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THE IMPACT OF CHEMOTHERAPY AND RADIOTHERAPY FOR BREAST CANCER ON COGNITION AND FUNCTIONAL PERFORMANCE: A COMPARATIVE ANALYSIS OF SURVEY DATA TAKEN AT THREE TIME POINTS POST-TREATMENT

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

by

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Dedication

This dissertation is dedicated to my husband, Sean Andrew Potter and our boys Eamon, Declan and Jesse.

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List of Abbreviations

Activities of Daily Living	ADL's
Aromatase Inhibitors	AIs
Central Nervous System	CNS
Computer Adaptive Testing	CAT
Functional Assessment of Cancer Therapy- Cognition version 3	FACT-Cog3
Ductal carcinoma *in situ*	DCIS
Human epidermal growth factor	HER2
Inflammatory breast cancer	IBC
Institute of Medicine	IOM
Institutional Review Board	IRB
Instrumental Activities of Daily Living	IADL's
International Classification of Functioning, Disability and Health	ICF
International Cognition and Cancer Task Force	ICCTF
Invasive ductal carcinoma	IDC
Invasive lobular carcinoma	ILC
Lobular carcinoma *in situ*	LCIS
Model of Human Occupation	MOHO
National Cancer Institute	NCI
National Comprehensive Cancer Network	NCCN

National Institute of Health	NIH
Post breast cancer treatment cognitive impairment	PBCCI
Patient-Reported Outcomes Measurement Information System	PROMIS®
Pathologic Complete Response	pCR
Research Electronic Data Capture	REDCap™
Virginia Commonwealth University	VCU
Young Survival Coalition	YSC

Abstract

THE IMPACT OF CHEMOTHERAPY AND RADIOTHERAPY FOR BREAST CANCER ON COGNITION AND FUNCTIONAL PERFORMANCE: A COMPARATIVE ANALYSIS OF SURVEY DATA TAKEN AT THREE TIME POINTS POST-TREATMENT

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

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Cognitive impairment related to treatment for breast cancer, affects as many as 75% of patients in study samples (Jansen, Cooper, Dodd & Miaskowski, 2011). Deficits in the cognitive domains of short-term memory, attention, speed of information processing, judgment, reasoning, spatial attention, and verbal memory have been documented. The extent to which these deficits impact functional performance within this population has not yet been quantified. The purpose of this study was to investigate the impact of breast cancer on self-reported cognition and functional performance in the six months post-completion in two groups of breast cancer survivors, a chemotherapy group and chemotherapy and radiotherapy group. Cognition and functional performance were measured with the Patient Reported Outcomes Measurement Information System (PROMIS®). Cognition was measured in terms of abilities and concerns. Functional performance measures addressed the constructs of physical function, ability to

participate in social roles and activities, and satisfaction with participation in social roles and activities.

Sixteen female participants (ages 28-45) completed online surveys three weeks following the conclusion of chemotherapy or radiotherapy and three and six months later. Linear mixed-effects models were used to analyze changes over time within groups and compare differences between groups. Over the six months post-treatment the chemotherapy group had a significant improvement in physical function ($p=.0178$), and the chemotherapy + radiotherapy group showed significant gains in the ability to participate in social roles and activities ($p=.0447$). Fatigue was a significant factor in the chemotherapy + radiotherapy group ($p=.015$). No significant differences between groups were noted for changes in cognition, functional performance or psychosocial factors.

This research provides insight into self-reported changes in cognition and functional performance in the six months following breast cancer treatment. Cognition and functional performance appear to be interrelated and impacted by a constellation of factors that occupational therapists and oncology providers need to be aware of in order to best support cancer survivors in the resumption of occupations after treatment. A comprehensive approach to assessment and intervention that considers the complexity of cognitive performance as it relates to physical capacity and concurrent symptoms is recommended.

Chapter 1: Introduction

This chapter summarizes current research on the impact of chemotherapy and radiotherapy on cognition and functional performance among patients with breast cancer. An overview of the problem of post breast cancer cognitive impairment is provided, followed by the purpose and specific aims for this study. The chapter concludes with discussion of the study rationale and a brief introduction to the theoretical underpinnings for this work.

Post Breast Cancer Cognitive Impairment

The relative survival rate for all stages of breast cancer in the United States is 89.5% (Howlander, et al. 2015). In response, clinicians are expanding care to include recovery and survivorship, including attention to symptoms and sequelae related to cancer treatment (Alfano, Ganz, Rowland & Hahn, 2012). Cognitive problems associated with breast cancer treatment are a major concern for survivors. The "impairment of patients' memory, learning, concentration, reasoning, executive function, attention, and visuospatial skills during and after the discontinuation of chemotherapy" is commonly referred to as *chemobrain* or *chemofog* (Argyriou, Assimakopoulos, Iconomou, Giannakopoulou & Kalafonos, 2011, p. 127). Chemotherapy induced cognitive impairment (CICI) and chemotherapy-related cognitive impairment (CRCI) are terms frequently used in the literature (Jansen, Cooper, Dodd & Miaskowski, 2011; Myers, 2009). This terminology originated from early assumptions that chemotherapy is

the cause of treatment-related cognitive impairment. Research has demonstrated that a variety of factors contribute to cognitive impairment, therefore I am using the term post breast cancer cognitive impairment (PBCCI) to better capture the essence of the phenomenon as it is now understood.

The impact of cognitive impairment on the resumption of life activities following cancer treatment is not well quantified or understood. Current research into PBCCI relies heavily on standardized batteries of neuropsychological tests and self-report measures. Standardized neuropsychological testing methods often fail to adequately address the impact of cognitive impairment on functional performance (Baddeley, 2004; Sbordone, 1996; Wilson, 2004). Functional performance encompasses the ability to perform activities of daily living (ADL's), instrumental activities of daily living (IADL's) and social participation. Self-reports of PBCCI frequently describe decreased functioning in these areas that neuropsychological testing fails to uncover (Nelson & Suls, 2013).

The National Comprehensive Cancer Network's (NCCN) guidelines for addressing cancer-related cognitive function recommend occupational therapy as a "first line" intervention to assist individuals experiencing specific functional limitations related to cognitive impairments associated with any type of cancer diagnosis and treatment (Denlinger et al., 2014). Occupational therapists are concerned with the impact of impairment on functional performance and how participation in personally meaningful activities can be improved. The extent to which cognitive impairment post-treatment for breast cancer impairs functional performance is not well documented. This study utilized the Patient Reported Outcomes Measurement Information System

(PROMIS®) to gain a better understanding of any relationship between self-reported cognitive abilities and cognitive concerns with functional performance experienced by breast cancer survivors who have undergone adjuvant chemotherapy as compared to those who have undergone both chemotherapy and radiotherapy.

Breast Cancer

Breast cancer is the most commonly diagnosed cancer among American women and the second leading cause of cancer death. The National Cancer Institute predicted approximately 252,710 new breast cancer diagnoses for 2017 (Howlander, et al. 2017). Men account for 1% of breast cancer cases (Howlander, et al. 2015). There are several different types of breast cancer: Ductal carcinoma *in situ* (DCIS), invasive ductal carcinoma (IDC), lobular carcinoma *in situ* (LCIS), invasive lobular carcinoma (ILC) and inflammatory breast cancer (IBC). Ductal carcinoma is the most common type of breast cancer and begins when the linings of the milk ducts transform into abnormal cancer cells. Lobular carcinoma begins in the lobes of the breast. *In situ* means the cancer is enclosed in either the duct or lobe and has not spread to surrounding tissue. Invasive cancer has spread into other parts of the breast tissue and possibly beyond to other tissues in the body. Inflammatory breast cancer is a rare and aggressive form that is caused by cancer cells blocking the lymph vessels in the skin (National Cancer Institute, 2012).

Breast cancer is staged according to the TNM classification system: (T) the size of the primary tumor, (N) the number of regional lymph nodes where the cancer has spread, and (M) distant spread or metastasis (NCI, 2015). DCIS and LCIS are stage 0. Stages I-IV are summarized in Table 1.

Table 1

Breast Cancer Staging According to the National Cancer Institute

Stage	TNM Description
IA	T<2cm, N=0, M=0
IB	T<2cm, N=small clusters, M=0
IIA	T<2 cm, N=1-3, M=0 or T= 2-5 cm, N=0, M=0
IIB	T=2-5 cm, N=small clusters T=2-5cm, N=1-4, M=0 T>5cm, N=0, M=0
IIIA	N=4-9 with or without tumor or T > 5cm, N=small clusters or T>5cm, N=1-3, M=0
IIIB	T=any size, M=spread to chest wall and/or skin and/or N=9+
IIIC	T=with or without, N=10+ or M: in nodes above or below the collar bone, axilla or near the breast bone
IV	M=other organs in the body

In addition to stages, breast cancer is categorized in groups based on hormone receptor and human epidermal growth factor (HER2) status. Hormone receptor (HR) positive (ER+/ PR+) breast cancers have receptors on the cell walls that are sensitive to naturally occurring estrogen and progesterone. HR negative (ER-/PR-) breast cancer does not have hormone receptors on the outside walls of the cells. The HER2 gene is a

growth promoting protein that helps control breast cell growth (Anderson, Rodenberg & Katki, 2014). In breast cancer that involves the HER+ genotype, there is uncontrolled cell division and rapid growth of cancer cells. Luminal A breast cancer is ER+ and/or PR+ and HER2- and accounts for approximately 70% of diagnosed breast cancer (Anderson et al., 2014). Luminal B breast cancer is ER+ and/or PR+ and HER 2+. This is an aggressive type of cancer and accounts for approximately 10% of all breast cancers (Anderson et al., 2014). HER2 type breast cancer is ER-/PR- and HER2 + and makes up 5% of breast cancers (Anderson et al., 2014). Basal-like or triple negative breast cancer (ER-/PR-/HER2-) makes up 12% of breast cancers and is more aggressive than the Luminal A and B types (Anderson et al., 2014). These typologies, along with tumor profiling are used to guide treatments for breast cancer.

Treatment for breast cancer may include surgery, radiation, hormone therapy, chemotherapy and/or targeted therapy (NCI, 2015). Surgery is used for stages I-IIIA to remove the primary tumor. Surgery may be a lumpectomy, breast conserving tumor removal, or mastectomy. Sentinel lymph node biopsy is used in conjunction with surgery to determine if cancerous cells have spread to the lymph system. Physical side effects of surgery include pain, tenderness and the development of scar tissue, which may result in limited range of motion and lymphedema. Surgery has traditionally preceded other types of adjuvant treatment for breast cancer. Recently, preoperative or neoadjuvant chemotherapy has come into greater use. The goal of neoadjuvant treatment is to shrink the tumor, which may make an unresectable tumor operable or downstage a tumor to allow for breast conservation (Schott & Hayes, 2012).

The goal of radiation therapy is to destroy any remaining disease in the breast tissue after surgery and prevent local recurrence. Short-term side effects of radiation may include swelling, skin changes such as burning, and fatigue. Possible long-term side effects of radiation are nerve damage in the arm, brachial plexopathy, lymphedema, and damage to the lungs and heart (Meric et al., 2002). Radiation treatment has been implicated in cognitive impairment, affecting verbal learning and memory, delayed recall, visual perception, and visual attention (Nguyen et al., 2013; Shibayama et al., 2014). Subsequent cognitive impairment may be related to fatigue or induced inflammation that elevates proinflammatory cytokines (Shibayama et al. 2014).

Hormone therapy is a systemic therapy that is used with ER+ breast cancer. The drug, Tamoxifen, works to reduce the risk for recurrence by blocking estrogen receptors (Dalmau, Armengol-Alonso, Muñoz, & Seguí-Palmer, 2014). Side effects of tamoxifen include blood clots and bone thinning. Aromatase inhibitors (AIs), Femara, Arimidex and Aromasin, prevent the body from making estrogen in post-menopausal women by blocking an enzyme in fat tissue. Side effects of AIs include muscle pain, joint stiffness and pain. (Niravath, 2013). Hormonal treatment is recommended for five years or more. Hormonal treatments are associated with declines in cognition, specifically in the domains of visual and verbal memory (Bender et al., 2009). Functional impairment related to the use of hormonal treatments is not documented in published literature.

Chemotherapy is a systemic treatment that kills fast growing cancer cells or stops them from dividing. Chemotherapy for breast cancer often consists of a combination of drugs given intravenously. There are five common regimes of chemotherapy: cyclophosphamide, doxorubicin and fluorouracil (CAF),

cyclophosphamide and doxorubicin (AC), cyclophosphamide, doxorubicin and taxol (AC-T), docetaxel, doxorubicin and cyclophosphamide (TAC) and taxotere or docetaxel and cyclophosphamide (TC) (NCI, 2015). Neoadjuvant chemotherapy is administered prior to the surgical removal of the primary tumor. Post-operative adjuvant chemotherapy is administered after surgical removal of the primary tumor. During chemotherapy individuals may experience hair loss, mouth sores, loss of appetite, nausea and vomiting, and fatigue. Long-term side effects of chemotherapy may include: menstrual changes, neuropathy, heart damage, hand-foot syndrome, decrease in cognitive functioning and fatigue (Howell, Jones & James, 2013). Neo-adjuvant chemotherapy is administered prior to surgery to shrink the tumor in more aggressive forms of breast cancer (stage III-IV). Targeted chemotherapies such as Trastuzumab and Pertuzumab block the HER-2 protein and are only used in individuals who test HER2+. Heart damage, hand and foot syndrome and fatigue are side effects associated with targeted chemotherapy.

Purpose

The original purpose of this study was to compare any changes in self-reported cognition to self-reported changes in functional performance among individuals with breast cancer following the completion of adjuvant chemotherapy or radiotherapy for breast cancer. Due to difficulty recruiting individuals receiving only radiotherapy and to maintain two groups for comparison, changes were made in the study design to include individuals receiving both chemotherapy and radiotherapy. This change limits the ability to make conclusions regarding the impact of radiation alone.

The practical goals of this study are to offer evidence-based guidance to occupational therapists and other clinicians who serve community dwelling breast cancer survivors regarding the functional impairments, activity limitations and participation restrictions that survivors face in order to develop more meaningful and effective assessment methods and treatment plans. The original specific aims of this survey research with the changes in italics were:

1. Measure changes in cognition for the chemotherapy and *chemotherapy* + radiotherapy groups over the 6 months following the completion of treatment.
2. Compare any changes in cognition between the chemotherapy and *chemotherapy* + radiotherapy groups.
3. Measure changes in functional performance for the chemotherapy and *chemotherapy* + radiotherapy groups over the 6 months following the completion of treatment.
4. Compare any changes in functional performance between the chemotherapy and *chemotherapy* + radiotherapy groups.
5. Compare any changes in cognition and changes in functional performance within each treatment group.
6. Compare any changes in cognition and changes in functional performance between the treatment groups.

In this study, cognition was operationalized as self-reported cognitive abilities and concerns. Functional performance was operationalized as self-reported physical function and social participation. The study assessed cognition and functional performance at three time points for women who have completed either chemotherapy

or chemotherapy + radiation therapy for breast cancer, comparing these parameters over time within groups and between groups. Assessment occurred at the conclusion of neoadjuvant chemotherapy (if not radiotherapy), adjuvant chemotherapy (if not radiotherapy), or radiation and 3 and 6 months afterward. The study used the Patient Reported Outcomes Measurement Information System (PROMIS®) to measure self-reported changes in cognition and functional performance.

The secondary aims for this study were:

7. Compare changes in cognition and functional performance with mediating factors, including anxiety, depression, fatigue, sleep disturbance and pain interference.

The Conceptual Model of Chemotherapy-Related Changes in Cognitive function recognizes the complex interplay of multidimensional factors affecting cognition after treatment (Hess & Insel, 2007). This model is addressed further in the literature review chapter. The PROMIS-57 scales of anxiety, depression, fatigue, sleep disturbance and pain interference were used to gather data about these mediating factors. Post-Hoc analysis explored trends over time in cognition and functional performance.

8. Compare caregiver/significant others perceptions of cognitive impairment with self-reports of breast cancer survivors.

Originally, I had hoped to compare subject self-ratings on the PROMIS instrument with caregiver surveys using the Patient Competency Rating Instrument, Caregiver Version (Wilson, 2004). This aim was not carried out. Caregiver referral was optional in the study. Only three participants provided contact information for a caregiver. No caregivers replied to the email invitations for the study.

Rationale

Cognitive impairment associated with treatment for cancer is receiving significant attention within the literature and the oncology, rehabilitation and survivorship communities (Denlinger, et. al., 2014; Player, Mackenzie, Willis & Loh, 2014; Wefel, Vardy, Ahles & Schagen, 2011). The greatest attention has been directed to the population of breast cancer survivors. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology- Survivorship: Cognitive Function Version 1.2014 (Denlinger, et. al., 2014) recommend occupational therapy as a first line intervention to address specific functional limitations associated with cognitive dysfunction. Within these guidelines, the lack of screening tools for assessment is acknowledged, and the panel recommends evaluation of cognitive impairment as a way to guide rehabilitation efforts. This study will help to inform the oncology community about any changes in self-reported cognition and functional performance over the six-month time span immediately following the completion of chemotherapy or chemotherapy + radiotherapy for breast cancer.

Theoretical Framework

The Conceptual Model of Chemotherapy-Related Changes in Cognitive Function developed by Hess & Insel (2007) is based on existing knowledge about cognitive impairment associated with all types of cancer. This model defines a constellation of factors and mediators that may lead to cognitive impairments and which result in functional performance limitations and decreased health-related quality of life. This model was expanded by Myers (2009) to include a greater recognition of the interrelationships and impacts of concurrent symptoms such as fatigue, pain and

depression. This study was based on findings by Hess & Insel (2007) and Myers (2009) that a confluence of factors causes PBCCI, and examined the relationship between cognitive changes and functional performance. This relationship is not well defined within either the original or revised model. The International Classification of Functioning, Disability and Health Core Set for breast cancer (World Health Organization, 2001), and the Model of Human Occupation (MOHO) (Kielhofner, 2008) served as lenses to view the relationship between cognitive impairment and functional performance.

Summary

PBCCI is a complex phenomenon and its true impact on functional performance in everyday life is not well understood. This study describes and compares changes in cognition and functional performance that may occur during the six months following the completion of chemotherapy or chemotherapy + radiotherapy for breast cancer. Additionally, this study compares changes in cognition following chemotherapy or chemotherapy + radiotherapy with changes in functional performance. The influence of mediating factors was explored. This study addresses a significant gap in the literature regarding the consequences of changes in cognition related to breast cancer treatment and functional performance. The study offers evidence-based insights on the impact of PBCCI on participation in daily activities that may assist occupational therapists in adapting assessments and interventions that will better assist breast cancer survivors in transitioning back to life's roles and responsibilities after treatment.

Chapter 2: Literature Review

Post breast cancer treatment cognitive impairment (PBCCI) is bothersome and troubling for cancer survivors and poses a challenge to clinicians who wish to determine the nature of its impact on everyday activity. As discussed in this chapter, PBCCI is characterized by deficits in short-term memory, attention, speed of processing information, judgment, reasoning, spatial perception, and verbal/nonverbal memory that may be noted in patients who have undergone treatment for breast cancer. Current research suggests that PBCCI negatively affects the everyday functioning of breast cancer survivors, however, the extent of impact has not been well quantified.

This chapter provides an overview of conceptual models from the disciplines of occupational therapy and oncology nursing that have guided the study. An overview of PBCCI is presented, including postulates of etiology, and domains of cognition that are impaired. Next, commonly reported cognitive sequelae and associated functional limitations are discussed. As noted by occupational therapy researchers Hartman-Maeir, Katz, and Baum (2009): “Cognition is embedded in many aspects of daily life where the individual is required to perform complex activities, formulate goals and carry them out effectively.” Cognitive skills are crucial in everyday living and it is important to understand the impact of PBCCI on everyday functioning in order to develop treatment strategies that will improve the quality of life for breast cancer survivors.

Theoretical Foundations

The Conceptual Model of Chemotherapy-Related Changes in Cognitive Function.

The Conceptual Model of Chemotherapy-Related Changes in Cognitive Function provides a means for examining "chemobrain" in regards to the relationship of physiological and psychosocial factors (Hess & Insel, 2007). Developed in the field of oncology nursing, the purpose of the model is to promote research into the mechanisms of cognition that may serve as a foundation for interventions aimed at improving cognitive functioning and overall wellbeing. This model defines two antecedents: physiological changes resulting from the treatment of cancer and psychosocial factors related to the experience of the diagnosis. Mediators of the physiological factors include the specific chemotherapy drugs used in treatment, their dose and duration, other medications taken, and radiation therapy and its associated toxicities. Psychosocial symptoms include anxiety, stress, depression, and distress (Hess & Insel, 2007). Hess and Insel (2007) point out that this is not an exhaustive list of symptoms. They assert that every individual will have a unique constellation of factors that may affect cognitive function. This model recognizes the potential impact of the following moderators or intervening variables: age, education, intelligence, genetic factors, and coexisting neurocognitive disorders. This model does not specifically include the impact of socio-economic status and social supports. Hess & Insel (2007) specifically note "until the domains of cognitive function affected by cancer treatment are identified and instruments are used consistently to measure the domains, knowledge will not progress concerning the prevention or treatment of the problem" (p. 991). The intention of this

model is to develop an understanding of the consequences of chemotherapy-related declines in cognition in the context of health-related quality of life and functional ability.

Green, Pakenham and Gardiner (2005) proposed a model of subjective and objective cognitive outcomes associated with cancer. The purpose of this model was to stimulate a greater understanding of the relationships among objective and subjective cognitive outcomes. Objective outcomes are those measured by neuropsychological tests and subjective outcomes are based in an individual's perceptions of their quality of life. Cancer treatments, psychosocial factors, and physical health have direct relationships with emotional health and objective cognitive impairment, while emotional health and objective cognitive impairment have a direct relationship to subjective cognitive impairment. In comparison to Hess & Insel's (2007) work, Green et al. (2005) provided a closer look at the relationship between the objective and subjective cognitive differences that are reported. A major shortfall of this model is that Green et al. did not discuss the outcomes of cognitive impairment in terms of function and health-related quality of life.

