WORK PERFORMANCE LIMITATIONS POST ANASTROZOLE TREATMENT FOR WOMEN WITH BREAST CANCER

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Due to early diagnosis and advancements in breast cancer treatments, an increasing number of women are living longer after treatment. Conversely, many women's experiences of extended life involve enduring long-term effects of breast cancer treatments possibly including pain, fatigue, decreased energy, sensory, and motor function, lymphedema, cognitive impairments, osteoporosis, nausea, and sleeping difficulties (American Cancer Society, 2013; Brach et al., 2004; Jenkins, Shilling, Fallowfield, Howell, & Hutton, 2004; Pullens, De Vries, & Roukema, 2010). Aromatase inhibitors, including anastrozole, have proven efficacy for adjuvant therapy in postmenopausal women with breast cancer (Nabholtz, 2008; Rinaldi, 2013). Adjuvant therapy may have negative effects on cognitive functioning (Bender et. al., 2007; Nattinger et al., 2013). Cognitive, physical, and affective impairments contribute to the likelihood of increased work problems. Largely, the condition, treatments, and consequential effects may alter body functions/structures, activities, and community participation. In theory, anastrozole treatment may increase the likelihood of work problems.

Work after a cancer diagnosis is highly desirable for individuals on a person, social, and economic level, ultimately contributing to quality of life, dignity, self-esteem, and purpose (Steiner, Cavender, Main, & Bradley, 2004). Women with breast cancer commonly report work-related concerns including job loss, demotion, unwanted changes in tasks, problems with the employer/co-workers, personal changes in attitudes to work and diminished physical capacity (Brisson, Dubois, Fraser, Lauzier, & Maunsell, 1999). The purpose of this study was to examine

the effects of the anastrozole breast cancer treatment, as it relates to the individuals' abilities to function at work. Through critical analysis of data from the Anastrozole Use In Menopausal Women (AIM) study, this study found that overall, the anastrozole group reported more work problems than the control group overtime. Pain emerged as a confounding variable that supports reason for further investigation of the effects and role of pain due to breast cancer and/or treatment, specifically as it pertains to work performance. Knowing that more individuals with breast cancer are surviving and are continuing to work or returning to work, additionally considering that treatment effects and residual symptoms are often present, this population likely would benefit from vocational rehabilitation support and services.

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1.0 INTRODUCTION

1.1 BREAST CANCER

Accounting for approximately 29% of newly diagnosed cancers in U.S. women, breast cancer is the most pervasive, aside from skin cancers. In 2013, there were an estimated 232,340 new cases of breast cancer diagnosed in U.S. women, resulting in approximately 39,620 deaths (American Cancer Society, 2013). Among the physical and emotional challenges that women with breast cancer and their families encounter, are an overwhelming number of decisions that they and their health care team confront. Screening the available therapeutic programs and treatment options are among these decisions. Multiple treatment options are offered for patients with different types of breast cancer and volumes of information are available to make the best treatment choices for the particular diagnosis. As incidence rates typically increase with age, approximately 79% of new cases of breast cancer occur in women 50 years of age and older (American Cancer Society, 2013). Due to early diagnosis and advancements in breast cancer treatments, including adjuvant treatments, an increasing number of women are living longer. Conversely, many women's experiences of extended life include enduring long-term effects of breast cancer treatments. Effects may include pain, limited range of motion, fatigue, decreased

energy, decreased sensory and motor function, lymphedema, cognitive impairments, osteoporosis, musculoskeletal symptoms, nausea, hair loss, and sleeping difficulties (American Cancer Society, 2013; Brach et al., 2004; Jenkin, Shilling, Fallowfield, Howell, Hutton, Hutton, 2004; Pullens, De Vries, and Roukema, 2010). Secondary effects may compound or arise from receiving treatments. Symptoms and experiences such as anxiety, depression, fear of recurrence or death, self-concept issues, social isolation, disruptions in family and sexual relationships, and decreased independence are commonly reported to occur (Brach et al., 2004; Schilder et al., 2012). Overall, the condition may alter body functions, structure, activities, community participation, and environmental factors.

An insufficient number of studies have directly addressed the activity limitations and participation restrictions faced by women with breast cancer (Karki, Simonen, Malkia, & Selfe, 2005). As affects of breast cancer and treatments have been well documented, it is imperative that a systematic framework be constructed for accurately defining and assessing clearly objectified functional limitations that impact activity and participation. The International Classification of Functioning, Disability and Health (ICF), published by the World Health Organization, is an international classification system and currently the standard for communicating health and health-related states through a common language over multiple contexts (World Health Organization, 2001). Core sets of functioning are described for numerous health conditions to distinctly label functional limitations that may present for an individual with that condition, in addition to environmental and personal factors that contribute to the overall effect of the limitations.

Within the past 10 years, a team of international healthcare experts identified and developed a core set of functional limitations for individuals with breast cancer, based on the ICF

framework (Brach et al., 2004). This was the first comprehensive list developed according to the standards of the ICF. ICF core sets for breast cancer intend to direct proper identification and definition of problems with daily functioning and guide multidisciplinary treatment (Brach et. al., 2004). Not until 2013 was the core sets validated by the perspective of women who had the condition. Qualitative research, conducted by Cooney, Galvin, Connolly, and Stokes (2013), exploring the perspective of women who have undergone breast cancer treatment strongly supported the validation of the ICF core set for breast cancer. Furthermore, the women identified additional ICF categories that were not included in the core sets. Reevaluation of the current core sets, potential addition of newly identified limitations, and continual modifications are essential to maintain the efficacy of the ICF core sets for breast cancer, in addition to facilitating proper treatment and promoting optimal functioning for women with breast cancer.

1.2 BREAST CANCER TREATMENTS

The current standard treatments for breast cancer may include surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy, and sentinel lymph node biopsy followed by surgery, depending on disease characteristics (Hartmann, 2012). Treatments are recommended based on numerous factors, one of the most important being the stage of breast cancer. Staging determines the extent to which the cancer has spread at the time of diagnosis. Through physical exams, scans, imaging, and tests, the cancer is evaluated and identified as being invasive or non-invasive, additionally considering if the cancer has spread to other parts of the body, the tumor size, and the number of lymph nodes involved. This process helps the clinical team determine

the stage of cancer. A most common staging system for breast cancer is the American Joint Committee on Cancer (AJCC) TNM system. Stage grouping based on the TNM system generates levels expressed with Roman numerals, with stage I being the least advanced stage to stage IV being the most advanced stage (American Cancer Society, 2013).

