	0.33, 12.49
						El vs. PF	0.42	0.04, 4.11
						En vs. PF	0.77	0.08, 7.36
						En vs. El	1.82	0.42, 7.84
Laxatives	3 (27.3)	2 (13.3)	3 (17.6)	8 (25.8)	9 (16.7)	EF vs. HD	2.25	0.20, 16.63
						PF vs. HD	1.75	0.28, 10.81
						El vs. HD	1.08	0.23, 5.09
						En vs. HD	1.83	0.41, 8.28
						PF vs. EF	0.78	0.11, 5.46
						El vs. EF	0.48	0.09, 2.62
						En vs. EF	0.82	0.16, 4.29
						El vs. PF	0.62	0.14, 2.72
						En vs. PF	1.05	0.25, 4.42
						En vs. El	1.70	0.58, 5.00

Table 5b: Continued

Variable	Highly distressed (*n* = 11)	Emotionally fatigued (*n* = 15)	Physically fatigued (*n* = 17)	Elevated (*n* = 31)	Energetic (*n* = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Minor tranqs	3 (27.3)	8 (53.3)	5 (29.4)	5 (16.1)	6 (11.1)	EF vs. HD	0.33	0.06, 1.74
						PF vs. HD	0.90	0.17, 4.87
						El vs. HD	1.95	0.38, 10.01
						En vs. HD	2.94	0.61, 14.20
						PF vs. EF	2.74	0.64, 11.75
						El vs. EF	**5.94**	**1.47, 23.97**
						En vs. EF	**8.95**	**2.38, 33.62**
						El vs. PF	2.17	0.53, 8.93
						En vs. PF	3.26	0.85, 12.53
						En vs. El	1.51	0.42, 5.42
Vitamins	6 (54.5)	11 (73.3)	14 (82.4)	19 (61.3)	35 (64.8)	EF vs. HD	0.44	0.08, 2.27
						PF vs. HD	0.26	0.05, 1.44
						El vs. HD	0.76	0.19, 3.04
						En vs. HD	0.62	0.17, 2.30
						PF vs. EF	0.59	0.11, 3.20
						El vs. EF	1.74	0.45, 6.72
						En vs. EF	1.41	0.39, 5.08
						El vs. PF	2.95	0.70, 12.46
						En vs. PF	2.40	0.61, 9.45
						En vs. El	0.81	0.33, 2.04

Table 5b: Continued

Variable	Highly distressed (*n* = 11)	Emotionally fatigued (*n* = 15)	Physically fatigued (*n* = 17)	Elevated (*n* = 31)	Energetic (*n* = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Other meds	6 (54.5)	3 (20.0)	9 (52.9)	12 (38.7)	18 (33.3)	EF vs. HD	4.80	0.85, 27.20
						PF vs. HD	1.07	0.23, 4.89
						El vs. HD	1.90	0.47, 7.63
						En vs. HD	2.33	0.63, 8.70
						PF vs. EF	0.22	0.05, 1.08
						El vs. EF	0.40	0.09, 1.70
						En vs. EF	0.49	0.12, 1.95
						El vs. PF	1.78	0.54, 5.89
						En vs. PF	2.19	0.72, 6.63
						En vs. El	1.23	0.49, 3.08
Medical comorbidities[b,c]								
Arthritis	3 (27.3)	3 (20.0)	6 (35.3)	3 (9.7)	7 (13.0)	EF vs. HD	1.50	0.24, 9.38
						PF vs. HD	0.69	0.13, 3.61
						El vs. HD	3.50	0.59, 20.81
						En vs. HD	2.46	0.53, 11.58
						PF vs. EF	0.46	0.09, 2.29
						El vs. EF	2.33	0.41, 13.26
						En vs. EF	1.64	0.37, 7.32
						El vs. PF	**5.09**	**1.08, 24.02**
						En vs. PF	**3.58**	**1.00, 12.81**
						En vs. El	0.70	0.17, 2.95