Myers (2009) (see Figure 1) revised Hess & Insel's (2007) model based on the Theory of Unpleasant Symptoms. This theory describes the interactions and relationships between physiological, psychological and situational factors on performance in the areas of functional status, cognition and physical performance (Myers, 2009). Functional status is similar to the concept of participation from the ICF. Myer's revision of the Hess and Insel model includes an acknowledgement of the interrelationship of the timing, intensity, distress and quality of concurrent symptoms including fatigue, pain, and depression. Additionally, Myers included situational factors

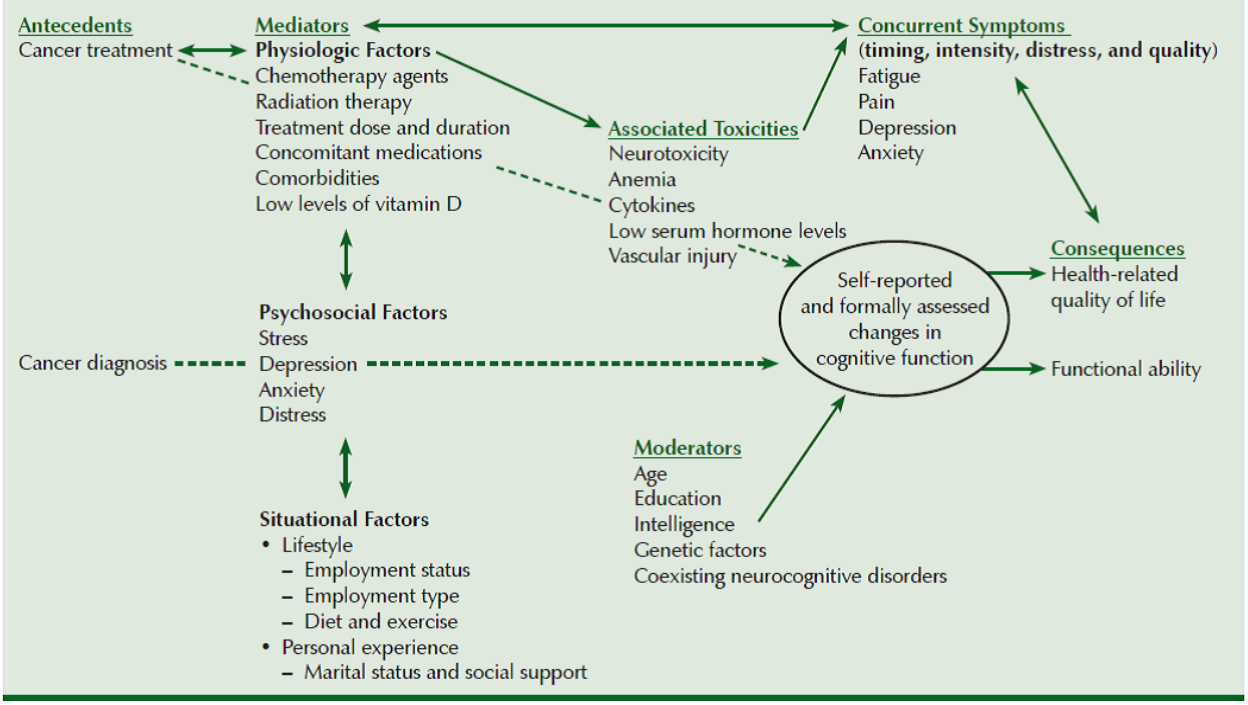

Figure 1: The Revised Conceptual Model of Chemotherapy-Related Changes in Cognitive Function Based on the Theory of Unpleasant Symptoms.

Note. From " A Comparison of the Theory of Unpleasant Symptoms and the Conceptual Model of Chemotherapy-Related Changes in Cognitive Function" by J.S. Myers, 2009, Oncology Nursing Forum, 36(1), p.E8. Copyright 2009 by the Oncology Nursing Society. Reprinted with permission.

as mediators. These include lifestyle factors, employment type and status, diet, exercise, personal experience, marital status, and social support. While the revision provides a more comprehensive view of the "symptom experience of cognitive impairment" it minimizes the multidimensionality of the concurrent symptoms. Both the original and revised model are lacking in definitions of the consequences or outcomes of chemotherapy-related cognitive function. Radiotherapy is viewed as a mediator and its specific role in cognitive impairment is not defined within this model. No models exist to explain the relationship of non-CNS radiotherapy for breast cancer with cognitive impairment. This study addresses the relationship between changes in function and the

cognitive sequelae related to chemotherapy and chemotherapy + radiation treatment for breast cancer. The following theoretical models provide the framework and nomenclature for the functional consequences of PBCCI.

International Classification of Functioning, Disability and Health.

The World Health Organization's (2001) International Classification of Functioning, Disability and Health (ICF), and the Model of Human Occupation (MOHO) (Kielhofner, 2008) provide a foundation for understanding how cognitive impairment post breast cancer impacts everyday functioning. The ICF also provides a systematic and uniform method to view the impact of cancer treatment on activities and participation. The ICF defines impairments as problems in body function or structure such as a significant deviation or loss. Activity is defined as the execution of a task or action by an individual. Participation is involvement in life situations. The ICF also considers the impact of both environmental and personal factors on an individual's activities and participation.

The ICF Core Set for breast cancer was validated in a study by Cooney, Galvin, Connolly & Stokes (2013). In this study, seven focus groups of a total of 34 women with breast cancer were utilized to confirm the ICF categories. Through these focus groups body functions in the categories of attention, memory, perceptual functions, and vision were identified by participants that were not included in the original breast cancer core set. These impairments in body structure and function result in activity limitations, such as the decreased ability to retain and make sense of verbal information and participation restrictions including the decreased ability to engage in work activities and social

relationships (Boykoff, Moieni & Subramanian, 2009; Jim et al., 2012; Player et al., 2014).

The Model of Human Occupation (MOHO).

MOHO offers a holistic mechanism for viewing an individual's function as a person transitions through the cancer diagnosis to survivorship continuum (Kielhofner, 2008). Secondly, MOHO offers an occupation-based perspective on activities and participation that are defined in the ICF model. Occupations are a major contributor to quality of life. According to MOHO, at the point an individual is diagnosed with cancer he/she commences into occupational transition. It is during this time that the individual attempts to maintain or reestablish new activity routines. Under this model, occupations are viewed as a product of three interrelated constructs; volition, habituation, and performance capacity (Kielhofner, 2008).

Volition is defined as "pattern of thoughts and feelings about oneself as an actor in one's world which occurs as one anticipates, chooses, experiences, and interprets what one does" (Kielhofner, 2008, p.5). Humans have an innate desire to participate in occupations and volition encompasses the role an individual's values play in determining the importance of participating and performing in chosen activities. Additionally, an individual's sense of their capacities and effectiveness are important motivators for participation. The volitional process is a cycle, in which an individual makes a choice of occupation, experiences the activity, interprets the experience, and anticipates or reacts to future potentials. The volition for occupation has been demonstrated in a study of Icelandic women with breast cancer (Palmadottir, 2010). Women in this study expressed fear of losing the ability to be in active control of their

functional abilities and emotions. An emergent theme in several works is the desire for individuals with cancer to maintain control in order to participate in activities (Palmadottir, 2010; Sviden, G.A., Tham, K. & Borell, L. 2010).

"Habituation is defined as an internalized readiness to exhibit consistent patterns of behavior guided by our habits and roles and fitted to the characteristics of routine temporal, physical and social environments" (Kielhofner, 2008 p. 18). Role performance is an important construct of habituation that may be impacted by PBCCI. The experience of breast cancer has been demonstrated to negatively impact the roles of parent, spouse, and worker (Boyle, 2006; Maunsell, Brisson, Dubois, Lauzier & Fraser, 1999; Shands, Lewis, Sinsheimer & Cochrane, 2006). Maintaining routines is important to individuals with cancer and individuals become distressed when they are unable to perform daily routines (Cheville, A. 2005: Palmadottir, 2010; Svidén, Tham & Borell, 2010). Resumption of activities of daily living and instrumental activities of daily living are equated with a return or maintenance of normalcy (Lyons, et al. 2010, Svidén, Tham & Borell, 2010).

Performance capacity is comprised of the physical and cognitive abilities an individual possesses that enable him/her to do activities (Kielhofner, 2008). MOHO values the individual's self-perceptions of functional ability. The cognitive functions such as memory, attention, planning, and processing speed all contribute to performance capacity. The three constructs -- volition, habituation, and performance capacity -- integrate with one another in the context of a multilayered environment to result in human occupation that is sustained through an organized pattern. Change occurs when an internal or external component is altered and results in a new pattern.

The ICF is a multidisciplinary model that provides a common framework for international collaboration and understanding of how health conditions relate to disability, while MOHO is discipline-specific to occupational therapy (Kramer, Bowyer & Kielhofner, 2008). Both models recognize the dynamic relationship between factors that contribute to an individual's ability to perform everyday activities and participate in society. In regards to this study, the body function of cognition was studied in association with activities and participation.

The Conceptual Model of Chemotherapy-Related Changes in Cognitive Function and MOHO together provide a conceptual foundation for examining the impact of PBCCI on participation in occupations. The antecedents and mediators have the potential to significantly impact an individual's volition, habits and performance capacity. The physiological factors and associated toxicities result in changes to the cognitive capacities of an individual. To understand the impact, both models call for self-report and formal assessment of the changes. "Persons with cancer frequently gauge their health or quality of life from an occupational perspective. They report feeling healthy or satisfied with life when they can do activities that are important to them" (Lyons, 2006 p. 6). This sense of satisfaction is representative of occupational competence. Occupational competence is a construct of MOHO representing an individual's ability to maintain routines and roles that are in line with one's personal values resulting in personal satisfaction (Kielhofner, 2008).

Post Breast Cancer Treatment Cognitive Impairment

The phenomenon of PBCCI is commonly referred to as "Chemobrain" or "Chemofog". Reports of chemotherapy-related cognitive impairment vary by type of

cancer (Hess & Insel, 2007; Raffa 2011). Cognitive problems are more frequently reported among breast cancer survivors than among ovarian cancer survivors (Hess & Insel, 2007). Cognitive problems have also been reported in populations of chemo-therapy treated patients with brain tumors, lung cancer, acute myeloid leukemia and testicular cancer (Von Ah, Jansen, Allen, Schiavone & Wulff, 2011). Across cancer types and treatments, survivors have reported cognitive problems following treatment in the areas of complex attention, concentration, verbal and visual memory, and processing speed. These symptoms are similar to the cognitive changes often observed in individuals with human immuno-deficiency virus (HIV), mild traumatic brain injury, multiple sclerosis, congestive heart failure, Type 2 diabetes mellitus, chronic obstructive coronary disorder (COPD) and depression (Raffa 2011; Vardy, Rourke & Tannock, 2007). Breast cancer has been the primary focus of research on cancer-related cognitive impairment (Hodgson, Hutchinson, Wilson & Nettleback, 2013; Holohan, Von Ah, McDonald & Saykin, 2013).

Currently, there is not a consensus on the specific etiology of PBCCI. The first published report of cognitive impairment associated with chemotherapy appeared in the early 1980's. Silberfarb (1983) described subtle losses in cognitive flexibility and the ability to think abstractly, as well as problems with word finding and forgetfulness, following chemotherapy for cancer. Initially, these symptoms were attributed to anxiety, depression and a predisposition of age toward delirium in cancer patients, and therefore the complaints of patients were not given much credence by physicians. Silberfarb (1983) likened the cognitive impairment experienced by cancer patients to delirium, "a relative global impairment of memory and thinking." In a second report focused on

breast cancer patients, Silberfarb (1984) hypothesized a multifactorial etiology consisting of chemotherapy, hypercalcemia, metabolic disorders, and cerebral metastasis. He also indicated possible roles of medications prescribed for pain, insomnia and anxiety in causing cognitive impairment.

In 1997, van Dam et al. published a landmark study exploring cognitive function in Dutch women with breast cancer two years after the completion of chemotherapy. Three groups were compared, high-dose chemotherapy plus radiotherapy and tamoxifen (n=34), standard-dose chemotherapy plus radiotherapy and tamoxifen (n=36) and a control group (n=34) of women with stage 1 breast cancer who did not undergo chemotherapy. Concentration and memory problems were reported by a significant number of subjects in each treatment group (*p=.006).* The high dose group showed greater cognitive impairment, higher depression scores, and lower physical function, role function and social function scores. This study was the first to identify a correlation between chemotherapy dosage and "chemobrain" based on the results of neuropsychological testing.

Despite a number of succeeding studies, we still do not know the definitive cause of cognitive changes among chemotherapy patients who have cancer (Ahles, 2012). Many early studies made the assumption that the cause was chemotherapy alone and did not take into consideration that most women receive additional treatments that may include surgery with general anesthesia, radiation therapy and endocrine therapy. A common postulate regarding the cause of "chemobrain" has been that chemotherapy agents cross the blood brain barrier and kill brain cells (Hess & Insel, 2007; Raffa, 2011). This is unlikely, however, since common chemotherapy agents do not easily

cross the blood-brain barrier. This has been a major problem in treating brain metastases (Raffa, 2011). In trying to unravel what is happening in the brain to cause cognitive problems in daily living several other postulates are currently under study. Scientists are investigating direct neurotoxic effects, oxidative stress and DNA damage, induced hormonal changes, immune dysregulation and release of cytokines, blood clotting in small CNS vessels, and genetic predispositions (Ahles, 2012; The International Cognition and Cancer Task Force, 2014). Therefore, the use of a broader term such as PBCCI, is necessary to better describe cognitive impairment related to breast cancer treatment.

Less is known about the role of localized (non-CNS) radiotherapy in PBCCI. Studies of chemotherapy-related cognitive impairment using radiation groups as comparison have shown changes in different cognitive domains unique to each group. Nguyen et al. (2013) found the chemotherapy group to have changes in general cognitive function, working memory, psychomotor speed and executive function with the radiotherapy group demonstrating deficits in verbal learning, visual perception, visual attention and short-term retention. Quesnel et al. (2009) identified changes in self-report cognitive failures, verbal memory, and verbal fluency in the chemotherapy group, and only verbal memory changes in the radiotherapy group. Jim et al. (2009) found attention deficits in the radiotherapy group and impaired episodic memory in the chemotherapy group. One hypothesis is that inflammation resulting from non-brain radiation elevates circulating levels of pro-inflammatory cytokines which in turn are associated with negative changes in cognition, specifically verbal memory and delayed recall (Shibayama et al., 2014). Changes in verbal learning, visual perception, visual attention,

and short-term retention have been noted more than ten years after the completion of radiotherapy for breast cancer (Nguyen et al., 2013). Within the existing literature, it is difficult to delineate changes in cognition related to breast cancer treatment due to the lack of consistency in the domains of cognition that are measured.

An inductive process has been used to identify other contributors to PBCCI, suggesting that fatigue, depression, anxiety and hormonal changes may play either a causative or confounding role in PBCCI. Vearncombe et al. (2009) studied predictors of cognitive decline in 136 Australian women diagnosed with breast cancer and treated with chemotherapy and a control group of 21 women diagnosed with breast cancer that did not receive chemotherapy. The subjects in the chemotherapy group were tested prior to chemotherapy and one month post-chemotherapy. Of the chemotherapy group, 16.9% showed cognitive decline in cognition 4 weeks post conclusion of chemotherapy. Declines in hemoglobin levels and increases in anxiety significantly correlated with multiple test impairment, a decline on two or more cognitive measures within the chemotherapy group. Jansen, Cooper, Dodd and Miaskowski (2011) reported similar findings in regards to a significant decrease in hemoglobin levels in a longitudinal study of 71 women undergoing a chemotherapy regime of AC (standard dose doxorubicin and cyclophosphamide) or AC+T (standard dose doxorubicin and cyclophosphamide + taxane). Significant increases were also noted in depression and fatigue scores, as well as decreases in subjects' self-perception of cognitive functioning. Self-reported cognition was significantly associated with anxiety ($p<0.001$), depression ($p<0.001$) and fatigue ($p<0.001$) using within subject analysis. Bender et al. (2009) concluded that depression was a covariate as women who indicated greater depressive

symptomatology self-reported more cognitive problems. Biglia et al. (2011) found that higher levels of anxiety and depression were correlated with lower self-reported cognition measured on the Functional Assessment of Cancer Therapy Cognitive Scale (Fact-Cog 2).

In regards to hormonal treatments and menopausal status, verbal memory impairments were noted in breast cancer survivors treated with anti-estrogens (tamoxifen, anastrozole or combined treatment) when compared with healthy controls (Jenkins et al. 2004). Bender et al. (2006) found that chemotherapy and tamoxifen combined treatment resulted in greater declines in visual and verbal memory in the year following treatment than in a chemotherapy only group. The subjects in the treatment groups of this study were all pre- or peri-menopausal while the non-treatment group did include women in menopause. Menopausal status differences may have skewed Bender et al.'s results as Jenkins et al. (2006) reported, in their 3-year prospective study of women with breast cancer in the UK, those who experienced treatment-induced menopause were at more risk for cognitive decline. This is an important finding as these women were younger and more likely to be dealing with different life tasks and roles than women who were post-menopausal.

In contrast, Hedayati, Alinaghizadeh, Schedin, Nyman and Albertson's (2012) prospective study found significantly lower memory scores for a chemotherapy group (n=18) but not for a hormone therapy group (n=45) when compared to a healthy control. It is difficult to determine if the changes are related to menopause status or hormonal treatment or both, as Bender et al.'s (2006) study included premenopausal women, Jenkins et al.'s (2006) study included both premenopausal and menopausal subjects

and Hedayati et al.'s sample consisted primarily of women who were in menopause. These studies support a confounding but not a definitive role for hormonal treatments and/or hormonal status in PBCCI. Menopausal status and the use of hormonal treatments were tracked in this study and analyzed as a covariant.

Cognition and Breast Cancer

Changes associated with chemotherapy.

The following domains of cognitive function -- attention, memory, concentration, intelligence, verbal ability, psychomotor function, executive function and spatial ability -- have been assessed to determine levels of cognitive impairment associated with breast and other types of cancers (Falleti, Sanfillipo, Maruff, Weih & Phillips, 2005; Hess & Insel, 2007; Jim et al., 2012). Memory declines have been associated with chemotherapy treatment (Bender et al., 2006; Collins et al. 2013; Ganz et al., 2013; Jim et al., 2009; Mehnert et al., 2007; Nguyen et al., 2013; Quesnel et al. 2009). Working memory deficits in chemotherapy groups were identified in multiple studies (Collins et al., 2013; Mehnert et al., 2007; Nguyen et al., 2013). Declines in the domain of verbal memory were reported by Bender et al. (2006) and Quesnel et al. (2009). Jim et al. (2009) report problems in the domain of episodic memory. Several studies have noted general cognitive decline and self-reports of cognitive dysfunction among subjects who have had chemotherapy (Collins et al., 2013; Ganz et al., 2013; Jenkins et al., 2006; Mehnert et al., 2006; Nguyen et al., 2013; Quesnel et al., 2009). Combined chemotherapy and radiotherapy treatment has been associated with changes in executive functioning, processing speed, subjective memory complaints and mental fatigue (Ganz et al., 2013; Phillips et al., 2012).

A pair of meta-analyses have examined the severity and nature of cognitive findings for individuals with breast cancer treated with chemotherapy. Falleti et al. (2005) analyzed 6 breast cancer studies in order to estimate the magnitude of changes in attention, motor function, memory, executive function, language and spatial ability. Effect sizes were calculated for each domain, with a negative effect size indicating lower performance in the chemotherapy group compared to controls. The effect sizes ranged from small (0.2) to moderate (0.5) with average effect sizes of -0.03 for attention, -0.051 for motor function, -0.26 for memory, -0.18 for executive function, -0.041 for language and -0.48 for spatial ability. There were significant associations between larger effect sizes across all domains and a shorter time since the culmination of chemotherapy, treatment with tamoxifen and younger patient age. The overall results of this meta-analysis suggest mild cognitive impairment (Falleti et al., 2005).

Jim et al. (2012) focused their meta-analysis on long-term changes in cognitive functioning experienced by breast cancer survivors. This meta-analysis included 17 studies, 4 that were included by Falleti et al. (2005) and the remainder which were published after 2004. Sixty-nine neuropsychological tests were utilized across the included studies and were categorized into eight domains: attention, executive functioning, information processing, motor speed, verbal ability, verbal memory, visual memory and visuo-spatial ability. Subjects in the chemotherapy groups demonstrated significantly worse functioning in the domains of verbal ability (*g* -0.19) and visuospatial ability (*g* -0.27) in comparison to controls and pre-chemotherapy baselines. Overall the magnitude of effect sizes across domains was small. This study suggests that cognitive impairment associated with breast cancer is slight. In contrast with Falleti et al. (2005),

there were not significant impairments in motor function, memory and executive function.

The meta-analyses discussed here are limited by the quality of the studies included, the wide variety of assessments used and small sample sizes that ranged from 18-97 subjects in chemotherapy groups. Additionally, there was no way to account for confounding variables, such as depression and anxiety. Jim et al. (2012) note that the longitudinal studies included in their meta-analysis may not have uncovered possible changes in cognitive functioning due to practice effects. Age, education, time since education and endocrine therapy were not associated with worse cognitive functioning by Jim et al. (2012), unlike the results of Falleti et al. (2005).

Changes associated with radiotherapy.

Changes in verbal memory, verbal learning, visual perception, visual attention, and executive functioning are associated with non-CNS radiation treatment for breast cancer (Jim et al., 2009; Nguyen et al., 2013; Phillips et al., 2012; Quesnel et al., 2009). These changes have been identified in studies in which a disease control of participants who received only radiotherapy was used for comparison to a chemotherapy group. Shibayama et al. (2014) set out to specifically examine changes in memory associated with radiation treatment. They identified lower levels of verbal memory and delayed recall in the radiation group when compared to a non-radiation group. A major limitation of this study was that approximately 50% of the radiation and non-radiation group had received chemotherapy and this was not controlled for in statistical analysis. Verbal learning, visual perception, visual attention and short-term retention were identified as long-term problems (greater than 10 years) in a radiation only breast cancer treatment

group when compared to women who had received chemotherapy and a non-cancer control group (Nguyen et al., 2013). These problems persisted when age was controlled for. This study did not control for endocrine therapy, which has been identified as a confounding factor in other studies. Moderate levels of attentional fatigue and a decreased capacity to direct attention as measured by self-report were found to persist over the course of radiotherapy extending out to 4 months after the conclusion of treatment (Merriman et al., 2010). These studies demonstrate a confounding role for radiotherapy in PBCCI, however none of these studies explored the impact of these cognitive problems on everyday activities and social participation.

Changes in Functional Performance Associated with Breast Cancer

Breast cancer treatment may cause a number of functional performance changes either aside from or in addition to cognitive changes. Functional performance includes changes in physical function and the performance of ADL's, IADL's, as well as social participation. In a systematic review of the literature, Ewertz and Jensen (2011) categorized problems associated with breast cancer treatment into three areas; focal problems, systemic problems, and psychosocial problems. Focal problems are related to therapies such as surgery and radiation. Lymphedema, pain and other arm and shoulder problems are included in this category. Systemic problems are attributed to the toxicities of chemotherapy and the side effects of endocrine treatment. Neuropathy, infertility, premature menopause and cardiovascular disease are common long-term systematic problems associated with breast cancer treatment (Ewertz & Jensen, 2011). Limited evidence is available about cancer-related neuropathy; however neuropathy is related to pain and sensory and motor impairment (Brearley et al., 2011, Ewertz &

Jensen, 2010). Evidence shows that chemotherapy treatment with a taxane produced deficits in motor function which were hypothesized as a result of peripheral neuropathy (Jansen, Cooper, Dodd & Miaskowski, 2011). Ewertz and Jensen (2011) delineate psychosocial problems as consequences of diagnosis and treatment, including depression, fear of recurrence, sleep disturbance, cognitive problems, fatigue, and sexual problems.