The hormone estrogen is a main contributor to the development of breast cancer. Hormonal therapies were designed to utilize endocrine agents in reducing the synthesis of estrogen or blocking the estrogen from binding with the breast tumor receptor site. For decades, the gold standard of hormonal treatment of early stage breast cancer in postmenopausal women has been tamoxifen. As resistance to tamoxifen developed, adjuvant therapies were created in the mid 1990's, to supplement or add to hormonal treatment options. Among these newer developments was an aromatase inhibitor (AI), anastrozole. The enzyme aromatase acts as a catalyst in the conversion of androgens to estrogens and provides as the principle factor in the synthesis of estrogen in postmenopausal women (Buzdar, 2006). Inhibiting aromatase is one approach to breast cancer prevention and treatment. Aromatase inhibitors, including anastrozole, have proven efficacy for adjuvant therapy in postmenopausal women with breast cancer (Nabholtz, 2008; Rinaldi, 2013).

New types of treatment are being tested in clinical trials in anticipation of discovering new methods and therapies that may ultimately lead to a cure for the disease. Although breast cancer treatments are extending the lives of thousands, the treatments are often accompanied with an array of side effects that may negatively impact daily functioning and quality of life (Pullens et al., 2010). Side effects vary based on the treatment type and may range from fatigue and nausea to pain, lymphedema, and osteoporosis (Hartmann, 2012). As it has been well recognized that unfavorable effects are often experienced as a derivative of treatments such as

chemotherapy, women's lives may be significantly altered as even routine activities of daily living become particularly difficult due to the decrease in function. Functionality is demonstrated through physical, cognitive, and psychological abilities. Among the more commonly reported side effects are fatigue, pain, and emotional distress (Bennett, Goldstein, Lloyd, Davenport, Hickie, 2004; Nabholtz, 2008; Tchen et. al., 2003; Pullens et al., 2010). As these symptoms often co-exist, they manifest differently for each individual and may compound or increase the impact of symptoms on the individual and their ability to function in daily activities. Bennett et al. (2004) encourage treatment providers to pay close attention to the patient's experience of fatigue and routinely assess the potential of psychological distress, such as depression and anxiety, that may be accompanying or associated with current problematic symptoms.

A decline in physical ability is most easily identifiable, whereas cognitive and psychological deteriorations are more difficult to clearly and objectively measure. Under the cognitive domain, executive functions, include a variety of higher level thought processes such as concentration, monitoring, regulating, initiation, planning, etc., and allow an individual to independently function. Executive functions are imperative for an individual to productively operate at home, work/school, and in society. Therefore, if cognitive function is inhibited as a result of treatment, problems in those settings, including work, will likely arise.

1.2.1. Effects of AIs/Anastrozole

Adverse effects of anastrozole treatment are reported to have included fatigue, infection, fractures, osteopenia, osteoporosis, nausea, hot flashes, vomiting, and cognitive impairments (Nabholtz, 2008; Tchen et. al., 2003; Pullens, et al., 2010). Cognitive dysfunction after treatment

has also been subjectively reported by women with breast cancer. Pullens et al. (2010) concluded that subjective reports of cognitive dysfunction, in women with breast cancer, may be more indicative of emotional distress than objective measures, due to the relationship between subjective cognitive dysfunction and anxiety and depression. The women's subjective reports are reflections of their satisfaction of their cognitive functioning and may be directly related to effects of treatment.

In a cross sectional study, Nattinger et al. (2013) compared cognitive function in a cohort of breast cancer survivors who had been exposed to AI agents to a control cohort of breast cancer survivors without AI exposure. Age and educational levels of the participants were comparable. The participants' cognitive function was measured by neuropsychological measures and task-activated fMRI. Due to the small sample size of 11 participants in each group, effect sizes were examined as an indicator of performance. A trend emerged for the AI group (effect size of 0.3 or greater), showing poorer performance on all 12 tests of the neuropsychological assessments administered, suggesting an overall trend of worse cognitive function in the participants exposed to AI. Additionally, during fMRI testing while completing a working memory task, the control group (no-AI) produced expected patterns of increased regional oxygenation as demands of the task increased, whereas the AI group failed to produce these results. This study indicates the possibility of adverse effects of AI exposure on cognition.

In another study with cross sectional design, Bender et al. (2007) examined memory impairments as a result of receiving tamoxifen compared to anastrozole. Thirty-one women, ages ranging from 21 to 65, who received tamoxifen (n=16) or anastrozole (n=15) treatment for a minimum of 3 months, were incorporated in the study. Age, therapy duration, years of education, depression, anxiety, and fatigue were controlled for upon analysis. A battery of validated and

reliable measures was used to assess cognitive function. The results showed that women who received anastrozole had poorer verbal and visual learning and memory than women who received tamoxifen. Bender et al. (2007) indicated in conclusion, cognitive impairments are capable of affecting overall quality of life, including occupational achievement.

1.3 WORK PROBLEMS ASSOCIATED WITH BREAST CANCER AND TREATMENTS

The literature suggests that adjuvant therapy, specifically anastrozole, may have negative affects on cognitive functioning (Bender et al., 2007; Nattinger et al., 2013). Cognitive impairments contribute to the likelihood of increased work problems. Therefore, in theory, anastrozole treatment may increase the likelihood of work problems.

Aside from earning a livelihood, work is a central component of most individuals' lives. Providing social and psychological benefits, work contributes to the overall wellbeing and identity of an individual (Szymanski & Parker, 2010). Work after cancer is highly desirable for individuals on a person, social, and economic level, ultimately contributing to quality of life, dignity, self-esteem, and purpose (Steiner, Cavender, Main, & Bradley, 2004).

Common concerns and experiences among women treated for breast cancer, in various positions and types of occupations, include job loss, demotion, unwanted changes in tasks, problems with the employer and co-workers, personal changes in attitudes to work and diminished physical capacity (Brisson et al., 1999). It is important to assess the deteriorations in cognitive function, as well as physical and emotional function, resulting from breast cancer therapies and the subsequent impact on work ability. Exploring these issues will promote better

understanding of work problems related to breast cancer, to facilitate better communication of functional limitations between employees, supervisors and coworkers and adjustment to potential work disability.

