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Daily Fatigue and Subjective Cognitive Function: What Influences Daily Quality of Life Issues among Breast Cancer Survivors?

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Daily Fatigue and Subjective Cognitive Function: What Influences Daily Quality of Life Issues among Breast Cancer Survivors?

by

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy Aging Studies School of Aging Studies College of Behavioral and Community Sciences University of South Florida

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Abstract

There are over 15.5 million cancer survivors in the U.S. currently, increasing to over 20 million by 2026. Long-term cancer survival has raised awareness for the issues that affect quality of life (QoL) after treatment. Fatigue and subjective cognitive dysfunction are common quality of life concerns for survivors but little is known regarding prevalence of these problems in daily life. The purpose of the current project is to examine these concerns after treatment using data from a 2 week daily diary study of breast cancer survivors up to 3 years post-treatment. Of importance is determining the factors that contribute to reporting decreased QoL.

Taken together, our findings suggest that within-persons, survivors who reported worse mood and physical function tended to also report higher levels of fatigue. Similarly, subjective reporting of cognitive function is influenced by current mood and physical symptoms such as fatigue. Demographic characteristics and depressive symptoms prior to the study were unrelated to fatigue and subjective cognitive function. This dissertation advances the current understanding of daily QoL issues. These findings also highlight the importance of capturing these experiences in daily life.
Chapter One: Introduction

The number of cancer survivors in the United States is expected to increase from 15.5 million in 2016 to 26.1 million by 2040 (Bluethmann, Mariotto, & Rowland, 2016). Due to the increasing numbers of survivors the American Cancer Society (ACS) has placed greater emphasis on research to help improve quality of life (QoL) after treatment (American Cancer Society, 2015). Key QoL outcomes identified include: fatigue, cognitive impairments, pain, depression, and sleep disturbance. These post-treatment outcomes have received much attention (Bower et al., 2011; Boykoff, Moieni, & Subramanian, 2009). Guidelines have been developed to improve QoL for long-term survivors and elucidate areas for future research (Denlinger et al., 2014; Runowicz et al., 2015). The goal is to alleviate, and in the future prevent, these issues (American Cancer Society, 2015) by raising awareness of the survivorship experience and identifying it as a public health concern including the development of care plans to deliver quality care (Hewitt, Greenfield, Stovall, & Board, 2006).

Fatigue and subjective cognitive dysfunction are the most commonly reported and may have the greatest impact on QoL (Bower, 2014; Boykoff et al., 2009). As elaborated below, fatigue and subjective cognitive function make it challenging for survivors to maintain usual function during daily life, but are not well-understood. Fatigue is considered a subjective general tiredness and lack of energy not alleviated by rest and makes it difficult to complete tasks (Curt et al., 2000; Minton et al., 2013). Identifying survivors with high levels of fatigue or at greater risk is difficult, but important to improve QoL (Piper & Cella, 2010). Research has identified demographic and psychological factors associated with fatigue. These factors include age and
education (Bower, Ganz, Aziz, & Fahey, 2002) and negative mood (Bower et al., 2000; S. L. Curran, Beacham, & Andrykowski, 2004). Subjective cognitive impairment is described as perceived problems in memory, concentration, language, and learning assessed via self-report and may interfere with daily life or negatively impact QoL (Pullens, De Vries, & Roukema, 2010). Subjective cognitive deficits can impact work and family roles (Boykoff et al., 2009).

Previous research has relied on retrospective self-report measures to examine QoL after treatment. Less emphasis has been placed on examining these issues in daily life contexts where they are experienced (Bower, 2014; Bower et al., 2011). Cross-sectional and longitudinal studies have found that individual differences in negative mood (Poppelreuter et al., 2004; Rey et al., 2012; Shilling & Jenkins, 2007), fatigue (Ribi et al., 2012), lower levels of education (Rey et al., 2012) are related to reporting increased cognitive dysfunction among cancer survivors.

Understanding these processes after treatment will help to guide treatment decisions and improve patient outcomes in the future (Ancoli-Israel et al., 2006). This includes the development and delivery of interventions to treat modifiable risk factors and viable treatment options for patients experiencing post-treatment side effects.

A limitation of the existing research is the lack of evidence on which to base guidelines (Runowicz et al., 2015). Overall, greater emphasis has been placed on QoL after treatment to understand how these experiences operate in daily life. How these processes are experienced in daily life has largely been overlooked. The current doctoral dissertation will address the need to examine daily experiences of QoL issues among breast cancer survivors. This was accomplished by using data from a daily diary study to determine which daily factors are associated with fatigue and subjective cognitive function. This research will help to identify survivors that have heightened fatigue or subjective cognitive dysfunction and make it possible to administer
treatments to alleviate the symptoms and improve function in daily life. The following chapter presents a review of what is known about fatigue and cognitive function after cancer treatment.
Chapter Two: Literature Review

Fatigue and subjective cognitive impairment are two of the most common QoL issues among survivors. This review will describe these post-treatment outcomes and summarize the literature on risk factors. Understanding what predicts daily fatigue and subjective cognitive impairments among cancer survivors is important for identifying individuals with these long-term QoL issues and to target life domains to improve outcomes. Existing knowledge of commonly reported QoL issues that cancer survivors experience in daily life will be presented. Lastly, this review will overview current methods of assessing QoL issues post-treatment and describe the approach taken in the current dissertation.

Cancer Survivors

In 2016 there were over 15.5 million cancer survivors (individuals undergoing treatment and post-treatment) in the U.S. and just over 3 million are breast cancer survivors (ACS, 2018). Earlier diagnosis and treatment advances have increased cancer survival rates. Survival rates are higher among breast cancer survivors (90%) compared to other cancers (60%) surviving 5 years after diagnosis (ACS, 2018). Breast cancer is also the most common site (41%) among female cancer survivors (DeSantis et al., 2014). Increased survival rates suggest that a greater emphasis on life after treatment is needed to address this growing public health concern. Both the cancer itself and its treatment are thought to contribute to decreased QoL in the months or years after treatment (Mehnert et al., 2007). As survivors resume work and family roles after treatment, QoL issues may have the greatest impact. Among breast cancer survivors, those treated with
chemotherapy may be at greater risk for worse long-term QoL and physical functioning compared to those that underwent other treatment (Ganz et al., 2002). Fatigue and subjective cognitive dysfunction are common among breast cancer survivors, although not all survivors are made aware of the potential long-term QoL issues associated with survivorship (DeSantis et al., 2014; Minton et al., 2013; Pinto & de Azambuja, 2011).

**QoL Outcomes**

**Fatigue**

Fatigue is one of the most frequently reported cancer- and treatment-related side effect (Bower, 2014; Curt et al., 2000; Fernandes, Stone, Andrews, Morgan, & Sharma, 2006) and the most important to patients due to the impact on physical and social function (P. C. Stone et al., 2000). Information about cancer-related fatigue has largely come from cross-sectional studies (Ancoli-Israel, Moore, & Jones, 2001). These studies compare individuals at a single time point, typically using a retrospective report. More recent studies have included multiple time points, but little research has examined fatigue on a daily basis. From this research the definition and prevalence of fatigue has remained elusive. Broadly, fatigue is considered a perceived experience of physical, cognitive, and/or emotional tiredness, exhaustion, and weakness with a lack of energy (Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, & Morrow, 2007; Mock et al., 2000; Schwartz, 2000). Often fatigue interferes with daily routines and usual function, but is not easily predictable by recent activity level (Curt et al., 2000; Mock et al., 2000). It is also considered the most distressing side effect due to the reduction in function for the months and years after treatment (Hofman et al., 2007; Minton et al., 2013). Persistent fatigue could prevent survivors from returning to activities that improve health and QoL (Hofman et al., 2007).
Depending on the cancer population studied and assessment mode, prevalence estimates of fatigue vary greatly. Rates of fatigue have been found to be higher among cancer patients (56-68%) during treatment compared to healthy controls (20-22%; Fernandes et al., 2006; Goldstein et al., 2012). These rates are higher among survivors undergoing chemotherapy with up to 80% having reported fatigue (Hofman et al., 2007). One study found that fatigue is often underreported by survivors in clinical settings (P. C. Stone et al., 2000). Some patients felt as though fatigue is an unavoidable and untreated issue during and after treatment. After treatment has concluded, approximately 33% to 42% of survivors have experienced fatigue (Goldstein et al., 2012; Hofman et al., 2007; Minton et al., 2013). Those who received chemotherapy treatment appear to be at higher risk. One example is that breast cancer survivors treated with chemotherapy are more susceptible to fatigue even when engaging in similar activities as healthy controls (S. L. Curran et al., 2004).

The course of fatigue after treatment is difficult to discern. One study found that even 6 years after treatment 1/3 of cancer survivors report fatigue and that it interferes with physical functioning (Jones et al., 2016). In contrast, another study found that fatigue symptoms improved over 12.5 years after cancer treatment (Hsu, Ennis, Hood, Graham, & Goodwin, 2013). Although fatigue is reported for years after treatment, some cross-sectional and longitudinal studies that examined the association between time since treatment and fatigue find no relationship (Mehnert et al., 2007; Servaes, Gielissen, Verhagen, & Bleijenberg, 2007). Discrepancies in prevalence rates and course present both a challenge to the research and an opportunity to identify individuals at greater risk for impairment.
Assessment of fatigue

Existing research utilizes various self-report measures which may not yield the same findings and helps to explain the wide range of fatigue reported after treatment. Commonly used questionnaire assessments developed for use among cancer survivors include the Functional Assessment of Cancer Therapy Fatigue (Yellen, Cella, Webster, Blendowski, & Kaplan, 1997) and the Fatigue Symptom Inventory (FSI; Minton & Stone, 2009). For example, the FSI is a validated, recommended measure of fatigue administered to cancer survivors after treatment (Hann et al., 1998). Emphasis is placed on fatigue severity and how much this interferes with activities, relationships, and life satisfaction experienced over the past week (Hann et al., 1998). This largely ignores variations that occur across days, but rather rely on survivors’ retrospective self-assessments of average fatigue intensity and interference. Responses depend on an individual’s perception and recollection of the experience which is susceptible to bias (P. C. Stone & Minton, 2008). Past experiences could be under or over reported, or influenced by an individual’s current state. To better understand fatigue in daily life and reduce bias more frequent measurement is required.

More recent studies have incorporated daily diary methods to assess fatigue daily, rather than over the past week. Typically, this is accomplished through the use of brief paper surveys or an electronic device to administer items (Banthia et al., 2006; S. L. Curran et al., 2004; Schwartz, 2000; Schwartz, Mori, Gao, Nail, & King, 2001). One study comparing traditional questionnaire and diary methods found a lack of agreeance between fatigue collected once via the FSI and fatigue collected for seven days during the corresponding week (Banthia et al., 2006). This suggests that unique experiences are assessed and questionnaires alone are not capturing the entire experience. Additionally, it presents an opportunity to focus on daily assessments of
fatigue and factors known to be associated to understand how these relationships operate in daily life.

**Factors associated with fatigue**

Multiple causes of fatigue and factors contributing to the symptoms have been identified. Factors associated with fatigue after treatment include genes related to inflammation, psychological factors (depression, ability to cope with the cancer diagnosis), level of fatigue before treatment, sleep disturbance, and level of physical activity (Bower, 2014; P. C. Stone & Minton, 2008). Although not the primary focus of this dissertation, underlying biological processes related to cancer and its treatment influence the experience of fatigue. For example, chemotherapy treatment is thought to increase inflammation and is one potential source of increased fatigue experienced by survivors (Bower & Lamkin, 2013). Also contributed to chemotherapy, disruptions of core body temperature commonly experienced by cancer survivors have been associated with hot flashes contributing to increased fatigue, sleep disruptions, reduced QoL (Carpenter, Gautam, Freedman, & Andrykowski, 2001). Several other studies have shown that sleep disturbance, difficulty functioning related to cancer, and tiredness were reported more frequently among those reporting greater fatigue up to 5 years after treatment (Ancoli-Israel et al., 2006; Goldstein et al., 2012). One study suggested that subjective tiredness is related to these biological processes (Dijk, Duffy, & Czeisler, 1992). Although sleep disturbance is often related to fatigue, when daily sleep disturbances and duration have been examined to explain greater levels of fatigue in breast cancer survivors, sleep factors were unrelated to daily reports of fatigue (S. L. Curran et al., 2004). Underlying biological processes of fatigue and the relation to psychological factors are still not well understood.
Influences on fatigue can be categorized as psychological factors, physical factors, and demographic characteristics. A substantial body of research has endorsed a relationship between negative mood states (e.g., depressive symptoms, anxiety) and fatigue among cancer survivors. Among female cancer patients undergoing treatment those with higher rates of depression and lower QoL have been associated with fatigue (Fernandes et al., 2006). Breast cancer survivors with worse mood, greater anxiety and depression, reported increased fatigue when assessed with common retrospective fatigue measures (Bower et al., 2000; Carpenter et al., 2001; Curt et al., 2000; Jones et al., 2016) and assessed monthly for two years after treatment (Servaes et al., 2007).

The studies above showed links between fatigue and mood in terms of individual differences: survivors who report worse mood relative to other survivors. There may also be links between fatigue and negative mood that unfold within individuals in real time. That is, to what extent is a survivor's fatigue higher when she is in a negative mood compared to her fatigue on a when she is not in a negative mood. There is evidence to suggest that when assessed over the course of 5 days, daily negative mood and fatigue are associated (S. L. Curran et al., 2004). An inverse relationship was found, greater fatigue was experienced on days when less positive mood was reported. Several explanations of this relationship have been proposed. One explanation is that worse mood and the distress experienced from increased fatigue are related. This finding suggests that although negative mood influences fatigue, it is only one component. A second explanation is that the relationship is reciprocal. Worse mood and inactivity lead to increased fatigue, due in part to the relationship between decreased physical functioning and fatigue following treatment (Mehnert et al., 2007). However, when examined daily, fatigue can be present when no negative psychosocial experiences are reported (S. L. Curran et al., 2004).
Associations between self-reported physical factors, activity, and fatigue are well established. Broadly, cross-sectional and longitudinal studies examining the relationship between physical function and fatigue find that survivors who are more functionally limited tend to experience worse fatigue (Jones et al., 2016; Servaes et al., 2007). Individual differences in long-term fatigue have been attributed to pain and activity. Survivors who report more pain tended to also report higher levels of fatigue (S. L. Curran et al., 2004; M. E. Schmidt et al., 2015).