Reduced arm function related to breast cancer surgery and radiotherapy has been linked to difficulties in performance of ADL's and a lower health-related quality of life (Hayes et al., 2012). O'Toole et al. (2015) studied breast cancer related lymphedema's impact on the ability to perform upper extremity activities of daily living. Their study followed 324 women who underwent unilateral mastectomy for approximately 30 months after surgery, finding lower functional scores, averaged from 19 items from the DASH, associated with fear of lymphedema, pain, mastectomy and axillary node dissection. Fatigue has also been shown to impact daily living activities for women with breast cancer during treatment up to twelve weeks afterward (de Jong, Candel, Schouten, Abu-Saad & Courtens, 2006). This study of 157 women with breast cancer showed that for women who had mastectomies, lower levels of activities were correlated with greater levels of fatigue. This was not observed in the group who had lumpectomies. Both of these studies calculated scores for function, but they did not account for the involvement of multiple factors related to treatment such as anxiety, depression and pain.

It is clear that surgical treatment for breast cancer can result in upper extremity physical impairments. These physical impairments include reduced upper extremity

range of motion and lymphedema. Pain and fatigue also contribute to reducing the ability to perform activities and maintaining social participation. The changes in upper extremity function may play a confounding role in measuring the cognitive domain of psychomotor speed as the tests that are used are typically pegboard tasks that require fine motor skills.

Current literature does not specifically correlate functional performance problems post breast cancer with PBCCI. However, cognitive skills are needed in order to successfully perform most everyday activities. Ogilvy, Livingstone and Prue (2008) identified problems in the areas of food preparation, household chores, social activities and employment related to fatigue. This study did not examine the role of changes in cognition as it relates to activities and participation. Braithwaite et al. (2010) report that the presence of functional limitations post breast cancer treatment results in a decreased overall survival. Braithwaite did not address cognitive impairment in relation to functional limitations. Loss of functional independence is also a concern for women experiencing PBCCI, including the inability to participate in family activities and frustrations at work due to problems in reading, anxiety and memory problems (Player, et al., 2014).

Changes in Functional Performance Associated with Cognition

Several studies looking at breast cancer and work provide insight into the challenges attributed to changes in cognition. In a qualitative study of 74 breast cancer survivors, Boykoff, Moieni and Subramanian (2009) describe PBCCI in terms of difficulty digesting new information, decreased focus, concentration and speed. The participants reported that decreased focus led to difficulty with job performance. Similar issues at

work were reported in a qualitative study of 22 breast cancer survivors by Von Ah et al. (2013). This study identified issues in the domains of short-term memory, long-term memory, speed of processing, attention and concentration, language and executive functioning. Participants reported that they had to work harder and utilize compensatory strategies at work. Additionally, participants reported that they did not notice the extent of their cognitive issues until after the completion of chemotherapy. The deficits for 16 of 22 participants did not improve over time (Von Ah et al., 2013).

Decreased self-confidence at work resulting from problems with memory were identified by Munir et al. (2011) through their qualitative interviews of 31 breast cancer survivors. These qualitative studies demonstrate that women may have difficulty in work performance related to PBCCI. No existing literature was located describing the impact of cognitive impairments related to non-CNS radiotherapy for breast cancer and functional abilities. This study is the first to specifically focus on the relationship of changes in cognitive abilities associated with chemotherapy and radiotherapy treatment for breast cancer with changes in everyday functional performance.

Conclusion

The impact of PBCCI on activities and participation is not well understood. The majority of existing research has focused on establishing evidence for the changes through neuropsychological assessment and determining the etiology as it is related to physiologic mechanisms. Several major issues are noted in the literature:

- A working definition of cognitive function does not exist in relationship to cancer;
- There is not a standardized diagnostic criteria for cancer related cognitive impairment;

- Current research focuses on different cognitive domains such as language, attention, processing, memory and concentration but not the impact on functional performance (Hess & Insel, 2007; Raffa, 2011; Von Ah et al., 2011).

Occupational therapists specialize in enabling individuals to perform personally meaningful occupations. Current literature points to functional limitations resulting from PBCCI. However, these limitations have not been well quantified. Additionally, PBCCI is most often associated with chemotherapy. Individuals who have been treated with non-CNS radiotherapy are also experiencing symptoms of PBCCI. This study measured self-report changes in cognitive abilities and concerns, functional abilities and social participation over 6 months following the completion of chemotherapy or chemotherapy + radiotherapy for breast cancer. This study also examined the impact of confounding factors such as age, menopausal status, sleep disturbance, pain interference, anxiety and depression on functional ability and social participation. A better understanding of the functional impact of PBCCI may be useful in designing more effective interventions and facilitating optimal performance of occupations by breast cancer survivors.

Chapter Three: Research Methodology

This study, as original proposed, aimed to compare self-reported cognitive function and everyday functional performance between two samples of patients with breast cancer who have received either adjuvant chemotherapy or radiotherapy, measured at the conclusion of treatment and 3 and 6 months later. Several months into participant accrual, no individuals receiving radiotherapy had enrolled. The dissertation committee was reconvened and approved the addition of a chemotherapy + radiation group. Therefore the two samples consist of individuals receiving only chemotherapy or those receiving chemotherapy + radiotherapy. The data from this study describe and measure changes in the domains of cognitive function and everyday functional performance over time in order to improve the predictive value of cognitive and functional screens in guiding occupational therapy interventions for this population. This study provides a better understanding of the extent to which PBCCI impacts the ability to perform daily activities, which thus far has not been well documented in published literature. This chapter describes the rationale, design, participant population, measurement tools, procedures, and data analysis plan. Chapter four provides an in depth description of challenges faced in recruitment and the changes made to the study to address the problems.

Approval

The original research plan was submitted and approved by the Massey Cancer Center Protocol Review and Monitoring Committee Cancer Prevention and Control Subcommittee in January 2016 (MCC-15-12217). The study (HM20006120) was approved by the Institutional Review Boards of Virginia Commonwealth University by expedited review according to 45 CFR 46.110 on 3/31/2017 under Expedited category 7. In April 2016, the study was approved by Exempt review through the Elizabethtown College Institutional Review Board. In August 2016 an amendment was approved to use Facebook for study recruitment, change eligibility requirements and to add a chemotherapy + radiation therapy group to the study. The rationale for these changes will be discussed later in the chapter. In February 2017 the study approved for continuation according to 45 CFR 46.108(b) and 45 CFR 46.109(e) and 45 CFR 46.110 by VCU IRB Panel A.

Design Rationale

The Revised Conceptual Model of Chemotherapy-Related Change in Cognitive Function provides the foundation for this study. In summary, this model views Post Breast Cancer Cognitive Impairment (PBCCI) resulting from two primary antecedents, cancer treatment and cancer diagnosis (Myers, 2009; Hess, 2010). The two types of breast cancer treatment compared in this study include completion of surgery, and either chemotherapy or chemotherapy + radiotherapy. This conceptual model goes on to view changes in functional abilities and health-related quality of life as consequences of changes in cognitive function (Hess, 2010; Myers, 2009). The changes in cognition and everyday functional performance are of particular concern to occupational

therapists, as treatment would focus on a compensatory or remedial approach to restore functional abilities.

Recommendations from the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology - Survivorship: Cognitive Function Version 1.2014 (Denlinger, et. al., 2014) and the International Cognition and Cancer Task Force (ICCTF) (Wefel, et al., 2011) are also integrated in this study design. The NCCN clinical practice guidelines (Denlinger, et al., 2014) cite occupational therapy as a first line intervention for cancer related cognitive impairment, along with neuropsychology. Occupational therapy typically addresses the ability to perform activities of interest in daily life, and the impact of underlying client factors, in this case cognition (American Occupational Therapy Association, 2014). This study examined the functional consequences of Post Breast Cancer Cognitive Impairment (PBCCI) through the use of the PROMIS Cancer Physical Function Scale, Ability to Participate Scale, and Satisfaction with Participation Scale. The ICCTF guidelines recommend a disease specific comparison group to control for the relative effects of the combination of treatments that are administered for breast cancer (Wefel et al., 2011).

In the original study proposal the radiotherapy group acted as the specific comparison group. A chemotherapy + radiotherapy treatment group was substituted to ensure that there would be a comparison group, as it was difficult to identify and recruit individuals receiving only radiotherapy. Nine individuals who were treated with only radiation entered the study. None qualified due to completing their course of treatment outside of the study parameters of the past 21 days. The study used a posttest-only design with nonequivalent groups (O'Farrell, et al., 2013; Shadish, Cook & Campbell,

2002). Both groups consisted of women who were diagnosed with breast cancer. One group consisted of those who had been treated with chemotherapy, and the other group consisted of those who had been treated with chemotherapy + radiotherapy.

Functional performance is defined in this study as performance of activities of daily living (ADL's) and instrumental activities of daily living (IADL's), including social participation and roles. The impact of the performance of roles in the areas of family and work has been recently highlighted as a major issue for survivors of breast cancer as it relates to cognitive impairment and an individual's ability to resume her/his prior lifestyle (Player et al., 2014). Therefore, the inclusion of the PROMIS Participation scales address role performance and satisfaction, in the areas of relationships, parenting, leisure and work (Bode, Hahn, DeVellis & Cella, 2010). This is also consistent with the Model of Human Occupation and the construct of habituation, as discussed in Chapter Two.

Within the Revised Conceptual Model of Chemotherapy-Related Changes in Cognitive Function, changes in cognition and functional performance are impacted by the interplay of lifestyle factors, situation factors and concurrent symptoms. These factors and symptoms include age, educational level, fatigue, anxiety, depression, sleep quality and hormonal status, all of which were measured for study participants. The PROMIS 57 v.2 measured self-reports of anxiety, depression, pain, and sleep disturbance at each observation. The demographic questionnaire collected related information about age, stage of cancer, treatment, employment, educational level and comorbidities.

The original study proposal included a caregiver observation to provide additional insight into changes in functional ability and participation experienced after chemotherapy or radiotherapy for breast cancer, because awareness of cognitive function may be over- or under-estimated when an individual has cognitive impairment (Kolakowsky-Hayner, 2010). Providing a referral to a caregiver for participation was optional. No caregivers entered the study, so no data is available for comparison.

Study Design

This descriptive study used a longitudinal posttest-only design at three assessment time points with nonequivalent groups (Shadish, Cook & Campbell, 2002). The intent of this study was to explore the relationship between changes in self-reported cognitive abilities and cognitive concerns with changes in functional performance to better understand the phenomenon of PBCCI for breast cancer survivors who have completed either chemotherapy or radiotherapy. No individuals with radiotherapy enrolled in the study. The results compare a chemotherapy only group with a chemotherapy + radiation group. Participants in both groups were assessed at three time points, O_1: at the completion of chemotherapy or radiotherapy (within 2-3 weeks to allow for recovery from immediate treatment effects) as a baseline, O_2: 3 months post, and O_3: 6 months post, in order to assess changes in cognition and function over time. Figure 2 provides an overview of the study flow for participants. This approach mirrors the common progression of clinical practice in occupational therapy, where a client's level of function is evaluated upon referral, not prior to receiving treatment for cancer. Additionally, these time frames match with medical oncology follow-ups. Analysis of the

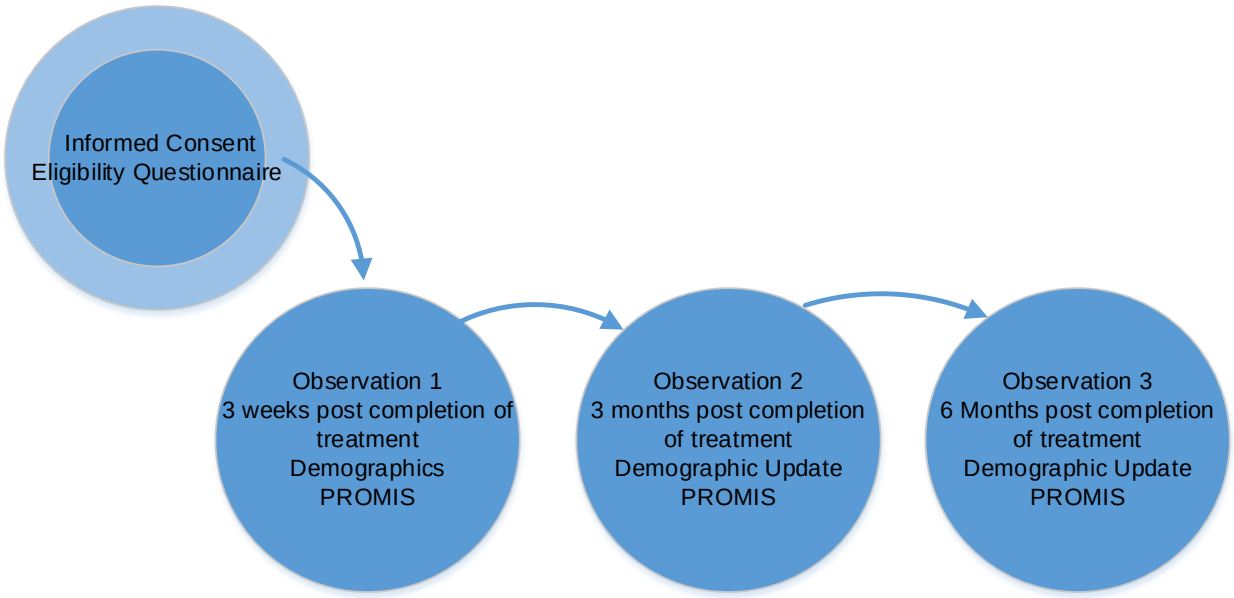

Figure 2: Study flow for participants beginning with enrollment.

resulting data from each time point may help inform medical and rehabilitation providers of areas to be addressed with this population at common follow-up time points.

Participants completed informed consent, demographics questionnaire, the PROMIS-57v2, the PROMIS Cognitive Abilities and Concerns Scales v1.0, PROMIS Cancer Physical Function Scale V1.0, PROMIS Ability to Participate in Social Roles and Activities (v2.0) and Satisfaction with Social Roles and Activities (v2.0) (See Appendix A-C) at O_1. Subsequently, at the next two observations participants completed the same battery with a demographics update form.

Determination of Variables

Type of treatment, chemotherapy or chemotherapy + radiotherapy, is the independent variable (IV) for comparison between groups in relationship to the dependent or outcome variables. In regards to the complexity of PBCCI, the

constellation of breast cancer treatment factors is the IV or predictor variable in this study for within subject analysis. This constellation includes type of surgery, physiologic factors including type of chemotherapy agent, radiotherapy, hormonal status, and psychological factors including depression, anxiety, sleep disturbance, fatigue, and pain interference as defined by the Revised Conceptual Model of Chemotherapy-Related Changes in Cognitive Function (Myers, 2009).

Cognitive function is a dependent variable for between and within group analysis. Cognitive function is measured in two ways, self-report assessment of cognitive abilities and self-report assessment of cognitive concerns via the PROMIS Applied Cognition - Abilities and the PROMIS Applied Cognition Concerns scales. These scales measure perceived functional abilities and concerns in the context of everyday activities, and the cognitive domains of memory, concentration, following directions, and learning. Functional performance is a dependent variable comprised of measures of physical function and social participation.

Physical function is measured by the score on the PROMIS Cancer Physical Function scale v1.0. This scale contains questions about mobility, activities of daily living and instrumental activities of daily living. This scale measures an individual's self-reports of their ability to perform specific activities and is not an observation of actual performance. The instrument is designed for use with any type of cancer diagnosis (PROMIS, 2015a). Two aspects of the dependent variable of participation, ability and satisfaction, were measured, using the PROMIS Ability to Participate in Social Roles and Activities V2.0 and the Satisfaction with Roles and Activities V 2.0. These scales

measure aspects of role performance in the areas of work, family life, friendships and other personal responsibilities.

Covariates include depression, anxiety, sleep disturbance, fatigue, and pain interference as measured by the PROMIS 57 Profile V2. Additional covariates including age, educational status, work status, stage of cancer, type of surgical intervention, concurrent treatments of hormonal, and/or targeted therapies, and lymphedema. These were measured through self-report on the demographics questionnaire. These covariates or moderators are included in the Revised Conceptual Model of Chemotherapy-Related Changes in Cognitive Function (Myers, 2009).

Measures

An enrollment questionnaire and demographics measure was created for this study (Appendix B). The collection of age, race and ethnicity follow current NIH guidelines. The demographics measure collected information on current employment status, caregiver status, menopausal status, stage of cancer including tumor size, number of positive lymph nodes, and metastasis, type of chemotherapy, type of surgery for breast cancer, tumor receptor status, and type of lymph node dissection, presence of lymphedema, radiotherapy, targeted therapy, and medical history including, anemia, thyroid disease, and vitamin D deficiency. The collection of demographics was based on factors included in Myers (2009) Revised Conceptual Model of Chemotherapy-Related Changes in Cognitive Function.

The Patient Reported Outcomes Measurement Information System (PROMIS®) is a measure of health domains that can be utilized universally across different disease types. PROMIS® (PROMIS, 2015b) consists of banks of questions on physical, social

and mental health domains. The system is designed to provide a technological infrastructure that supports NIH-funded clinical investigations across Institutes, disciplines, diseases and subpopulations. PROMIS® instruments were developed using Item Response Theory (IRT) "a family of statistical models that link individual items to a presumed underlying trait or concept represented by all items in the item bank. (PROMIS, 2015 c).

This study utilized the PROMIS v 1.0 Applied Cognition – Abilities and General Concerns scales, the Ability to Participate in Social Roles and Activities v 2.0, Satisfaction with Social Roles and Activities v 2.0, and the Physical Function Ca Bank, v 1.1 and the PROMIS-57 Profile v2.0 (Appendix C). For all the PROMIS® scales the raw scores are converted to a standardized T-score for each subject. A T-score has a mean of 50 and a standard deviation of 10. The development of the PROMIS® scales specified procedures to ensure construct, concurrent and, criterion validity (PROMIS, 2013).

The PROMIS Applied Cognitive Abilities v1.0 and the PROMIS Applied Cognitive General Concerns v1.0 (Appendix C) were used as the self-report measure of cognition. The abilities scale is positively worded and asks the respondent to rate items about attention, memory, concentration and other cognitive tasks for the past 7 days on a scale of not at all, a little bit, somewhat, quite a bit and very much. The concerns scale is negatively worded or problem focused asking the respondent to rate difficulty or trouble with the same tasks on abilities scale. The questions are rated on a scale of never, rarely (once), sometimes (two or three times), often (about once a day) or very often (several times a day). Both scales place the cognitive domain within the context of

an everyday activity (PROMIS, 2015d). For example, new learning is represented as an ability in the item “I have been able to learn new things easily, like telephone numbers or instructions. The concerns scale has the question worded “I have trouble remembering new information, like phone numbers or simple instructions.” These scales are based on the Functional Assessment of Cancer Therapy-Cognitive Function scale (FACT-Cog) that was designed to measure both abilities and concerns (Lai, et al., 2014). The PROMIS instruments were designed “to better understand cognitive function during and following cancer treatment from a patient’s perspective” (Lai, et al., 2014). These scales were developed with a sample of 509 participants. Items were generated through interviews and field testing. Conceptual models were tested using unidimensional and multidimensional item response theory. Results showed “separation in the clusters of factor loadings between concerns and abilities to support separate reporting of concerns and abilities” (Lai, et al., 2014). This was confirmed in the cognitive interviewing process of the instrument development. As such, this study used the conservative approach advocated by Lai, et al. and measured both concerns and abilities.

Reliability and validity of the PROMIS cognitive scales has been assessed with individuals with multiple sclerosis, revealing high internal consistency with a reliability Cronbach α coefficient of .97 (Becker, Stuifbergen, Lee & Kullberg, 2014). Becker, et al. (2014) also found participants who were unemployed due to their disabilities reported lower cognitive abilities and greater concerns. This study measured both abilities and concerns related to cognition in order to get a fuller picture of the experiences of participants and any changes over the 6-month study period.

The PROMIS-Ca Physical Function Scale (Appendix C) was used to measure activities of daily living and instrumental activities of daily living. The participant rates their level of difficulty on each item from “no difficulty” to “unable to do”. The instrument covers activities inside and outside the home, including dressing, bathing, shopping, laundry, doing dishes and other household tasks as well as getting in and out of a car, traveling overnight and participation in sports. The adult cancer instrument was developed for use with any type of cancer diagnosis. This scale contains 45 items as compared to 38 in the general physical function scale (PROMIS, 2014a). Internal consistency for the 38 item general physical function scale is high with a Cronbach α of .99 (PROMIS, 2014a). The additional items on the cancer scale were developed by content experts to address items that may convey a different meaning to individuals with cancer and then calibrated with adult cancer patients (PROMIS, 2014a). The T-score of 50 on this scale represents the norm of the calibration sample, not the national sample as other PROMIS scales do (PROMIS, 2014a). This instrument addresses the MOHO construct of performance capacity.

The Ability to Participate in Social Roles and Activity scale (Appendix C) measures perspectives about the ability to perform roles in work, family and social environment (Bode, et al., 2010). The Satisfaction with Social Roles and Activity scale (Appendix C) looks at how well the individual is satisfied with the performance of family, work and social roles. For example, the abilities scale has the participant rate ability items such as: “I have trouble doing my regular daily work around the house, I have trouble meeting the needs of my family.” These items are rated as never, rarely, sometimes, usually and always. The satisfaction scale has the participant rate “I am

satisfied with my current level of family activities and I am satisfied with how much work I can do (include work at home)." This scale addresses the MOHO constructs of habituation and role performance. The internal consistency of both scales is high with a Cronbach α of .99 (PROMIS, 2015e). These scales were calibrated with a sample that included more individuals with chronic illnesses, therefore, they do not reflect the average of the United States general population as many of the other PROMIS scales do (PROMIS, 2014e).

The PROMIS-57 v2 scale (Appendix C) contains short form scales for anxiety, depression, fatigue, pain interference and intensity, physical function, sleep disturbance and the ability to participate in social roles and activities. This profile instrument includes "high information items" that have been ranked through Computer Adapted Testing (CAT) simulations and reviewed by content experts. The PROMIS-57 v2 is administered as short forms that "enable a more direct comparability across people or time" (PROMIS, 2015f). The anxiety scale asks how often, never, rarely, sometimes, often and always, in the past seven days a participant has experienced related feelings of worry, fear and uneasiness. The depression, fatigue, sleep disturbance, ability to participate in social roles and activities and pain interference use the same rating procedure. The physical function questions ask the participant to rate how difficult tasks such as walking and doing chores are and to rate their limitations on doing house work activities. The physical function scale of the PROMIS- 57 has overlapping items with the PROMIS-Ca Physical Function Scale. The PROMIS-Ca Physical Function Scale is used for analysis since it was developed with a population of individuals diagnosed with cancer. The computer administration was set up to avoid having participants answer

items more than once as there is overlap of the PROMIS 57 scales with the other scales being administered.