In 2004, Steiner et al. (2004) published a commentary recognizing gaps in the existing literature concerning the work impact of cancer and its treatments. The commentary concluded that most of the research on return to work and work roles after cancer contained methodological errors, which limited the available literature. Steiner added that while the reviewed literature recognized return to work rates, it failed to address contextual factors and economic impacts. The current study findings may add insight to the ICF core sets for breast cancer specifically related to the workplace. It may also direct treatment decision making for breast cancer patients who are particularly concerned about their ability to perform at work post treatment.

1.4 SIGNIFICANCE OF STUDY

As higher percentages of breast cancer survivors are returning to work and/or continuing to maintain employment after and even during treatment, it is necessary to examine the effects of breast cancer treatments as it relates to the individual's ability to function at work. Furthermore, identifying work problems and analyzing the impact in specific work contexts will supplement the current literature.

Ethical considerations need to be upheld when making the ultimate decision on breast cancer treatment, based on healthcare provider recommendations and patient concerns. *Do the potential benefits from particular treatments outweigh the potential harm caused by the selected treatment?* Women with breast cancer who plan to return to or continue to work, will need to

evaluate the potential outcomes of treatment and how that will impact their functioning in the workplace, in addition to other areas of life. Necessary vocational rehabilitative supports, services, and funding for services should also be a point of priority in discussion when considering post-treatment plans for maintaining or returning to work.

1.5 SPECIFIC AIMS

The purpose of this study was to examine work problems through a critical analysis of self-reported data of women receiving breast cancer treatment, specifically anastrozole. Additionally, the study aimed to identify potential work performance limitations after receiving anastrozole treatment as compared with controls (women that were postmenopausal, who did not have breast cancer nor had undergone any systemic therapy or treatment) and compared within-subjects overtime. Work performance limitations and functions were analyzed under three domains (affective, physiological, and cognitive), as they impact functioning associated with work.

1.5.1 Hypotheses

After a critical review of the current available literature, the following hypotheses were established:

Hypothesis 1: Postmenopausal women with breast cancer self-report (a) higher numbers and (b) greater severity of work problems as compared with the control group, at baseline, prior to treatment.

Hypothesis 2: Postmenopausal women with breast cancer receiving anastrozole treatment self-report (a) higher numbers and (b) greater severity of work problems as compared to the control group, at pre-treatment, 6 months, and 18 months post initial treatment.

Hypothesis 3: Postmenopausal women with breast cancer will self-report (a) higher numbers and (b) greater severity of work problems over time.

2.0 METHODS

2.1 STUDY DESIGN

This study was a retrospective analysis of data that was collected longitudinally to evaluate the impact on work performance through self-reported data of postmenopausal women receiving anastrozole treatment for breast cancer. A control group was incorporated in the study that included women that were postmenopausal, who did not have breast cancer nor had undergone any systemic therapy or treatment. The longitudinal data was originally collected for the Anastrozole Use In Menopausal Women (AIM) study (R01 CA 107408), directed by primary investigator, Dr. Catherine Bender. The National Institutes of Health (NIH) provided funding for the AIM study. Approval for the present study was obtained from the University of Pittsburgh Institutional Review Board (IRB) prior to receiving access to data (PRO14010224). Records gathered from the original study and used in this secondary analysis were data collected by self-report from the participants during the AIM study from October 2005 through 18-months post treatment. A comparison of the treatment and control groups and a critical analysis of the data was conducted at baseline, 6 months post treatment, and 18 months post treatment to examine the magnitude of change in work problems over time. The specific time points were selected for this analysis due to greater amounts of subjective data were reported and available at those time points.

2.2 PARTICIPANTS

Participants consisted of a sample of postmenopausal women who participated in the AIM study from October 2005 through 18-months post treatment. The AIM study recruited the participants from the Comprehensive Breast Care Program of the University of Pittsburgh Cancer Institute and the University of Pittsburgh Medical Center Cancer Centers. The women were diagnosed with stage I, II, and IIIa breast cancer and were eligible to receive hormonal therapy with or without chemotherapy. Random digit dialing was used to recruit controls that were healthy menopausal women. The controls were matched with treatment participants on age and years of education (Bender et al., 2013).

A member of the team from the original study de-identified the data, prior to providing it to the investigator, assigned linkage codes, but did not provide the investigator with access to the linkage codes. The member of the team from the original study was not associated with this research study and only had access to the records for this study for the purpose of de-identifying the data.

2.2.1 Eligibility

Participants' eligibility criteria for this study were adopted from the original AIM study. According to the previous study (R01 CA 107408), the inclusion criteria for all participants were as follows: (a) female; (b) postmenopausal, defined as: 1) amenorrhea persisting for an entire

year, 2) oophorectomy, or 3) hysterectomy and age greater than 51 years (average age of menopause in the U.S.); (c) maximum age of 75 years; (d) able to speak and read English, (neuropsychological tests are normed on English speakers); (e) have completed a minimum of 8 years of education, due to the 8th-grade reading levels required to complete some neuropsychological tests. Additional inclusion criteria for the anastrozole treatment intervention group included: (a) diagnosed with stage I, II, and IIIa breast cancer based on the Tumor, Node, Metastasis Classification System and confirmed by each subject's medical oncologist; (b) eligible to receive either chemotherapy + anastrozole, chemotherapy alone or anastrozole alone. Additional inclusion criteria for the control group included: (a) matched on age, race and level of education with experimental participants; (b) no current or history of any cancer, due to the potential confounding effects of preexisting disease and treatment; (c) not currently taking any form of hormone replacement therapy (HRT).

Exclusion criteria for all participants included the following: (a) self-report of hospitalization for psychiatric illness within the last 2 years, due to the increased risk for cognitive impairment in patients with a history of psychiatric illness; (b) have a prior diagnosis of neurologic illness such as stroke, multiple sclerosis, dementia syndrome, or Parkinson’s disease or of HIV-related dementia or chronic fatigue syndrome, due to the potential confounding effect of these illnesses on cognitive function. Additional exclusion criteria for the anastrozole treatment intervention group included: (a) clinical evidence of distant metastases including the central nervous system, due to the potential confounding effect of metastatic disease on cognitive function; or (b) prior diagnosis of cancer, due to the potential confounding effects of preexisting disease and therapy. The table below is included to clearly show the eligibility inclusion and exclusion criteria for participants in study.