Similarly, breast cancer survivors who report reduced activity also report higher levels of fatigue (S. L. Curran et al., 2004; M. E. Schmidt et al., 2015). Most studies focusing on the relationship between fatigue and physical activity have been intervention studies; however there is only mild support for a connection. There is stronger support for the efficacy of psychological interventions (Jacobsen, Donovan, Vadaparampil, & Small, 2007). Some studies have found that fatigue symptoms are alleviated with increased physical activity (Jacobsen et al., 2007; Minton et al., 2013; Mormont et al., 2000). One study examining the efficacy of an exercise program found that daily reported fatigue was lessened and function increased among breast cancer survivors (Schwartz, 2000). Engaging in appropriate activities for an individual may improve health and QoL. The ACS recommends at least 150 minutes of exercise per week for cancer survivors (Rock et al., 2012). However, intensity of the activity should be considered rather than activity alone (S. L. Curran et al., 2004). Over activity throughout the day could lead to increased fatigue. A study examining daily activity patterns of cancer survivors found greater morning activity lead to higher levels of fatigue later in the day (Timmerman, Weering, Tönis, Hermens, & Vollenbroek-Hutten, 2015).

Demographic characteristics have been associated with reporting increased fatigue among breast cancer survivors. Younger age (Bower et al., 2002; Schwartz, 2000) and being
unmarried (Bower et al., 2002; Jones et al., 2016) has been associated with increased fatigue. One explanation is that less social support is related with increased fatigue. However, the role of social support has not been extensively examined in the literature (Servaes, Verhagen, & Bleijenberg, 2002). Employment-related factors, such as level of education and income among breast cancer survivors have been associated with fatigue. Fatigue is higher among survivors with lower educational attainment (Bower et al., 2002; M. E. Schmidt et al., 2015) and lower income (Bower et al., 2002; Jones et al., 2016). After treatment has concluded, decreased function often experienced by survivors with fatigue could impact work activities and earning capacity (Minton et al., 2013). Additionally, increased fatigue has been related to change in employment status or type (Curt et al., 2000). Taken together, fewer social and financial resources contribute to increased fatigue.

**Cognitive Function**

Cognitive declines have been documented in numerous domains and across cancers (Small, Scott, Jim, & Jacobsen, 2015; Wefel, Kesler, Noll, & Schagen, 2015). Subjective declines in attention, memory, language, and concentration are the most frequently reported problems (Ahles, Root, & Ryan, 2012; Mehnert et al., 2007). Additionally, studies have reported objectively assessed impairments in two or more cognitive domains after chemotherapy treatment (Jim et al., 2009; Poppelreuter et al., 2004). This can include general cognitive function, attention, executive function, working memory, processing speed, verbal memory, and visual memory (Ahles et al., 2012; Collins, MacKenzie, Tasca, Scherling, & Smith, 2013; Jim et al., 2012; Kreukels, van Dam, Ridderinkhof, Boogerd, & Schagen, 2008; Ono et al., 2015). These impairments are found when compared to healthy controls and survivors who received other treatments for cancer (Donovan et al., 2005; Jim et al., 2009; K. M. Phillips et al., 2012).
Slower reaction time and processing speed have even been associated with self-reported history of cancer and chemotherapy among older adults (Anstey, Sargent-Cox, Cherbuin, & Sachdev, 2015). Another study found that although all treatment groups improved in processing speed, the chemotherapy group reported more subjective cognitive dysfunction (Ahles et al., 2010). Regardless of the improvements in objective function, cognitive complaints remained. Attention has been identified as the most affected and subjective reports revealed that attention difficulties were reported by 22% of survivors (Poppelreuter et al., 2004).

There is considerable variation in the definition and assessment of self-reported cognitive function and impairments. Subjective cognitive impairment is a broad label that often subsumes other terms used to describe similar constructs (Hill, Mogle, Munoz, Wion, & Colancecco, 2015). In a recent review, Pullens et al. (2010) defined subjective cognitive impairment as deficits in attention, memory, language, and learning that are experienced in everyday life by an individual. Among cancer survivors these impairments are often collectively termed ‘chemobrain’ and described as frustrating and upsetting, and in more severe cases decreased independence occurred (Boykoff et al., 2009). These experiences are perceived and may not translate to objective impairment assessed with neuropsychological tests.

Further, those who experience cognitive declines have more difficulties in daily life post-treatment compared to those that remain stable (Wefel et al., 2015). Impairments in executive functioning are associated with reduced social functioning and involvement, and occupational complications (Wefel et al., 2015). This can include decreased job performance and efficiency as survivors transition back into daily life (Boykoff et al., 2009). One study found that over the two years post-treatment, subjective memory and attention problems increased from 21% to 42% of the survivors, which could be attributed to survivors transitioning back to activities of daily life.
(Rey et al., 2012). Findings highlight the importance of examining these problems at beyond the first few years after treatment.

**Subjective and objective cognition**

Research has largely focused on the relationship between subjective and objective cognitive function post-treatment with the assumption that individuals who report worse subjective cognitive function tend to also score worse on assessments of objective function. However, the relationship is mixed at best and research suggests that the constructs are separate (Hulur, Hertzog, Pearman, & Gerstorf, 2015; Sunderland, Harris, & Baddeley, 1983). Subjective cognitive dysfunction is more common than objective cognitive impairment among cancer survivors (Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012). Up to 70% subjectively report memory loss and difficulty concentrating (Boykoff et al., 2009), whereas only 15-25% exhibit impairment in objective performance based on normative criteria (Boykoff et al., 2009; Wefel et al., 2004). Survivors may experience objective decline, but it remains undetected by neuropsychological test batteries and the norms used to determine impairment (Wefel et al., 2015). Most studies find little to no association and only a third of studies find any association (Hutchinson et al., 2012; Mehnert et al., 2007; Poppelreuter et al., 2004). Recent meta-analyses have found small effect sizes (0.06 and 0.15) in the relationship between objective and subjective cognitive function (Beaudoin & Desrichard, 2011; Crumley, Stetler, & Horhota, 2014).

Several explanations have been proposed for the discrepancy between the subjective reports of cognitive difficulties and impairment defined by objective criteria. One explanation for the lack of association is the issue of reference periods (Poppelreuter et al., 2004). Objective function is typically measured at one time point and compared to norms used for clinical diagnosis or a threshold for cognitive impairment, rather than comparing to an individual’s
previous level of function. Subjective function is recollection-based and involves an appraisal of current function and past function which is susceptible to bias during longer recall periods (Cavanaugh, Feldman, & Hertzog, 1998; Poppelreuter et al., 2004). In sum, objective cognitive assessments and subjective function reports may not overlap in the periods that they are assessing.

Other explanations have also been proposed. A second explanation is that anxiety and depression has been found to explain the relationship between subjective impairments and cognitive performance (Poppelreuter et al., 2004). Evidence suggests that current mood may influence reporting of subjective impairments and objective performance. For example, depressive symptoms have been associated with increased subjective cognitive dysfunction among breast cancer survivors (Janelsins et al., 2017). Anxiety and depression may have a greater impact in daily life rather than on objective measures of function and may explain the relatively consistent relationship with subjective cognitive function. Finally, age-related changes, underlying biological processes, and the type of comparison group may elucidate the differences between subjective and objective cognitive performance (Beaudoin & Desrichard, 2011; Cavanaugh et al., 1998; Crumley et al., 2014; Gunstad et al., 2006).

Subjective cognitive impairment may have a greater impact on daily function than objective impairment (Shilling & Jenkins, 2007) and is one of the most commonly reported side effects of treatment (Boykoff et al., 2009). Six months after chemotherapy treatment 37% of breast cancer survivors reported subjective cognitive decline compared to pre-treatment reports (Janelsins et al., 2017). Lower QoL among those who reported subjective cognitive problems indicated that perceived problems impact daily life during the 2 years following breast cancer treatment (Rey et al., 2012). This indicates a long-term QoL issue that is disruptive to daily life.
Previous research among older adults has indicated that greater experiences of subjective impairment and memory lapses are related to subjective psychological factors such as anxiety, depression, and activity (Rey et al., 2012; Ribi et al., 2012; Shilling & Jenkins, 2007). At the individual difference level, survivors who report worse negative mood tend to also rate subjective cognitive function as worse. Self-reported cognitive dysfunction was associated with health-related QoL but the link between objective cognitive impairment and the subjectively reported experiences is less clear (e.g. cognitive complaints, fatigue, and health-related QoL; Mehnert et al., 2007). In sum, the subjective experience of survivorship appears to be different from objective measurements of cognition and there is a more consistent relationship among self-reported cognition and other QoL factors exists.

Assessment of subjective cognitive function

Beliefs about cognition and memory may influence subjective ratings (Cavanaugh et al., 1998). Typically, one does not assess memory unless prompted, responses are often mood- and thought-based with question wording potentially influencing the answer (Cavanaugh et al., 1998). Most adults have difficulty accurately assessing memory and cognitive function (Crumley et al., 2014; Pearman, Hertzog, & Gerstorf, 2014; Sunderland et al., 1983). Assessments of subjective cognitive function range from interview questions focused on one domain (typically memory) to standard questionnaires (Pullens et al., 2010). Self-report measures that utilize Likert (or similar) scales with a recent past timeframe (i.e., over the past week) are most commonly used to assess subjective cognitive function (Rabin et al., 2015). The Functional Assessment of Cancer Treatment Cognitive is a validated questionnaire administered to cancer survivors (FACT-Cog; Cella et al., 1993). Questions focus on subjective cognitive impairments, abilities, QoL, and comments from others over the past seven days. Whether knowing that subjective
cognitive dysfunction is a side effect of treatment, or priming, has been proposed as a potential source of increased reporting of problems among cancer survivors. After participants were primed with information on cognitive issues experienced post-treatment, those who received chemotherapy reported more problems on a subjective cognitive function questionnaire (Schagen, Das, & Vermeulen, 2012). However, general knowledge of cognitive issues did not influence reported problems suggesting that priming alone does not explain the prevalence of subjective cognitive dysfunction (Schagen et al., 2012).

More recently, subjective cognition has been assessed with questions concerning daily memory lapses administered via smartphones among healthy adults (Mogle, 2011; Mogle, Munoz, Hill, Smyth, & Sliwinski, 2017). Although this method captures daily subjective cognition in the environment that it is experienced, the focus is primarily on memory. It is difficult to discern the prevalence of subjective cognitive dysfunction and what puts some survivors at greater risk when measures tend to focus primarily on memory. A recent review of studies that examined subjective cognitive impairment among breast cancer survivors found that less than half of the included studies reported prevalence and were inconsistent ranging from 21% to 90% (Pullens et al., 2010). This indicates that this is a relatively understudied issue despite the daily QoL implications.

**Factors associated with subjective cognitive function**

The potential causes and factors associated with cognitive dysfunction among aging adults and cancer survivors have long been a focus of research. Similar to mechanisms that may underlie fatigue, the biology of cancer and inflammation impair cognition (Ahles & Saykin, 2007). Shared risk factors and biological mechanisms place a subset of cancer patients at higher risk for objectively measured cognitive changes including older age, genes, and less cognitive
reserve (Ahles et al., 2012; Ahles & Saykin, 2007; Bower, 2014; Mandelblatt et al., 2013; Ono et al., 2015; Small et al., 2015; Wefel et al., 2015). Subjective cognitive complaints and objective cognitive performance have also been shown to be related to structural changes in the brain assessed via neuroimaging (Wefel et al., 2015). These problems are bothersome enough to disrupt daily function and this becomes particularly important as survivors transition back to regular responsibilities post-treatment.

Previous research has further identified chemotherapy treatment, psychological factors (e.g., depressive symptoms), and demographic characteristics (e.g., education and employment) related to subjective cognitive dysfunction (Rey et al., 2012). Chemotherapy is increasingly used to treat cancer and its potential role in cognitive function has been investigated both cross-sectionally and longitudinally (Ahles et al., 2012; Wefel, Saleeba, Buzdar, & Meyers, 2010; Wefel, Vardy, Ahles, & Schagen, 2011). When compared to other cancer treatment groups over time, survivors who received chemotherapy reported greater changes in subjective memory and concentration and a third reported that the changes were noticeable to others one year after treatment (Shilling & Jenkins, 2007). Potential sources of the chemotherapy effect have been proposed. One explanation posits that increased inflammation after treatment which contributes to DNA damage and continues the inflammatory response (Ahles & Saykin, 2007). Another explanation is that small amounts of chemotherapy cross the blood-brain barrier and damage cells (Ahles et al., 2012; Ahles & Saykin, 2007).

Psychological characteristics relating to mood and tiredness have also been found to impact subjective cognitive function. Individual differences in negative affect (e.g., anxiety and depression), sleep disturbances, fatigue, and QoL issues have been associated with subjective complaints of memory and concentration (Pullens et al., 2010; Shilling & Jenkins, 2007). Studies
utilizing retrospective questionnaire measures have reported consistent findings between-persons. Findings suggest a connection between negative mood and survivors reporting worse subjective cognitive function (Klemp et al., 2018; Poppelreuter et al., 2004; Von Ah & Tallman, 2015). Other studies have found that depressive symptoms at one year (Shilling & Jenkins, 2007) and up to 2 years (Rey et al., 2012) after treatment were associated with reporting more subjective cognitive dysfunction. One explanation for the connection is that depressive symptoms and anxiety may heighten awareness of memory problems or increase the negative impact of perceived problems leading to increased reporting.