Table 5b: Continued

Variable	Highly distressed (*n* = 11)	Emotionally fatigued (*n* = 15)	Physically fatigued (*n* = 17)	Elevated (*n* = 31)	Energetic (*n* = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Neck or back diseases	2 (18.2)	5 (33.3)	5 (29.4)	4 (12.9)	8 (14.8)	EF vs. HD	0.44	0.07, 2.89
						PF vs. HD	0.53	0.09, 3.40
						El vs. HD	1.50	0.23, 9.61
						En vs. HD	1.25	0.23, 6.89
						PF vs. EF	1.20	0.27, 5.36
						El vs. EF	3.38	0.75, 15.15
						En vs. EF	2.81	0.76, 10.43
						El vs. PF	2.81	0.64, 12.36
						En vs. PF	2.34	0.65, 8.48
						En vs. El	0.83	0.23, 3.03
Headache	2 (18.2)	5 (33.3)	5 (29.4)	6 (19.4)	12 (22.2)	EF vs. HD	0.44	0.07, 2.89
						PF vs. HD	0.53	0.09, 3.40
						El vs. HD	0.93	0.16, 5.45
						En vs. HD	0.76	0.14, 4.00
						PF vs. EF	1.20	0.27, 5.36
						El vs. EF	2.08	0.52, 8.41
						En vs. EF	1.71	0.49, 5.97
						El vs. PF	1.74	0.44, 6.85
						En vs. PF	1.42	0.42, 4.85
						En vs. El	0.82	0.27, 2.46

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
High blood pressure	2 (18.2)	5 (33.3)	2 (11.8)	6 (19.4)	8 (14.8)	EF vs. HD	0.44	0.07, 2.89
						PF vs. HD	1.67	0.20, 13.98
						El vs. HD	0.93	0.16, 5.45
						En vs. HD	1.25	0.23, 6.89
						PF vs. EF	3.75	0.61, 23.25
						El vs. EF	2.08	0.52, 8.41
						En vs. EF	2.81	0.76, 10.43
						El vs. PF	0.56	0.10, 3.11
						En vs. PF	0.75	0.14, 3.93
						En vs. El	1.35	0.42, 4.33
Asthma	3 (27.3)	4 (26.7)	3 (17.6)	3 (9.7)	1 (1.9)	EF vs. HD	1.03	0.18, 5.95
						PF vs. HD	1.75	0.28, 10.81
						El vs. HD	3.50	0.59, 20.81
						En vs. HD	**19.50**	**1.80, 211.21**
						PF vs. EF	1.70	0.31, 9.22
						El vs. EF	3.39	0.65, 17.70
						En vs. EF	**18.91**	**1.92, 185.95**
						El vs. PF	2.00	0.36, 1.22
						En vs. PF	**11.14**	**1.08, 115.54**
						En vs. El	5.57	0.55, 56.09

Table 5b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Other diseases	3 (27.3)	2 (13.3)	5 (29.4)	1 (3.2)	7 (13.0)	EF vs. HD	2.44	0.33, 17.91
						PF vs. HD	0.90	0.17, 4.87
						El vs. HD	**11.25**	**1.03, 123.24**
						En vs. HD	2.46	0.53, 11.58
						PF vs. EF	0.37	0.06, 2.27
						El vs. EF	4.62	0.38, 55.51
						En vs. EF	1.01	0.19, 5.47
						El vs. PF	**12.50**	**1.32, 118.48**
						En vs. PF	2.74	0.74, 10.17
						En vs. El	0.22	0.03, 1.87

Note. [a]*M* (*SD*); [b]*n* (%); [c]reference is yes; Comp vs. Ref: Comparison vs. Reference; OR: Odds ratio; 95% CI: 95% Confidence Interval; BMI: Body Mass Index; Lumpect: Lumpectomy; Mastect: Mastectomy; Antidepres: Antidepressant; Antihistam: Antihistamine; Antihypert: Antihypertensive; Minor tranqs: Minor tranquilizers; Other meds: Other medications; HD: Highly distressed; EF: Emotionally fatigued; PF: Physically fatigued; El: Elevated; En: Energetic; Bolded statistics are significant at $\alpha = .05$. The relationship between each medical variable and group membership was explored in a separate, bivariate logistic regression analysis due to sample size constraints. The following variables had insufficient variability to enable analysis: Anticonvulsants, Antiparkinson medications, Cardiac medications, Cardiovascular diseases, Central nervous system diseases, Connective tissue diseases, Dementia, Diabetes, Diuretics, Edema, Emphysema, Endocrine diseases, Epilepsy, Esophageal diseases, Gastroenterological diseases, Hiatal hernias, Infections, Insulins, Kidney diseases, Major tranquilizers, Over-the-counter hypnotics, Oxygens, Pulmonary diseases, Renal diseases, Sedative hypnotics, Stimulants, Stroke, Thyroid diseases, Ulcers, and Vasodilators.