Table 1. Eligibility criteria

Participants	Inclusion Criteria	Exclusion Criteria
All participants	(a) female (b) postmenopausal, defined as: 1) amenorrhea persisting for an entire year, 2) oophorectomy, or 3) hysterectomy and age greater than 51 years (c) maximum age of 75 years (d) able to speak and read English (e) have completed a minimum of 8 years of education	(a) self-report of hospitalization for psychiatric illness within the last 2 years (b) have a prior diagnosis of neurologic illness such as stroke, multiple sclerosis, dementia syndrome, or Parkinson's disease or of HIV-related dementia or chronic fatigue syndrome
Anastrozole only	(a) diagnosed with stage I, II or IIIa breast cancer based on the Tumor, Node, Metastasis Classification System and confirmed by each subject's medical oncologist (b) eligible to receive either chemotherapy + anastrozole, chemotherapy alone or anastrozole alone.	(a) clinical evidence of distant metastases including the central nervous system (b) prior diagnosis of cancer
Controls only	(a) matched on age, race and level of education with experimental participants (b) no current or history of any cancer (c) not currently taking any form of hormone replacement therapy (HRT).	

2.3 OUTCOME INSTRUMENTATION

All data were de-identified prior to the investigator's access. Data were analyzed at baseline (prior to treatment), 6 months post initial treatment, and 18 months post initial treatment. The self-reported questionnaire data, containing the variables being examined, included: (a) Baseline

Demographic/Health Questionnaire, (b) Follow-up Health Questionnaire, (c) Patient Assessment of Own Functioning Inventory (PAOFI), (d) Medical Outcomes Study Short Form 36 Health Survey (SF-36), (e) Beck's Depression Inventory-II (BDI-II), (f) Fatigue/Inertia Subscale of the Profile of Mood States (POMS), and (g) Brief Pain Inventory (BPI). The PAOFI and SF-36 – *work items* were primarily used to measure work problems, the Follow-up Health Questionnaire was incorporated to assess open-ended qualitative information, which may include work problems. The BDI-II, POMS, and BPI were also incorporated to explore potential covariates that could impact cognitive, affective, and physiological functioning and the perception of work limitations.

Table 2. Description of study objectives and corresponding data needed for analysis

Data measure(s)	Objective(s)	Scoring
Baseline Demographic/Health Questionnaire	To establish baseline demographics of research participants to compare with data collected at succeeding time points.	26-question survey was designed to capture information pertaining to personal demographics, physical health, breast cancer, and hormonal status/reproductive history.
Follow-up Health Questionnaire	To identify self-reported changes occurred at specific time points (6 months post initial treatment and 18 months post initial treatment).	6 didactic questions, additionally requesting open-ended detail when necessary. Questions asked about the occurrence of significant changes since the individual's previous meeting.
Patient Assessment of Own Functioning Inventory (PAOFI)	To analyze participants' self-reported assessment of own functioning.	6-point scale ranging from almost never to almost always. *Higher scores representing worse impairment and lower scores denoting less to no impairment.*

Table 2. (continued)

Data measure(s)	Objective(s)	Scoring
Medical Outcomes Study Short Form 36 Health Survey (SF-36)–*work items*	To identify participants self-reported problems at work as a result of physical health and emotional health.	36-item self-report measure of functional ability. Of the SF-36 - work items that were analyzed, scores ranging from 7-35 were possible. These scores assessed physical and psychological functioning. *Higher scores indicated better functioning.*
Beck's Depression Inventory-II	To identify factors associated with affective and cognitive limitations as related to work problems.	21-question self-report inventory measuring the degree and severity of depression. Scores range from 0-63 and *the higher the score, the more severe the depression.*
Fatigue/Inertia Subscale of the Profile of Mood States (POMS)	To identify factors associated with physiological and affective issues as related to work problems.	7-item self-report survey, a portion of the full Profile of Mood States (POMS). A 5-point Likert scale format is used to indicate the degree to which the adjective describes the subject's condition over the last week. *High scores indicated increased fatigue.*
Brief Pain Inventory (BPI)	To identify factors associated with physiological issues as related to work problems.	7-item medical questionnaire to assess the severity of pain and the impact of pain on daily functions. Pain is scored from 0-10 for each items. *The higher the total or average, the more severe the pain.*

2.3.1 Baseline Demographic/Health Questionnaire and Follow-up Health Questionnaire

The Baseline Demographic/Health Questionnaire was a 26-question survey was designed to capture information pertaining to personal demographics (i.e. age, education, occupation, language, etc.), physical health, breast cancer, and hormonal status/reproductive history. The Follow-up Health Questionnaire included 6 "yes or no" questions, additionally requesting open-ended detail when necessary. The questions asked about the occurrence of significant changes since the individual's previous meeting. The Follow-up Questionnaire was completed during the 6-month post treatment and 18-month post treatment intervals. Both the Demographic/Health Questionnaire and the Follow-up Questionnaire consisted of subjective information provided by the study participants. Psychometric properties of these questionnaires have not been evaluated due to the creation of the Follow-up Health Questionnaire as an alternative method of gathering information at 6-months and 18-months post treatment. While administering the Baseline Demographic/Health Questionnaire repeatedly would provide test-retest reliability, the Follow-up Health Questionnaire consisted of items that targeted post treatment results specifically.

2.3.2 Patient Assessment of Own Functioning Inventory (PAOFI)

The Patient Assessment of Own Functioning Inventory (PAOFI) was a 47-item survey that incorporated both physiological and cognitive function into 5 domains. The PAOFI inquired about the participant's frequency of everyday difficulties including memory, higher-level cognition and intellectual functions, use of hands, sensory-perceptual functions, and language and communication. With thirty-three questions related to difficulties with functioning, the inventory used a 6-point scale ranging from *almost never* to *almost always*; higher scores (198

highest possible) on the PAOFI indicated no perceived impairment and lower scores (33 lowest possible score) indicated highest degree of perceived impairment (Chelune, Heaton, & Lehman, 1986). For the present study the scoring scale was reversed to reflect higher scores representing worse impairment and lower scores denoting less to no impairment.