Some studies have found that individual differences in tiredness and fatigue are associated with subjective cognitive function. Among breast cancer survivors one year after treatment tiredness was associated with subjective cognitive function (Ribi et al., 2012). Similarly, two years after treatment alertness and tiredness are related to cognitive function (Rey et al., 2012). Among studies examining individual differences in fatigue and subjective cognitive function, reporting higher levels of fatigue is associated with worse subjective cognitive function (Klemp et al., 2018; Myers, Wick, & Klemp, 2015; Von Ah & Tallman, 2015). Taken together increased levels of fatigue and tiredness negatively impact ratings of subjective cognitive function in the years after treatment. Another study found that fatigue and subjective cognitive function were not related; however, cognitive complaints were more common among those with fatigue (Mehnert et al., 2007). Subjective tiredness and alertness are thought to underlie cognitive function and help to explain the relationship between fatigue subjective cognitive function (Dijk et al., 1992).

Demographic characteristics such as education, age, and memory aids have been proposed as possible explanations in both the aging and cancer survivorship literature. Previous
research on cognitive function after treatment has focused on objective assessments which has led to less knowledge about subjective cognitive function and demographic factors. Studies of aging have consistently found that individuals with more education also rate subjective memory as better (Hulur, Hertzog, Pearman, Ram, & Gerstorf, 2014; Hulur et al., 2015). A recent meta-analysis found that higher levels of education are associated with better assessment of memory and cognitive function among older adults (Crumley et al., 2014). Among breast cancer survivors the relationship between education and subjective cognitive function is mixed. One cross-sectional study found that five years after treatment for breast cancer there was no association between educational attainment and subjective cognitive function (Mehnert et al., 2007). Across a two year study following treatment education and employment were both associated with reporting more subjective cognitive problems (Rey et al., 2012). Consistent with this research another longitudinal study found that survivors not only had lower cognitive function and worse financial standing compared to healthy controls, but cognitive function did not improve 12 years after treatment (Hsu et al., 2013).

The association between subjective cognitive function and age is mixed. Among breast cancer survivors, younger survivors report worse subjective cognitive function than older survivors (Jansins et al., 2017; Myers et al., 2015). Longitudinal studies in the aging literature highlight the inconsistent relationship. One study found that older participants tend to rate their memory as better than younger participants (Hulur et al., 2014). In contrast, another study found that older age was associated with worse subjective memory (Hulur et al., 2015). Tools to improve memory function, such as lists or reminder notes may explain better ratings of subjective cognitive function in later life. Memory aids are a potential coping strategy that are easy to employ in daily life. However, when the influence of memory aid usage on subjective
memory was examined among older adults, evidence did not support a relationship (Parisi et al., 2011).

**Function in Daily Life**

Traditionally, studies have examined fatigue and subjective cognitive function from cross-sectional or longitudinal designs with time points ranging from months to years. Daily behavior and experiences are collected via questionnaire in a different environment than they naturally occur, such as a laboratory setting (Shiffman, Stone, & Hufford, 2008). Furthermore, assessment often takes the form of retrospective reporting about experiences that happened during the prior week or beyond (Shiffman et al., 2008). A different approach is the use of intensive periods of study such as ecological momentary assessment (EMA) and daily diary methods. These are applicable in a broad range of research (Moskowitz & Young, 2006). However, Fahrenberg, Myrtek, Pawlik, and Perrez (2007) argue that EMA is still used far less in psychology, despite the increasing evidence that questionnaires are poorly suited to capture situations that occur in daily life. Further, questionnaires are often inferior to EMA methods, yet continue to be widely used (Fahrenberg et al., 2007; Moskowitz & Young, 2006). Recall bias (Runyan & Steinke, 2015) and ambiguous time frames prevent questionnaires from capturing daily events accurately, rather it is a representation (Fahrenberg et al., 2007).

Multiple assessments of behavior and experiences can be collected in real-time and in natural settings with EMA and diary methods (Runyan & Steinke, 2015; Shiffman et al., 2008). Assessments can be completed throughout the day or once per day. Two primary advantages of diary studies are increased ecological validity and reduced retrospective bias (Bolger, Davis, & Rafaeli, 2003; Moskowitz, Russell, Sadikaj, & Sutton, 2009; Shiffman et al., 2008). Ecological validity is improved when experiences are assessed in natural settings compared to a clinical or
laboratory setting. Retrospective bias is reduced due to a shorter recall time compared to traditional questionnaires. Relationships can then be examined over shorter periods of time (Heron & Smyth, 2010). For example, variation in daily fatigue can be observed across days and factors that are associated with reporting increased fatigue. Comparisons across survivors and variations within survivors from day-to-day are possible. For example, it is possible to compare survivors who are higher in negative affect to survivors lower in negative affect in general, and how negative affect may vary within each survivor across days.

Several benefits and drawbacks of collecting data in daily life exist. First, technology (e.g., smartphones and tablets) is increasingly used in daily diary research (Runyan & Steinke, 2015; Trull & Ebner-Priemer, 2013). The prevalence of smartphone use translates to familiarity for participants and a non-invasive, practical tool for researchers (Miller, 2012; Runyan et al., 2013; Runyan & Steinke, 2015). Unfamiliar laboratory or clinical settings may influence reporting of fatigue and subjective cognitive function thus natural settings are ideal to measure experiences. Further, questionnaires administered at one time point fail to capture variability in experiences (Runyan & Steinke, 2015) and are susceptible to potential ‘good’ or ‘bad’ measurement days in which a participant is not having a typical week. Multiple assessments over shorter intervals are needed to capture a more reliable measure and understand how processes operate in daily life. Compared to traditional research designs however, daily diary studies require a greater investment from the participant (Bolger et al., 2003). Burden and compliance could impact reliability (Moskowitz et al., 2009). Therefore, the number of assessments should be carefully considered. The lack of experimental control in daily life is another potential drawback of diary studies and limits the ability to determine cause and effect, but time-ordered
relationships can be examined (Fahrenberg et al., 2007). Nevertheless, to understand how processes operate in daily life natural settings are most appropriate.

In addition, both specific and average measures are calculated (Moskowitz et al., 2009). Specific measures obtained through assessing behavior at multiple time points, across situations in order to observe variability in behavior based on context (Bolger et al., 2003; Moskowitz et al., 2009; Shiffman et al., 2008). Previous research has demonstrated that subjective ratings can fluctuate throughout the day and across days (C. Schmidt, Collette, Cajochen, & Peigneux, 2007; Valdez, Ramirez, & Garcia, 2012). Repeated sampling is necessary to assess these effects and to account for intraindividual variation in responses (Blatter & Cajochen, 2007; Mansell, 1985). These are changes that occur within-person, from day-to-day. If ratings are collected only at one time point (i.e., retrospective questionnaires) variation across settings (i.e., EMA and dairy methods) is not captured. The ability to find consistent associations is likely due to the time frames in which a construct is measured.

Sampling behavior across days also provides a more accurate estimate (Mansell, 1985) and improves validity (Sliwinski, 2008). Average measures can be obtained by aggregating across assessments (i.e., person-averages) or the entire day to provide a summary measure (Bolger et al., 2003) and are able to provide a more reliable estimate by averaging across multiple observations rather than relying on a single observation (Mansell, 1985).

**Between and Within Persons Comparisons**

Within-person processes are of interest in most psychological studies, yet many only collect data between-person (P. J. Curran & Bauer, 2011). For example, whether survivors who report higher depression experience worse self-reported cognitive function could be examined using between or within-person comparisons. Between-persons comparisons identify
characteristics that differ across individuals (e.g., age, education) and contribute to differences in an outcome, and on the other hand within-person comparisons examine characteristics that differ within an individual. In other words, an individual is compared to themselves, rather than others. Cross-sectional studies are not able to provide within-person comparisons as previously mentioned. Typical behavior may not be accurately represented, but rather one individual on a good day and another on a bad day. This ignores the within-person variability, how people are changing from day-to-day. In order to better understand the daily impact of cancer survivorship and associated factors, research will need to focus on studying this in daily life and across multiple days.

Within persons comparisons examine the variability associated with an individual’s responses on multiple occasions. For example, we can examine how a survivor’s fatigue is higher or lower relative to her own average and then identify predictors of this variation. Daily diary methods are able to collect longitudinal data (multiple measures over multiple moments) and to identify peak experiences, when reports are highest across days. This within-person variability and the factors that contribute to greater daily fatigue or subjective cognitive function can be examined rather than only between-person differences. This is an advantage of longitudinal designs, EMA and diary studies. Advanced statistical methods, such as multilevel modeling (MLM) are also required to distinguish differences (and what predicts these) in survivors on average and fluctuations within survivors across days (P. J. Curran & Bauer, 2011; Hoffman & Stawski, 2009).

**Current Study**

The purpose of the current study was to determine the factors that impact daily reported
of fatigue and subjective cognitive function. Using daily diaries it is possible to determine which patients are at the highest risk for decreased QoL and on what days (Wefel et al., 2015).

Aim 1 described between person differences and within person variation in daily fatigue collected at the end of each day. Within person (day-level) predictors (e.g., mood, pain, and activity from daily diary surveys) and between person (person-level) predictors (e.g., person-averages of day-level predictors, age, income, time since treatment, retrospective fatigue, depressive symptoms) on ratings of daily fatigue collected at the end of the day were examined. Research questions of interest for the first Aim included: 1) Does daily reported fatigue differ across days (within-person variation) and across individuals (between-person differences)? 2) Are daily diary measures, such as mood and physical activity related to daily fatigue? Are these predictors able to account for variation across days and individuals? 3) Are traditional in-person measures related to daily fatigue? Specifically, what are the relationships between daily fatigue and demographic and clinical characteristics, and retrospective measures of fatigue and depressive symptoms?

Aim 2 described between person differences and within person variation in daily subjective cognitive functioning (thinking as fast as usual, memory as good as usual, and mind as sharp as usual) collected at the end of the day. Within person (day-level) predictors (e.g., ratings of mood, fatigue, and memory lapses from daily diary surveys) and between person (person-level) predictors (e.g., person means of day-level predictors, age, education, time since treatment, retrospective subjective cognitive function, depressive symptoms) on ratings of daily subjective cognitive performance collected at the end of the day were examined. Important questions for Aim 2 included: 1) Does daily reported subjective cognitive function differ across days (within-person variation) and across individuals (between-person differences)? 2) Are daily diary
measures, such as mood and memory lapses related to daily subjective cognitive function? Are these predictors able to account for variation across days and individuals? 3) Are traditional in-person measures related to daily subjective cognitive function? Specifically, what are the relationships between daily subjective cognitive function and demographic and clinical characteristics, and retrospective measures of subjective cognitive function and depressive symptoms?
Chapter Three: Methods

Participants

Data from the larger Daily Cognitive Function among Breast Cancer Survivors study (H. Lee Moffitt Cancer Center’s American Cancer Society Institutional Research Grant 93-032-16; National Cancer Institute Grant R03 CA191712) was used for the current analyses. The study utilized daily diary subjective surveys completed at the end of the day and ecological momentary assessment (EMA) ambulatory cognitive assessments and subjective surveys as well as questionnaires. The study was approved by the IRB at the University of South Florida and the H. Lee Moffitt Scientific Review Committee.

Eligible participants were recruited from Moffitt Cancer Center and were 6-36 months post-chemotherapy for stage II or lower breast cancer, are female, have no cancer recurrence, and were 40-65 years of age. Medical records were reviewed by trained study coordinators; eligible participants were sent an invitation letter with an option to opt out of the study before a research team member contacted by phone. Participants that did not opt out were contacted and screened for interest and eligibility (age, no vision or hand movement issues which could interfere with ability to follow study protocol). Eligible participants were also recruited from the breast clinic where survivors attend post-treatment follow-up visits. For individuals recruited from the clinic, participants were approached and screened in-person before or after their follow-up appointment. A separate visit to the research offices for data collection and training was then scheduled. Figure 3.1 displays participant recruitment and enrollment.
During an in-person visit to the research offices participants signed informed consent and completed a standard neuropsychological test battery administered by a trained research assistant assessing memory, processing speed, executive function, and attention. Testing was completed in 35 to 45 minutes. Next, participants completed self-report questionnaires assessing depressive symptoms, cancer-related fatigue, subjective cognitive function, mood and thoughts, activity, and demographics. The questionnaire packet took approximately 20 minutes to complete. Participants were then trained to use a study provided smartphone to answer survey questions and cognitive tasks that were completed for 14 days beginning the next day. Participants were exposed to all possible question branches and completed an additional survey independently to ensure that the procedures were understood. Instructions for contacting study staff in the event of any questions or problems while at home with the study phones were provided. The phone training typically took 45 minutes.

As part of the 14 day smartphone data collection, participants completed beeped and daily diary surveys each day. Beeped surveys were prompted quasi-randomly by the phone 5 times per day. Prompts occurred every 2-3 hours and participants were instructed to complete the survey as close to the prompt as possible. During the smartphone training session, participants provided their typical wake times. Beep prompts occurred following study schedules that were assigned based on participants’ self-reported wake time. Beeped surveys collected momentary self-reported context, experiences, mood, alertness, fatigue, and activity. Following each beeped survey three brief cognitive tasks were completed to assess attention, working memory, and perceptual speed, respectively. Beeped surveys and cognitive tasks were typically completed in approximately 3 minutes.
Daily diary surveys were self-initiated each night prior to bedtime. The phone did not prompt the participant to complete the survey. Questions were similar to the beeped survey and were concerned with the entire day as a whole. This dissertation focuses on participants’ reports of daily fatigue and daily subjective cognitive function – assessments of memory, thinking, and mental sharpness. In addition, participants rated questions on each day’s memory lapses (type of information forgotten), memory aids, mood, physical symptoms, and physical activity. Diary surveys were completed in approximately 2 minutes.