Table 6a. Differences in T1 psychosocial characteristics among groups identified at T1

Variable	Distressed	Elevated	Energetic	Statistics		
	(*n* = 29)	(*n* = 77)	(*n* = 46)	Comp vs. Ref	*OR*	*95% CI*
CES-D total[a]	21.45 (10.04)	12.34 (7.27)	4.29 (3.48)	**D vs. En**	**1.52**	**1.34, 1.73**
				D vs. El	**1.13**	**1.07, 1.21**
				El vs. En	**1.34**	**1.20, 1.50**
Greene psychological[a]	13.97 (4.83)	7.26 (3.67)	3.02 (2.37)	**D vs. En**	**2.34**	**1.85, 2.98**
				D vs. El	**1.50**	**1.27, 1.76**
				El vs. En	**1.57**	**1.32, 1.86**
Greene somatic[a]	5.30 (3.45)	2.49 (1.96)	1.33 (1.60)	**D vs. En**	**2.30**	**1.70, 3.12**
				D vs. El	**1.58**	**1.25, 1.99**
				El vs. En	**1.46**	**1.16, 1.84**
Greene vasomotor[a]	2.17 (1.93)	1.01 (1.33)	0.87 (1.39)	**D vs. En**	**1.64**	**1.20, 2.25**
				D vs. El	**1.51**	**1.16, 1.97**
				El vs. En	1.09	0.82, 1.44
SF-36 MCS[a]	35.86 (8.68)	45.74 (9.87)	54.88 (5.72)	**D vs. En**	**0.77**	**0.71, 0.84**
				D vs. El	**0.90**	**0.86, 0.95**
				El vs. En	**0.85**	**0.80, 0.91**
SF-36 PCS[a]	36.76 (8.61)	43.94 (9.54)	46.42 (9.23)	**D vs. En**	**0.89**	**0.84, 0.95**
				D vs. El	**0.92**	**0.87, 0.97**
				El vs. En	0.97	0.93, 1.01

Table 6a: Continued

Variable	Distressed	Elevated	Energetic	Statistics		
	(*n* = 29)	(*n* = 77)	(*n* = 46)	Comp vs. Ref	*OR*	*95% CI*
FACT-B total[a]	86.68 (14.30)	104.28 (12.60)	121.35 (9.22)	**D vs. En**	**0.78**	**0.73, 0.84**
				D vs. El	**0.91**	**0.87, 0.95**
				El vs. En	**0.87**	**0.82, 0.91**

Note. [a]*M* (*SD)*; Comp vs. Ref: Comparison vs. Reference; OR: Odds ratio; 95% CI: 95% Confidence Interval; CES-D: Center for Epidemiological Studies-Depression; MCS: Mental Component Score; PCS: Physical Component Score; FACT-B: Functional Assessment of Cancer Therapy-Breast; D: Distressed; El: Elevated; En: Energetic; Bolded statistics are significant at $\alpha = .05$. The relationship between each psychosocial variable and group membership was explored in a separate, bivariate logistic regression analysis due to sample size constraints.

Table 6b. Differences in T1 psychosocial characteristics among groups identified at T2

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
CES-D[a]	19.64 (10.86)	18.16 (12.47)	12.47 (9.17)	12.13 (4.97)	6.98 (6.56)	EF vs. HD	0.99	0.92, 1.06
						PF vs. HD	0.92	0.85, 1.00
						El vs. HD	**0.92**	**0.85, 0.99**
						En vs. HD	**0.82**	**0.75, 0.90**
						PF vs. EF	0.94	0.87, 1.01
						El vs. EF	**0.93**	**0.87, 1.00**
						En vs. EF	**0.83**	**0.77, 0.90**
						El vs. PF	1.00	0.93, 1.07
						En vs. PF	**0.89**	**0.82, 0.96**
						En vs. El	**0.89**	**0.83, 0.96**
Greene psych[a]	11.82 (5.00)	11.27 (7.55)	7.96 (5.22)	7.52 (3.20)	4.30 (3.03)	EF vs. HD	0.98	0.86, 1.13
						PF vs. HD	0.86	0.73, 1.01
						El vs. HD	**0.84**	**0.72, 0.97**
						En vs. HD	**0.67**	**0.56, 0.79**
						PF vs. EF	0.87	0.75, 1.01
						El vs. EF	**0.85**	**0.74, 0.98**
						En vs. EF	**0.68**	**0.58, 0.80**
						El vs. PF	0.98	0.85, 1.12
						En vs. PF	**0.78**	**0.67, 0.90**
						En vs. El	**0.80**	**0.70, 0.91**