Reliability and validity studies have been limited and not yet established in diverse populations, including breast cancer (Bell, Terhorst, & Bender, 2013). To assess the psychometric properties of the PAOFI in the population of interest, Bell et al. (2013) conducted secondary analysis of reliability and validity of the PAOFI in a sample of postmenopausal women with early-stage breast cancer prior to adjuvant therapy. By correlating PAOFI scores with Profile of Moods States (POMS) and Medical Outcome Study Short Form-36 (SF-36) scores, construct validity was examined. Exploratory factor analysis was performed to further explore the factor structure of the PAOFI. Baseline data from a sample of 259 participants from the Anastrozole Use in Menopausal Women (AIM) Study (R01 CA107408) was used in this secondary analysis. The baseline data was collected after participants (postmenopausal women who had undergone surgery for early-stage breast cancer) completed primary breast surgery but prior to the start of adjuvant therapy. The five-factor structure generated the following categories: Higher Level Cognitive & Intellectual Function, Language & Communication, Memory I, Sensorimotor, and Memory 2. Using Cronbach's alpha, reliabilities for the PAOFI subscale were calculated resulting in the following Cronbach's alpha scores: Memory I = .818, Memory 2 = .744, Language & Communication = .792, Sensorimotor = .572, and Cognitive/Intellectual Functions = .883. All categories were considered to have adequate internal consistencies except for Sensorimotor (Bell et al., 2013). Using the exploratory factor

analysis categories, correlations of PAOFI subscales with POMS Fatigue and SF-36 subscales supported the construct validity of the use of the tool in the particular population.

2.3.3 Medical Outcomes Study Short Form 36 Health Survey (SF-36)

The Medical Outcomes Study Short Form 36 Health Survey (SF-36) was a 36-item self-report measure of functional ability to monitor and assess care outcomes in adult patients (Ware, Snow, Kosinski, & Gandek, 1993; Ware & Sherbourne, 1992). The survey assesses eight health concepts, including: limitations in physical activities because of health problems, limitations in social activities because of physical or emotional problems, limitations in usual role activities because of physical health problems, bodily pain, general mental health (psychological distress and well-being), limitations in usual role activities because of emotional problems, vitality (energy and fatigue), and general health perceptions. Standardized scores, ranging from 0-100, were used to assess physical and psychological functioning. Higher scores indicated better functioning (Bell et al., 2013). From the SF-36, only items numbered 4 and 5, which covered the 'limitations in usual role', were incorporated in the study as those items specifically targeted work limitations due to physical health problems and psychological health problems. The work items were the only items of the SF-36 that were used for analysis.

McHorney, Ware, Rachel Lu, and Sherbourne (1994) studied the psychometric properties of the SF-36 across diverse populations with 3,445 patients with 24 subgroups to reflect diversity. The study supported the measure's item-internal consistency and item-discriminant validity across all groups. Reliability coefficients varied some across subgroups and ranged from 0.65 to 0.94 across scales. These findings support the use of the SF-36 tool in populations of various socioeconomic characteristics, health conditions or diseases, and disease severity.

2.3.4 Beck's Depression Inventory – II

Incorporated as a study measure of affective functioning, Beck's Depression Inventory-II was a 21-question self-report inventory measuring the degree and severity of depression (Beck, Steer, Brown, 1996). The highest possible score on a BDI-II is sixty-three and the lowest possible score is zero. The higher the score, the more severe the depression. The BDI-II is a widely accepted and extensively utilized assessment for evaluating depression in patients with psychiatric diagnoses and in non-psychiatric populations. The original BDI has demonstrated efficacy in adequately maintaining internal consistency, test-retest reliability, and construct validity (Dozois, Dobson, & Ahnberg, 1998). The BDI-II was developed to be more compatible with the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria once the DSM-IV was developed. In a study sampling 1,022 college students the BDI–II has been found to demonstrate high levels of internal consistency with an alpha coefficient of 0.89 for the BDI and 0.91 for the BDI-II. The correlation of validity scores between the two instruments (0.93) supported the convergent validity of the BDI-II. In the same study, factor analysis was also run which identified two main factors, Cognitive-Affective and Somatic-Vegetative, summarized the data (Dozois, Dobson, & Ahnberg, 1998). The source suggests that the BDI-II is more congruent with the DSM-IV and more robust in its factor structure than the BDI.

2.3.5 Fatigue/Inertia Subscale of the Profile of Mood States (POMS)

The Fatigue/Inertia Subscale was a 7-item self-report survey, a portion of the full Profile of Mood States (POMS), and utilized in the study as a physiological measure of (McNair, Lorr, & Droppleman, 1992). The complete POMS comprises of 65 adjectives under 6 subscales: tension-

anxiety, depression, anger-hostility, vigor-activity, fatigue, and confusion-bewilderment. The Fatigue/Inertia Subscale measures the impact of fatigue among the overall context and purpose of the tool to ultimately assess psychological distress. A 5-point Likert scale format is used to indicate the degree to which the adjective describes the subject's condition over the last week. High scores indicated increased fatigue. The tool is used across a variety of clinical and research settings and has achieved acceptance as a measure of psychological distress in healthy, physically ill, and psychiatric populations (Curran, Andrykowski, & Studts, 1995). Internal consistency estimates for the Subscale Scores for the Profile of Mood States (POMS) and the POMS-Short Form (POMS-SF) were assessed in a population of breast cancer patients, and other populations. The Cronback's alpha for the fatigue scales resulted in 0.90 for the POMS and 0.89 for the POMS-SF (Curran et al., 1995). These results justify the usage of the subscales as opposed to the entire original POMS survey in clinical and research settings. Additionally, the POMS has concurrent validity with the BDI.

2.3.6 Brief Pain Inventory

Operating as a study measure of physiological function, the Brief Pain Inventory (BPI) was a 17-item medical questionnaire to assess the severity of pain and the impact of pain on daily functions (Cleeland, 1991). Pain is scored from 0-10 for each item. The higher the total or average score, the more severe the pain. Both total scores and average scores are used clinically. Recognized as a standard tool for assessing self-reported pain, the instrument is widely used in clinical settings and numerous studies for individuals with chronic diseases or conditions, including cancer. Designed with a two-factor structure, the BPI aims to capture severity and interference of pain. Furthermore, it also intends to capture the activity and affective

components of *interference*. Among the original studies of the tool, the BPI was tested across four language versions. Factor analysis was applied to the matrix of intercorrelations for each item. Results revealed that the individuals experiencing cancer and pain who completed the BPI responded to the items in a similar fashion, although living in different countries and speaking various languages (Cleeland, 2009).

A larger factor analysis study completed in the US involving 1261 subjects concluded good internal consistency, with Cronbach alphas ranging from 0.80 to 0.87 for the severity of pain items and from 0.89 to 0.92 for the interference items (Cleeland, 2009). The BPI has proven a reliable tool supported by the assessment of its high test-retest reliability and alternate-form reliability examined in a study completed in 1999 based on 100 patients with cancer taking both the English and Hindi forms of the BPI on different days. The alternate-form reliability of the interference subscale was 0.88 and the reliability of the severity subscales was 0.95. These high rates of reliability are demonstrated when pain is stable or when pain changes in a predictable way (Cleeland, 2009).