To ensure that the smartphone was functioning properly and to answer any additional questions about the surveys participants were contacted on the 1st day and halfway through the study. Compliance was checked prior to the phone calls to confirm that survey data was stored on the secure server and to remind participants to keep the smartphone with them throughout the day. Additionally, at the end of the 14 day study period (day 15) participants were contacted to provide detailed instructions for powering the phone down and mailing all materials back the research offices via a prepaid postage mailer. Upon receipt of the smartphone, compliance was confirmed by downloading all data from the phone. Participants received up to $110 for completing the study. Incentives were provided to those completing 80% or more of the smartphone surveys. For a schematic of the study protocol see Figure 3.2.

Predetermined guidelines were followed to establish compliance and rules for excluding daily diary observations. First, surveys completed outside of the two week study period were excluded. This included surveys launched on the training day before the 14 day study period began (day of the in-person visit) or after the study period ended (day 15 or after). Next, incomplete and duplicate surveys were examined. Surveys were considered incomplete if less than half of the items were answered and were excluded. Duplicates were defined as more than
one daily diary survey completed on the same day. For example, daily diary surveys were excluded if completed in place of a beeped survey. This was determined if a diary survey was completed in place of any beeped survey during the day, which likely indicated that the participant accidently launched an diary survey rather than a beeped when she received the prompt. When two were completed at the end of the day, the first survey was excluded to ensure that the survey reflected entire day’s experiences. Lastly, diary surveys completed after 4 AM (e.g., the cutoff selected for participants with late bedtimes) were excluded.

**Measures**

The following are variables from in-person measures (person-level) and diary surveys (day-level) used in the current study (see Figure 3.3).

**In-person Measures**

Responses on the retrospective fatigue, subjective cognitive function, and depressive symptoms measures correspond to the week prior to the 14 day smartphone portion of the study.

**Demographic and clinical characteristics**

Demographic and clinical characteristics were used to describe the sample. Age, ethnicity, race, education, income, marital status, and work status were all collected using a demographics questionnaire during the in-person visit. Age and years of education were treated as continuous variables in analyses. Clinical characteristics, such as time since treatment was collected via medical record review, were included as covariates.

**Fatigue**

The Fatigue Symptom Inventory (FSI) is a 14 item questionnaire that was administered as part of a larger packet of measures during the in-person visit (Hann et al., 1998). The severity subscale was utilized from this measure which is a sum of 4 items that asked participants to rate
levels of most, least, and average fatigue over the past week, as well as current level fatigue. Responses for items ranged from 0 not at all fatigued to 10 as fatigued as I could be on an 11 point scale and scores can range from 0-40. The interference subscale is a sum of 7 items that asked participants to rate, in the past week, how much fatigue interfered with general activities, self-care, work, concentration, relationships, enjoyment of life, and mood. Responses for items ranged from 0 no interference to 10 extreme interference on an 11 point scale and scores can range from 0-70. Frequency of fatigue was one item that assessed how many days of the week that fatigue was experienced from 0-7 days. The intensity subscale was included in analyses and Cronbach’s alpha for this sample was 0.91.

**Subjective cognitive function**

The Functional Assessment of Cancer Therapy-Cognition (FACT-Cog) is a 37 item questionnaire that assesses retrospective cognitive function over the past seven days (Chelune, Heaton, & Lehman, 1986). Item responses ranged from never to several times a day on a five point scale. All negatively worded items were reverse scored. Items assessed four subscales perceived cognitive impairments (range: 0-80), quality of life (range: 0-16), comments from others (range: 0-16), and perceived cognitive abilities (range: 0-36). A total score was calculated by taking the sum of all 37 items and can range from 0-148. Total score was used in analyses and Cronbach’s alpha for this sample was 0.97.

**Depressive symptoms**

The Center for Epidemiologic Studies-Depression scale is a 20 item questionnaire that assesses depressive symptoms over the past week (Radloff, 1977). Item responses ranged from 1-4 and were rarely or none of the time (less than 1 day), some or a little of the time (1-2 days), occasionally or a moderate amount of the time (3-4 days), or most or all of the time (5-7 days).
All positively worded items were reverse scored. A total score was calculated by taking the sum of all items and can range from 0-60. Cronbach’s alpha for this sample was 0.87.

**Daily Diary Surveys**

For all daily ratings completed before bed, participants were instructed to consider the entire day as a whole and to respond to each question accordingly. For all items with a sliding visual analog scale no numbers were visible to the participant and responses were rescaled to 0-100 scale.

**Fatigue**

Daily fatigue was measured with the item “How fatigued did you feel today?” from no fatigue to worst possible fatigue on a sliding scale. The item was adapted from the FSI (Hann et al., 1998). Higher scores indicated worse fatigue. Daily fatigue was used as an outcome variable for Aim 1.

**Subjective cognitive function**

Three items concerning daily subjective cognitive function included: was your mind as sharp as usual, memory as good as usual, and thinking as fast as usual. These questions have been used in a previous study (Mogle et al., 2017; Scott et al., 2015) and are similar to items from the FACT-Cog (Chelune et al., 1986). Special instructions were provided for this question during phone training at the in-person visit. Usual functioning was treated as the recent past, within the past two weeks, rather than before cancer. Responses ranged from not at all to very much and were specified on a sliding scale. Higher ratings indicate better subjective cognitive performance. The three items were highly correlated (see Table 1), therefore a daily composite was calculated by taking the mean of mental sharpness, memory, and thinking speed each day.
for each participant. Daily subjective cognitive function composite was used as outcome variable for Aim 2.

**Auxiliary daily variables**

**Mood**

Daily mood was assessed with positive and negative affect means. All items were rated using a sliding scale. Daily positive affect was measured with 4 items (happiness, joyfulness, how pleased, and enjoyment). Happiness, joyfulness, and how pleased items were rated from *not at all* to *extremely*; enjoyment was rated from *not at all* to *very much* on a sliding scale. Higher scores indicated higher levels of positive affect (i.e., better mood). Daily negative affect was measured with 5 items (anxiety, depression, anger, unhappiness, and frustration). Negative affect items were rated from *not at all* to *extremely* on a sliding scale. Higher scores indicated higher levels of negative affect (i.e., worse mood). Daily means of positive and negative affect were obtained by averaging responses across respective items that day.

**Physical activity**

To assess daily physical activity the question “how much time did you spend doing moderate to vigorous activities today, these are activities that make you breathe somewhat harder than normal or much harder than normal” was presented. Participants were instructed to only include activities that were engaged in for at least 10 minutes at a time. Drop down menus for both hours (0-12) and minutes (5 minute increments) were used to indicate time spent doing physical activity that day. Total time spent engaging in activity was converted from hour-minute format to minutes per day.
**Overall physical health**

Daily overall physical health was assessed with the item “overall how have you felt physically today” rated from *very unhealthy* to *very healthy* on a sliding scale. Higher scores indicated better perceived physical health.

**Pain**

The physical symptom of daily pain was assessed with the item “how much pain did you feel today” and responses ranged from *no pain* to *worst possible pain* on a sliding scale. Higher ratings indicated more pain that day.

**Memory lapses**

Participants were instructed to check all memory lapses that occurred that day, prompted by the question “did you forget any of the following today?” (Mogle, 2011). Options for memory lapses were: *an errand/chore, take a medicine, finish a task, appointment, why you entered a room, someone’s name, where something was put, a word, important information, and other*. A response of *none of the above* indicated that the participant did not have a memory lapse that day. Total number of lapse types was calculated by summing all items endorsed that day and was used in analyses.

**External memory aids**

To assess the use of external memory aids participants were instructed to check all items that were used to help remember information that day. A list of common memory aids was presented: *lists, reminder notes, appointment book, had someone else remind you, repeat in your head, and none of these things*. Memory aid usage was treated as a dichotomous variable, any reported usage (one or more endorsed items) or no usage that day.
Data Analysis

Demographic and clinical variables were examined to describe the sample. Summary statistics were conducted to describe outcome variables (daily fatigue and daily subjective cognitive function) and predictors. In addition, summary statistics on retrospective questionnaire subscales (FSI and FACT-Cog) and daily subjective cognitive functioning questions (thinking as fast as usual, memory as good as usual, and mind as sharp as usual), average number of memory lapses, percentage of days that lapses were reported, frequency of each type of memory failure, and severity of lapses were examined to describe the sample. Compliance was calculated for each participant and the overall sample. The total number of usable completed surveys was divided by the number of possible surveys. Analyses indicated that overall compliance for the sample was 87.23% (574 completed/ 658 possible) for daily diary surveys.

Person-averages of daily predictor variables from the diary measures were calculated by obtaining an individual’s mean across study days (Hoffman, 2015). Correlation analyses were conducted to examine univariate associations between fatigue and diary (mood, physical activity, pain, physical health) and in-person measures (age, education, time since treatment, FSI, CES-D). Similarly, correlation analyses were also conducted to observe associations between subjective cognitive function and diary (mood, fatigue, memory lapses, memory aid usage) and in-person measures (age, education, time since treatment, FACT-Cog, CES-D). Person-averages of daily predictors were used in correlation analyses.

Reactivity refers to the accuracy of responses and understanding of a construct that may occur as familiarity with assessment increases (Bolger et al., 2003; Moskowitz et al., 2009). Although little evidence exists to suggest this is a major concern to validity (Bolger et al., 2003),
to account for measurement reactivity study day (sequence of days 1-14) was included as a within-person covariate (Hoffman, 2015).

**Centering of Variables**

Recommendations for centering variables vary across the literature. While no one rule applies to all MLM, general guidelines can be applied according to the research question of interest. In the current study centered variables were used when doing so aids interpretation (e.g., age, CES-D; P. J. Curran & Bauer, 2011; Hoffman & Stawski, 2009; Wang & Maxwell, 2015). Between-person variables were grand-mean centered (i.e., the practice of subtracting a constant from a raw variable), prior to analysis. First, the grand mean was obtained by calculating the mean across all participants and then subtracted from the score of each participant. For example, grand-mean centered (CES-Dgmc) was calculated as follows: CES-Dgmc = CES-D (of individual participant) – CES-D (of sample) (P. J. Curran & Bauer, 2011; Hoffman & Stawski, 2009; Wang & Maxwell, 2015). Time since treatment was centered on shortest time since treatment (6.17 months) and education was centered at 12 years to aid interpretation. Daily predictors each have a meaningful zero (e.g., physical activity in minutes) and were used in their raw, un-centered forms (Wang & Maxwell, 2015). Person-averages were grand-mean centered to indicate individual differences in responses. Only the person-average of memory aid usage (dichotomous variable) was used in its un-centered form (Wang & Maxwell, 2015).

**Multilevel Modeling**

Multilevel model analysis was conducted to investigate the predictors of daily fatigue and subjective cognitive function. Daily diary surveys completed across the study (up to 14 per participant) are nested within survivors, measurement occasions nested within individuals, and MLM is recommended. Generalized mixed models were utilized, which include fixed and
random effects (Bolger et al., 2003; P. J. Curran & Bauer, 2011; Hoffman & Stawski, 2009). Missing data is common among daily diary studies due to repeated assessment and does not exclude cases with missing data (Walls & Schafer, 2006). For example, if an assessment was not completed the rest of that participant’s assessments will still be used. Therefore, differing numbers of assessments and unequal time intervals across participants, due in part to missing data or missed surveys do not violate the assumptions of MLM (Hox, 2010). Data were is assumed to be missing at random and refers to missingness that is attributed to a predictable source, such as other observations (Hoffman, 2015). Day of study (i.e., 1 – 14) was unable to account for missing observations from daily diaries. To satisfy the missing at random assumption maximum likelihood estimation was used for all models (Hox, 2010) and all complete assessments from each participant were included in analyses. Proc Mixed (SAS Version 9.4) was used to estimate all models. Daily variables contain both within and between-person variation. Therefore, person-averages of daily predictors were included at the person-level in all models that contained diary measures in order to help separate between and within effects (Hoffman & Stawski, 2009). Unconditional models were estimated for each daily predictor as the outcome to examine the variance at each level.

The MLM assumptions of normality, independence, and homogeneity of variance were examined using previously established recommendations. Normality refers to the normal distribution of level-1 and level-2 residuals. Histograms and probability plots were used to visually inspect normality (Hoffman, 2015; Hox, 2010). Independence implies that residuals at each level are unrelated and was examined visually via scatterplots (Hoffman, 2015). Lastly, homogeneity of variance assumes equal variance within each level and was examined with scatterplots (Hox, 2010).
Aim 1

Aim 1 was to describe between person differences and within person variation in daily fatigue collected at the end of each day. The influence of within person (day-level) predictors (e.g., daily diary measures) and between person (person-level) predictors (e.g., person averages of day-level predictors, in-person measures) on ratings of daily fatigue were examined. We hypothesized that daily fatigue will exhibit both between person and within person variation. Both daily negative affect and daily pain were hypothesized to be positively related to daily fatigue. Daily physical activity was negatively associated with daily fatigue. Finally, retrospective fatigue completed prior to the daily diary portion of the study will be positively associated with daily fatigue.

MLM of increasing complexity were used to determine the predictors of daily fatigue. First, an unconditional model with a random intercept and no predictors was conducted with daily fatigue as the dependent variable (outcome). This model provided an estimate of the intercept, which was the average daily fatigue across all participants and days (Hox, 2010). The variance estimate of the intercept indicated whether individuals differ on daily reported fatigue (Hayes, 2006). The within-person variance estimate indicated whether or not individuals vary across days in daily reported fatigue. Intraclass correlation coefficients (ICC) was calculated to examine the proportion of variance at the between-person and within-person level using variance estimates from the unconditional model (Hox, 2010). The equation can be conceptualized as the variance at a given level (between or within) over the total variance (between + within).