Hypotheses

The original purpose of this study was to examine changes in self-report cognition and everyday functional ability, as measured at three evenly spaced time points over the first six months after the completion of either adjuvant chemotherapy or radiotherapy for individuals with breast cancer. Due to challenges to enrollment, the study compares chemotherapy only to chemotherapy + radiotherapy groups. Study research hypotheses include:

H_A 1: Cognition, as measured by the PROMIS Applied Cognition abilities and concerns scales, will improve within each group across the three measurement time points.

H_A2: Functional performance as measured by the PROMIS Cancer Physical Function Scale, the PROMIS Ability to Participate Scale, and the PROMIS Satisfaction with Social Roles and Activities will improve within each group across the three measurement time points.

H_A3: Change in cognition will positively correlate with change in functional performance within each group.

H_A4: Cognition, as measured by the PROMIS Applied Cognition abilities and concerns scales will differ between the chemotherapy and chemotherapy + radiotherapy groups.

H_A5: Functional performance as measured by the PROMIS Cancer Physical Function Scale, the PROMIS Ability to Participate Scale, and the PROMIS

Satisfaction with Social Roles and Activities will differ between the chemotherapy and chemotherapy + radiotherapy groups.

Participants

Individuals diagnosed with Stage I-IIIa breast cancer were recruited for the originally proposed groups, adjuvant chemotherapy and radiotherapy. In August 2016 recruitment was expanded to include individuals receiving both chemotherapy and radiotherapy. At this point in the progression of treatment the participants were eligible if they were receiving targeted therapies such as Herceptin, and/ or hormonal treatments (i.e. aromatase inhibitors or Tamoxifen). Although, concurrent treatments have been implicated in the constellation of causes for PBCCI, excluding individuals with concurrent treatments would have significantly decreased the ability to recruit subjects.

Eligibility

In order for a person to participate in this study he or she must have been 18 years or older, diagnosed with breast cancer stages I-IIIa and nearing the end of either chemotherapy or radiotherapy. The original eligibility criteria was limited to having undergone surgical intervention (mastectomy or lumpectomy) prior to adjuvant chemotherapy. To improve accrual, the eligibility was changed to allow for neoadjuvant chemotherapy with surgery at a later time. Anthracycline/taxane-based adjuvant chemotherapy was required for participation. Limiting subjects to an anthracycline/taxane-based treatment reflects current oncology practice and helped eliminate variability due to type of chemotherapy. Subjects in the chemotherapy + radiotherapy group must have completed a fully prescribed course of radiation

treatment. Participants needed to understand and communicate in English at a level to access and complete the PROMIS and demographic questionnaires.

Exclusion criteria included a diagnosis of Stage IIIB or 4 breast cancer, non-anthracycline/taxane chemotherapy regimens, a history of chemotherapy for any other type of cancer, a history of cognitive impairment related to a brain injury, stroke, dementia, epilepsy or a current or past disorder/ disease of the central nervous system, a history of substance abuse, presence of a developmental disorder impacting cognition, or a history of hospitalization for mental illness. Individuals with stage IIIb or 4 breast cancer were not eligible, as they are more likely to receive longer and more intense treatment regimens.

Recruitment

Recruitment for this study was open from May 2016 through February 2017. A multi-pronged recruitment approach of convenience sampling with snowballing was used for this study. Oncology clinics that were part of the Johns Hopkins Medical Center and Andrews & Patel Associates in the Harrisburg, Pennsylvania area were provided flyers (Appendix D) and agreed to distribute the flyers for the study. The Young Survival Coalition (YSC), a national organization based in New York City, advertised the study in their electronic newsletter and on their Facebook page. Additionally, YSC and Living Beyond Breast Cancer, a national organization based in Philadelphia, allowed for a study announcement posting in their closed Facebook Support Groups. In October YSC posted a guest blog that discussed my journey from breast cancer survivor to researcher. This blog post contained a link to the study (Appendix D).

A Facebook page titled 'The impact of breast cancer treatment on cognition research study', @chemoandcognition, was created for this study. This page was linked to Facebook announcements as well as shared with personal friends and breast cancer survivors for snowballing. Posts were made on this page with reminders that the study was still open. Additionally, articles and blogs were shared on the topic of cognition and breast cancer. The decision was made not to use Facebook paid advertisements as they could not be targeted precisely enough to reach eligible individuals.

Study announcements were emailed to twenty one face-to-face support groups in the state of Pennsylvania (Appendix E). One hundred twenty five flyers were distributed to attendees at the 2016 Young Survival Coalitions Midwest Symposium in Minneapolis, MN and 200 flyers at the West Coast Regional Symposium in Long Beach, CA. Additionally, ten flyers were given to individuals at the San Antonio Breast Cancer Symposium in December 2016 for nurses and advocates to distribute. It was expected that recruitment would occur over a period of 2-3 months. In total recruitment was open for 8 months. The plan to recruit through clinics and local support groups combined with online recruiting was an attempt to reduce coverage error by capturing both social media users and non-users (Dillman, Smyth & Christian, 2014).

Participants were recruited prior to the completion of chemotherapy or radiation in order to initiate the first administration of assessments approximately 2-3 weeks post completion of treatment. The time span of 2-3 weeks provided for flexibility, allowed for immediate side effects of the chemotherapy or radiotherapy to clear, but still reflected the baseline cognitive and functional status at the conclusion of treatment. Prior to enrollment in the study, volunteers were asked to complete an informed consent and

eligibility questionnaire. These were available through a public link to the VCU REDCap™ System. The flyer provided an option to call or email for a paper copy of the consent form and survey. No participants requested this option. Each eligible participant was asked to recommend a caregiver to participate. Only three participants provided a caregiver referral. One caregiver referral was the same as a participant and was not contacted. The other caregivers were contacted via email and did not respond. Table 2 provides an overview of the participant timeline, tasks and time commitment.

Table 2

Participant Timeline

Observation	Required Tasks	Estimated Time Commitment	Actual Time Commitment
Study Entry	Informed Consent		2-5 minutes
O_1: Completion of treatment (within 3 weeks)	Demographics PROMIS assessments Incentive form.	30-45 minutes	15-35 minutes
O_2: 3 months post O_1	Update of demographics PROMIS assessments	30-45 minutes	10-30 minutes
O_3: 6 months post O_1	Update of demographics PROMIS assessments	30-45 minutes	10-30 minutes

Sample Size

The original proposal had the goal of recruiting approximately 46 individuals for each group in this study to achieve a reasonable number of participants anticipated to complete the six-month study (n=32/group). This corresponds to an approximate 30%

attrition rate. This rate is similar to the attrition rate reported by Bender et al. (2006) in their 6-month study of cognition and breast cancer. The sample size was determined based on feasibility of recruitment and time constraints. If 32 subjects per group completed the study, then there would be 80% statistical power to detect a difference between the groups on the order of 0.8 standard deviation units (Cohen's d = 0.8, considered a moderate-to-large large effect size). In August 2016, the recruitment goal was adjusted to achieve a sample size of 16 in each group, which corresponded to a one SD difference. The final sample size for this study was 16 with seven chemotherapy subjects and nine chemotherapy + radiation subjects.

Attrition

The risk of attrition was significant as this study followed participants over the span of six months. Several strategies were employed to reduce the potential loss. Participants were scheduled for O_2 upon completion of O_1 and for O_3 at the completion of O_2. Participants were sent automatic email from REDCap™. If a participant did not respond I sent an additional reminder originating from REDCap™. Participants were provided a $10 gift card or donation to YSC incentive upon completion of the first survey. This amount served as a small thank you token and was not at the amount to be viewed as coercive (Singer & Couper, 2009). Advance token incentives have been shown to be effective in improving response rates through establishment of trust and creation of a social exchange (Dillman et al., 2014). Advance incentives have been shown to increase response rates more than lotteries and those offered for completion (Dillman et al., 2014). These incentives were funded through an internal faculty grant from Elizabethtown College. During the study, participant progress on surveys was

monitored through REDCap™. If a participant did not complete any surveys an email reminder was sent to invite the respondent to return to REDCap™ and complete the survey.

Data Collection

Study data were collected and managed using REDCap™ electronic data capture tools hosted at Virginia Commonwealth University (Harris et al. 2009). REDCap™. (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. Upon IRB approval an account was established in REDCap™.

A welcome page was set up with access to the informed consent and demographic survey (Appendix A-B). The study was set up into two arms. The first arm included the welcome, informed consent and eligibility survey. The second arm was for eligible individuals. As fields were created in REDCap™ they were designated as private health information as necessary and data permissions were set up to maintain participant confidentiality. Automatic invitations were set up in the system to invite participants to complete their first survey three weeks after the treatment finish date provided in the eligibility survey. REDCap™ generated a unique link for each participant. The system was set up to send email invitations with a personally unique URL to the second arm of the study. The second arm contained the demographic surveys and PROMIS® instruments. The PROMIS® instruments were available in the

REDCap™ shared library and were uploaded into the study (Obeid et al 2013). The instruments were programmed to capture Computer Adaptive Testing (CAT) scoring (Cella, Gershon, Bass & Rothrock, 2014). In CAT the survey questions are adapted by the computer based on the responses provided on a previous question. CAT decreases administration time, while maintaining measurement precision (PROMIS, 2015g). The PROMIS® instruments were set up to avoid redundancy in asking the same item multiple times in each administration. Prior to launching, the project was tested by myself and a research assistant/ graduate student from Elizabethtown College.

Statistical Analysis

Data collected through REDCap™ was downloaded into an Excel worksheet. Data was cleaned and examined for outliers and missing data. The REDCap™ format of the PROMIS instruments required participants to complete all items, therefore there was no missing data in this section. Missing data from demographic questionnaires are indicated in the results section. The data was then uploaded into SAS for analysis. Descriptive statistics are provided in Chapter 5 for all demographics and scales to provide a picture of the sample. These include measures of central tendency and variance.

The original proposed data plan was to use univariate and multivariate repeated measures analysis of covariance (RM ANCOVA) to compare the changes in cognition and functional performance variables within groups (H_A1-3). This was changed to linear mixed effects models for H_A1-2 and a correlation matrix comparing changes in cognition related variables with changes in functional performance variables for H_A3. For the between group analysis (H_A4-5), the groups were not matched within the study design;

therefore, the original analysis plan used propensity scores to account for the inability to randomly assign participants to treatment groups (Austin, 2011). Due to the small sample size (N=16) and attrition, linear mixed-effects models were calculated instead. This approach allowed for both within and between subject analyses and accounted for the repeated measures. In ANCOVA analysis, missing time point data results in dropping all the data from analysis. The linear mixed-effects model allowed for the inclusion of data from eight participants that missed one time point data collection.

Likewise linear mixed-effects modeling was used to examine changes in fatigue, pain interference, sleep, anxiety and depression both within and between groups. The small sample size was not adequate to perform the proposed exploratory ANCOVA analysis to examine the impact of education level, sleep disturbance, pain, depression and anxiety on T-scores.

This chapter provided an overview of the study design and the changes that were implemented in the areas of recruitment and data analysis. The following chapter will provide an in depth presentation of the challenges encountered in recruitment and enrollment in the study and the actions taken to address the associated issues. The study results are presented in Chapter 5 and discussed in Chapter 6.

Chapter Four: Study Recruitment and Enrollment Challenges

"If it doesn't work, it's not failure, it's data."

-Dorie Clark 2017

In designing research, we typically try to foresee and address threats to validity and completion of research. These are weighed in relationship to resources available such as time, money, infrastructure, and researcher capacity. In the design of this study, efforts were made to balance rigor in research methods with the reality of the disease of breast cancer treatment profiles and the availability of eligible research subjects. This chapter provides an overview and discussion of the challenges and obstacles faced in the enrollment phase. The process of responding to these challenges and the actions implemented in an attempt to improve enrollment are presented.

Challenges in Recruitment

The proposed design of this study aimed to compare changes in cognition and everyday functional performance of individuals receiving chemotherapy treatment for breast cancer to those receiving radiation therapy. The radiation only arm served as the comparison group to control for the relative effects of the combination of treatments (Wefel et al., 2011). In order to limit variability and promote homogeneity, regarding type of chemotherapy, eligible participants must have received an anthracycline/ taxane based treatment. Additionally, original eligibility required surgery prior to the initiation of treatment. Initial recruitment was through flyer distribution to patients at Andrews &

Patel in Central Pennsylvania, Johns Hopkins Medical Center and e-newsletter/ social media posting by the Young Survival Coalition (YSC). The study announcement provided options to go online or to obtain paper surveys for participation. A dedicated phone number was established. The announcements by YSC provided a direct link to the study informed consent form.

Recruitment initially relied on the cooperation of clinicians, doctors and nurses, to provide flyers to eligible patients, but this approach did not work effectively. Results from a focus group study examining the barriers to clinical trial recruitment describe "a hidden recruitment element' in which it is necessary to gather support from other personnel at the clinical site (Stein et al. 2015). Furthermore, Stein et al. report that investigator/clinicians found it difficult to balance and integrate their own research with their clinical care. In this study, clinicians were being asked to recruit for a study that they were not personally invested in. It is possible that issues of this nature impacted distribution of flyers by medical professionals in this study.

A second recruitment challenge may have been that the clinic flyers placed the onus on the participant to either go online or call the researcher to enroll in the study. In retrospect, this approach most likely led to the loss of potential participants. Cancer treatment is stressful and tiring. Patients may have put the flyer aside instead of taking the next step. In an effort to encourage flyer distribution, beginning in June 2016 through February 2017, and monthly follow up emails were sent to both clinic contacts to encourage recruitment. The clinical liaisons replied to all inquiries stating that they would continue to encourage clinic staff to distribute flyers. This points to another issue within the study, the lack of tracking for flyer distribution. The clinical sites offered to

make their own copies to distribute. If numbered flyers were sent to the site, the site liaison would have been able to easily report the number of flyers distributed.

The ability to recruit participants for this study within a reasonable time frame was overestimated. This common tendency of researchers, especially novice or junior researchers, is referred to as a 'funnel effect' or Lasagna's Law (Gul & Ali, 2010; Stein et al. 2012). Low enrollment and nonresponse rates can prolong the time of studies, can lead to invalid or inconclusive results secondary to diminished statistical power, results in poorly used human and material resources and threatens the internal and external validity of research studies (Carlisle et al. 2015; Gul & Ali, 2010; Williams, Tse, DiPiazza & Zarin, 2015).

Insufficient accrual of participants for clinical trials is often a top reason for termination. In 2013, a review of the ClinicalTrials.gov database found 57% of 619 trials terminated for nonscientific reasons resulted from insufficient rate of accrual (Williams et al. 2015). A study utilizing the National Library of Medicine clinical trial registry identified 481 (19%) out of 2579 studies terminated for less than 85% of expected enrollment (Carlisle et al. 2015). Finally, volunteers participate in research studies to contribute to meaningful scientific knowledge. When studies are not sufficiently enrolled an ethical issue arises in regards to the volunteers and may deplete the available pool of participants (Carlisle et al, 2015; Williams et al. 2015).

Efforts to Expand Enrollment

Within two months of opening enrollment to the study, it became apparent that many interested participants were not qualifying for the study. In July a page for the study was created on Facebook (https://www.facebook.com/ chemoandcognition/) and

an amendment to the study IRB was submitted and approved. The study link was shared on two closed Facebook support groups. This resulted in over twenty new logins to the survey. The initial analysis of participant characteristics showed that interested participants were ineligible due to receiving both chemotherapy and radiation, or because they were receiving neoadjuvant treatment. The dissertation committee was reconvened in August 2016 and the study design was altered to include a chemotherapy and radiation treatment group, as well as including individuals receiving neoadjuvant treatment. The protocol changes were approved by the VCU IRB. Individuals who completed the consent process and were then eligible to participate were emailed and invited to return to the study.

In addition to the changes in protocol, recruitment efforts were expanded. Twenty-one in person support groups in the state of Pennsylvania were contacted via email between June and September 2016 (Appendix E). Three groups responded and agreed to distribute the study flyer. Study announcements were posted in eight closed Facebook support groups with permission from the group administrator. Closed groups on Facebook require approval to join and individuals must demonstrate that they have been diagnosed with breast cancer. Monthly re-posts of the study announcement were made between August 2016 and January 2017.

Posting on Facebook was intentionally made within closed support groups. This did not prevent the link from being shared. In Mid-July 2016 over a span of three days, 56 records were created on REDCap™. Evidently the link was shared and there were attempts to gain access to receive the incentive gift card. The eligibility screening questionnaire worked well in this case. Responses for date of diagnosis and end of

treatment dates needed to match up in order to qualify. This type of misrepresentation is associated with the lack of face-to-face contact in the recruitment process and is a clear risk associated with the use of Facebook for recruitment (Pedersen & Kurz, 2016). The low yield and completion rate observed in this study is consistent with other studies utilizing Facebook for recruitment (Kapp, Peters & Oliver, 2013; Ramo & Prochaska, 2012).

One hundred and twenty five flyers were distributed at the Young Survival Midwest Symposium in June 2016 and 200 copies at the West Coast Symposium in October 2016. In October, 2016 a guest blog was posted on the YSC website about my journey from breast cancer survivor to doctoral student researcher which included a link to the study (Appendix D).

In November, 2016 an electronic flyer was emailed and 20 paper copies were mailed to committee member Dr. Albrecht for distribution through her clinic work setting. Additionally, three local nursing oncology groups were emailed with a request to distribute flyers and to make a presentation at their local meetings. One group replied stating they would distribute the flyer to their members. A presentation to the Oncology research group at Penn State Hershey Medical center was given in November 2016 and both medical oncologists and radiation oncologists agreed to distribute flyers. An electronic copy of the flyer was sent to research group coordinator and twenty paper flyers were passed out at the meeting. In December 2017, an electronic copy and 5 paper flyers were provided to an oncology nurse in San Francisco and to the Cancer Resource Center in Ithaca, NY.

Eligibility Challenges

The initial study design required that participants had surgery prior to initiating chemotherapy or radiotherapy. This design did not recognize a shift in breast cancer treatment toward the use of neoadjuvant chemotherapy and/ or radiotherapy, treatment provided before surgery, and negatively impacted enrollment. Of the first 50 individuals to start the enrollment process in the study three did not qualify because they were receiving neoadjuvant treatment. Additionally, comments to the Facebook announcements indicated interest among individuals who were ineligible because they had not had surgery prior to chemotherapy.

The study design was based on the traditional approach in which breast cancer is treated with surgery and adjuvant treatment of chemotherapy, and/or radiation therapy, and/or endocrine therapy. The recent shift to neoadjuvant chemotherapy allows oncologists to determine if an individual has a pathologic complete response (pCR), meaning that there is no tumor left after the treatment. A pCR is associated with a survival benefit (Teshome & Hunt, 2014). With newer molecular technology, neoadjuvant treatment models identify both exceptional responders and non-responders (Chatterjee & Erban 2017). This approach also improves rates of less-invasive breast conservation surgery, quicker recovery and post-operative complications such as lymphedema (Chatterjee & Erban 2017; Steenbrugen et al. 2017; Teshome & Hunt, 2014). Shifts in standards of care, such as experienced with this study, are known to impact clinical accrual (Carlisle, Kimmelman, Ramsay & MacKinnon, 2015). The inclusion of individuals with surgery before or after chemotherapy treatment introduces additional confounding variability. The study protocol was changed in August 2016, with

committee approval, to include individuals receiving neoadjuvant treatment. With this change five participants entered and completed the study.

Technology Issues

At least ten times during data collection there was a glitch in REDCap™ and the survey queue failed to load automatically for participants. One participant emailed regarding the problem. Additionally, the problem was observed through monitoring of REDCap™ confirmation emails. The VCU REDCap™ administrators were contacted regarding this issue and they confirmed it was a problem within the entire REDCap™ system. When this occurred, an invitation to return and complete the survey was sent to the participant via REDCap™. This strategy helped to reduce missing data in these instances.

Summary

Throughout the recruitment phase of the study the researcher was responsive to recruitment challenges and attempted to develop new sources for participants. Prior to implementation, strategies were discussed with the dissertation advisor and/or committee. When necessary, IRB amendments were submitted for approval. Despite these best efforts, the desired sample size was not met. This study included the following barriers to enrollment: a significant number of eligibility criteria, reliance on clinic staff to provide flyers to eligible patients, and reliance on volunteers to go online to enroll in the study. Positive recruitment efforts included modifying eligibility, adding recruitment sites and support group outreach.

The following chapter provides a summary of the progression of participants through the study and the results of the study. Demographics, descriptive data and

hypothesis analysis are provided. Chapter 6 provides a discussion of the results in the context of current published literature, study limitations and implications of this study for occupational therapy and oncology professions.

Chapter Five: Results

The purpose of this study was to better understand the impact of PBCCI on activities and participation during the six months following the conclusion of chemotherapy and/or radiotherapy for breast cancer. In this study participants receiving either chemotherapy or chemotherapy + radiotherapy completed online self-report surveys regarding their physical function, social function, cognition and related confounding factors including sleep interference, pain, depression, fatigue and anxiety, at the conclusion of treatment, and at three and six months later. This descriptive study utilized a longitudinal post-test only design with nonequivalent groups (Shadish, Cook & Campbell, 2002). In this chapter, the study results are presented, beginning with an overview of the participants followed by descriptive data framed by Hess & Insel's (2007) Conceptual Model of Chemotherapy-Related Changes in Cognitive Function concluding with the hypothesis related analysis.

Participants

Participants were recruited through clinics, snowballing, support groups, and Facebook. Sixteen women, ages (28-45) participated in this study. The majority of these participants (n=12, 75%) are considered younger women (age<40 years) in the oncology field (Gabriel & Domchek, 2010). Nine received chemotherapy + radiotherapy and seven received chemotherapy. Nine women that received radiotherapy only completed the consent process, but were ineligible due to being more than 3 weeks out

of treatment. Recruitment for this study was challenging and an in-depth review of recruitment procedures and challenges is provided in Chapter 4. Figure 3 provides an overview of the progression of participants in the study and reasons for ineligibility. There was an overall 50 percent attrition rate over the six month follow up. The chemotherapy group had an initial enrollment of n=7, decreasing to n=3 at the three month follow up and n=2 at the six month follow up. In the chemotherapy + radiotherapy the initial enrollment was n=9, decreasing to n=7 at three months and n=6 at six months.