2.4 DATA COLLECTION

Following approval for the study (PRO14010224), granted by the University of Pittsburgh Institutional Review Board (IRB), data were obtained from its source through an honest broker. Records gathered from the original study and used in this secondary analysis were teleform data that was collected by self-report from the participants and all data were de-identified prior to the investigator's viewing. Specific variables of selected measures, namely the Baseline Demographic/Health Questionnaire, Follow-up Health Questionnaire, and SF-36, were requested

based on utility and relevance of the variables to the aims of the study. Other measures required that all items be requested to assess the value of the individual items and of the test as a whole. The following table lists the data measures and the specific variables requested from the respective instrument.

Table 3. Data measures and key variables requested for analysis.

Data measure(s) requested	**Data variable(s)**
Baseline Demographic/Health Questionnaire	Item #s (including additional corresponding details for each item): *Section A*: 2, 3, 4, 5, 6, 7, 8, 9, 10 *Section B*: 11 *Section C*: 12, 13, 14, 15, 16 *Section D*: 20, 21
Follow-up Health Questionnaire	All items (including additional corresponding details for each item)
Patient Assessment of Own Functioning Inventory (PAOFI)	All items
Medical Outcomes Study Short Form 36 Health Survey (SF-36)	Item #s: 4 and 5 only (*work items*)
Beck's Depression Inventory-II	All items
Fatigue/Inertia Subscale of the Profile of Mood States (POMS)	All items
Brief Pain Inventory (BPI)	All items

2.4.1 Data condensing of Baseline Demographic/Health Questionnaire

Due to small sample sizes, multiple variables from the original data were collapsed into transformed data to simplify the information for the utility of analysis. Below in Table 4 is a reference identifying the variable, original measures, and transformed measures. A few measures were recorded as continuous data but were transformed to intervals for simpler understanding. Any original measures that did not appear in the transformed column were because there were no data for that specific measure. Handedness, for instance, had original measures of "Yes", "No", or "Both", but none of the participants reported to be "Both", therefore the transformed measure did not include the "Both" measure. Other measures, which were similar in nature, were combined to form measures such as marital statuses like "Currently married or living with partner" and "Separated or divorced", instead of standing independent. For the purposes of this study these details were used as a general understanding of the demographics of the participants and did not need to be examined closely unless outliers or skewness presented.

Table 4. Original and transformed demographic data.

Variable	**Original Measure**	**Transformed Measure**
Age in years	Continuous	40-60 y OR 61-80 y
Years of Education	Continuous	6-13 y OR 14-17 y OR 18-29 y
English as native language	Yes OR No	Yes OR No

Table 4. (Continued)

Race	White OR Black/African American OR American Indian OR Alaska Native OR Native Hawaiian or Pacific Islander OR Asian OR Unknown OR Other	White OR African American
Handedness	Right OR Left OR Both	Right OR Left
Marital Status	Never married OR Currently married OR Living with partner/significant other OR Widow OR Separated OR Divorced	Never married or widowed OR Currently married or living with partner OR Separated or divorced
Number of children	Continuous	No children OR 1-4 OR 5-8
Occupation	Higher execs, major professionals, owners of large businesses OR Managers of medium sized businesses, nurses, opticians, pharmacists, social workers, teachers OR Administrative personnel, managers, minor professionals, owners/proprietors of small businesses: bakery... OR Clerical and sales, technicians, bank teller, bookkeeper, clerk, draftsperson, timekeeper, secretary... OR Skilled manual – usually having had training (baker, barber, brake-person, chef, electrician, fireperson...OR Semi-skilled (hospital aide, painter, bartender, bus driver, cutter, cook, drill press, garage guard... OR Unskilled (attendant, janitor, construction helper, unspecified labor, porter, including unemployed.) OR Homemaker OR Student, disabled, no occupation, retired.	Major professionals OR Minor professionals OR Clerical, sales, technicians OR Skilled or semi-skilled OR Unskilled, homemaker OR Student, disabled, retired, no occupation

Table 4. (Continued)

Gone through natural menopause	Yes OR No OR Does not know	Yes OR No or does not know
Date of BC diagnosis	Continuous	1/1/2005 – 12/31/2007 OR 1/1/2008 – 12/31/2010 OR 1/1/2011 – 12/31/2013
Date of first surgery	Continuous	1/1/2005 – 12/31/2007 OR 1/1/2008 – 12/31/2010 OR 1/1/2011 – 12/31/2013
Type of surgery (first surgery)	Modified Radical Mastectomy OR Total or Simple OR Breast-conserving surgeries (BCS) OR BCS & Sentinel Node Biopsy OR BCS & Axillary Node Dissection OR Other	Modified Radical Mastectomy OR Total or Simple OR Breast-conserving surgeries (BCS) OR BCS & Sentinel Node Biopsy OR BCS & Axillary Node Dissection OR Other
Date of second surgery	Continuous	1/1/2005 – 12/31/2007 OR 1/1/2008 – 12/31/2010 OR 1/1/2011 – 12/31/2013
Type of surgery (second surgery)	Modified Radical Mastectomy OR Total or Simple OR Breast-conserving surgeries (BCS) OR BCS & Sentinel Node Biopsy OR BCS & Axillary Node Dissection OR Revision OR Other	Modified Radical Mastectomy OR Total or Simple OR Breast-conserving surgeries (BCS) OR BCS & Sentinel Node Biopsy OR BCS & Axillary Node Dissection OR Revision OR Other

Table 4. (Continued)

Stage of breast cancer	LCIS OR DCIS OR Stage 1 OR Stage 2a OR Stage 2b OR Stage 3a	Stage 1 OR Stage 2a OR Stage 2b OR Stage 3a

2.4.2 Selected variables of the Follow-up Health Questionnaire

Originally, all of the items of the Follow-up Health Questionnaire were requested for analysis and selected to undergo evaluation. Each question required a "yes" or "no" response and if the participant responded "yes", further open-ended description was requested. Of the six items, the results from question 5, "Have you had any other significant changes in life since our last meeting," were found to be most applicable for this study and therefore were the only data incorporated in the results for hypothesis #3. As the other questionnaire items mostly pertained to health related concerns, question 5 remained open for potential reports of work related issues. Only the anastrozole group's results were assessed, in line with the aims of the hypothesis.