Successive models included time-varying and time-invariant predictors to account for the variance at each level. Time-varying predictors were collected daily at each assessment and were considered to vary across time (P. J. Curran & Bauer, 2011). Time-invariant predictors remained
constant over time and can explain between-person variance (P. J. Curran & Bauer, 2011). Using this as a general framework, predictor variables were added at the day-level (varies) or person-level (does not vary). To examine the impact of diary measures on daily fatigue Model 2 included fixed effects for daily negative affect, daily positive affect, daily overall physical health, daily physical activity, daily pain, and study day at the day-level. The daily predictors were entered into the model un-centered. These represent the within-person influences on daily fatigue. To account for individual differences in daily predictors, grand-mean centered person-averages of these predictors were also included. Estimates from Model 2 indicate the relationship between diary measures and daily fatigue. Model 3 examined fixed effects for person-level predictors: demographic (age, education) and clinical characteristics (time since treatment), the FSI intensity subscale, and depressive symptoms collected during the in-person visit in addition to the Model 2 predictors. All person-level predictors were grand-mean centered. Estimates indicated the relationship between the person-level predictors and daily fatigue across the study.

Model fit was examined using a Chi-square goodness of fit test with the change in -2 log-likelihood and the difference in the number of model parameters as the degrees of freedom (Hoffman & Stawski, 2009) indicated which model explains the data best. Each subsequent model was compared to the previous model. If the result was significant the more complex model (more parameters) was chosen. The simpler model (fewer parameters) should be retained if the result was not significant. In addition, AIC and BIC fit indices were examined to determine the most appropriate model (Hoffman, 2015). Although not a true measure of model fit pseudo $R^2$ was calculated to determine the amount of variance explained by each successive model (Singer & Willett, 2003).
Aim 2

Aim 2 described between-person differences and within-person variation in daily subjective cognitive functioning composite (thinking as fast as usual, memory as good as usual, and mind as sharp as usual) collected at the end of each day. The influence of within-person (day-level) predictors (e.g., daily diary measures) and between-person (person-level) predictors (e.g., person means of day-level predictors, in-person-measures) on ratings of daily subjective cognitive function were examined. We hypothesized that daily subjective cognitive function will exhibit both between person and within person variation. Daily ratings of fatigue, memory lapses, and negative affect were negatively associated with daily subjective cognitive function. Lastly, retrospective cognitive function and depressive symptoms prior to the daily diary portion of the study were hypothesized to be positively associated with daily subjective cognitive function.

Successive MLMs were conducted to determine the predictors of daily subjective cognitive function. As described in Aim 1, an unconditional model was estimated with daily subjective cognitive function as to outcome and the ICC was calculated. In Model 2 fixed effects of daily negative affect, daily positive affect, daily fatigue daily memory lapses, daily use of memory aids, and study day represented within-persons influences on daily subjective cognitive function. The daily predictors were entered into the model un-centered. Person-averages of daily predictors were included as between-person influences on daily subjective cognitive function. Model 2 estimates indicated the relationship between day-level predictors and daily subjective cognitive function.

In Model 3 age, education, time since treatment, FACT-Cog (total score), and depressive symptoms collected during the in-person visit were examined in addition to the Model 2
predictors. All person-level predictors were grand-mean centered, with the exception of memory aid usage. Estimates indicated the relationship between the person-level predictors and daily subjective cognitive function across the study. As described in Aim 1, model fit was examined using a Chi-square goodness of fit test, and AIC and BIC fit indices (Hoffman & Stawski, 2009) and pseudo $R^2$ was calculated.
Figure 3.1 Participant recruitment and enrollment.
**Recruitment:**
Sent a letter or approached in clinic

**Eligibility:**
Female, 40-65 years old, treated for stage 0, 1, or 2 breast cancer at Moffitt, ≥4 cycles of chemotherapy, completed treatment 6-36 months ago, no recurrence

**Screen and Schedule:**
Those who did not opt out are called by research staff
Screened to confirm eligibility, verbal consent to participation, and scheduled in-person visit

**In-person Visit:**
Provided Informed Consent
Completed neuropsychological tests and self-report surveys
Trained on study protocol and smartphones

**EMA and Daily Diary:**
Carried study smartphones for 14 days
Answered brief surveys and cognitive assessments each day

**End of Study Phone Return and Payment:**
Equipment mailed back via postage paid boxes
Upon return compliance was confirmed and payment sent (Maximum: $110 for completing study, incentives for completing 80% of surveys)

*Figure 3.2.* Study design, how participants moved through the study. EMA= Ecological momentary assessment.
**Person-level** (In-person Questionnaires):
- FSI
- FACT-Cog
- CES-D
- Demographics
- Clinical Characteristics

**Day-level** (Daily Diary Surveys):
- Fatigue (Outcome)
- Subjective Cognitive Function (Outcome)
- Mood
- Pain
- Physical Activity
- Memory Lapses
- Memory Aid Usage

*Figure 3.3.* Description of data collection at each level of the study and specific information collected. FSI = Fatigue Symptom Inventory; FACT-Cog = Functional Assessment of Cancer Treatment - Cognitive; CES-D = Center for Epidemiological Studies-Depression.
Table 3.1

*Intercorrelations among Subjective Cognitive Function Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Thinking as fast as usual</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Mind as sharp as usual</td>
<td>.83*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Memory as good as usual</td>
<td>.86*</td>
<td>.87*</td>
<td></td>
</tr>
</tbody>
</table>

*Note. N = 47; * = p < .001.*
Chapter Four: Results

The purpose of the present study was to examine daily quality of life concerns among breast cancer survivors. Demographic characteristics of the sample are presented first, including daily diary compliance. Next, the first aim described between-person differences and within-person variation in daily fatigue collected at the end of the day. Additionally, day-level and person-level predictors were examined. Aim 2 described between-person differences and within-person variation in daily subjective cognitive functioning collected at the end of the day. The associations of day-level and person-level predictors were examined.

Sample Characteristics

Sample characteristics are presented in Table 4.1. Briefly, 47 female breast cancer survivors who were an average age of 53.34 years ($SD = 6.46$; range = 40.79-64.54), and were also 17.07 months ($SD = 7.23$; range = 6-36) post-chemotherapy treatment comprised the final sample. Ninety-eight percent of the sample completed at least high school. Seventy-nine percent of the sample was white and 85% were Non-Hispanic or Latino. Descriptive statistics for study variables are presented in Table 4.2 (in-person measures) and Table 4.3 (dairy measures).

Compliance was examined prior to completing analyses related to the study aims. A total of 658 daily diary surveys were possible (47 participants for 14 days). In all, 677 surveys were completed by participants. Seventy surveys were completed outside of the two week study period, launched on the training day (before the 14 day study period began) or after the study period ended and were excluded. Additionally, 33 were duplicates in which more than one survey was completed on the same day. This was determined by examining survey times and
excluded if completed in place of a beeped survey (e.g., if diary survey was completed prior to, or in place of, the last beeped survey of that day likely the participant accidently launched a diary survey rather than a beeped when she received the prompt) or after 4 AM (e.g., the cutoff selected for participants with late bedtimes). Average compliance was 87.23% (~12.2 surveys; 574 usable/ 658 possible; range = 7.14% - 100%, $Mdn = 92.86\%$) for daily diary surveys completed at the end of the day (see Table 4.4 for a breakdown of compliance). We examined the influence of participants with low compliance (i.e., less than 50% of survey completed). Results remained the same when low compliance individuals were included. To not bias our findings, and represent of individuals with low compliance, these participants were included in analyses.

**Aim 1 – Daily Fatigue**

To examine the predictors of daily fatigue, diary measures and in-person measures were utilized. Both day-level and person-level predictors from diary measures were included. Daily predictors were un-centered and grand-mean centered person-averages of each of these daily variables were also included to disentangle between and within effects. All daily variables showed significant variability within-persons across days and between-persons ($ps < .001$) and ICCs are displayed in Figure 4.1. The majority of variance ($> 50\%$) was between-persons for all daily variables. In-person measures were grand-mean centered.

Correlations between daily fatigue and predictor variables are shown in Table 4.5. Person-averages of daily variables were utilized when calculating correlations. Fatigue had positive correlations with negative affect and physical activity. Fatigue had a negative correlation with positive affect. Demographic and clinical characteristics, such as retrospective fatigue
severity during the prior week and depressive symptoms, had positive correlations with fatigue. Age, education, and time since treatment were not correlated with fatigue.

**Fatigue Multilevel Model Results**

Normality, independence, and homogeneity of variance assumptions were evaluated for each model that examined the predictors of daily fatigue. Histogram and probability plots indicated that residuals appeared to be normally distributed. Independence and homogeneity of variance assumptions did not appear to be violated as indicated by scatterplots.

Results for all daily fatigue models are displayed in Table 4.6. To determine if ratings of daily fatigue exhibit both between person and within person variation an unconditional model was conducted. The intraclass correlation coefficient (ICC) indicated that 67.8% of variance in daily fatigue was between individuals and 32.1% of the variance was within persons. The unconditional model showed that mean fatigue across days was 35.23 (SE = 3.26, p < .001) and on average survivors differed in daily reports of fatigue, SD = 21.87, Z = 4.62, p < .001.

The effects of within- and between-person predictors from the diary measures were examined in Model 2. Daily variables included mood (negative affect, positive affect), pain, physical activity, and overall physical health collected each day; we also included the grand mean-centered person averages of each of these variables. Within-person daily fluctuations in negative affect, pain, and overall physical health were significant predictors of daily fatigue. On days when a survivor reported higher negative affect, she tended to report greater fatigue that day (b = 0.18, SE = 0.07, p = .007). Reporting higher pain was related to reporting higher fatigue that day (b = 0.31, SE = 0.06, p < .001). Finally, on days when worse overall physical health was experienced higher fatigue was reported that day (b = -0.14, SE = 0.05, p = .002). Daily fluctuations in positive affect and moderate to vigorous physical activity did not predict
fluctuations in fatigue. Study day was unrelated to daily fatigue ratings. No between-person effects (person-averages) were related to daily fatigue across the study. Chi-square goodness of fit test ($\chi^2 (11) = 111, p < .05$), suggests that Model 2 should be retained. A pseudo $R^2$ that compared a model that included diary measures to the unconditional model revealed that 59% of the variation of daily fatigue was explained at the between-person level and 13% was explained at the within-person level.

Demographic and clinical variables (i.e., age, education, time since treatment, retrospective fatigue, and depressive symptoms) collected from in-person measures were included in Model 3 to help account for between-person variation in addition to the diary measures. Individual differences prior to the study in fatigue severity the week prior to the diary phase of the study and time since treatment were a significant predictors of average daily fatigue. As expected, persons who reported greater fatigue severity on the in-person measure also rated average daily fatigue as greater across the study ($b = 1.16, SE = 0.30, p < .001$). Greater time since treatment was related to higher fatigue across the study ($b = 0.55, SE = 0.26, p = .044$). Age, education, and depressive symptoms from the in-person measures were unrelated to average daily fatigue.

Day-level effects remained significant after all measures were included in the combined model (Model 3). When survivors reported higher negative affect and pain then fatigue was rated as higher that day. In contrast, on days when better overall physical health was reported related to lower fatigue. The within-person effect of reporting 1 unit higher daily negative affect was related to reporting higher fatigue by 0.18 that day ($b = 0.18, SE = 0.07, p = .02$). Within person fluctuations in pain predicted daily fatigue - reporting 1 unit higher pain than average was related to reporting higher fatigue by 0.31 that day ($b = 0.31, SE = 0.06, p < .001$). Last, the within-
person effect of overall health on daily fatigue was significant \((b = -0.15, SE = 0.05, p = .002)\).

On days when worse overall health was reported fatigue was rated as higher. Daily fluctuations in positive affect and physical activity did not predict fluctuations in daily fatigue. Study day was unrelated to daily fatigue ratings. Individual differences in person-averages of daily predictors were unrelated to fatigue across the study. Chi-square goodness of fit test \((\chi^2 (5) = 20.1, p < .05)\), suggests that Model 3 should be retained. Including retrospective questionnaires and demographic and clinical characteristics explained the data significantly better than the previous model. A pseudo \(R^2\) that compared the full model to a model without demographic and clinic characteristics revealed that 38% of the variation of daily fatigue was explained at the between-person level.

**Aim 2 – Daily Subjective Cognitive Function**

To examine the predictors of daily subjective cognitive function (i.e., a composite of memory as good, thinking as fast, and mind as sharp), diary measures and in-person measures were utilized. Diary measures were included as day-level and person-level predictors. Day-level predictors were un-centered and person-level predictors were included as grand-mean centered person-averages, with the exception of the dichotomous variable for memory aid usage. ICCs for daily variables are displayed in Figure 4.1, variability within-persons across days and between-persons was significant \((ps < .001)\). All in-person measures were grand-mean centered.

Correlations among subjective cognitive function and predictor variables are displayed in Table 4.7. Person-averages of daily variables were utilized when calculating correlations. Subjective cognitive function had negative correlations with diary measures of negative affect, fatigue, memory aid usage, and memory lapses. Subjective cognitive function had a positive correlation with positive affect. Demographic and clinical characteristics were correlated with
subjective cognitive function. Retrospective subjective cognitive function prior to the study had a positive correlation with subjective cognitive function. In contrast, depressive symptoms prior to the study had a negative correlation with subjective cognitive function. Age, education, and time since treatment were not correlated with subjective cognitive function.

**Subjective Cognitive Function Multilevel Model Results**

Normality, independence, and homogeneity of variance assumptions were evaluated for each model. Histogram and normal probability plots were used to evaluate normality. Residuals appeared to be normally distributed. Similarly, the independence and homogeneity of variance assumptions did not appear to be violated as indicated by scatterplots.

Results for all daily subjective cognitive function models are displayed in Table 4.8. To determine if ratings of subjective cognitive function made at the end of the day exhibit both between person and within person variation the unconditional model was examined. The ICC indicated that 69.7% of variance in daily subjective cognitive function was between individuals and 30.3% of the variance was within persons. The unconditional model showed that mean subjective cognitive function across days was 61.56 ($SE = 2.44$, $p < .001$). Survivors differed on average in daily subjective cognitive function, $SD = 16.42$, $Z = 4.49$, $p < .001$.