Table 6b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
Greene som[a]	5.16 (4.50)	3.47 (3.60)	3.74 (2.47)	2.33 (1.84)	1.67 (1.73)	EF vs. HD	0.86	0.67, 1.10
						PF vs. HD	0.89	0.71, 1.11
						El vs. HD	**0.71**	**0.54, 0.92**
						En vs. HD	**0.59**	**0.45, 0.77**
						PF vs. EF	1.03	0.81, 1.32
						El vs. EF	0.82	0.63, 1.06
						En vs. EF	**0.69**	**0.53, 0.89**
						El vs. PF	0.80	0.62, 1.02
						En vs. PF	**0.66**	**0.52, 0.85**
						En vs. El	0.84	0.66, 1.06
Greene vaso[a]	1.64 (1.36)	1.53 (1.85)	1.94 (1.98)	1.17 (1.82)	0.80 (1.07)	EF vs. HD	0.97	0.62, 1.51
						PF vs. HD	1.09	0.72, 1.66
						El vs. HD	0.84	0.56, 1.27
						En vs. HD	0.69	0.46, 1.03
						PF vs. EF	1.13	0.77, 1.67
						El vs. EF	0.87	0.59, 1.27
						En vs. EF	0.71	0.49, 1.03
						El vs. PF	0.77	0.54, 1.09
						En vs. PF	**0.63**	**0.44, 0.89**
						En vs. El	0.82	0.59, 1.13

Table 6b: Continued

Variable	Highly distressed (*n* = 11)	Emotionally fatigued (*n* = 15)	Physically fatigued (*n* = 17)	Elevated (*n* = 31)	Energetic (*n* = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
SF-36 MCS[a]	41.62 (10.47)	37.94 (9.85)	47.73 (10.12)	45.31 (9.84)	52.17 (8.40)	EF vs. HD	0.97	0.90, 1.04
						PF vs. HD	1.06	0.98, 1.15
						El vs. HD	1.04	0.97, 111
						En vs. HD	**1.13**	**1.05, 1.21**
						PF vs. EF	**1.10**	**1.02, 1.18**
						El vs. EF	**1.07**	**1.01, 1.14**
						En vs. EF	**1.17**	**1.09, 1.25**
						El vs. PF	0.98	0.92, 1.04
						En vs. PF	1.06	1.00, 1.13
						En vs. El	**1.09**	**1.03, 1.15**
SF-36PCS[a]	37.25 (7.62)	41.31 (9.24)	40.96 (9.11)	42.69 (10.73)	45.70 (9.00)	EF vs. HD	1.05	0.96, 1.14
						PF vs. HD	1.05	0.96, 1.14
						El vs. HD	1.07	0.99, 1.15
						En vs. HD	**1.10**	**1.02, 1.19**
						PF vs. EF	1.00	0.92, 1.07
						El vs. EF	1.02	0.95, 1.09
						En vs. EF	1.05	0.99, 1.12
						El vs. PF	1.02	0.96, 1.09
						En vs. PF	1.06	0.99, 1.12
						En vs. El	1.04	0.99, 1.09

Table 6b: Continued

Variable	Highly distressed (n = 11)	Emotionally fatigued (n = 15)	Physically fatigued (n = 17)	Elevated (n = 31)	Energetic (n = 54)	Statistics		
						Comp vs. Ref	*OR*	*95% CI*
FACT-B[a]	93.97 (17.47)	92.96 (18.18)	101.31 (15.63)	105.59 (12.28)	117.00 (10.30)	EF vs. HD	1.00	0.95, 1.05
						PF vs. HD	1.03	0.98, 1.09
						El vs. HD	**1.06**	**1.01, 1.11**
						En vs. HD	**1.14**	**1.08, 1.21**
						PF vs. EF	1.04	0.99, 1.09
						El vs. EF	**1.06**	**1.01, 1.11**
						En vs. EF	**1.15**	**1.09, 1.21**
						El vs. PF	1.02	0.98, 1.07
						En vs. PF	**1.10**	**1.05, 1.16**
						En vs. El	**1.08**	**1.04, 1.12**

Note. [a]*M* (*SD*); Comp vs. Ref: Comparison vs. Reference; OR: Odds ratio; 95% CI: 95% Confidence Interval; CES-D: Center for Epidemiological Studies-Depression; MCS: Mental Component Score; PCS: Physical Component Score; FACT-B: Functional Assessment of Cancer Therapy-Breast; HD: Highly distressed; EF: Emotionally fatigued; PF: Physically fatigued; El: Elevated; En: Energetic; Bolded statistics are significant at $\alpha = .05$. The relationship between each psychosocial variable and group membership was explored in a separate, bivariate logistic regression analysis due to sample size constraints.