2.4.3 Selected variables of the Medical Outcomes Study Short Form 36 Health Survey (SF-36)

Based on the aims of the study, only items #4 and #5 of the SF-36 were used for analysis because the variables directly inquired about the impact of either physical or emotional health on ability to perform at work or other regular activities. For both questions and sub-questions, a Likert scale was used to score the responses. The following are examples of questions #4 and #5.

Question 4: During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

a) Cut down on the amount of time you spent on work or other activities
b) Accomplished less than you would like
c) Were limited in the kind of work or other activities
d) Had difficulty performing the work or other activities (for example, it took extra effort)

Question 5: During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

a) Cut down on the amount of time you spend on work or other activities
b) Accomplished less than you would like
c) Did work or other activities less carefully than usual

2.5 STATISTICAL ANALYSIS

Data were analyzed using IBM SPSS Statistics Version 22.0. IBM SPSS statistics was a software program used for statistical analysis (IBM Inc., 2013). Distributions were analyzed using frequencies, means, and standard deviations. Alpha levels set at 0.05 a priori. Descriptive statistics were run. Baseline differences were analyzed using χ^2 (categorical data) and t-tests for continuous data.

Hypothesis 1: Postmenopausal women with breast cancer self-report (a) higher numbers and (b) greater severity of work problems as compared with the control group, at baseline, prior to treatment.

Hypothesis 1 was tested at baseline with independent sample t-tests to assess if differences existed between the group with anastrozole treatment and the control group. Prior analysis was also conducted to identify if missing or skewed data were present in the samples at baseline and to adjust for if necessary. Descriptive statistics were used to assess missing and skewed data using frequencies and percentages for all categorical variables, means, and standard deviations for all continuous variables as applicable.

Hypothesis 2: Postmenopausal women with breast cancer receiving anastrozole treatment self-report (a) higher numbers and (b) greater severity of work problems as compared to the control group, at pre-treatment, 6 months, and 18 months post initial treatment.

Hypothesis 2 was assessed using repeated measures to control for experimental variability and to examine changes in number and severity of work problems. Participants will act as their own controls (within-subject design). A 2 x 3 mixed analysis of variance (ANOVA) was conducted to determine if there were significant differences in self-reported work problems or limitations on work performance, between the group receiving anastrozole and the control group, at baseline, 6 months, and 18 months post initial treatment. This analysis was used to identify if there were differences in work problems between the two groups, overtime. Figure 1 is provided as a visual diagram to assist in depicting the method of analysis.

	Pre-treatment	6 months	18 months
Anastrozole Group			
Control Group			

Figure 1. 2x3 Mixed Model ANOVA conceptual diagram

Hypothesis 3: Postmenopausal women with breast cancer receiving anastrozole will self-report (a) higher numbers and (b) greater severity of work problems over time.

Hypothesis 3 was assessed using repeated measures to examine changes in frequency and severity of work problems. Only results from the anastrozole group were assessed to target the aim of Hypothesis #3. Due to the limited open-ended response rate of work problems, qualitative analysis was conducted to identify reported changes in work, including both positive and negative changes.

3.0 RESULTS

3.1 DESCRIPTIVE STATISTICS

Two hundred and seventy-one total individuals participated in the study, all of who were females. The participants were divided into two groups. The first group, referred to as the anastrozole group, included women with breast cancer who received anastrozole treatment and the second group, controls, consisted of women of like demographic makeup but did not have breast cancer nor the anastrozole treatment.

Based on the information collected from the participants' de-identified baseline demographics, the mean age of the participants in the anastrozole group was 59.9 years (SD= 5.6; range= 44.3 – 71.5) and the mean age of the participants in the control group was 59.5 (SD= 5.8; range= 42.5 – 74.9). To examine distribution and concentration of age, age was also separated by age range for each group (Table 5). For both groups, there were more participants in the 40-60 age range than the 61-80 range. The years of education of the samples were likewise divided into ranges to further examine the distribution of years of education. The categories of years of education were 6-13 years, 14-17 years, and 18-29 years. The racial

makeup of the sample was predominantly white (anastrozole: 93.8%, n= 126; control: 97.9%, n= 140) and the only other ethnicity reported for each group was African American (anastrozole: 6.3%, n= 8; control: 8.4%, n= 12).

Information on participants' occupational levels was examined at baseline. The data were grouped into multiple categories with occupational labels but an explanation for how the categories were originally created was not available. For purpose of statistical analysis, some categories were consolidated to create six total occupational categorical groupings: (1) major professionals, (2) minor professionals, (3) clerical, sales, technicians, (4) skilled or semi-skilled, (5) unskilled, homemaker, (6) student, disabled, retired, no occupation. Major professionals (anastrozole: 21.9%, n= 28; control: 24.5%, n= 35) consisted of occupations such as: higher executives, major professionals, owners of large businesses, managers of medium sized businesses, nurses, opticians, pharmacists, social workers, teachers. Minor professionals (10.2%, n= 13; control: 27.3%, n= 39) consisted of occupations such as: administrative personnel, managers, minor professionals, and owners/proprietors of small businesses. The clerical, sales, technician category (anastrozole: 22.7%, n=29; control: 23.8%, n= 34) consisted of occupations such as: clerical and sales, technicians, bank teller, bookkeeper, clerk, draftsperson, timekeeper, and secretary. Skilled or semi-skilled occupations (anastrozole: 11.7%, n= 15; control: 7%, n= 10) consisted of: usually having training (baker, barber, brake person, chef, electrician, fireperson) or semi-skilled jobs (hospital aide, painter, bartender, bus driver, cutter, cook, drill press, garage guard). Unskilled, homemaker occupations category (anastrozole: 8.6%, n= 11; control: 6.3%, n= 9) consisted of: attendant, janitor, construction helper, unspecified labor, porter, including unemployed and homemaker. Lastly, the sixth category consisted of students, individuals who were disabled, and individuals who had no occupation or were retired

(anastrozole: 25.0%, n=32; control: 11.2%, n= 16). Information was additionally collected on participants' demographic reports on native speaking language, handedness, marital status, number of children, and whether they had gone through menopause. See table 5 for frequencies and percentages of each domain of demographic information at baseline.

Between groups at baseline, there were no significant differences found in demographic information in all categories except for occupations. The occupations between the anastrozole group and the control group were significantly different (p= .001). Overall, there were higher percentages of women from the control group reporting employment as major professionals, minor professionals, and clerical/sales/technicians as there were from the anastrozole group. Additionally to be recognized, 25.0% of the anastrozole group, over double the 11.2% of the control group, reported to be in the category of "student, disabled, retired, or no occupation". These results likely contributed greatly to the skewness of baseline demographic data for occupations.