The effects of within-person and between-person predictors from the diary measures were examined in Model 2. Study day was associated with daily subjective cognitive function. For each additional day in the study, subjective cognitive function was rated as better that day ($b = 0.31$, $SE = 0.11$, $p = .005$). Daily variables included mood (negative affect, positive affect), fatigue, memory aid usage, and memory lapses collected each day; person-averages of each of the daily variables were also included. Within-person variability in positive affect, fatigue, and memory lapses related to daily subjective cognitive function. On days when a survivor reported
higher positive affect, she tended to report better subjective function that day ($b = 0.20, SE = 0.05, p < .001$). On days when a survivor reported higher fatigue, she tended to rate her subjective cognitive function worse ($b = -0.15, SE = 0.03, p < .001$). Reporting more types of memory lapses was related to reporting worse subjective cognitive function that day ($b = -1.62, SE = 0.42, p < .001$). Daily fluctuations in negative affect and memory aid usage did not predict fluctuations in subjective cognitive function. Between-person effects for diary measures were also observed. Overall, survivors who reported greater positive affect on average also rated subjective cognitive function as better across the study ($b = 0.32, SE = 0.13, p = .019$). No other significant between-person effects were found. Chi-square goodness of fit test ($\chi^2 (11) = 128.7, p < .05$), suggests that Model 2 should be retained. A pseudo $R^2$ that compared a model that included diary measures to the unconditional model revealed that 65% of the variation of daily subjective cognitive function was explained at the between-person level and 14% was explained at the within-person level.

Demographic and clinical variables (e.g., age, education, time since treatment, retrospective subjective cognitive function the week prior to the study, depressive symptoms) collected from in-person measures were included in Model 3 to help account for between-person variation in addition to the diary measures. Individual differences in demographic and clinical variables from the in-person measures were unrelated to subjective cognitive function.

Day-level effects remained significant after all measures were included in the combined model (Model 3). Study day was associated with daily subjective cognitive function. For each additional day in the study, subjective cognitive function was 0.31 units higher that day ($b = 0.31, SE = 0.11, p = .005$). Daily fluctuations in positive affect, fatigue, and memory lapses significantly predicted daily fatigue. Within persons, positive affect was related to better
subjective cognitive function. For every one-unit higher positive affect, subjective cognitive function was 0.20 units higher that day ($b = 0.20, SE = 0.05, p < .001$). Greater fatigue was associated with worse subjective cognitive function within persons. For every 1 unit higher fatigue, subjective cognitive function was 0.15 lower that day ($b = -0.15, SE = 0.03, p < .001$). Within persons, for each additional type of memory lapse reported subjective cognitive function was expected to decrease by 1.62 that day ($b = -1.62, SE = 0.42, p < .001$). For a survivor with 1.76 more types of memory lapses than the sample average (+1 SD), her average subjective cognitive function was 6.13 units lower than the average in the sample. Daily fluctuations in negative affect and memory aid usage did not predict fluctuations in subjective cognitive function. No significant between-person effects were found for these variables. The between-person positive affect effect was no longer associated with subjective cognitive function, which was significant in the previous model. Chi-square goodness of fit test ($\chi^2 (5) = 3.6, p > .05$), suggests that Model 2 should be retained. Including retrospective questionnaires and demographic and clinical characteristics did not explain the data significantly better than the previous model. A pseudo $R^2$ that compared the full model to a model without demographic and clinic characteristics revealed that 8% of the variation of daily subjective cognitive function was explained at the between-person level.
### Table 4.1

**Participant Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Sample ((n = 47))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M (SD)</strong></td>
<td><strong>% (n)</strong></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>53.34 (6.46)</td>
</tr>
<tr>
<td><strong>Time since treatment (in months)</strong></td>
<td>17.07 (7.23)</td>
</tr>
<tr>
<td><strong>Breast Cancer Stage</strong></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>25.53 (12)</td>
</tr>
<tr>
<td>Stage II</td>
<td>74.47 (35)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>Some high school</td>
<td>2.13 (1)</td>
</tr>
<tr>
<td>Completed high school or GED</td>
<td>17.02 (8)</td>
</tr>
<tr>
<td>Some college</td>
<td>31.91 (15)</td>
</tr>
<tr>
<td>Completed college</td>
<td>25.53 (12)</td>
</tr>
<tr>
<td>Graduate or professional degree</td>
<td>23.40 (11)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>78.72 (37)</td>
</tr>
<tr>
<td>Black</td>
<td>14.89 (7)</td>
</tr>
<tr>
<td>Asian</td>
<td>4.26 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>2.13 (1)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic/Latino</td>
<td>82.98 (39)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>14.89 (7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2.13 (1)</td>
</tr>
<tr>
<td><strong>Work Status</strong></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>48.94 (23)</td>
</tr>
<tr>
<td>Retired</td>
<td>31.91 (15)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>19.15 (9)</td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>68.08 (32)</td>
</tr>
<tr>
<td>Divorced or separated</td>
<td>19.15 (9)</td>
</tr>
<tr>
<td>Un-married</td>
<td>10.64 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>2.13 (1)</td>
</tr>
</tbody>
</table>
Table 4.1 (Continued)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Sample (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
</tr>
<tr>
<td>Household Income</td>
<td></td>
</tr>
<tr>
<td>Less than 4,999</td>
<td>4.26 (2)</td>
</tr>
<tr>
<td>5,000-19,999</td>
<td>8.51 (4)</td>
</tr>
<tr>
<td>20,000-39,999</td>
<td>10.64 (5)</td>
</tr>
<tr>
<td>40,000-59,999</td>
<td>12.77 (6)</td>
</tr>
<tr>
<td>60,000-79,999</td>
<td>4.26 (2)</td>
</tr>
<tr>
<td>80,000-99,999</td>
<td>12.77 (6)</td>
</tr>
<tr>
<td>100,000-149,999</td>
<td>10.64 (5)</td>
</tr>
<tr>
<td>150,000 or more</td>
<td>12.77 (6)</td>
</tr>
<tr>
<td>Chose not to answer</td>
<td>8.51 (4)</td>
</tr>
<tr>
<td>Missing</td>
<td>14.89 (7)</td>
</tr>
</tbody>
</table>

*Note. For age the range = 40.91-64.58 years and for time since treatment the range = 6.17-36.40 months.*
Table 4.2

Summary Statistics for In-Person Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Total Sample (n = 47)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>M (SD)</td>
<td>% (N)</td>
<td>Range</td>
</tr>
<tr>
<td>Pre-Study Paper Questionnaires FSI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSI severity</td>
<td>13.45 (8.35)</td>
<td>0-28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSI interference</td>
<td>14.99 (15.61)</td>
<td>0-56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSI frequency</td>
<td>3.36 (2.27)</td>
<td>0-7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT – Cog</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT perceived cognitive impairments</td>
<td>54.16 (16.78)</td>
<td>6-80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT quality of life</td>
<td>12.23 (4.43)</td>
<td>0-16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT comments from others</td>
<td>14.38 (2.50)</td>
<td>6-16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT perceived cognitive abilities</td>
<td>24.64 (9.50)</td>
<td>5-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT total score</td>
<td>105.41 (30.36)</td>
<td>21-148</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D total score</td>
<td>11.81 (7.94)</td>
<td>3-41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note. FSI = Fatigue Symptom Inventory; FACT = Functional Assessment of Cancer Treatment; CES-D = Center for Epidemiological Studies-Depression; Range is the observed range in the sample.*
Table 4.3

**Summary Statistics for Daily Diary Measures**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Total Sample ((n = 47))</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>% (N)</td>
<td>Range</td>
</tr>
<tr>
<td><strong>End of Day Smartphone Surveys</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Fatigue</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fatigue severity</td>
<td>33.96 (26.57)</td>
<td>0-100</td>
<td></td>
</tr>
<tr>
<td>Fatigue interference</td>
<td>26.49 (26.28)</td>
<td>0-100</td>
<td></td>
</tr>
<tr>
<td>Subjective cognitive function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mind as sharp</td>
<td>62.07 (21.20)</td>
<td>0-100</td>
<td></td>
</tr>
<tr>
<td>Memory as good</td>
<td>62.00 (21.38)</td>
<td>2-100</td>
<td></td>
</tr>
<tr>
<td>Thinking as fast</td>
<td>62.13 (20.66)</td>
<td>0-100</td>
<td></td>
</tr>
<tr>
<td>Composite</td>
<td>62.06 (20.03)</td>
<td>8.7-100</td>
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<td><strong>Memory lapses</strong></td>
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<tr>
<td>Memory lapse by type</td>
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<td></td>
</tr>
<tr>
<td>Chore</td>
<td>12.37 (71)</td>
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<tr>
<td>Task</td>
<td>18.29 (105)</td>
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<tr>
<td>Why entered a room</td>
<td>16.72 (96)</td>
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<td></td>
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<tr>
<td>Medication</td>
<td>11.32 (65)</td>
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<tr>
<td>Appointment</td>
<td>3.48 (20)</td>
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<tr>
<td>A word</td>
<td>21.25 (122)</td>
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<td></td>
</tr>
<tr>
<td>Where something was put</td>
<td>19.16 (110)</td>
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<td></td>
</tr>
<tr>
<td>Someone’s name</td>
<td>13.76 (79)</td>
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<td></td>
</tr>
<tr>
<td>Information</td>
<td>9.06 (52)</td>
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<td></td>
</tr>
<tr>
<td>Other</td>
<td>10.98 (63)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than one</td>
<td>35.19 (202)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>42.33 (243)</td>
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<td></td>
</tr>
<tr>
<td>Total lapses per day</td>
<td>1.42 (1.76)</td>
<td>0-9</td>
<td></td>
</tr>
<tr>
<td>Memory lapse severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bother</td>
<td>25.28 (28.77)</td>
<td>0-100</td>
<td></td>
</tr>
<tr>
<td>Interfere</td>
<td>14.41 (21.03)</td>
<td>0-96</td>
<td></td>
</tr>
<tr>
<td>Future consequences</td>
<td>23.29 (29.59)</td>
<td>0-99</td>
<td></td>
</tr>
<tr>
<td>Severity</td>
<td>20.99 (23.27)</td>
<td>0-97.5</td>
<td></td>
</tr>
<tr>
<td><strong>Memory aid usage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lists</td>
<td>33.97 (195)</td>
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<td></td>
</tr>
<tr>
<td>Notes</td>
<td>28.22 (162)</td>
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<tr>
<td>Book</td>
<td>24.22 (139)</td>
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<tr>
<td>Someone</td>
<td>12.02 (69)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeat</td>
<td>17.25 (99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aid</td>
<td>38.33 (220)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any used</td>
<td>61.67 (354)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>19.72 (26.76)</td>
<td>0-100</td>
<td></td>
</tr>
</tbody>
</table>
Table 4.3 (Continued)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Total Sample (n = 47)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$M$ ($SD$)</td>
<td>$%$ ($N$)</td>
</tr>
<tr>
<td>Physical activity (minutes)</td>
<td>93.14 (111.01)</td>
<td></td>
</tr>
<tr>
<td>Sitting (minutes)</td>
<td>419.98 (166.91)</td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive affect</td>
<td>65.33 (18.81)</td>
<td></td>
</tr>
<tr>
<td>Negative affect</td>
<td>16.24 (17.07)</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Range is the observed range in the sample; Memory lapses were reported via checklists each night; Frequencies are across all participants over the 14 day ecological momentary assessment study. Memory lapse severity questions bother, interfere, and future consequences were only asked if a memory lapse was reported.
Table 4.4

Participant Compliance for Daily Diary Surveys

<table>
<thead>
<tr>
<th>Number of Daily Diary Surveys completed</th>
<th>N</th>
<th>%</th>
<th>Cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>17</td>
<td>36.17</td>
<td>36.17</td>
</tr>
<tr>
<td>90%-99%</td>
<td>12</td>
<td>25.53</td>
<td>61.70</td>
</tr>
<tr>
<td>80%-89%</td>
<td>7</td>
<td>14.89</td>
<td>76.59</td>
</tr>
<tr>
<td>70%-79%</td>
<td>5</td>
<td>10.64</td>
<td>87.23</td>
</tr>
<tr>
<td>60%-69%</td>
<td>4</td>
<td>8.51</td>
<td>95.74</td>
</tr>
<tr>
<td>50%-59%</td>
<td>0</td>
<td>0</td>
<td>95.74</td>
</tr>
<tr>
<td>&lt; 50%</td>
<td>2</td>
<td>4.26</td>
<td>100</td>
</tr>
</tbody>
</table>

Note. Breakdown of participant compliance for daily diary surveys across the 14 day study.
Figure 4.1. Variance of daily predictors from the daily diary surveys. Breakdown of within- and between-persons variance in daily variables (day-level). ICCs were calculated from individual unconditional models run for each daily variable.
### Table 4.5

*Correlations among Daily Fatigue and Predictors*

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Daily fatigue</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Daily negative affect</td>
<td>.53**</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Daily positive affect</td>
<td>-.44**</td>
<td>-.49**</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Daily pain</td>
<td>.70**</td>
<td>.42**</td>
<td>-.38**</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Daily sitting</td>
<td>-.06</td>
<td>.12</td>
<td>-.07</td>
<td>.25</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Daily physical activity</td>
<td>.29*</td>
<td>-.08</td>
<td>-.05</td>
<td>.39**</td>
<td>-.11</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Daily physical health</td>
<td>-.58**</td>
<td>-.58**</td>
<td>.67**</td>
<td>.57**</td>
<td>-.19</td>
<td>.02</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Age</td>
<td>-.12</td>
<td>-.22</td>
<td>.15</td>
<td>-.01</td>
<td>.07</td>
<td>.05</td>
<td>.10</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Education</td>
<td>-.07</td>
<td>-.11</td>
<td>-.37*</td>
<td>-.15</td>
<td>-.07</td>
<td>-.16</td>
<td>-.24</td>
<td>-.41**</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Time since treatment</td>
<td>.20</td>
<td>.10</td>
<td>-.14</td>
<td>.05</td>
<td>.27</td>
<td>-.11</td>
<td>-.24</td>
<td>.01</td>
<td>.03</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. FSI severity</td>
<td>.71**</td>
<td>.43**</td>
<td>-.46**</td>
<td>.51**</td>
<td>.02</td>
<td>.13</td>
<td>-.46**</td>
<td>-.28</td>
<td>-.07</td>
<td>.03</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>12. CES-D</td>
<td>.68**</td>
<td>.59**</td>
<td>-.39**</td>
<td>.68**</td>
<td>.21</td>
<td>.24</td>
<td>-.48**</td>
<td>-.09</td>
<td>-.11</td>
<td>-.02</td>
<td>.59**</td>
<td>-</td>
</tr>
</tbody>
</table>