Cancer Related Demographics

Table 3 provides an overview of breast cancer related demographics. The table covers diagnosis, treatment and physiologic factors that are known to be involved in cognitive changes associated with cancer treatment (Hess & Insel, 2007; Myers 2009). Two participants in the chemotherapy group had zero positive lymph nodes and five did not report a number of positive nodes. In the chemotherapy + radiotherapy group, one participant reported zero positive nodes. The other participants in this group ranged from 1-7 positive nodes. This is expected as radiotherapy is more prevalent when there is lymphatic involvement.

Situational Factors

In the Conceptual Model Of Chemotherapy-Related Changes in Cognitive Function, Hess and Insel (2007) define the situational factors of lifestyle and personal experience. Lifestyle includes employment, and personal experience includes marital status and social support. Fifteen women identified themselves as white and one as other. All the women in the chemotherapy + radiotherapy group were married (n=9), one

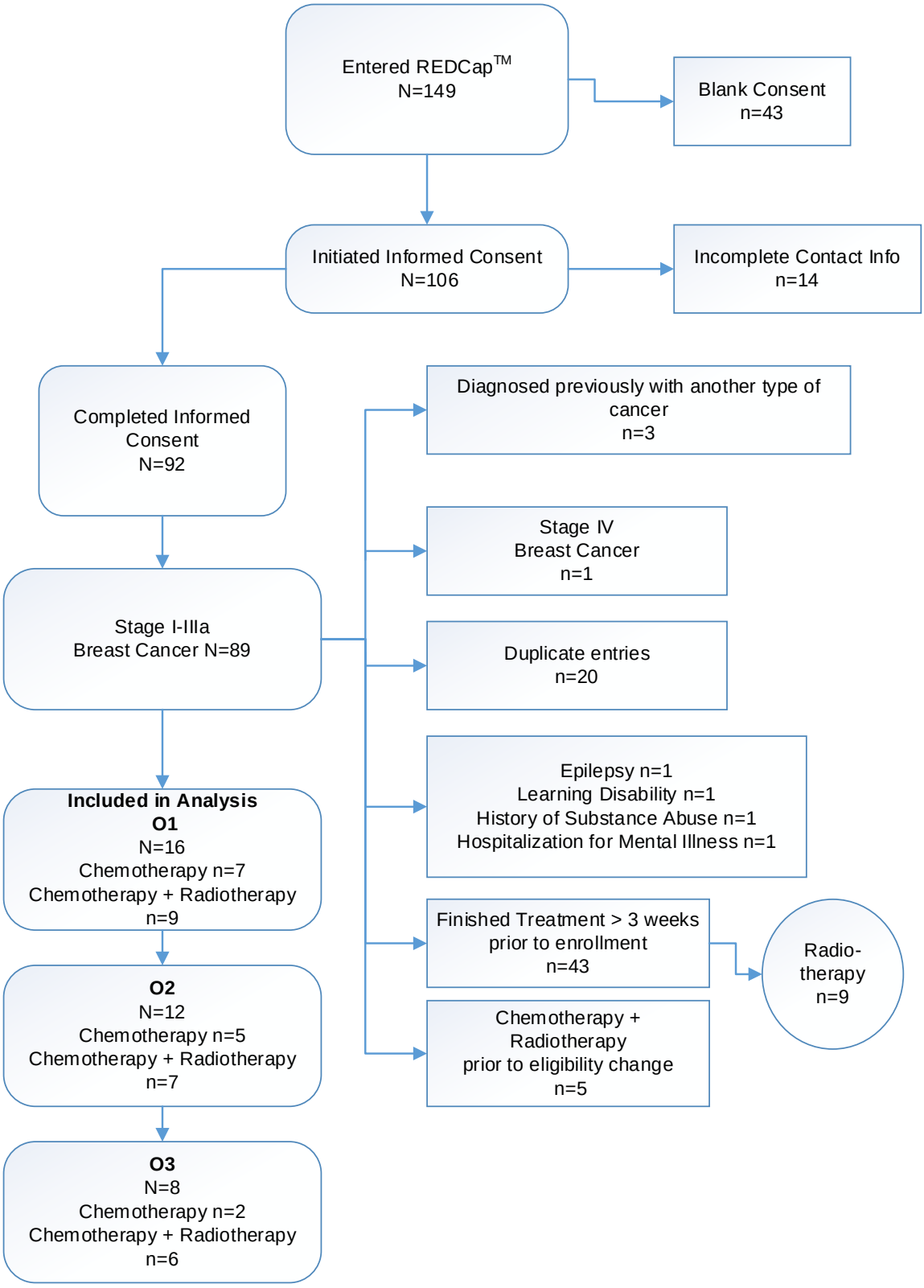

Figure 3: Participant enrollment and retention.

Table 3

Demographics: Antecedents and Physiologic Mediators According to the Revised Conceptual Model of Chemotherapy-Related Changes.

	Chemotherapy (n=7)	**Chemotherapy + Radiotherapy (n=9)**	**Total (N=16)**
Stage of Cancer at Diagnosis	I: 2 II: 5 III: 0	I:2 II: 4 III: 3	I: 4 II: 9 III: 3
Surgery Type			
Lumpectomy	0	3	3
Simple Mastectomy	4	3	7
Modified Radical Mastectomy	0	4	4
Type of Chemotherapy			
Standard AC-T	1	2	3
Dose-Dense AC-T	2	1	4
TAC	2	2	4
TC	0	1	1
Other	2	3	5
Tumor Characteristics			
ER+	0	8	8
ER-	4	1	5
PR+	2	5	7
PR-	4	1	5
HER2+	0	0	0
HER2-	4	6	10
Menopausal status at diagnosis			
Pre-menopause	6	9	15
Peri-menopause	1	0	1
Menopausal status at start of study			
Pre-menopause	3	0	3
Peri-menopause	1	0	1
Post-menopause	0	2	2
Chemo-induced menopause	3	7	10
Type of Hormonal Therapy			
Tamoxifen	0	1	1
Zoladex	2	0	2
Lupron	1	1	2
Arimidex	0	2	2
Aromasin	0	1	1
Lymphedema Diagnosis	3	2	5
Low Levels of Vitamin D	4	3	7
Anemic at start of study	1	2	3

woman in the chemotherapy group (n=7) reported living with a partner, the others were married. None of the participants reported that they smoke or vape. Table 4 provides an overview of the education status and Table 5 shows employment status. A total of 7 participants (chemotherapy n=2, chemotherapy + radiotherapy n=5) reported their employment status changed after their diagnosis with breast cancer. Four participants in the chemotherapy group were parents compared with six in the chemotherapy + radiotherapy group. One participant in the chemotherapy group reported caregiving for an adult.

Table 4

Education Level.

	Doctoral or Professional Degree	Master Degree	Bachelor Degree	Associate Degree	Post-Secondary Non-degree Award	Some College No Degree	Total
Chemotherapy	0	2	2	0	1	2	7
Chemotherapy + Radiotherapy	1	1	4	1	1	1	9
Total	1	3	6	1	2	3	16

Table 5

Employment Status.

	Full-time	Part-time	Volunteer	Homemaker	Total
Chemotherapy	4	2	0	1	7
Chemotherapy + Radiotherapy	6	1	1	1	9
Total	10	3	1	2	16

Psychosocial Factors

Stress, depression, anxiety and distress are psychosocial factors associated with cognitive changes in the Conceptual Model Of Chemotherapy-Related Changes in

Cognitive Function (Hess & Insel, 2007). Depression and anxiety may also be a concurrent symptom related to cancer treatment that impacts health-related quality of life. Participants were asked if they had a history of anxiety and if they had a history of depression. Six participants reported a history of anxiety, one in the chemotherapy group and four in the chemotherapy + radiotherapy group. Four individuals reported a history of depression, all in the chemotherapy + radiotherapy group. Two participants in the chemotherapy group did not answer this question.

PROMIS® Descriptive Data

Each participant completed the PROMIS® instruments measuring cognition, physical function, social participation, anxiety, depression, fatigue, pain interference, and sleep interference at the three time points. Table 6 provides a summary for each domain for the chemotherapy group and the chemotherapy + radiotherapy group at each observation point. Using Computer Adaptive Testing (CAT) in REDCap™, participant scores were automatically converted from raw scores to a standardized T-score. For all PROMIS® measures, the T-score has a mean of 50 and a standard deviation of 10. The PROMIS-57 Profile v2.0 contains scales to measure depression, anxiety, fatigue, sleep interference and pain interference (PROMIS 2015f). These scales were normed on the general population of the United States. Higher scores represent more of the concept being measured and lower scores represent less. Fatigue and anxiety were one standard deviation higher than the norm for the general population of the US for the chemotherapy + radiation group, across all three time points. Depression scores were one standard deviation higher than the norm for the

Table 6

Summary of T-Score Means on PROMIS Domains.

		Observation 1 (Baseline)		Observation 2 (3 Months)		Observation 3 (6 Months)	
PROMIS Domain		**Chemo n=7**	**Chemo+Rad n=9**	**Chemo n=4**	**Chemo+Rad n=7**	**Chemo n=2**	**Chemo+Rad n=6**
Physical Function	Mean	44.96	42.59	48.20	43.17	52.80	42.93
	Median	43.9	42.90	45.20	41.40	54.10	43.50
Cognition-Concerns	Mean	**36.59***	41.22	**37.18***	42.56	**38.45***	45.72
	Median	42.60	39.60	37.25	41.20	38.45	42.25
Cognition- Abilities	Mean	49.10	44.24	50.98	43.27	46.40	**38.83***
	Median	48.50	43.60	51.75	43.50	46.40	41.45
Ability to Participate	Mean	46.21	47.68	51.35	44.40	54.60	46.77
	Median	43.80	47.80	48.85	44.70	54.60	51.20
Satisfaction with participation	Mean	50.91	45.77	50.23	43.30	48.15	44.58
	Median	48.00	45.80	51.55	44.30	48.15	49.05
Depression	Mean	59.07	57.64	55.25	**60.70****	57.75	**61.85****
	Median	59.80	57.60	58.40	62.25	57.75	59.60
Anxiety	Mean	58.16	**61.10****	57.50	**66.05****	**61.20****	**67.17****
	Median	60.00	63.40	60.25	67.45	61.20	67.80
Fatigue	Mean	56.66	**62.28****	52.80	**61.30****	55.50	**61.58****
	Median	57.50	61.20	53.40	60.90	55.50	61.95
Pain Interference	Mean	59.07	55.89	49.65	**60.70****	50.85	58.18
	Median	62.80	56.40	49.35	61.60	50.85	54.05
Sleep Interference	Mean	52.43	56.41	49.65	55.22	48.60	59.47
	Median	51.10	56.30	49.35	53.45	48.60	59.10

Note. PROMIS® T-Scores have a mean of 50 and a standard deviation of 10. * One standard deviation below the PROMIS® instrument population norm. **One standard deviation above the PROMIS® instrument population norm.

three and six month time points. This means the participants in this sample report higher levels of fatigue, anxiety and depression than would be expected.

The PROMIS Physical Function Ca Bank v1.1 was calibrated with individuals diagnosed with different types of cancer (PROMIS 2015a). The PROMIS Ability to Participate in Social Roles v2.0 and PROMIS Satisfaction with Social Roles and

Activities v2.0 scales were calibrated with individuals with chronic illness that were sicker than the general population (PROMIS 2015e). The PROMIS Applied Cognitive Abilities v1.0 and the PROMIS Applied Cognitive General Concerns v1.0 were calibrated on samples enriched for chronic illness (PROMIS, 2015d). In this study, the chemotherapy only group was more than one standard deviation below the norm on the cognitive concerns scales across the six month span of the study (see Table 6). This may be interpreted as the group having fewer concerns than the normed population which was enriched for individuals with chronic illnesses. Cognitive ability t-scores for the chemotherapy + radiotherapy group did not change significantly during the study but fell to one standard deviation below the norm at the six month follow up. This result shows lower cognitive abilities than expected for a chronically enriched population

Hypothesis Tests

H_A 1: Cognition, as measured by the PROMIS Applied Cognition abilities and concerns scales, will improve within each group across the three measurement time points.

There was no significant change in cognition for either group over the six months post treatment as measured on either the abilities scale or the concerns scale (See Table 7). Cognitive concerns were one standard deviation lower than the PROMIS norm across all three time points for the chemotherapy only group, meaning this sample reported lower level of concerns with cognition. At the six month follow up the chemotherapy + radiotherapy group was one standard deviation below the norm for cognitive abilities. This may be interpreted as the group having lower cognitive abilities than expected.

Table 7

Linear Mixed Effects Model Summarizing Changes in Cognition as Measured by the PROMIS Applied Cognition Scales According to Treatment Group Over The Six Months Following the Completion of Treatment.

	Estimate	Standard Error	df	t-Value	PR>ltl
Chemotherapy Slope					
Cognition- Concerns	1.6971	1.3756	14	1.23	0.2376
Cognition- Abilities	-0.4419	1.5505	14	-0.29	0.7798
Chemotherapy+Radiotherapy Slope					
Cognition- Concerns	-0.4751	0.6919	14	-0.69	0.5035
Cognition- Abilities	-0.9322	0.9953	14	-0.94	0.3649

Note. Slope estimates were calculated using mean changes in PROMIS ® T-scores at the three time points- three weeks post treatment, three months post treatment and six months post treatment.

H_A2: Functional performance as measured by the PROMIS Cancer Physical Function Scale, the PROMIS Ability to Participate Scale, and the PROMIS Satisfaction with Social Roles and Activities will improve within each group across the three measurement time points.

Physical function as measured on the PROMIS scale improved significantly in the six months post treatment in the chemotherapy only group, but not in the chemotherapy + radiotherapy group. Ability to participate, as measured on the PROMIS scale, improved significantly for the chemotherapy + radiation group, but not for the chemotherapy only group. There was no significant change for either group in satisfaction with social roles and activities (see Table 8).

H_A3: Change in cognition will positively correlate with change in functional performance within each group

Table 8

Linear Mixed Effect Model Summarizing Changes in Functional Performance by Treatment Group Over the Six Months Following the Completion of Treatment.

	Estimate	Standard Error	df	t-Value	PR>ltl
Chemotherapy Slope					
Physical Function	3.3142	1.2340	14	2.69	**0.0178***
Ability to Participate	3.3969	2.4752	14	1.37	0.1915
Satisfaction with Social Roles	-0.6809	2.6353	14	-0.26	0.7999
Chemotherapy + Radiotherapy Slope					
Physical Function	1.8450	0.9147	14	2.02	0.0633
Ability to Participate	2.8475	1.2976	14	2.20	**0.0447***
Satisfaction with Social Roles	1.8454	1.6475	14	1.12	0.2815

Note. Slope estimates were calculated using mean changes in PROMIS ® T-scores at the three time points- three weeks post treatment, three months post treatment and six months post treatment. *significant at $p<0.05$

A Pearson's correlation matrix was used to examine the correlation of changes in cognitive variables with changes in the functional performance variables for eachgroup over time. A 95% confidence interval (CI) was calculated to determine significance of the correlations. The correlations provide only descriptive data about the direction of relationships. All correlations fell within the 95% CI for the chemotherapy + radiotherapy group, this was not the case for the chemotherapy only group. Appendix F contains the 95% CI tables for all variables in both groups.

Table 9 provides a summary of all correlations for the chemotherapy group. Of the three constructs used to define functional activity, physical activity, ability to participate and satisfaction with participation, only physical activity showed a significant

Table 9

Chemotherapy: Correlations among Mean PROMIS® T-score Changes over Six Months Post Treatment.

Variable	Physical Function	Cognitive Concerns	Cognitive Abilities	Depression	Anxiety	Fatigue	Pain Interference	Sleep Interference	Ability to Participate in Social Roles
Physical Function									
Cognitive Concerns	**-0.6661***								
Cognitive Abilities	0.6252	-0.6075							
Depression	-0.5265	0.5471	**-0.7156***						
Anxiety	**-0.7559***	**0.8321***	**-0.6556***	0.5068					
Fatigue	**-0.7306***	**0.6864***	**-0.7484***	0.5675	**0.6574***				
Pain Interference	**-0.6693***	0.3967	-0.4655	0.4364	0.4986	0.6283			
Sleep Interference	0.5154	-0.4826	0.5019	-0.5203	-0.5584	-0.5584	-0.5765		
Ability to Participate in Social Roles	**0.7338***	-0.5461	0.6192	-0.5592	-0.4834	-0.6222	-0.4823	0.3759	
Satisfaction with Social Roles	-0.4048	0.4504	-0.5841	0.4088	0.4745	0.5306	0.4449	-0.3473	-0.4956

Note. Appendix F contains a full listing of the 95% Confidence Intervals.
*significant at p<.05

negative correlation (p<.05) with cognitive concerns, *r*=.-.66, 95% CI [-.91, -.05]. Likewise, a similar relationship of a significant negative correlation was observed for these two constructs in the chemotherapy + radiotherapy group (see Table 10). The chemotherapy + radiotherapy group showed a significant (p<.05) negative correlation for cognitive concerns and the ability to participate in social roles *r*=-.59, 95% CI [-.79, -.27]. Within the chemotherapy + radiotherapy group, cognitive abilities were significantly, positively correlated with these two variables. This means as cognitive concerns decreased or lessened over time and cognitive abilities improved over time, physical function and ability to participate in social roles improved. An inverse

Table 10

Chemotherapy + Radiotherapy: Correlations among Mean PROMIS® T-score Changes over Six Months Post Treatment.

Variable	Physical Function	Cognitive Concerns	Cognitive Abilities	Depression	Anxiety	Fatigue	Pain Interference	Sleep Interference	Ability to Participate in Social Roles
Physical Function									
Cognitive Concerns	**-0.6917***								
Cognitive Abilities	**0.6551***	**-0.6367***							
Depression	**-0.5659***	**0.5821***	**-0.7377***						
Anxiety	**-0.7781***	**0.8455***	**-0.6864***	**0.5536***					
Fatigue	**-0.7542***	**0.7118***	**-0.7698***	**0.6061***	**0.6917***				
Pain Interference	**-0.6994***	**0.4483***	**-0.5132***	**0.4895***	**0.5507***	**0.6651***			
Sleep Interference	**0.5722***	**-0.5387***	**0.5592***	**-0.5799***	**-0.6456***	**-0.6155***	**-0.6331***		
Ability to Participate in Social Roles	**0.7478***	**-0.5877***	**0.6396***	**-0.5834***	**-0.5158***	**-0.6437***	**-0.5148***	**0.4261***	
Satisfaction with Social Roles	**-0.4366***	**0.4781***	**-0.6047***	**0.4404***	**0.5041***	**0.5555***	**0.4765***	**-0.3945***	**-0.5164***

Note. Appendix F contains a full listing of the 95% Confidence Intervals.
*significant at p<.05

relationship occurred in respect to the correlation of cognition and the satisfaction with participation in social roles. As cognitive concerns lessened over time and cognitive abilities improved, satisfaction with participation in social roles increased. No causation or significance may be determined from correlational analysis.

H_A4: Cognition, as measured by the PROMIS Applied Cognition abilities and concerns scales will differ between the chemotherapy and chemotherapy + radiotherapy groups.

The linear mixed-effects model was used to compare the slopes of the cognition variables for the chemotherapy group with the chemotherapy + radiotherapy group. No significant differences were observed between the two groups over time for cognitive

concerns (Estimate: 2.1723, SE: 1.5397, DF: 14, t: 1.141, PR>ltl 0.1801) and cognitive abilities concerns (Estimate: 0.4903, SE: 1.8425, DF: 14, t: 0.27, PR>ltl 0.7941).

H_A5**:** Functional performance as measured by the PROMIS Cancer Physical Function Scale, the PROMIS Ability to Participate Scale, and the PROMIS Satisfaction with Social Roles and Activities will differ between the chemotherapy and chemotherapy + radiotherapy groups.

No significant differences between the two groups were observed on the functional performance variables when analyzed in the linear mixed-effects model as seen in Table 11.

Table 11

Comparison of Chemotherapy and Chemotherapy + Radiotherapy Groups on Functional Performance

	Estimate	Standard Error	df	t-Value	PR>ltl
Physical Function	1.4692	1.5361	14	0.96	0.3551
Ability to Participate	0.5494	2.7919	14	0.20	0.8468
Satisfaction with Social Roles	-2.5263	3.1079	14	-0.81	0.4299

Exploratory Analysis of Psychosocial Factors and Concurrent Symptoms

Depression and anxiety are viewed as both psychosocial factors and concurrent symptoms in the Revised Conceptual Model of Chemotherapy-Related Changes in Cognitive Function (Myers, 2009). Fatigue and pain interference are considered concurrent symptoms. Sleep interference is not specifically mentioned in this guiding model, but is included as a construct in the PROMIS-57 and was included in this study's analysis. Table 12 provides a summary from the linear mixed-effects model examining

Table 12

Slope Estimates for Psychosocial Factors and Concurrent Symptoms Within and Between Treatment Groups.

	Estimate	Standard Error	DF	t-Value	PR>ltl
Chemotherapy Slope					
Depression	-2.7139	2.2720	14	-1.19	0.2521
Anxiety	1.2185	1.5136	14	0.81	0.4343
Fatigue	-0.2326	2.1281	14	-0.11	0.9145
Pain Interference	-3.5960	2.1679	14	-1.66	0.1194
Sleep Interference	-0.6226	1.5570	14	-0.40	0.6953
Chemotherapy + Radiotherapy Slope					
Depression	-2.1571	1.3080	14	-1.65	0.1214
Anxiety	0.8805	0.8326	14	1.06	0.3082
Fatigue	-3.3835	1.2210	14	-2.77	**0.0150***
Pain Interference	0.7311	1.3360	14	.055	0.5929
Sleep Interference	1.2085	0.9488	14	1.27	0.2235
Chemotherapy Vs Chemotherapy + Radiotherapy					
Depression	-0.5567	2.6216	14	-0.21	0.8349
Anxiety	0.3381	1.7275	14	0.20	0.8477
Fatigue	3.1509	2.4535	14	1.28	0.2199
Pain Interference	-4.3271	2.5465	14	-1.70	0.1114
Sleep Interference	-1.8311	1.8233	14	-1.00	0.3323

Note. Slope estimates were calculated using mean changes in PROMIS-57 T-scores at the three time points- three weeks post treatment, three months post treatment and six months post treatment.
*significant at p<.05

depression, anxiety, fatigue, pain interference and sleep interference. There were no significant differences between groups on these five constructs.

Fatigue was significant (Table 12) in the chemotherapy + radiotherapy group with fatigue decreasing in the six months following treatment. Mean t-scores for fatigue were above 60 for all time points in this group (Table 10). This is one standard deviation greater than the general population of the United States. Although there were not significant changes over time for anxiety and depression in this group, their T-scores were also one standard deviation below the norm (Table 10).