Table 7a. Analyses of covariance evaluating differences in psychosocial outcomes at T2 based on sleep and fatigue groups identified at T1

Outcome	*df*	*F*	$p\eta^2$	*Estimated Marginal Mean* (*Standard Error*)		
				Distressed	Elevated	Energetic
CES-D	2, 98	1.75	.03	19.86 (3.16)	14.08 (2.53)	14.38 (2.80)
Greene psych	2, 98	2.19	.04	11.30 (1.49)	8.70 (1.07)	7.39 (1.20)
Greene som	2, 98	2.08	.04	3.81 (0.77)	3.37 (0.63)	2.27 (0.66)
Greene vaso	2, 98	0.02	< .01	2.14 (0.48)	2.08 (0.42)	2.15 (0.46)
SF-36 MCS	2, 98	2.90	.06	38.37 (2.98)	43.82 (2.52)	47.40 (2.83)
SF-36 PCS	2, 98	2.51	.05	36.37 (2.22)	40.69 (1.89)	42.10 (2.03)
FACT-B	2, 98	0.06	< .01	96.49 (5.12)	98.32 (4.10)	98.11 (4.82)

Note. All analyses controlled for age at T1, marital status at T1, use of analgesics at T1, diagnosis of asthma at T1, diagnosis of an "other" disease at T1, stage of cancer at diagnosis, chemotherapy formulation, type of surgical intervention, and score on outcome measure at T1; *df*: degrees of freedom; $p\eta^2$: partial eta-squared from omnibus ANCOVA; CES-D: Center for Epidemiological Studies-Depression; psych: psychological; som: somatic; vaso: vasomotor; MCS: Mental Component Score; PCS: Physical Component Score; FACT-B: Functional Assessment of Cancer Therapy-Breast.

Table 7b. Analyses of covariance evaluating differences in psychosocial outcomes at T2 based on sleep and fatigue groups identified at T2

Outcome	*df*	*F*	$p\eta^2$	*Estimated Marginal Mean (Standard Error)*				
				Highly distressed	Emotionally fatigued	Physically fatigued	Elevated	Energetic
CES-D	**4, 107**	**28.95**	**.52**	32.68 $(2.91)_{aeg}$	29.31 $(2.40)_{bfh}$	16.78 $(2.05)_{cgh}$	18.97 $(2.30)_{def}$	7.54 $(2.12)_{abcd}$
Greene psych	**4, 106**	**30.17**	**.53**	16.53 $(1.26)_{aeg}$	15.22 $(1.10)_{bfh}$	10.03 $(0.91)_{cgh}$	8.94 $(1.01)_{def}$	5.18 $(0.92)_{abcd}$
Greene som	**4, 106**	**20.78**	**.44**	8.19 $(0.82)_{aefg}$	3.44 $(0.70)_{bg}$	4.53 $(0.62)_{cf}$	2.71 $(0.66)_{de}$	1.36 $(0.60)_{abcd}$
Greene vaso	**4, 106**	**4.82**	**.15**	3.68 $(0.64)_{ac}$	1.87 (0.55)	3.22 $(0.48)_{b}$	1.92 $(0.52)_{c}$	1.53 $(0.48)_{ab}$
SF-36 MCS	**4, 106**	**30.15**	**.53**	30.28 $(2.88)_{aeg}$	29.61 $(2.40)_{bfh}$	46.72 $(2.07)_{cgh}$	41.79 $(2.35)_{def}$	53.35 $(2.17)_{abcd}$
SF-36 PCS	**4, 106**	**9.31**	**.26**	32.41 $(2.61)_{acf}$	40.13 $(2.10)_{ef}$	32.71 $(1.89)_{bde}$	39.73 $(2.13)_{cd}$	43.41 $(1.95)_{ab}$
FACT-B	**4, 107**	**19.64**	**.42**	71.88 $(4.70)_{aef}$	83.23 $(4.21)_{bg}$	96.99 $(3.56)_{cfg}$	91.04 $(3.90)_{de}$	110.59 $(3.70)_{abcd}$

Note. Within each row, means with the same subscript are significant different from one another at $\alpha = .010$; Bolded statistics are significant at the omnibus level $\alpha = .05$; All analyses controlled for use of antidepressants at T1, use of minor tranquilizers at T1, asthma diagnosis at T1, arthritis diagnosis at T1, diagnosis of an "other" disease at T1, education, marital status at T1, BMI at T1, and score on outcome measure at T1; *df*: degrees of freedom; $p\eta^2$: partial eta-squared from omnibus ANCOVA; CES-D: Center for Epidemiological Studies-Depression; psych: psychological; som: somatic; vaso: vasomotor; MCS: Mental Component Score; PCS: Physical Component Score; FACT-B: Functional Assessment of Cancer Therapy-Breast.