*Note. Within person correlations (N = 47); FSI = Fatigue Symptom Inventory; CES-D = Center for Epidemiological Studies-Depression.*

* p < .05. ** p < .01.
### Table 4.6

**Fixed and Random Effects of Daily Fatigue**

<table>
<thead>
<tr>
<th>Fixed Effects</th>
<th>Model 1 (Unconditional)</th>
<th>Model 2 (Diary Measures)</th>
<th>Model 3 (Diary + In-person Measures)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intercept</strong></td>
<td>35.23** (3.26)</td>
<td>33.63** (6.11)</td>
<td>30.41** (7.34)</td>
</tr>
<tr>
<td><strong>Level 1 (day)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study day</td>
<td>-</td>
<td>0.15 (0.15)</td>
<td>0.15 (0.15)</td>
</tr>
<tr>
<td>Negative affect</td>
<td>-</td>
<td>0.18* (0.07)</td>
<td>0.18* (0.07)</td>
</tr>
<tr>
<td>Positive affect</td>
<td>-</td>
<td>0.02 (0.07)</td>
<td>0.02 (0.07)</td>
</tr>
<tr>
<td>Vigorous activity</td>
<td>-</td>
<td>-0.01 (0.01)</td>
<td>-0.003 (0.01)</td>
</tr>
<tr>
<td>Pain</td>
<td>-</td>
<td>0.31** (0.06)</td>
<td>0.31** (0.06)</td>
</tr>
<tr>
<td>Overall physical health</td>
<td>-</td>
<td>-0.14* (0.05)</td>
<td>-0.15* (0.05)</td>
</tr>
<tr>
<td><strong>Level 2 (person)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative affect – person average</td>
<td>-</td>
<td>0.27 (0.23)</td>
<td>0.11 (0.21)</td>
</tr>
<tr>
<td>Positive affect – person average</td>
<td>-</td>
<td>-0.06 (0.21)</td>
<td>0.10 (0.18)</td>
</tr>
<tr>
<td>Vigorous activity – person average</td>
<td>-</td>
<td>0.03 (0.03)</td>
<td>0.04 (0.02)</td>
</tr>
<tr>
<td>Pain – person average</td>
<td>-</td>
<td>0.05 (0.13)</td>
<td>-0.12 (0.12)</td>
</tr>
<tr>
<td>Overall physical health – person average</td>
<td>-</td>
<td>-0.11 (0.22)</td>
<td>0.001 (0.19)</td>
</tr>
<tr>
<td>Age</td>
<td>-</td>
<td>-</td>
<td>0.19 (0.35)</td>
</tr>
<tr>
<td>Time since treatment</td>
<td>-</td>
<td>-</td>
<td>0.55* (0.26)</td>
</tr>
<tr>
<td>FSI severity</td>
<td>-</td>
<td>-</td>
<td>1.16** (0.30)</td>
</tr>
<tr>
<td>CES-D total</td>
<td>-</td>
<td>-</td>
<td>0.39 (0.36)</td>
</tr>
<tr>
<td>Education</td>
<td>-</td>
<td>-</td>
<td>0.47 (0.92)</td>
</tr>
</tbody>
</table>

**Random effects**

\[
\begin{align*}
N, \text{ Level 2} & = 47 \\
N, \text{ Level 1} & = 574 \\
\tau_{00} \text{ (Intercept)} & = 478.37** \\
\sigma^2 \text{ (Residual)} & = 227.60** \\
\end{align*}
\]

**Fit Statistics**

\[
\begin{align*}
\text{Deviance (-2LL)} & = 4896.8 \\
\text{AIC} & = 4902.8
\end{align*}
\]
### Table 4.6 (Continued)

<table>
<thead>
<tr>
<th></th>
<th>Model 1 (Unconditional)</th>
<th>Model 2 (Diary Measures)</th>
<th>Model 3 (Diary + In-person Measures)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BIC</strong></td>
<td>4908.3</td>
<td>4835.9</td>
<td>4835.0</td>
</tr>
<tr>
<td><strong>Pseudo-$R^2$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between individuals</td>
<td>-</td>
<td>.59</td>
<td>.38</td>
</tr>
<tr>
<td>Within individual</td>
<td>-</td>
<td>.13</td>
<td>-</td>
</tr>
</tbody>
</table>

*Note.* Unstandardized parameter estimates were displayed; Level 2 variables were grand-mean centered; FSI = Fatigue Symptom Inventory; CES-D = Center for Epidemiological Studies-Depression.  
* $p < .05$. ** $p < .01$. 

Table 4.7

Correlations among Daily Subjective Cognitive Function and Predictors

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Daily subjective cognitive function</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Daily negative affect</td>
<td>-.48**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Daily positive affect</td>
<td>.65**</td>
<td>-.49**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Daily fatigue</td>
<td>-.62**</td>
<td>.53**</td>
<td>-.44**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Daily memory aid usage</td>
<td>-.36*</td>
<td>.28</td>
<td>-.44**</td>
<td>.41**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Daily memory lapse</td>
<td>-.58**</td>
<td>.51**</td>
<td>-.39**</td>
<td>.56**</td>
<td>.42**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Age</td>
<td>.11</td>
<td>-.22</td>
<td>.15</td>
<td>-.12</td>
<td>.26</td>
<td>.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Education</td>
<td>-.14</td>
<td>.04</td>
<td>-.26</td>
<td>-.15</td>
<td>.01</td>
<td>-.07</td>
<td>-.35*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Time since treatment</td>
<td>-.21</td>
<td>.10</td>
<td>-.14</td>
<td>.20</td>
<td>.10</td>
<td>.07</td>
<td>.01</td>
<td>-.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. FACT-cog</td>
<td>.41**</td>
<td>-.49**</td>
<td>.31*</td>
<td>-.59**</td>
<td>-.34*</td>
<td>-.77**</td>
<td>.15</td>
<td>.16</td>
<td>.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. CES-D</td>
<td>-.46**</td>
<td>.58**</td>
<td>-.39**</td>
<td>.68**</td>
<td>.30*</td>
<td>.63**</td>
<td>-.09</td>
<td>-.17</td>
<td>-.02</td>
<td>-.79**</td>
<td></td>
</tr>
</tbody>
</table>

*Note. Within person correlations (N = 47); EOD = end of day; FACT-cog = Functional Assessment of Cancer Treatment cognitive subscale; CES-D = Center for Epidemiological Studies-Depression.*

* p < .05. ** p < .01.
### Table 4.8

**Fixed and Random Effects of Daily Subjective Cognitive Function**

<table>
<thead>
<tr>
<th>Fixed Effects</th>
<th>Model 1 (Unconditional)</th>
<th>Model 2 (Diary Measures)</th>
<th>Model 3 (Diary + In-person Measures)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate (SE)</td>
<td>Estimate (SE)</td>
<td>Estimate (SE)</td>
</tr>
<tr>
<td>Intercept</td>
<td>61.56** (2.44)</td>
<td>55.06** (5.10)</td>
<td>58.29** (6.00)</td>
</tr>
<tr>
<td>Level 1 (day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study day</td>
<td>-</td>
<td>0.31** (0.11)</td>
<td>0.31** (0.11)</td>
</tr>
<tr>
<td>Negative affect</td>
<td>-</td>
<td>-0.01 (0.05)</td>
<td>-0.01 (0.05)</td>
</tr>
<tr>
<td>Positive affect</td>
<td>-</td>
<td>0.20** (0.05)</td>
<td>0.20** (0.05)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-</td>
<td>-0.15** (0.03)</td>
<td>-0.15** (0.03)</td>
</tr>
<tr>
<td>Memory aid usage</td>
<td>-</td>
<td>-0.53 (1.27)</td>
<td>-0.53 (1.27)</td>
</tr>
<tr>
<td>Memory lapses</td>
<td>-</td>
<td>-1.62** (0.42)</td>
<td>-1.62** (0.42)</td>
</tr>
<tr>
<td>Level 2 (person)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative affect – person average</td>
<td>-</td>
<td>0.12 (0.16)</td>
<td>0.13 (0.17)</td>
</tr>
<tr>
<td>Positive affect – person average</td>
<td>-</td>
<td>0.32* (0.13)</td>
<td>0.26 (0.14)</td>
</tr>
<tr>
<td>Fatigue – person average</td>
<td>-</td>
<td>-0.10 (0.09)</td>
<td>-0.13 (0.10)</td>
</tr>
<tr>
<td>Memory aid usage – person average</td>
<td>-</td>
<td>3.99 (5.16)</td>
<td>3.08 (5.46)</td>
</tr>
<tr>
<td>Memory lapses – person average</td>
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<td>-1.89 (1.39)</td>
<td>-3.61 (1.83)</td>
</tr>
<tr>
<td>Age</td>
<td>-</td>
<td>-</td>
<td>0.12 (0.31)</td>
</tr>
<tr>
<td>Education</td>
<td>-</td>
<td>-</td>
<td>-0.51 (0.70)</td>
</tr>
<tr>
<td>Time since treatment</td>
<td>-</td>
<td>-</td>
<td>-0.09 (0.22)</td>
</tr>
<tr>
<td>FACT total</td>
<td>-</td>
<td>-</td>
<td>-0.12 (0.10)</td>
</tr>
<tr>
<td>CES-D total</td>
<td>-</td>
<td>-</td>
<td>-0.08 (0.35)</td>
</tr>
<tr>
<td>Random effects</td>
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<td></td>
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</tr>
<tr>
<td>N, Level 2</td>
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<td>47</td>
<td>47</td>
</tr>
<tr>
<td>N, Level 1</td>
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<td>574</td>
<td>574</td>
</tr>
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<td>Intercept (τ₀₀)</td>
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<td>93.46**</td>
<td>85.68**</td>
</tr>
<tr>
<td>Residual (σ²)</td>
<td>117.21**</td>
<td>100.39**</td>
<td>100.41**</td>
</tr>
<tr>
<td>Fit Statistics</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Deviance (-2LL)</td>
<td>4519.9</td>
<td>4391.2</td>
<td>4387.6</td>
</tr>
<tr>
<td>AIC</td>
<td>4525.9</td>
<td>4417.2</td>
<td>4423.6</td>
</tr>
<tr>
<td>BIC</td>
<td>4531.5</td>
<td>4441.2</td>
<td>4456.9</td>
</tr>
</tbody>
</table>
Table 4.8 (Continued)

<table>
<thead>
<tr>
<th></th>
<th>Model 1 (Unconditional)</th>
<th>Model 2 (Diary Measures)</th>
<th>Model 3 (Diary + In-person Measures)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pseudo-$R^2$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between individuals</td>
<td>-</td>
<td>.65</td>
<td>.08</td>
</tr>
<tr>
<td>Within individual</td>
<td>-</td>
<td>.14</td>
<td>-</td>
</tr>
</tbody>
</table>

*Note.* Unstandardized parameter estimates are displayed; Level 2 were grand-mean centered with the exception of memory aid usage; FACT = Functional Assessment of Cancer Treatment; CES-D = Center for Epidemiological Studies-Depression.

* $p < .05$. ** $p < .001$. 


Chapter Five: Discussion

As cancer survival rates continue to increase there is a need to focus on life after cancer. Self-reports of memory and attention difficulties and fatigue are common quality of life concerns for breast cancer survivors but less is known regarding prevalence and predictors of these problems in daily life. This dissertation expanded the literature on fatigue and subjective cognitive function after cancer treatment using data from daily diary assessments. Specifically, our findings highlight both which individuals are at risk for high levels of fatigue and subjective cognitive problems in daily life and types of days when fatigue is higher and subjective cognitive problems are worse. Further, QoL concerns were reported up to three years after treatment among a sample of breast cancer survivors.

Daily Fatigue

The present study evaluated within-person and between-persons relationships between daily fatigue and diary measures, as well as associations with in-person measures (e.g., retrospective questionnaires and demographic characteristics). Variability in daily fatigue was largely between-persons (67.8%), attributed to individual differences. Diary measures explained a substantial amount of the variance in daily fatigue, 59% between-persons and 13% within-persons. Of the daily factors examined, greater negative affect and worse subjective physical functioning were most consistently associated with fatigue. Previous research has linked fatigue with negative affect (Carpenter et al., 2001) and worse physical function (S. L. Curran et al., 2004; Mehnert et al., 2007) at the between-persons level, whereas our study detected within-person influences on daily fatigue. As expected, at the within-person level, daily negative affect
(i.e., depressive symptoms, anxiety, anger, unhappiness, and frustration) was associated with 
daily fatigue. On days when survivors reported elevated levels of negative affect she also tended 
to rate fatigue as higher.

Previous research has established an association between two aspects of physical function - pain and general physical health - and fatigue (Jones et al., 2016; Servaes et al., 2007). At the 
within-person level, pain was related to fatigue and was consistent with previous research (S. L. 
Curran et al., 2004). That is, on days when survivors reported greater pain, they tended to also 
report higher levels of fatigue that day. Our findings also support a concurrent, within-person 
association between fatigue and a marker of physical health. At the within-person level, on days 
when physical health was rated as better survivors also rated fatigue as lower.