Summary

In summary, the sample (N=16) in this study is considered young (ages 28-45) in regards to breast cancer research. Depression, anxiety and fatigue were at least one standard deviation higher than the normal US population in the chemotherapy + radiotherapy group. A significant improvement in physical function was found in the chemotherapy only group in the 6 months post treatment. Ability to participate in social roles and activities significantly improved in the chemotherapy + radiation group. Fatigue was a significant symptom for the chemotherapy + radiation group. There were no significant differences between the groups on any of the constructs measured in the study. There were no significant changes in self-reported cognition over the course of the study in either group. The following chapter will discuss these results and the study limitations within the context of current evidence and provide recommendations for future research and occupational therapy practice.

Chapter 6: Discussion

The goal of this study was to better understand how cognition and functional performance change after breast cancer treatment in order to better inform occupational therapists and oncology professionals about the challenges breast cancer survivors face after treatment in returning to their life's roles and responsibilities. The original proposal for this study intended to compare individuals who underwent chemotherapy for breast cancer to individuals who received only radiotherapy for their breast cancer at 3 evenly spaced time periods in the six months after completion of treatment. It became apparent several months into the study enrollment that it was going to be challenging to enroll the radiotherapy only group. The study enrollment criteria were expanded to include a group of individuals that received both chemotherapy and radiotherapy which served the purpose of maintaining a comparison group. The sample size (N=16), with seven participants in the chemotherapy group and nine participants in the chemotherapy + radiotherapy group, limits the ability to generalize results and draw conclusions from this study.

Much can be learned from both the process of research and study design employed in this study. In this chapter an overview of the findings placed in the context of study aims and existing literature will be presented. Next, the limitations of the study will be discussed followed by a summary of implications for occupational therapy research and practice, and suggestions for further research.

Cognitive Performance Findings

The primary aims of this study were to measure changes in cognition and functional performance over the 6 months following the completion of treatment for breast cancer and to compare the changes between the two groups. Survivors of breast cancer report problems with cognition for many years after treatment. It is not clear how the reported changes in cognition impact the ability to participate in everyday activities. In this study, cognition was measured in terms of concerns or negative effects, and abilities or positive effects. There were no significant differences between the chemotherapy only group and the chemotherapy + radiotherapy group in regards to either measure of cognitive functioning. Neither group showed significant changes in cognition over the 6 months after the conclusion of treatment. This is in contrast to the study hypothesis predicting an improvement in cognition over time. It was surprising that the chemotherapy group was one standard deviation below norms on the PROMIS Applied Cognition Cognitive Concerns scale across all three time points. In the chemotherapy + radiotherapy group, there was a decline in cognitive abilities that dipped to one standard deviation below normal at the six month follow up. If chemotherapy is the primary contributor to cognitive impairments then one would expect for cognition to improve as the drugs clear the system. Consideration must be made for other physiologic, psychosocial and situational factors that are simultaneously impacting cognition and functional ability.

Within the published literature, self-reported cognitive declines are common for women who have been diagnosed with breast cancer and undergone treatment (Collins et al., 2013; Ganz et al., 2013; Jenkins et al., 2006; Quesnel et al., 2009). Anecdotal

self-reports of cognitive problems occurred during recruitment for this study in response to the Facebook recruitment postings in closed support groups. Survivors that were too far out of treatment to participate provided encouragement and shared their challenges in their comments:

"Cool, We're not dead yet"

"I'm struggling with short term memory loss"

"I have been out of treatment since 2007 but was wondering how you managed to go back to school? I was on 26 at dc, now 35 and I want to but am terrified bc I still have cognitive issues"

"If u ever do 5yrs out id love to help. Because im affected everyday"

Functional Performance Findings

Within current published literature there is a gap in the understanding of resumption of functional performance for cancer survivors. Functional performance as narrowly defined in terms of physical impairments and the ability to perform basic activities of daily living, as measured in previous studies, stops short of considering the full spectrum of activities humans participate in (Brearly et al., 2011; Jansen et al., 2011; O'Toole et al., 2015). Several qualitative studies have explored areas of instrumental activities of daily living and employment (Braithwaite et al., 2010; Ogilvy, Livingstone & Prue, 2008; Player et al., 2014). This is the first study to quantitatively look at cognitive performance and functional performance in broad terms including physical abilities, social participation and personal satisfaction with social participation.

Functional performance was represented by the constructs of physical function, ability to participate in social roles and activities, and satisfaction with social roles and

activities in this research. In the six months following treatment the chemotherapy only group showed significant gains in physical function. For both groups the mean T-scores were lower than 50 which is below the average for a general cancer population (but within 1SD). The chemotherapy group reported higher levels of physical functioning than the chemotherapy + radiotherapy group, however this was not a significant difference. In a 6 month longitudinal study of breast cancer survivors, Jansen et al. (2011) reported greater deficits in motor function associated with taxane based treatment (Jansen et al. 2011). All participants in this study received a taxane based chemotherapy treatment.

The chemotherapy + radiotherapy group showed significant positive changes in their ability to participate in social roles and activities over the six month time period after treatment. There was not a significant change in the reported satisfaction with participation in social roles and activities in either group. Occupational therapists are concerned with both the ability to participate in meaningful activities and an individual's satisfaction. The levels of anxiety, depression and fatigue were one standard deviation higher than the norms for the general US population. These concurrent psychosocial factors may potentially be impacting satisfaction.

Psychosocial Factors and Concurrent Symptoms

An additional aim of this study was comparison of changes in cognition and functional performance with the mediating factors of anxiety, depression, fatigue, sleep disturbance and pain interference. Participants in this study provided self-reports about their feelings of depression, anxiety, fatigue, and how well they sleep, in addition to how pain interferes in their ability to participate in everyday activities. The chemotherapy +

radiotherapy group's mean anxiety scores were one standard deviation higher than the average US population for the entire six month time follow up period. Anxiety has been associated with self-reported cognitive problems for individuals treated for breast cancer (Biglia et al., 2011; Jansen et al., 2011). In designing this study, evidence relating to fear of reoccurrence, which is most likely tied into levels of anxiety, in breast cancer survivors was not examined. With the high levels of anxiety reported by participants and evidence showing a correlation of anxiety with decreases in self-reported cognition, exploration of the impact of fear of reoccurrence on participation in occupations is warranted. In the clinical setting, occupational therapists can provide interventions to assist clients with coping and compensating for their anxiety.

Mean t-scores for reports of depression did not change significantly during the study for either group and were above the standardized score of 50. Depression has been associated with an increase in self-report cognitive problems in several studies (Bender et al., 2009; Biglia et al., 2011; Jansen et al., 2011). Higher levels of depression were also associated with higher levels of fatigue (Jansen et al., 2011). Positive correlations between depression and fatigue were present for both groups in this study (Refer to Tables 9 & 10).

Fatigue scores dropped significantly in the chemotherapy + radiotherapy group during the six month period after treatment. The mean fatigue T-score for this group immediately after treatment was 62.28 dropping to 61.58 at six months, over 1SD greater than average over the entire study period. Fatigue scores were lower in the chemotherapy only group than the chemotherapy + radiotherapy group and did not significantly change over the six month follow up. The higher rates of fatigue in the

chemotherapy + radiotherapy group may be the result of the cumulative effects on the body from the treatments. In a recent study by Kishan et al. (2016) breast cancer patients reported increasing fatigue over the course of treatment, interestingly one of the predictors for higher level fatigue was younger age (>45). The majority of participants in this study were also younger. Fatigue is commonly associated with tiredness. The quality of sleep also impacts tiredness. In this study participants reported sleep disturbance levels above average, and the chemotherapy + radiotherapy group reported an increase in sleep disturbance further out from treatment. Anxiety, depression, fatigue, pain and sleep disturbance appear to be interrelated and it is extremely difficult to tease out the influence of each on cognition and functional performance. The small sample size limited the ability to perform post hoc analysis to explore trends in the relationship of these mediating factors to changes in cognition and functional performance.

Limitations

This was a small study with limited generalizability. The recruitment goal was for 92 participants (46 per group) with the expectation of a 30% attrition rate. Recruitment for this study took place over a period of 10 months and only 16 participants met eligibility requirements and participated. Over the six month time period for follow up the attrition rate was approximately 50%. Follow ups during this study consisted of email communications.

The small sample size and high attrition rate resulted in a need to alter the data analysis plan. The planned analysis with RM ANOVA and RM ANCOVA were replaced with linear mixed-effects models. Linear mixed-effects modeling allow for analyzing

repeated measures at the independent level, can be used when independence is violated and can use all data points, even if the individual did not complete the time series (Tabachnik & Fidell, 2007). The small sample size eliminated the ability to control for covariates such as age, menopause status, hypothyroid, and surgery effects, as well as performing post-hoc analysis.

The study does not have a non-disease control group and did not have a pure disease control group of radiotherapy only. Therefore, no inference can be made regarding the impact of radiotherapy alone. The results of this study are not representative of the general breast cancer population and cannot be compared to the general population. Participants in this study self-selected, therefore self-selection bias is a concern. There is potential that some individuals did not participate because they predetermined they would not qualify.

There is a tendency for breast cancer studies to have samples of middle class, white women. Fifteen out of the sixteen participants indicated they were white. According to the Institute of Medicine (IOM, 2010) only 3-5% of individuals diagnosed with cancer enroll in clinical trials. Through a systematic review covering 304 peer-reviewed publications from 2001-2010, over 80% of the participants were white (Kwiatkowski, Coe, Bailar & Swanson, 2013).

Individuals with diverse backgrounds did not volunteer to participate in this study. Recruitment in the city of Harrisburg and Baltimore, as well as through a national organization did not result in an increase of diversity in the sample. This study attempted to address the bias of recruiting through social media by also recruiting

through oncology clinics and providing non-Internet users an alternative to participate with paper surveys. No requests for paper surveys were received.

This study did not directly measure cognition through standardized, objective neurological testing. Additionally, functional performance was not measured on a standardized observational scale. The study relied entirely on self-report measures which may be impacted by recall bias, social desirability and errors in self-observation (National Collaborating Centre for Primary Care). Additionally, no conclusions about the causality of cognitive and functional changes may be drawn due to the lack of a pre-treatment cognitive assessment. The optimal design would include pre-surgical cognitive assessment and pre-chemotherapy assessment with follow-ups (Wefel et al., 2011).

Implications for Occupational Therapy

Occupational therapists have a strong tradition in the provision of cognitive rehabilitation services for developmental, traumatic, psychological and neurodegenerative conditions. An assumption is made that these skills will carry over to the cancer population and to some extent they do. However, occupational therapists must understand not only the etiology of the cognitive impairments but also the manifestations in the performance of occupations. This study is a beginning point for understanding some of the cognitive and functional performance difficulties that may occur after treatment for breast cancer. This study brings to light the complexity of PBBCI. Higher levels of fatigue, depression and anxiety were all highly correlated with lower levels of cognitive function, physical function and participation in social roles.

In the clinic, occupational therapist are responsible for assessing occupational performance. Many individuals with breast cancer receive occupational referrals as a result of lymphedema. Occupational therapists need to look beyond the physical performance and remediation of lymphedema symptoms and screen for changes in cognition, as well as the presence of anxiety, depression and fatigue. These areas can quickly be screened through self-report with the PROMIS® scales.

The top-down approach of occupational therapy views the client in a holistic manner and provides treatment with a broad based focus on the performance of personally meaningful activities**.** Occupational therapists can assist individuals in the period following the conclusion of chemotherapy and radiotherapy treatment through the instruction and implementation of energy conservation, pain management and relaxation techniques, mindfulness training, developing compensatory strategies to cope with memory changes and cognitive behavioral therapy. Home based and technology based delivery of occupational therapy and cognitive behavioral therapy are beginning to emerge with successful outcomes (Cheng, Lim, Koh, & Tam, 2017; Ferguson et al., 2016; Lyons, Erickson & Hegel, 2012; Morean, O'Dwyer, & Cherney, 2015). Additionally, group of researchers in Spain are currently recruiting for a randomized trial examining the use of occupational therapy for supportive care using a m-health approach (Lozano-Lozano et al., 2016).

Breast cancer survivors may be referred to occupational therapy for only lymphedema treatment. It is the occupational therapists responsibility to thoroughly assess occupational performance and to look at the impact changes in cognition, anxiety, depression and fatigue may be having on their participation. The PROMIS®

instruments offer a quick, standardized way to assess and measure change in these factors. Additionally, they offer norms for easy comparison. The items on the PROMIS® scales provide insight into areas that should be evaluated in greater depth.

Recently the American Occupational Therapy Association began promoting the role of occupational therapy in oncology rehabilitation. Again this is primarily based in the assumption that assessment and intervention will transfer from other areas of practice. There is a paucity of occupational therapy specific research addressing cognitive impairment within cancer rehabilitation. Recently published research reviews published in the *American Journal of Occupational Therapy* (AJOT) are based on the analysis of evidence from other disciplines (Baxter, Newman, Longpré, & Polo, 2017; Hunter, Gibson, Arbesman & D'Amico, 2017a; Hunter, Gibson, Arbesman & D'Amico, 2017b). This study is a beginning point to better understanding the impact of PBCCI on functional performance. Furthermore, no occupational therapy studies were located in a recent search of currently funded NIH projects related to intervention for cognitive impairment related to cancer.

The PROMIS® instruments used in this study were designed for both research and clinical use and serve as a convenient method for gathering information on multiple factors related to cognition and cancer. Occupational therapists can use these instruments to screen clients and to measure changes over the course of treatment. In fact, PROMIS® instruments are readily available in some of the major electronic medical record systems.

In this sample, the ability to participate in social roles and activities was lower than the average for a chronic illness enriched general US population. This is an area in

which occupational therapists can provide intervention to improve participation. The theoretical foundation for this study, the Model of Human Occupation, is focused on understanding the performance of occupations by taking into account volition, habits and performance capacity. From this study it may be hypothesized that depression and anxiety may impact an individual's volition. Performance capacity may be impacted by cognitive and physical changes resulting from the disease process and associated treatment.

Additionally, it is vital that occupational therapists work collaboratively with the oncology team. The Conceptual Model of Chemotherapy-Related Changes in Cognitive Function developed in the nursing field provides a framework for occupational therapists to understand the complexity of factors that contribute to PBCCI. The model provides a basic definition of functional performance. Occupational therapy models, such as MOHO, provide a way to extend the model to reflect the functional trajectory of the client with cancer.

Despite the attention that PBCCI is receiving in the research community, this information does not appear to be changing clinical intervention for survivors. In a study of over 2,000 breast cancer survivors in the US, 60% of the sample self-reported cognitive problems (Buchanan, et al., 2015). Of these, 37% discussed these concerns with their medical provide and a mere 15% of these individuals reported receiving any type of treatment (Buchanan, et al., 2015). Survivors are not being referred to services such as occupational therapy that address changes they are noticing in their cognition and ability to perform everyday activities. Occupational therapy provides a unique and holistic approach to the treatment of cognitive impairment with a focus on participation

in meaningful occupations. As a profession, occupational therapists must advocate for our role in the cognitive rehabilitation of cancer survivors.

Recommendations for Future Research

This study scratched the surface in understanding the connection of self-reported cognitive impairment and its relationship to changes in functional performance. Further research needs to better describe the impact of cancer treatment, not only as it concerns changes in cognition but as a whole, on the participation in daily meaningful occupations. The design of this study can be improved upon to provide one approach to this end. First, a better design would be to enroll participants prior to beginning treatment to provide a baseline for functional performance and cognition. The study might also include additional comparison groups: a chemotherapy only group, a chemotherapy and radiotherapy group, a radiotherapy only group and a hormone therapy only group. The inclusion of standardized neurological assessments may also strengthen the design. Objective neurological assessments would provide a way to pinpoint specific deficit areas. For example, the Rivermead Behavioral Memory Assessment would provide better information about the domains of memory that are impaired and the extent of the impairment. Likewise, the Test of Everyday Attention can provide more detail about deficits in attention. The sample size should be increased to adequately power the study. Special attention should be paid to recruitment procedures and methods for follow-up to limit attrition. This study followed participants for 6 months. This is a very short period. A greater length of follow up is needed to understand the long term impacts of cancer diagnosis and treatment on cognition and function.

This study depended on self-report measures. Other studies attempting to measure cognition related to breast cancer treatment heavily relied on standardized neuropsychological testing (Ahles, Root & Ryan, 2012). Standard neuropsychological testing is heavily decontextualized from the demands of everyday living with testing environments that remove all distractors (Nelson & Suls, 2013; Hutchinson, et al. 2011). This poses a problem, as the impact of PBCCI on activities and participation has not been measured with standardized, valid and reliable assessments. Research utilizing an ecological approach to the evaluation of cognition is needed. Ecological assessments are designed to measure cognitive function within the demands of real life living. Occupational therapists often use ecological approaches to evaluation and are well suited to perform research that would examine the utility of an ecological approach in assessing cognitive impairments associated with cancer treatment.

Additionally, well designed studies are needed to examine the efficacy of occupational intervention for cognitive impairment. Studies are needed to compare occupational intervention to other interventions and also in combination with other treatments, in order to provide cancer survivors with the best options.

This study excluded participants with metastatic breast cancer and several women expressed disappointment about not being able to participate. They too, face cognitive impairments that impact their ability to do the things they want to do. Research is needed in understanding the unique changes in cognition and activities and participation of this population. As current treatments are extending the life expectancies of individuals living with Stage VI cancer, these people want to continue

doing things they like to do. Occupational therapy has the potential to provide interventions that will improve the quality of life for these individuals.

Conclusion

When people complete cancer treatment they are forced into a life transition. This follows a period in which medical appointments, surgeries, invasive radiation or chemotherapy treatments and recovery periods have dominated their days. The big question for survivors is “What’s next?” or “How do I get back to normal?” There are no guides for this transition and little support is provided from the medical establishment. Survivors may go from one day to the next wondering when they will feel like themselves again. As survivors transition back into fuller levels of participation, the after effects of treatment become more visible. Perhaps when the car keys were misplaced before the cancer diagnosis it was viewed as the temporary absent-mindedness of a busy person. After cancer such a miscue may be viewed as a symptom of the disease or a result of invasive treatment and put in a category with forgetting names and appointments or having trouble doing calculations. It is difficult to determine if self-reports are the result of changes in brain function or if they are the result of heightened awareness and a desire to live as one recalled living before cancer. In either scenario, occupational therapy intervention can facilitate increased participation and engagement in occupations for cancer survivors.

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Appendix A

Research Subject Information and Consent Form

TITLE: The Impact of Chemotherapy and Radiotherapy for Breast Cancer on Cognition and Functional Performance: A Comparative Analysis of Survey Data taken at Three Time Points Post-Treatment

VCU IRB PROTOCOL NUMBER: HM20006120
INVESTIGATOR: Lynwood Gentry, PhD

If any information contained in this consent form is not clear or you have any questions, please contact the study staff, by phone or email using the contact information at the end of this document, to explain any information that you do not fully understand. You may take time to think about or discuss this consent form with family or friends before making your decision. When you are ready to decide return to this website to continue.

PURPOSE OF THE STUDY

The purpose of this research study is to find out how cognition and the ability to do everyday activities changes in the 6 months after the completion of treatment for breast cancer. You are being asked to participate in this study because you are nearing the end of chemotherapy or radiotherapy for breast cancer

DESCRIPTION OF THE STUDY AND YOUR INVOLVEMENT

If you decide to be in this research study, you will be asked to indicate that you consent to participate in the research by checking a box after you have had all your questions answered and understand what you will need to do.

Once you submit your consent form, you will be directed to an eligibility questionnaire. This questionnaire will ask you questions about your breast cancer diagnosis and treatment, and your medical history. If you are eligible to continue in the study you will be redirected to the study surveys about your daily activities and cognitive function.

If you are eligible for this study you will be asked to complete online surveys three different times. The first time you complete the surveys will be about two weeks after you complete either chemotherapy or radiation. Then you will complete the same surveys 3 and 6 months later. You will receive an email or text reminders to keep on schedule. The survey will ask you demographic and medical history questions, as well as questions about your general health, activities that you are able to do and how well you feel you do these activities, your attention and memory, and concerns that you have

such as feeling nervous or fearful. The surveys will take 15-30 minutes to complete. During the first survey you will also be asked to refer a caregiver or someone close to you that you see on a regular basis, and is over 18 years of age, to participate by providing an email address or phone number (text or voice) for that person. The caregiver will be asked similar questions about how they observe your ability to do daily activities. If you do not have a caregiver to refer or do not want to refer a caregiver you will still be able to participate in the study.

RISKS AND DISCOMFORTS

Sometimes thinking about these subjects causes people to become upset. Several questions will ask about feeling depressed or anxious. You do not have answer any questions that you do not want to and you may leave the study at any time. If you become upset, you may contact the study staff with the information provided at the end of this document and you will be given the name of a support group to contact so you can get help in dealing with these issues.

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Authority to Request Protected Health Information

The following people and/or groups may request my Protected Health Information:

- Principal Investigator and Research Staff
- Institutional Review Boards
- Government/Health Agencies

Authority to Release Protected Health Information

The VCU Health System (VCUHS) may release the information identified in this authorization from my medical records and provide this information to:

- Health Care Providers at the VCUHS
- Study Sponsor
- Data Coordinators
- Data Safety Monitoring Boards
- Others as Required by Law
- Principal Investigator and Research Staff
- Research Collaborators
- Institutional Review Boards
- Government/Health Agencies

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

Type of Information that may be Released

The following types of information may be used for the conduct of this research:

☐ Complete health record	☒ Diagnosis & treatment codes	☐ Discharge summary
☒ ☒ Laboratory test results	☐ Consultation reports ☐ X-ray reports	☐ Progress notes ☐ X-ray films /

☐ Photographs, videotapes ☐ Complete billing record ☐ Itemized bill
☒ Information about drug or alcohol abuse ☐ Information about Hepatitis B or C tests
☒ Information about psychiatric care ☐ Information about sexually transmitted diseases

☐ Other (specify):

Expiration of This Authorization

☒ This authorization will expire when the research study is closed, or there is no need to review, analyze and consider the data generated by the research project, whichever is later.

☐ This research study involves the use of a Data or Tissue Repository (bank) and will never expire.

☐ Other (specify):

Right to Revoke Authorization and Re-disclosure

You may change your mind and revoke (take back) the right to use your protected health information at any time. Even if you revoke this Authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization you may no longer be allowed to participate in the research study. To revoke this Authorization, you may write, email or text message the Principal Investigator with your request.

BENEFITS TO YOU AND OTHERS

You may not get any direct benefit from this study, but, the information we learn from people in this study may help us design treatments that will help individuals transition out of treatment and back to full living.

COSTS

There are no costs for participating in this study other than the time you will spend filling out questionnaires.

PAYMENT FOR PARTICIPATION

If you are eligible to participate in this study, you will receive an electronic $10.00 gift certificate to Amazon.com or Starbucks, at an email address you provide, once you have completed the first survey. You will also have the option to donate $10 to the Young Survival Coalition if you do not want a gift certificate.

ALTERNATIVES

If you would like to complete this study with paper surveys please contact the primary investigator, Ann Marie Potter, listed below. You may call, email or text message. You will be asked to provide a mailing address where you would like to receive the consent form and surveys. You will first receive the consent form and eligibility survey. Once

your completed consent forms are received and you are determined eligible, the study surveys will arrive by mail. This will be about 2 weeks after you complete radiation or chemotherapy, and again 3 and 6 months later.

CONFIDENTIALITY
Potentially identifiable information about you will consist of your name, birth date, email address, home address, breast cancer diagnosis, and survey data. Data is being collected only for research purposes.

Your data will be identified by a computer assigned ID numbers, not names, and stored separately from research data in a password protected file. All personal identifying information will be kept in separate password protected files and these files will be deleted in 5 years. Access to all data will be limited to study personnel. If you are not eligible for the study your data will be deleted prior to the data analysis phase of the project.

We will not tell anyone the answers you give us; however, information from the study may be looked at or copied for research or legal purposes by Virginia Commonwealth University. Personal information about you might be shared with or copied by authorized officials of the Department of Health and Human Services or other federal regulatory bodies.

What we find from this study may be presented at meetings or published in papers, but your name will not ever be used in these presentations or papers.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
You do not have to participate in this study. Your decision not to take part will involve no penalty or loss of benefits to which you are otherwise entitled. If you choose to participate, you may stop at any time without any penalty. Your decision to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled. You may also choose not to answer particular questions that are asked in the study.

Your participation in this study may be stopped at any time by the study staff without your consent. The reasons might include:

- the study staff thinks it necessary for your health or safety;
- you have not followed study instructions;
- administrative reasons require your withdrawal.

QUESTIONS
If you have any questions, complaints, or concerns about your participation in this research, contact:

Ann Marie Potter, MA, OTR/L - Doctoral Candidate, Researcher Email: pottera2@vcu.edu
Phone/Text: 717-298-7005 Mail: Elizabethtown College,
One Alpha Drive, Occupational Therapy Department,
Elizabethtown, PA 17022
and/or
Tony Gentry, PhD. – Advisor Email: logentry@vcu.edu Phone: 804-828-3397
Mail: Department of Occupational Therapy 730 East Broad Street
P.O. Box 980008
Richmond, Virginia 23298-0008

The researcher/study staff named above is the best person(s) to call for questions about your participation in this study.

If you have any general questions about your rights as a participant in this or any other research, you may contact:

Office of Research
Virginia Commonwealth University 800 East Leigh
Street, Suite 3000
P.O. Box 980568 Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk with someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

Last name

_____

[first_name], are you over 18 years of age?

◯ Yes
◯ No

Consent
I
[first_name] [last_name] have been given the chance
to read this consent form. I understand the
information about this study. Questions that I
wanted to ask about the study have been answered.

◯ By checking this box I agree that I am willing to take part in this research. I may print a copy of the consent form once I have agreed to participate.
◯ I do not wish to participate in this study.

You may print a copy of the consent form for your records here.

[Attachment: "HM20006120 Consent Form .pdf"]

Please provide an email address. _____

You will receive a survey link to this address if you meet all the eligibility requirements to participate in this study.

Please enter your birthdate _____

[first_name], Please provide a phone number where we can contact you during the study. _____

May we send you a text message at the number you provided?

◯ Yes
◯ No

Have you been diagnosed with breast cancer?

◯ Yes
◯ No

Appendix B

Demographics

What date where you diagnosed? **If** you do not recall the exact day please list the **f**irst day of the month that you were diagnosed. **F**or example if you were diagnosed in **D**ecember 2015 and do not remember the exact date enter 12/01/2015.

_____

[first_name], have you ever been diagnosed with any type of cancer before this breast cancer diagnosis?

- ◯ Yes
- ◯ **N**o

What stage is your breast cancer?

- ◯ Stage 0
- ◯ Stage **I**
- ◯ Stage **II**
- ◯ Stage **III**
- ◯ Stage IV

Have you been diagnosed or told by the doctor that you have any of the **f**ollowing conditions? **P**lease check all that apply.

- ☐ **H**ead trauma or brain injury
- ☐ Stroke
- ☐ **E**pilepsy
- ☐ **D**ementia
- ☐ **L**earning disability
- ☐ **D**evelopmental disability impacting cognitive **f**unction
- ☐ Central nervous disease impacting cognitive **f**unction such as Multiple Sclerosis, **P**arkinson's disease or **A**LS
- ☐ none of the above

Do you have a history of substance abuse?

- ◯ Yes
- ◯ **N**o

Have you ever been hospitalized **f**or mental illness?

- ◯ Yes
- ◯ **N**o

Please indicate they type of breast cancer treatment you are currently receiving, plan to receive or recently completed.	◯ Radiation Treatment ◯ Chemotherapy Treatment ◯ Both Radiation and Chemotherapy Treatment
[first_name], are you currently receiving or recently finished (within the past 3 weeks) radiation therapy for your breast cancer?	◯ Yes ◯ No
[first_name], are you currently receiving or recently finished (within the past 3 weeks) chemotherapy for your breast cancer?	◯ Yes ◯ No

Thank you for your interest in this study. You are not eligible to continue. We appreciate your time and willingness to participate. Please email me at pottera2@vcu.edu if you have any concerns or comments.
Ann Marie Potter, MA, OTR/L
Doctoral Candidate in Health Related Sciences-Occupational Therapy

Thank you for completing this first survey in the study. You will receive an email to the address your provided containing a link to the other surveys. This email will arrive about 2 weeks after you complete your breast cancer treatment. We hope that your remaining treatment goes well and look forward to you sharing your experiences with us. Please email pottera2@vcu.edu if you have any concerns. Once again thank you for your participation.
Ann Marie Potter, MA, OTR/L
Doctoral Candidate in Health Related Sciences-Occupational Therapy

At the time of your diagnosis, what was your menopausal status?

- ◯ Pre-menopause
- ◯ Peri-menopause
- ◯ Post-menopause

What is your current menopausal status?

- ◯ Pre-menopause
- ◯ Peri-menopause
- ◯ Post-menopause
- ◯ Chemotherapy induced menopause

Are you currently taking a hormonal therapy to treat your breast cancer?

- ◯ Yes
- ◯ No

What type of hormonal therapy are you taking?

- ◯ Tamoxifen
- ◯ Evista or Fareston
- ◯ Zoladex
- ◯ Lupron
- ◯ Arimidex
- ◯ Femara
- ◯ Aromasin
- ◯ Faslodex
- ◯ Not sure

When did you start your hormonal therapy? If you do not know the exact date please list the first day of the month.

_____

Please check any of targeted therapies below that you are receiving.

- ◯ Trastuzumab (Herceptin)
- ◯ Pertuzumab (Perjeta)
- ◯ Ado-trastuzumab emtansine (Kadcyla)
- ◯ Lapatinib (Tykerb)
- ◯ Other type of targeted therapy
- ◯ Not receiving any type of targeted therapy

Are you currently anemic?

- ◯ Yes
- ◯ No
- ◯ Don't know

Are you currently receiving any thyroid treatment?

- ◯ Yes
- ◯ No

Do you have a history of anxiety?

- ◯ Yes
- ◯ No

Do you have a history of depression?

- ◯ Yes
- ◯ No

How many positive lymph nodes did you have? If you do not know please insert a ? in the box.

_____

For this study we would also like to hear from a caregiver or someone close to you about how they observe your ability to do your everyday activities. This is not mandatory. Please provide the name of your caregiver if you feel comfortable with having us contact them to complete a short survey. If you would like to see the caregiver survey please email pottera2@vcu.edu

_____

Please provide an email contact for your caregiver? If you do not have an email please leave blank.

_____

Please provide a phone number for you caregiver? If you do not have a phone number for your caregiver please leave blank.

Gift card

Please complete the survey below.

Thank you!

Thank you for your participation in this research study. You are eligible to receive a one time $10 electronic gift certificate.

Please indicate what type of gift you would like.

- ◯ Starbucks gift card
- ◯ Amazon gift card
- ◯ Donation to Young Survival Coalition

Please provide an email address for us to send your gift card to. This may take a couple of weeks. _____

Please tell us if you would like to make your donation to the Young Survival Coalition in memory or honor of someone. _____

Appendix C

PROMIS® Instruments

Applied Cognition-Abilities

Please respond to each item by marking one box per row.

	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
PC20	I have been able to bring to mind words that I wanted to use while talking to someone	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC24	I have been able to remember where I put things, like my keys or my wallet.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC27	I have been able to remember to do things, like take medicine or buy something I needed	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC29_2	I have been able to pay attention and keep track of what I am doing without extra effort.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC4	I have been able to think clearly	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC43_2	My mind has been as sharp as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC44_2	My memory has been as good as usual ..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC45_2	My thinking has been as fast as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC46_2	I have been able to shift back and forth between two activities that require thinking	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC47_2	I have been able to keep track of what I am doing, even if I am interrupted	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC6	I have been able to concentrate	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

In the past 7 days…

		Not at all	A little bit	Somewhat	Quite a bit	Very much
PC-CaPS1	I have been able to form thoughts clearly.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS10	I have been able to remember telephone numbers	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS11	I have been able to get my point across when talking with someone	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS12	I have been able to remember the name of a familiar object	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS13	I have been able to think as clearly as usual without extra effort	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS14	I have been able to remember things as easily as usual without extra effort	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS16	My ability to remember important dates has been as good as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS17	My ability to remember names has been as good as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS19	My ability to keep track of lists has been as good as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS2	My thinking has been clear	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS20	My ability to count money has been as good as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS21	My ability to follow driving directions has been as good as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS22	I have been able to handle many tasks at once without losing track of what I was doing	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS23	My ability to remember things that I need to do has been as good as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

In the past 7 days…

		Not at all	A little bit	Somewhat	Quite a bit	Very much
PC-CaPS24	I have been able to multi-task as easily as usual without extra effort	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS3	I have been able to think clearly without extra effort	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS4	My ability to concentrate has been good ...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS5	I have been able to focus my attention	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS6	I have been able to mentally focus.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS7	I have been able to add and subtract numbers in my head without difficulty.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS8	I have been able to remember the name of a familiar person	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC-CaPS9	I have been able to learn new things easily, like telephone numbers or instructions.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Applied Cognition-General Concerns

Please respond to each item by marking one box per row.

	In the past 7 days…	Never	Rarely (Once)	Sometimes (Two or three times)	Often (About once a day)	Very often (Several times a day)
PC1	I have had trouble forming thoughts	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC2	My thinking has been slow	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC3	My thinking has been foggy	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC5	I have had trouble adding or subtracting numbers in my head	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC7	I have made mistakes when writing down phone numbers	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC8	I have had trouble concentrating.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC10	I have had trouble finding my way to a familiar place	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC11	I have had trouble remembering where I put things, like my keys or my wallet.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC12	I have had trouble remembering whether I did things I was supposed to do, like taking a medicine or buying something I needed	☐ 1	☐ 2	☐ 3	☐ 4	☐
PC13	I have had trouble remembering new information, like phone numbers or simple instructions	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC14	I have had trouble recalling the name of an object while talking to someone.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC15	Words I wanted to use have seemed to be on the "tip of my tongue"	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

	In the past 7 days…	Never	Rarely (Once)	Sometimes (Two or three times)	Often (About once a day)	Very often (Several times a day)
PC16	I have had trouble finding the right word(s) to express myself	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC18	I have had trouble speaking fluently.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC21	I have walked into a room and forgotten what I meant to get or do there	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC22	I have needed medical instructions repeated because I could not keep them straight	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC25	I have had to work really hard to pay attention or I would make a mistake.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC26	I have forgotten names of people soon after being introduced	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC28	My reactions in everyday situations have been slow	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC30	Other people have told me I seemed to have trouble remembering information ..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC35	It has seemed like my brain was not working as well as usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC36	I have had to work harder than usual to keep track of what I was doing.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC37	My thinking has been slower than usual..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC38	I have had to work harder than usual to express myself clearly.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC39	I have had more problems conversing with others.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC40	I have had to use written lists more often than usual so I would not forget things....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

	In the past 7 days…	Never	Rarely (Once)	Sometimes (Two or three times)	Often (About once a day)	Very often (Several times a day)
PC41	I have had trouble keeping track of what I was doing when interrupted.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC42	I have had trouble shifting back and forth between different activities that require thinking.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC48	I have hidden my problems with memory, concentration, or making mental mistakes so that others would not notice.....	☐ 1	☐ 2	☐ 3	☐ 4	☐
PC49	I have been upset about my problems with memory, concentration, or making mental mistakes.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PC50	My problems with memory, concentration, or making mental mistakes have interfered with my ability to work.....	☐ 1	☐ 2	☐ 3	☐ 4	☐
PC51	My problems with memory, concentration, or making mental mistakes have interfered with my ability to do things I enjoy	☐ 1	☐ 2	☐ 3	☐ 4	☐
PC53	My problems with memory, concentration, or making mental mistakes have interfered with the quality of my life.....	☐ 1	☐ 2	☐ 3	☐ 4	☐
PC-CaPS25	I have had difficulty multi-tasking.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Ability to Participate in Social Roles and Activities – Calibrated Items

Please respond to each item by marking one box per row.

		Never	Rarely	Sometimes	Usually	Always
RP1	I have trouble doing my regular daily work around the house.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
RP6	I have trouble meeting the needs of my friends	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER_ CaPS1	I have to limit social activities at home ..	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER01 r1	I have trouble meeting the needs of my family.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER02 r1	I am limited in doing my work (include work at home).....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER03 r1	I have to limit social activities outside my home	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER04 _CaPS	I have trouble participating in recreational activities with others	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER05 _CaPS	I have trouble doing everything for my family that I feel I should do.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER06 _CaPS	I have trouble accomplishing my usual work (include work at home).....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER07 _CaPS	I have trouble doing all of the family activities that I feel I should do.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER08 _CaPS	I have trouble doing all of the family activities that are really important to me.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER09 CaPS	I have trouble doing everything for work that I want to do (include work at home).	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

		Never	Rarely	Sometimes	Usually	Always
SRPPER11_CaPS	I have trouble doing all of my regular leisure activities with others	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER13_CaPS	I have to limit social activities with groups of people	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER14r1	I have to limit my regular family activities	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER15_CaPS	I have to limit the things I do for fun with others	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER16r1	I have to do my work for shorter periods of time than usual (include work at home)	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER17r1	I feel limited in the amount of time I have for my family	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER18_CaPS	I have trouble doing all of the family activities that I want to do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER20_CaPS	I have trouble doing all of the activities with friends that are really important to me	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER21_CaPS	I have trouble doing all the leisure activities with others that I want to do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER22_CaPS	I have trouble keeping up with my family responsibilities	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER23_CaPS	I have trouble doing all of my usual work (include work at home)	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER26_CaPS	I have trouble doing all of the work that is really important to me (include work at home)	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER28r1	I have to limit my regular activities with friends	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

		Never	Rarely	Sometimes	Usually	Always
SRPPER31_CaPS	I have trouble taking care of my regular personal responsibilities.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER35_CaPS	I have trouble doing everything for my friends that I want to do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER36_CaPS	I have trouble doing all of the activities with friends that I feel I should do.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER37_CaPS	I have trouble doing all of the work that I feel I should do (include work at home)...	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER42r1	I feel limited in my ability to visit friends	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER43r1	I have trouble keeping in touch with others.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER46_CaPS	I have trouble doing all of the activities with friends that I want to do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER47_CaPS	I have trouble keeping up with my work responsibilities (include work at home)....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER54_CaPS	I have trouble doing everything for my friends that I feel I should do	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
SRPPER55r1	I feel limited in the amount of time I have to visit friends.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Satisfaction with Social Roles and Activities – Calibrated Items

Please respond to each item by marking one box per row.

		Not at all	A little bit	Somewhat	Quite a bit	Very much
SRPSAT17_CaPS	I am satisfied with the extent of my social activities outside my home	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
RP14_CaPS	I am satisfied with my current level of family activities.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
RP7_CaPS	I am satisfied with my ability to maintain friendships.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT03_CaPS	I am satisfied with how often I go out for entertainment	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT04_CaPS	I am satisfied with my ability to socialize with friends	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT05r1	I am satisfied with the amount of time I spend doing leisure activities.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT05_CaPS	I am satisfied with the amount of time I spend doing leisure activities with others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT06r1	I am satisfied with my ability to do things for my family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT07r1	I am satisfied with how much work I can do (include work at home).....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT09r1	I feel good about my ability to do things for my family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT09r1	I am satisfied with my ability to do the work that is really important to me (include work at home).....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT10r1	I am satisfied with my current level of social activity.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

		Not at all	A little bit	Somewhat	Quite a bit	Very much
SRPSAT15_CaPS	I am satisfied with my ability to participate in family activities.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT19r1	I am satisfied with my ability to do all of the community activities that are really important to me.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT20r1	I am satisfied with my ability to do things for my friends.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT21r1	I am satisfied with the amount of time I spend doing work (include work at home)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT22r1	I am happy with how much I do for my family.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT23r1	I am satisfied with my ability to do leisure activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT23_CaPS	I am satisfied with my ability to do leisure activities with others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT24r1	I am satisfied with my ability to work (include work at home).....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT25r1	I am satisfied with my current level of activities with my friends.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT29_CaPS	I am satisfied with my ability to engage in activities with friends.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT33r1	I am satisfied with my ability to do things for fun outside my home	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT33_CaPS	I am satisfied with my ability to do things for fun with others.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT34r1	I feel good about my ability to do things for my friends.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

		Not at all	A little bit	Somewhat	Quite a bit	Very much
SRPSAT35r1	The quality of my work is as good as I want it to be (include work at home).....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT36r1	I am happy with how much I do for my friends	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT37r1	I am satisfied with the amount of time I spend visiting friends.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT39r1	I am satisfied with the amount of time I spend performing my daily routines.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT38_ CaPS	I am satisfied with the amount of time I spend doing things for my family.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT39r1	I am satisfied with my ability to do household chores/tasks	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT41_ CaPS	I am satisfied with the extent of my social activities with groups of people....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT43_ CaPS	I am satisfied with my ability to keep in touch with others.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT45_ CaPS	I am satisfied with my ability to meet the needs of my family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT46_ CaPS	I am satisfied with my ability to meet the needs of my friends.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT47r1	I am satisfied with my ability to do regular personal and household responsibilities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT47_ CaPS	I am satisfied with my ability to do regular personal responsibilities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT48r1	I am satisfied with my ability to do things for fun at home (like reading, listening to music, etc.).....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

		Not at all	A little bit	Somewhat	Quite a bit	Very much
SRPSAT49r1	I am satisfied with my ability to perform my daily routines	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT50r1	I am satisfied with my ability to meet the needs of those who depend on me	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT51r1	I am satisfied with my ability to run errands	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT51_CaPS	I am satisfied with my ability to run errands for others	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT52r1	I am satisfied with my ability to do all of the leisure activities that are really important to me.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
SRPSAT52_CaPS	I am satisfied with my ability to do all of the group activities that are really important to me.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

PROMIS–57 Profile v2.0

Please respond to each question or statement by marking one box per row.

	Physical Function	**Without any difficulty**	**With a little difficulty**	**With some difficulty**	**With much difficulty**	**Unable to do**
1	Are you able to do chores such as vacuuming or yard work?	☐	☐	☐	☐	☐
2	Are you able to go up and down stairs at a normal pace?	☐	☐	☐	☐	☐
3	Are you able to go for a walk of at least 15 minutes?	☐	☐	☐	☐	☐
4	Are you able to run errands and shop?	☐	☐	☐	☐	☐
		Not at all	**Very little**	**Somewhat**	**Quite a lot**	**Cannot do**
5	Does your health now limit you in doing two hours of physical labor?	☐	☐	☐	☐	☐
6	Does your health now limit you in doing moderate work around the house like vacuuming, sweeping floors or carrying in groceries?	☐	☐	☐	☐	☐
7	Does your health now limit you in lifting or carrying groceries?	☐	☐	☐	☐	☐
8	Does your health now limit you in doing heavy work around the house like scrubbing floors, or lifting or moving heavy furniture?	☐	☐	☐	☐	☐
	Anxiety **In the past 7 days…**	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
9	I felt fearful	☐	☐	☐	☐	☐
10	I found it hard to focus on anything other than my anxiety	☐	☐	☐	☐	☐
11	My worries overwhelmed me	☐	☐	☐	☐	☐
12	I felt uneasy	☐	☐	☐	☐	☐
13	I felt nervous	☐	☐	☐	☐	☐
14	I felt like I needed help for my anxiety	☐	☐	☐	☐	☐

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	Anxiety **In the past 7 days…**	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
15	I felt anxious	☐	☐	☐	☐	☐
16	I felt tense	☐	☐	☐	☐	☐
	Depression **In the past 7 days...**	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
17	I felt worthless	☐	☐	☐	☐	☐
18	I felt helpless	☐	☐	☐	☐	☐
19	I felt depressed	☐	☐	☐	☐	☐
20	I felt hopeless	☐	☐	☐	☐	☐
21	I felt like a failure	☐	☐	☐	☐	☐
22	I felt unhappy	☐	☐	☐	☐	☐
23	I felt that I had nothing to look forward to.	☐	☐	☐	☐	☐
24	I felt that nothing could cheer me up	☐	☐	☐	☐	☐
	Fatigue **During the past 7 days…**	**Not at all**	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
25	I feel fatigued	☐	☐	☐	☐	☐
26	I have trouble starting things because I am tired	☐	☐	☐	☐	☐
	In the past 7 days…					
27	How run-down did you feel on average?	☐	☐	☐	☐	☐
28	How fatigued were you on average?	☐	☐	☐	☐	☐
29	How much were you bothered by your fatigue on average?	☐	☐	☐	☐	☐
30	To what degree did your fatigue interfere with your physical functioning?	☐	☐	☐	☐	☐

PROMIS–57 Profile v2.0

Ability to Participate in Social Roles and Activities

		Never	Rarely	Sometimes	Usually	Always
46	I have to limit my regular activities with friends	☐	☐	☐	☐	☐
47	I have to limit my regular family activities	☐	☐	☐	☐	☐
48	I have trouble doing all of the work that is really important to me (include work at home)	☐	☐	☐	☐	☐

Pain Interference
In the past 7 days…

		Not at all	A little bit	Somewhat	Quite a bit	Very much
49	How much did pain interfere with your day to day activities?	☐	☐	☐	☐	☐
50	How much did pain interfere with work around the home?	☐	☐	☐	☐	☐
51	How much did pain interfere with your ability to participate in social activities?	☐	☐	☐	☐	☐
52	How much did pain interfere with your enjoyment of life?	☐	☐	☐	☐	☐
53	How much did pain interfere with the things you usually do for fun?	☐	☐	☐	☐	☐
54	How much did pain interfere with your enjoyment of social activities?	☐	☐	☐	☐	☐
55	How much did pain interfere with your household chores?	☐	☐	☐	☐	☐
56	How much did pain interfere with your family life?	☐	☐	☐	☐	☐

Pain Intensity
In the past 7 days…

57	How would you rate your pain on average?	☐ 0 **No pain**	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10 **Worst imaginable pain**

Physical Function

Please respond to each item by marking one box per row.