Additionally, another aspect of daily physical function, physical activity, was examined 
as a predictor of daily fatigue. Findings of no associations, within- or between-persons, between 
physical activity and fatigue were contrary to expectations based on previous research (Jacobsen 
et al., 2007; Minton et al., 2013; Mormont et al., 2000). The assessment of physical activity is a 
potential explanation. We operationalized physical activity as the total amount of time (in 
minutes) engaging in moderate to vigorous activity that day, which may not be a sensitive 
enough measure of activity. For instance, participants were instructed to report any physical 
activity when they were active for longer than 10 minutes at a time. Despite engaging in activity, 
participants that did not reach the 10 minute threshold may report less activity or no activity that 
day. Further, type of activity was not accounted for, only level of exertion, which may not 
capture the entire experience. Objective measures of activity, such as those available from 
wearable sensors, would contribute additional information about activity levels and provide a 
comparison for self-report measures.
Including between-person influences (e.g., demographic and clinical characteristics, retrospective fatigue) from the in-person visit did not significantly change the relationships between diary measures and daily fatigue. In regards to within-person findings, this suggests that individual differences in demographic and clinical characteristics and retrospective questionnaires did not account for within-persons associations. Between-person effects of the person-averages of daily variables remained unrelated to daily fatigue across the study. Individual differences in retrospective fatigue, corresponding to the week prior to the daily diary portion of the study, were predictive of daily fatigue across the study. At the between-person level, survivors who recalled higher levels of fatigue prior to the study tended to report higher levels of fatigue across the two weeks. There are several possible explanations for this consistency. Fatigue levels may be consistent across short periods of time (e.g., less than a month). Another explanation is that fatigue a persistent problem for some survivors regardless of the timeframe in which it assessed. Our finding of an association between time since treatment was completed and fatigue was in contrast to previous studies that found no relationship (Mehnert et al., 2007; Servaes et al., 2007). At the between-person level, survivors who had completed treatment longer ago (in months) tended to report higher levels of fatigue. We did not observe an association between daily fatigue and age, education, and depressive symptoms from the week prior.

**Daily Subjective Cognitive Function**

Subjective cognitive function represented multiple aspects of daily cognition (i.e., memory, mental sharpness, and thinking speed) in the current study. We examined the within-person and between-persons relationships between daily subjective cognitive function and diary measures, along with associations with in-person measures (e.g., retrospective questionnaires and
demographic characteristics). The majority of the variance in daily subjective cognitive function was between-persons (69.7%). Diary measures explained a substantial amount of variance in daily subjective cognitive function, 65% between-persons and 14% within-persons. Of the daily factors examined, positive affect, fatigue, and memory lapses were most consistently associated with subjective cognitive function.

There is an extensive body of research connecting mood and fatigue to subjective cognitive function among cancer survivors. From this research it is evident that at the between-person level, better mood is associated with better subjective cognitive function (Pullens et al., 2010; Rey et al., 2012; Shilling & Jenkins, 2007). Our study found support for this relationship at the within-person level. We found that on days when positive affect (the day mean of happiness, joyfulness, pleasure, and enjoyment) was rated as higher, better subjective cognitive function was reported. Fatigue is another well-established as a predictor of subjective cognitive function (Mehnert et al., 2007; Rey et al., 2012; Ribi et al., 2012). Our study provides further support for the connection and the understanding that tiredness and fatigue likely underlie cognition (Dijk et al., 1992). At the within-person level, on days when higher levels of fatigue were reported subjective cognitive function was rated as worse that day. Memory performance is one component of subjective cognitive function, and potentially the easiest for participants to identify. At the within-person level, memory lapses were associated with daily subjective cognitive function. On days when a survivor reported more memory lapses she also rated subjective cognitive function as worse.

In this study, between-person predictors from the diary and in-person measures were not associated with subjective cognitive function. That is, person-averages of daily variables were not associated with subjective cognitive function at the between-persons level, with the
exception of positive affect in the model that included only diary measures. However, this association was no longer significant when demographic and clinical characteristics were included. Contrary to predictions, depressive symptoms and retrospective subjective cognitive function corresponding to the week prior to the daily diary portion of the study were not related to daily subjective cognitive function. In general, the timeframes of questionnaire measures and daily diaries do not correspond to the same experiences which may make it difficult to observe an association. That is, the retrospective questionnaire assessed the week prior to the daily diary period. Our lack of an observed association with retrospective depressive symptoms could be the inclusion of daily negative affect, which included depressive symptoms. That is, fatigue and negative affect assessed on the same day are more closely related. In regards to retrospective subjective cognitive function, another potential explanation is that the FACT-Cog total score may have been too broad a measure. A subscale focusing on perceived cognitive abilities or impairments may relate better to daily subjective cognitive function items used during the diary portion of the study.

Individual differences in demographic and clinical characteristics (i.e., age, education, and time since treatment completed) were also unrelated to daily subjective cognitive function across the study. Time since treatment completed was unable to predict subjective cognitive function experienced in daily life. Our study contributes to the body of literature that suggests the course of subjective cognitive dysfunction is difficult to discern (Pullens et al., 2010). Taken together, our findings do not suggest that individual differences in demographic and clinical characteristics are able identify survivors at greater risk for worse subjective cognitive function.
**Function in Daily Life**

Much of the previous research in survivorship has been limited to traditional in-person measures with little focus on daily life. Findings from this study support the movement towards examining function in natural settings, rather than relying on retrospective self-report measures. Importantly, traditional measures largely ignore variations that occur across days, but commonly rely on survivors’ self-assessments experiences that occurred over the past week. Responses depend on an individual’s perception and recollection of the experience which is susceptible to bias (P. C. Stone & Minton, 2008). Our study combined both diary data and retrospective questionnaire data to examine the within- and between person influences on daily fatigue and subjective cognitive function. We demonstrated that to better understand fatigue and subjective cognitive function in daily life more frequent measurement, such as daily diaries, is required.

**Strengths and Limitations**

Strengths and limitations of this dissertation should be acknowledged. First, a strength was the use of daily diary surveys that allowed us to follow survivors for 14 days and examine QoL issues that occurred in natural settings. Daily diary surveys should reduce retrospective bias by shortening reporting windows (A. A. Stone & Shiffman, 2002). Rather than participants recalling fatigue over the past week they only had to recall experiences from that day. Our methods allowed us to examine both individual differences and within-person fluctuations that contributed to daily QoL issues. This is among the first studies to examine within-person relationships between QoL issues and previously identified related factors (e.g., negative affect, pain). Although daily fatigue and daily subjective cognitive function were measured with few items, there was sufficient within-person variability to detect effects at the within-person level. Another strength was that average compliance among this sample was close to 90%, although
two participants completed less than 60% of surveys; these participants were included in analyses in order to represent individuals with low compliance. We also had no attrition during the 14 day dairy study period, therefore there were no differences between participants that completed versus those that did not.

Several limitations of our study should be acknowledged. First, our sample was female, predominantly white, breast cancer survivors. This limits the generalizability to males, and to other cancers. This is a widespread issue in survivorship research. However, the prevalence of breast cancer and high rates of survival make it an ideal population to study. Expanding this research to other cancers such as prostate and colorectal would remedy the issue and provide information about how these issues operate in daily life across cancers.

Despite the majority of variance being between-persons few demographic, clinical, and retrospective questionnaire variables were significant predictors of daily fatigue and subjective cognitive function. We did not find any associations between demographic variables (i.e., age and education) and daily variables of fatigue and subjective cognitive function. Our ability to detect individual differences was partially dependent upon the number of level-2 units (Hoffman, 2015; Hox, 2010). That is, although we had 574 observations in total, we only had 47 survivors for our tests of individual differences. In addition, a restricted age range and overall high educational attainment of the sample may have reduced our ability to observe associations between these demographic characteristics and daily QoL. An expanded age range that included adults over the age of 65 would improve generalizability and provide important information about older cancer survivors as this population continues to grow. An alternative explanation is that daily reported measures were more consistently related to our daily outcomes indicating that relationships at the same level (i.e., daily) were stronger and more predictive of outcomes. Daily
experiences may have a greater influence over daily QoL. These relationships may occur on a short time scale, and the daily variability is important. For example, variation in negative affect across days is different than being higher in negative affect compared to others.

Another limitation was the time of measurement. In the current study we opted to use diary surveys completed at the end of the day. Reports made at the end of the day are susceptible to retrospective bias, although less so than traditional retrospective questionnaires. Recent or peak (e.g., a time when pain was particularly high that day) events may influence reporting. Additionally, daily variables were reported concurrently each night which does not permit us to determine causation. The use of daily diaries, rather than the momentary data collected throughout the day, captured variation across days but not variability throughout the day. Recent evidence suggests that EMA and diary reports of mood, fatigue, and activities completed on the same day were associated and similar (Kim, Kikuchi, & Yamamoto, 2013). Only small differences in reports were detected, diary reports of activities were shorter in duration and depression was higher compared to EMA reports (Kim et al., 2013). Lastly, no baseline data was available to compare change. Therefore, we were only able to examine individual differences and day-level effects.

**Future Directions**

Our results indicate areas where future work is needed. Fatigue not only interferes with physical function, but may also impact daily subjective cognitive function (S. M. Phillips, Lloyd, Awick, & McAuley, 2017). Moving forward, future work should explore the connections between daily QoL issues. This information will be important for survivors that are experiencing worse fatigue and subjective cognitive function in daily life compared other survivors. Additionally, although only the retrospective fatigue questionnaire was a significant predictor of
fatigue across the study there is utility in traditional validated measures. Retrospective fatigue measures administered once could be used to determine which survivors should be followed with daily diaries (i.e., those reporting higher fatigue compared to other survivors). The present analyses were able to examine within-person and between-person associations. However, assessments would ideally occur pre-treatment, during treatment, and after treatment has completed to examine change. In addition, common risk factors such as pre-cancer cognitive function, life-style factors, and genetic factors should be collected and controlled for when available to help elucidate inconsistent relationships (Wefel et al., 2015).

Using methodologies currently available it is possible to survivors at highest risk for issues in order to reduce long-term disability and improve QoL (Wefel et al., 2015). Currently, interventions to improve cognitive outcomes post-treatment include web-based cognitive training (Damholdt et al., 2016), increased physical activity and yoga (Derry et al., 2015), and pharmacology (Wefel et al., 2015). One approach to delivering interventions is ecological momentary intervention (EMI). EMI provides an intervention or tailored support (content and timing) in the real-world where the target behavior occurs and has been used to increase physical activity and reduce anxiety (Heron & Smyth, 2010). Our results indicated that daily mood corresponds with fatigue and subjective cognitive function. A tailored intervention for breast cancer survivors to increase positive affect and decrease negative affect could be beneficial. Further, assessments can increase awareness of a behavior and potential triggers, track past behaviors, and provide information about high risk contexts (Runyan & Steinke, 2015). Daily diary assessments could be used in combination with EMI to improve daily fatigue and subjective cognitive function among breast cancer survivors. Although delivering interventions
in this form is likely the future, specific aspects of interventions still need to be determined (e.g.,
length of intervention, frequency and length of each assessment) (Runyan & Steinke, 2015).

**Clinical Implications and Considerations**

Our findings have clinical implications for breast cancers survivors experiencing
decreased QoL post-treatment. Daily variation in fatigue and subjective cognitive functioning
has received little attention in the existing survivorship research. Identifying sources of
variability will provide areas of daily life on which to intervene, and this study contributed to this
body of knowledge at the within-person level. Further, survivors want self-perceived changes,
especially subjective cognitive dysfunction, to be acknowledged by doctors and informed of
these potential changes prior to treatment (Boykoff et al., 2009). Appropriate coping methods
could then be provided to patients undergoing chemotherapy and after treatment. The questions
remain: who is best suited to provide care for post-treatment side-effects and when this care is
appropriate (Rowland & Bellizzi, 2014). Educating high risk survivors may begin at diagnosis to
inform patients on treatment decisions and the associated QoL issues. In the future, this will
guide treatment options and continue monitoring QoL during administration (Curt et al., 2000).

Further, understanding these relationships in daily life will be increasingly important as
cancer survivors age. Due to the aging of the population, increased cancer risk with age, and
improved survival rates, individuals over age 65 currently make up 2/3 of cancer survivors,
representing a significant public health concern (Bluethmann et al., 2016). Previous research has
also found the older breast cancer survivors report higher levels of anxiety, depression, and
fatigue and lower levels of QoL compared to healthy controls (Mandelblatt et al., 2014). These
self-reported experiences are associated with higher fatigue and worse subjective cognitive
function, as demonstrated in this study. Future work should follow survivors as they age to disentangle cancer- and age-related effects.

**Summary**

A primary goal of this dissertation was to examine QoL issues among a sample of breast cancer survivors. Specifically, we focused on daily life after treatment when survivors experience a decrease in physical, cognitive, and social function. We accomplished this using data from daily diaries. Our findings suggest that diary surveys completed once per day were able to capture the relationships between fatigue and subjective cognitive function and daily reported experiences. Taken together, our findings represent long-term QoL issues that persists up to 3 years after treatment for some survivors. Further research after treatment is needed to address these issues.
References


Appendix A:

IRB Approval Letter

2/1/2018

Brent Small, Ph.D.
School of Aging Studies
4202 E Fowler Ave., MHC1300
Tampa, FL 33620

RE: Expedited Approval for Continuing Review
IRB#: CR3_Pro00015048
Title: Daily Cognitive Functioning Among Cancer Survivors

Study Approval Period: 2/27/2018 to 2/27/2019

Dear Dr. Small:

On 1/31/2018, the Institutional Review Board (IRB) reviewed and APPROVED the above application and all documents contained within including those outlined below.

Approved

Item(s): Protocol

Document(s):

2016.06.23 V10 Moffitt protocol_clean.docx

The IRB determined that your study qualified for expedited review based on federal expedited category number(s):
(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

As the principal investigator of this study, it is your responsibility to conduct this study in accordance with USF HRPP policies and procedures and as approved by the USF IRB. Any changes to the approved research must be submitted to the IRB for review and approval by an amendment. Additionally, all unanticipated problems must be reported to the USF IRB within five (5) calendar days.

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

Sincerely,

Kristen Salomon, Ph.D., Vice Chairperson USF Institutional Review Board