		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
PFA8	Are you able to move a chair from one room to another?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA9	Are you able to bend down and pick up clothing from the floor?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA11	Are you able to do chores such as vacuuming or yard work?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA12	Are you able to push open a heavy door?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA13	Are you able to exercise for an hour?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA14	Are you able to carry a heavy object (over 10 pounds)?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA18	Are you able to use a hammer to pound a nail?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA19	Are you able to run or jog for two miles?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA21	Are you able to go up and down stairs at a normal pace?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA24	Are you able to climb several flights of stairs?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA25	Are you able to do yard work like raking leaves, weeding, or pushing a lawn mower?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA26	Are you able to do two hours of physical labor?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

PROMIS - Ca Bank v1.1 – Physical Function

		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
PFA27	Are you able to run on uneven ground?...	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA29	Are you able to pull heavy objects (10 pounds) towards yourself?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA31	Are you able to get up off the floor from lying on your back without help?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA41	Are you able to squat and get up?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA42	Are you able to carry a laundry basket up a flight of stairs?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA53	Are you able to run errands and shop?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA56	Are you able to get in and out of a car?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB10	Are you able to climb up five steps?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB11	Are you able to wash dishes, pots, and utensils by hand while standing at a sink?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB12	Are you able to make a bed, including spreading and tucking in bed sheets?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB13	Are you able to carry a shopping bag or briefcase?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB17	Are you able to put on and take off your socks?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB24	Are you able to run a short distance, such as to catch a bus?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB32	Are you able to stand unsupported for 10 minutes?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

		Not at all	Very little	Somewhat	Quite a lot	Cannot do
PFB44	Does your health now limit you in doing moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB46	Does your health now limit you in doing housework or jobs around the house?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB47	Does your health now limit you in doing recreational activities which require little exertion (e.g., card playing, knitting, etc.)?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB49	Does your health now limit you in going for a short walk (less than 15 minutes)?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB51	Does your health now limit you in participating in active sports such as swimming, tennis, or basketball?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB52	Does your health now limit you in pursuing your hobbies or other leisure activities?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFB55	Does your health now limit you in traveling out of town for an overnight stay?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
		No difficulty at all	**A little bit of difficulty**	**Some difficulty**	**A lot of difficulty**	**Can't do because of health**
PFB50	How much difficulty do you have doing your daily physical activities, because of your health?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Appendix D

Related Recruitment Documents

You are invited to participate in a research study

The Impact of Chemotherapy and Radiotherapy for Breast Cancer on Cognition and Functional Performance: A Comparative Analysis of Survey Data taken at Three Time Points Post-Treatment

Are you completing chemotherapy, radiation, or chemotherapy and radiation for Stage 1-3 breast cancer by the end of 2016? Or have you completed treatment in the past three weeks.

If so, you may be eligible to participate in a research study looking at the changes in the ability to do daily activities and in cognition that may occur after breast cancer treatment.

The purpose of this study is to compare changes in cognition and functional performance in the 6 months after completing breast cancer treatment. Participants in this study will complete an online survey three times - at the end of your treatment, 3 months after completing treatment and 6 months after completing treatment. The survey will take about 15 minutes. Participants can choose to receive a $10 gift card to Starbucks or Amazon.com, or have a $10 donation made to the Young Survival Coalition.

If you would like to participate go to http://bit.ly/bccognition

If you would like to participate in this study and prefer paper copies of surveys to be mailed to you please call Ann Marie at 717-298-7005

This study is being conducted by Ann Marie Potter, a doctoral candidate in the Health Related Sciences- Occupational Therapy program at Virginia Commonwealth University-Richmond, VA.

Please call/text or email Ann Marie with any questions.
717-298-7005 pottera2@vcu.edu

Turning the Corner

YSC YOUNG SURVIVAL COALITION

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(/blog/blog/author/AnnMariePotter)

Turning the Corner

by Ann Marie Potter , MA, OTR/L, Survivor, YSC RISE Legacy Advocate (/blog/blog/author/AnnMariePotter) on Oct 17

Changing My Identity

In December 2006, I was diagnosed with Stage 3 breast cancer at the age of 38. At this point in my life, my identity was wife, mother of three boys--ages 3, 2, and 11 months--and lecturer of occupational therapy. In a moment, my identity changed to breast cancer patient. My personal

journey through treatment was arduous with life threatening surgical complications, overwhelming due to chemotherapy side effects and anxiety-filled "waiting for the other shoe to drop."

As an occupational therapist, I had helped many people reconstruct their lives after illness and traumatic accidents. Now, I found myself having to reconstruct my own life. I was adrift and needed to figure out my roles of mom, wife, breast cancer survivor, occupational therapist and lecturer. My mother-in-law, offered some sage advice--that one day I would wake up and have turned the corner. Now I'll be honest here, I'm a little impatient and was constantly looking for the corner.

Finding That Corner

While in treatment, I attended the YSC National Summit in Washington D.C. One session focused on advocacy and the National Breast Cancer Coalition's

(http://www.breastcancerdeadline2020.org/) work. Now this was something I could get into! I was able to see the direct relationship between advocacy, research and my own treatment. It was clear there was a lot more work to be done. In my mind, I was trying to put together how all my roles interconnected.

I quickly realized that occupational therapy should be included in cancer treatment. For example, I was told not to lift more than 30 pounds, yet no one offered me any advice or strategies of how to take care of a 30+ pound toddler. This is something I would address with a client if they couldn't take care of their child. I also thought about energy conservation and lymphedema prevention and role performance. As I bumbled along in a post treatment haze, I was approached by some OT graduate students that wanted to do their research project related to breast cancer. We decided to look at how roles change for women with breast cancer. Things were beginning to mesh for me and I saw that I could contribute to research on survivorship using my skills as an occupational therapist.

Back To School

I attended NBCC's Project Lead in 2010. During lunch, I discussed my work as an occupational therapist and spoke of my interest in survivorship research. I was encouraged to look at cognition and how it changes related to breast cancer treatment, and how it impacts everyday life. As I reassessed where I was at, I decided that it was time to go back to school for a PhD so I could do better research. I enrolled at Virginia Commonwealth University in the Health Related Sciences-Occupational Therapy Doctoral Program. Between attending boys soccer and little league games and helping with homework-- it was the support of my family and work colleagues who helped me balance life and being a student.

Where It All Lead

Now I am a doctoral candidate. I'm currently researching the impact of breast cancer treatment on cognition and functional performance. Many a breast cancer survivor has complaints of cognitive changes, but we really haven't quantified how much this impacts our abilities to do our everyday life activities. Occupational therapy has been named a first line intervention for cancer associated cognitive impairment by the National Comprehensive Cancer Network. So there is a need within my profession to learn more about the cognitive and functional changes after cancer treatment. My cancer journey hasn't been mapped out well, but I have turned the corner. I'm now able to put together the meaningful things in my life.

The Impact of Chemotherapy and Radiotherapy for Breast Cancer on Cognition and Functional Performance

Ann Marie is currently enrolling individuals, who are Stage 1-3, nearing the completion of treatment--chemotherapy only, radiation only or chemotherapy and radiation. For more information about the study, click here (https://redcap.vcu.edu/surveys/?s=L3HFWRKTTN).

Leave a comment

To leave a message, please login or register for an account.

Ann Marie Potter [ampotter.otr@gmail.com]

Actions

To:
Potter, Ann M

Sunday, July 05, 2015 3:58 PM

---------- Forwarded message ----------
From: **Stacie Jeter** <e>
Date: Thu, May 21, 2015 at 4:33 PM
Subject: RE: Follow up from Thursday
To: Ann Marie Potter <ampotter.otr@gmail.com>

Ann Marie, I wanted to follow-up with you as I was finally able to connect with one of the folks in our IRB. If not to have the study approved by our IRB here at Hopkins, we are not allowed to post information in our clinic about the study or include the study in a list of "our" clinical trials on our websites/handouts; however, our medical oncologists could hand a flier to potentially eligible patients when they see them in clinic that gives them info about the study and invites them to contact you directly. I think that this should still work/help – and save the regulatory effort. Good news! Stacie

Gmail Ann Marie Potter <ampotter.otr@gmail.com>

New flyer for research study

3 messages

Ann Marie Potter <ampotter.otr@gmail.com> Fri, Aug 19, 2016 at 11:38 AM
To: Stacie Jeter <Sjeter1@jhmi.edu>

Hi Stacie
I have attached an updated flyer to my research study. Due to low enrollment since the study opened in May, my dissertation committee approved some changes to the eligibility criteria. Now volunteers will qualify if they are in treatment for both chemotherapy and radiation. Additionally there treatment may neoadjuvant. This change was made since several individuals did not qualify because their surgery was occurring after their chemotherapy treatment.

I have also extend the timeline for the enrollment to include individuals completing their treatment by the end of November 2016.
Please let me know if you need any clarifications or have any questions.
As always, thank you for your support.
Sincerely
Ann Marie

--
Ann Marie Potter

HM20006120 recruitment flyer v9 clean 8_8_2016.approved.pdf
80K

Stacie Jeter <Sjeter1@jhmi.edu> Tue, Sep 27, 2016 at 1:17 PM
To: Ann Marie Potter <ampotter.otr@gmail.com>

Hi Ann Marie, I emailed others, but just noted that I never sent this reply in my draft folder to you. That doesn't usually happen, I'm so sorry! Have you heard from anyone? How is accrual overall?

I'll see what we can do to push a few patients your way these next few weeks! Can you please remind me if the patients can have already started chemo and/or radiation, or if you must get them prior to starting? We have a group meeting tomorrow afternoon and want to "plug" it (again) for you.

Thank you!

Stacie

From: Ann Marie Potter [mailto:ampotter.otr@gmail.com]
Sent: Friday, August 19, 2016 11:38 AM
To: Stacie Jeter
Subject: New flyer for research study

[Quoted text hidden]

Ann Marie Potter <ampotter.otr@gmail.com> Wed, Sep 28, 2016 at 8:17 AM
To: Stacie Jeter <Sjeter1@jhmi.edu>

Hi Stacie
Thanks so much for checking in with me. I was planning to get in touch with you on Friday. I currently have 9 individuals in the study, pretty evenly distributed between the chemo only group and the chemo+rad group. I do not have anyone in the radiation only group. 7 have completed the first survey. I would be very grateful is you could push some more my way. The participants should be close to finishing their treatment (chemo, radiation or at the end of the chemo+rad). The first survey is three weeks after the last day of treatment. If they are going to be finishing treatment before the end of November they can go to the website and enroll. Part of the enrollment/ qualification survey asks the end date for treatment. They will be sent the survey automatically according to the date they indicate. As I get closer to November I will let you know if I will continue enrolling. My ultimate goal would be to have about 30 in each group so I have a solid sample size for analysis even if I lose a few during the course of the 6 months.

I truly appreciate your support and encouragement.
Thank you.
Ann Marie
[Quoted text hidden]
--
Ann Marie Potter

Hi Ann Marie!

I reviewed the submission for your research project "The Relationship between Post Breast Cancer Cognitive Impairment and Function." YSC would be glad to post about your study on social media to aid in your recruitment efforts. Since it looks like participants must be in the Pennsylvania/Baltimore area, I am thinking that our NorthEast Regional Facebook page would be the best place to advertise, but we can also post on the national YSC Facebook page too and Twitter. When your study is IRB approved and you're ready to recruit patients, please send me your proposed text for posting.

I hope you are well. Are you going to BCY2?

Best,

Michelle

Michelle Esser

Program Manager, Research and Advocacy • Survivor

YOUNG SURVIVAL COALITION

Young women facing breast cancer together.

Work days: Monday through Thursday

c 215.588.5572 I youngsurvival.org

Like us on Facebook and Follow us on Twitter and Instagram

Appendix E

List of support groups contacted

List of support groups contacted

Pink Ribbon Friends
Cancer Caring Center
Pink Ribbon Girls
The Small Group Ministry for Breast Cancer Support
P.I.N.K Partners York
Celebrating Hope in Cancer Survivors (CHICS)
ABC Breast Cancer Support Group (YWCA of Carlisle)
Hanover Area Breast Cancer Support Group
ENCORE (YWCA of Allentown) Breast Cancer Recovery Program
Cancer Support Community of the Greater Lehigh Valley
Breast Cancer Support Services of Berks
Breast Friends of PA Breakfast Club
The Cancer Support of Greater Philadelphia
The Healing Foundation of Bucks County
Linked By Pink (Erie)
Looking Ahead Breast Cancer Support Group (Meadville)
Warren County Women's Cancer Support Group
Mercer County Breast Cancer Support Group
Our Clubhouse (Pittsburgh)
Pink Steel Dragon
Butler Breast and Women's Cancer Support Group

Appendix F

Confidence Intervals Tables

Table F1

Chemotherapy + Radiation group 95% Confidence Intervals for Correlations among T-Score Changes over the Six Months Post Treatment

Variable_1	Variable_2	Correlation	Correlation_LCL	Correlation_UCL
Physical Function T Score	Cognitive Concerns T Score	-0.6917	-0.8472	-0.4271
Physical Function T Score	Cognitive Abilities T Score	0.6551	0.3708	0.8272
Physical Function T Score	Depression T Score	-0.5659	-0.7764	-0.2417
Physical Function T Score	Anxiety T Score	-0.7781	-0.8928	-0.5687
Physical Function T Score	Fatigue T Score	-0.7542	-0.8804	-0.5283
Physical Function T Score	Pain Interference T Score	-0.6994	-0.8513	-0.4392
Physical Function T Score	Sleep T Score	0.5722	0.2505	0.7801
Physical Function T Score	Ability to Participate T Score	0.7478	0.5176	0.8770
Physical Function T Score	Satisfaction to Participate T Score	-0.4366	-0.6977	-0.0730
Cognitive Concerns T Score	Cognitive Abilities T Score	-0.6367	-0.8169	-0.3432
Cognitive Concerns T Score	Depression T Score	0.5821	0.2643	0.7859
Cognitive Concerns T Score	Anxiety T Score	0.8455	0.6886	0.9268
Cognitive Concerns T Score	Fatigue T Score	0.7118	0.4589	0.8580
Cognitive Concerns T Score	Pain Interference T Score	0.4483	0.0875	0.7051
Cognitive Concerns T Score	Sleep T Score	-0.5387	-0.7604	-0.2045
Cognitive Concerns T Score	Ability to Participate T Score	-0.5877	-0.7891	-0.2722
Cognitive Concerns T Score	Satisfaction to Participate T Score	0.4781	0.1250	0.7237
Cognitive Abilities T Score	Depression T Score	-0.7377	-0.8717	-0.5009
Cognitive Abilities T Score	Anxiety T Score	-0.6864	-0.8443	-0.4188
Cognitive Abilities T Score	Fatigue T Score	-0.7698	-0.8885	-0.5546
Cognitive Abilities T Score	Pain Interference T Score	-0.5132	-0.7451	-0.1705
Cognitive Abilities T Score	Sleep T Score	0.5592	0.2325	0.7725
Cognitive Abilities T Score	Ability to Participate T Score	0.6396	0.3475	0.8185
Cognitive Abilities T Score	Satisfaction to Participate T Score	-0.6047	-0.7988	-0.2965
Depression T Score	Anxiety T Score	0.5536	0.2248	0.7692
Depression T Score	Fatigue T Score	0.6061	0.2985	0.7996
Depression T Score	Pain Interference T Score	0.4895	0.1396	0.7307
Depression T Score	Sleep T Score	-0.5799	-0.7846	-0.2612
Depression T Score	Ability to Participate T Score	-0.5834	-0.7866	-0.2662
Depression T Score	Satisfaction to Participate T Score	0.4404	0.0777	0.7002
Anxiety T Score	Fatigue T Score	0.6917	0.4271	0.8472
Anxiety T Score	Pain Interference T Score	0.5507	0.2208	0.7675
Anxiety T Score	Sleep T Score	-0.6456	-0.8219	-0.3565
Anxiety T Score	Ability to Participate T Score	-0.5158	-0.7467	-0.1739
Anxiety T Score	Satisfaction to Participate T Score	0.5041	0.1586	0.7396
Fatigue T Score	Pain Interference T Score	0.6651	0.3859	0.8327
Fatigue T Score	Sleep T Score	-0.6155	-0.8050	-0.3121

Table F1 continued

Chemotherapy + Radiation group 95% Confidence Intervals for Correlations among T-Score Changes over the Six Months Post Treatment

Variable_1	Variable_2	Correlation	Correlation_LCL	Correlation_UCL
Fatigue T Score	Ability to Participate T Score	-0.6437	-0.8208	-0.3536
Fatigue T Score	Satisfaction to Participate T Score	0.5555	0.2274	0.7703
Pain Interference T Score	Sleep T Score	-0.6331	-0.8149	-0.3379
Pain Interference T Score	Ability to Participate T Score	-0.5148	-0.7461	-0.1726
Pain Interference T Score	Satisfaction to Participate T Score	0.4765	0.1229	0.7227
Sleep T Score	Ability to Participate T Score	0.4261	0.0602	0.6911
Sleep T Score	Satisfaction to Participate T Score	-0.3945	-0.6707	-0.0222
Ability to Participate T Score	Satisfaction to Participate T Score	-0.5164	-0.7471	-0.1747

Table F2

Chemotherapy + Radiation group 95% Confidence Intervals for Correlations among T-Score Changes over the Six Months Post Treatment

Variable_1	Variable_2	Correlation	Correlation_LCL	Correlation_UCL
Physical Function T Score	Cognitive Concerns T Score	-0.6661	-0.9151	-0.0496
Physical Function T Score	Cognitive Abilities T Score	0.6252	-0.0206	0.9029
Physical Function T Score	Depression T Score	-0.5265	-0.8715	0.1672
Physical Function T Score	Anxiety T Score	-0.7559	-0.9403	-0.2284
Physical Function T Score	Fatigue T Score	-0.7306	-0.9334	-0.1742
Physical Function T Score	Pain Interference T Score	-0.6693	-0.9160	-0.0554
Physical Function T Score	Sleep T Score	0.5154	-0.1819	0.8678
Physical Function T Score	Ability to Participate T Score	0.7338	0.1808	0.9343
Physical Function T Score	Satisfaction to Participate T Score	-0.4048	-0.8285	0.3137
Cognitive Concerns T Score	Cognitive Abilities T Score	-0.6075	-0.8975	0.0491
Cognitive Concerns T Score	Depression T Score	0.5471	-0.1389	0.8783
Cognitive Concerns T Score	Anxiety T Score	0.8321	0.4144	0.9602
Cognitive Concerns T Score	Fatigue T Score	0.6864	0.0868	0.9209
Cognitive Concerns T Score	Pain Interference T Score	0.3967	-0.3224	0.8255
Cognitive Concerns T Score	Sleep T Score	-0.4826	-0.8566	0.2238
Cognitive Concerns T Score	Ability to Participate T Score	-0.5641	-0.8838	0.1147
Cognitive Concerns T Score	Satisfaction to Participate T Score	0.4504	-0.2626	0.8452
Cognitive Abilities T Score	Depression T Score	-0.7156	-0.9292	-0.1435
Cognitive Abilities T Score	Anxiety T Score	-0.6556	-0.9120	-0.0310
Cognitive Abilities T Score	Fatigue T Score	-0.7484	-0.9383	-0.2120
Cognitive Abilities T Score	Pain Interference T Score	-0.4655	-0.8506	0.2447
Cognitive Abilities T Score	Sleep T Score	0.5019	-0.1995	0.8632
Cognitive Abilities T Score	Ability to Participate T Score	0.6192	-0.0303	0.9010
Cognitive Abilities T Score	Satisfaction to Participate T Score	-0.5841	-0.8902	0.0852
Depression T Score	Anxiety T Score	0.5068	-0.1932	0.8649
Depression T Score	Fatigue T Score	0.5675	-0.1098	0.8849
Depression T Score	Pain Interference T Score	0.4364	-0.2787	0.8402
Depression T Score	Sleep T Score	-0.5203	-0.8694	0.1755
Depression T Score	Ability to Participate T Score	-0.5592	-0.8822	0.1218
Depression T Score	Satisfaction to Participate T Score	0.4088	-0.3094	0.8300
Anxiety T Score	Fatigue T Score	0.6574	0.0342	0.9125
Anxiety T Score	Pain Interference T Score	0.4986	-0.2037	0.8621
Anxiety T Score	Sleep T Score	-0.5891	-0.8917	0.0776
Anxiety T Score	Ability to Participate T Score	-0.4834	-0.8569	0.2228
Anxiety T Score	Satisfaction to Participate T Score	0.4745	-0.2338	0.8538
Fatigue T Score	Pain Interference T Score	0.6283	-0.0154	0.9038
Fatigue T Score	Sleep T Score	-0.5584	-0.8820	0.1229

Table F2 continued

Chemotherapy + Radiation group 95% Confidence Intervals for Correlations among T-Score Changes over the Six Months Post Treatment

Variable_1	Variable_2	Correlation	Correlation_LCL	Correlation_UCL
Fatigue T Score	Ability to Participate T Score	-0.6222	-0.9020	0.0255
Fatigue T Score	Satisfaction to Participate T Score	0.5306	-0.1616	0.8729
Pain Interference T Score	Sleep T Score	-0.5765	-0.8878	0.0965
Pain Interference T Score	Ability to Participate T Score	-0.4823	-0.8565	0.2242
Pain Interference T Score	Satisfaction to Participate T Score	0.4449	-0.2689	0.8433
Sleep T Score	Ability to Participate T Score	0.3759	-0.3441	0.8175
Sleep T Score	Satisfaction to Participate T Score	-0.3473	-0.8063	0.3728
Ability to Participate T Score	Satisfaction to Participate T Score	-0.4956	-0.8611	0.2075

Vita

Ann Marie Potter (née Knecht) was born on July 20, 1967 in Queens County, New York. She graduated from Vernon Township High School, Vernon, New Jersey in 1985. She received her Bachelor of Arts in Psychology from Luther College, Decorah, Iowa in 1989. She received a Master of Arts in Occupational Therapy from University of Southern California, Los Angeles, California in 1995. She worked as an occupational therapist specializing in Spinal Cord Injury at Rancho Los Amigos Medical Center, Downey, California from 1992-1995. From 1997- 2002, she was a Clinical Assistant Professor at Florida International University, Miami, Florida in the Occupational Therapy Department. In 2002, she took a position as a lecturer in the Occupational Therapy Department at Elizabethtown College, Elizabethtown, Pennsylvania where she continues to teach and mentor occupational therapy students.