Separately, information was gathered on the women with breast cancer, at baseline, prior to having anastrozole treatment. This information, displayed in table 6, included date of breast cancer diagnosis, date of first surgery and type of surgery, date of second surgery and type, and stage of breast cancer. All 128 total women with breast cancer reported on this information.

Table 5. Baseline demographics.

Variable, mean (SD) or no. (%)	Anastrozole n=128	Control n=143	Anastrozole group vs. Control group p Value
Age in years			0.688
Mean (SD)	59.9 (5.6)	59.5 (5.8)	
Minimum	44.3	42.5	
Maximum	71.5	74.9	
Age			0.688
40 – 60 y	73 (57.0)	85 (59.4)	
61 – 80 y	55 (43.0)	58 (40.6)	
Years of Education			0.608
6 – 13 y	48 (37.5)	47 (32.9)	
14 – 17 y	49 (38.3)	63 (44.1)	
18 – 29 y	31 (24.2)	33 (23.1)	
English as native language			0.744
Yes	126 (93.8)	140 (97.9)	
No	2 (1.6)	3 (2.1)	
Race			0.501
White	120 (93.8)	131 (91.6)	
African American	8 (6.3)	12 (8.4)	
Handedness*			0.111
Right	117 (91.4)	120 (85.1)	
Left	11 (8.6)	21 (14.9)	
Marital Status			0.128
Never married or widowed	22 (17.2)	21 (14.7)	
Currently married or living with partner	85 (66.4)	84 (58.7)	
Separated or divorced	21 (16.4)	38 (26.6)	
Number of children			0.740
No children	27 (21.1)	25 (17.5)	
1 – 4	89 (69.5)	103 (72.0)	
5 - 8	12 (9.4)	15 (10.5)	
Occupation			0.001
Major professionals	28 (21.9)	35 (24.5)	
Minor professionals	13 (10.2)	39 (27.3)	
Clerical, sales, technicians	29 (22.7)	34 (23.8)	
Skilled or semi-skilled	15 (11.7)	10 (7.0)	
Unskilled, homemaker	11 (8.6)	9 (6.3)	
Student, disabled, retired, no occupation	32 (25.0)	16 (11.2)	
Gone through natural menopause			0.369
Yes	104 (81.3)	122 (85.3)	
No or does not know	24 (18.8)	21 (14.7)	

*Missing data: 2

Table 6. Baseline demographics – Anastrozole only group

Variable, no. (%)	**Anastrozole n=128**
Date of BC diagnosis	
1/1/2005 – 12/31/2007	47 (36.7)
1/1/2008 – 12/31/2010	61 (47.7)
1/1/2011 – 12/31/2013	20 (15.6)
Date of *first* surgery*	
1/1/2005 – 12/31/2007	42 (32.8)
1/1/2008 – 12/31/2010	63 (49.2)
1/1/2011 – 12/31/2013	20 (15.6)
Type of surgery (first surgery)	
Modified Radical Mastectomy	10 (7.8)
Total or Simple	15 (11.7)
Breast-conserving surgeries (BCS)	3 (2.3)
BCS & Sentinel Node Biopsy	83 (64.8)
BCS & Axillary Node Dissection	9 (7.0)
Other	24 (18.8)
Date of *second* surgery**	
1/1/2005 – 12/31/2007	15 (11.7)
1/1/2008 – 12/31/2010	22 (17.1)
1/1/2011 – 12/31/2013	6 (4.7)
No second surgery	81 (63.3)
Type of surgery (second surgery)**	
Modified Radical Mastectomy	0
Total or Simple	4 (3.1)
Breast-conserving surgeries (BCS)	0
BCS & Sentinel Node Biopsy	0
BCS & Axillary Node Dissection	3 (2.3)
Revision	7 (5.5)
Other	29 (22.7)
Stage of breast cancer	
Stage I	50 (39.1)
Stage IIa	41 (32.0)
Stage IIb	22 (17.2)
Stage IIIa	15 (11.7)

*3 missing data

**4 missing data

3.2 HYPOTHESIS 1

Hypothesis 1: Postmenopausal women with breast cancer self-report (a) higher numbers and (b) greater severity of work problems as compared with the control group, at baseline, prior to treatment.

Prior to running t-tests, some data needed transformed, recoded, and/or restructured preceding running statistical testing. Assessment of skewness and missing data were also accounted for and noted before statistical analysis and guided proceeding steps.

T-tests were conducted for each PAOFI subscale to analyze limitations to functioning in participants with anastrozole treatment as compared to controls, prior to treatment being administered. Although each PAOFI sub-scale varies in numerical scoring, all sub-scale sum scores are understood that the ***higher scores indicate worse impairment***. Each subscale was examined individually and generated independent p-values (Table 7). There was no significant difference in the *memory* subscale sum scores for anastrozole group (M=8.02, SD=5.39) and control group (M=8.25, SD=4.94) conditions; t(256)= -.352, p= .724. There was no significant difference in the *language and communication* subscale sum scores for anastrozole group (M=5.93, SD=5.44) and control group (M=5.80, SD=4.52) conditions; t(256)= .210, p= .691. There was no significant difference in the *use of hands* subscale sum scores for anastrozole group (M=1.21, SD=1.37) and control group (M=1.76, SD=1.90) conditions; t(256)= -.2.615, p= .051. There was no significant difference in the *sensory/perceptual* subscale sum scores for anastrozole group (M=.62, SD=1.11) and control group (M=1.06, SD=1.77 conditions; t(256)= -2.912, p= .081. There was no significant difference in the *higher level of cognitive and intellectual functioning* subscale sum scores for anastrozole group (M=4.01, SD=4.65) and control group (M=3.76, SD=4.50) conditions; t(256)= .443, p= .639.

A t-test was conducted for the SF-36–*work items* sum scores to compare limitations in work performance in participants with anastrozole treatment and controls, prior to treatment being administered. Sum scores for work items alone would fall between 7 and 35, with ***higher scores indicating better functioning***. There was a significant difference in the scores for anastrozole group (M=26.92, SD=6.62) and control group (M=31.25, SD=5.30) conditions; t(258)= -5.86, p= .001 (Table 7). The results suggest that prior to treatment, there were significant differences related to pain between the anastrozole group and the control group.

A t-test was conducted for the BDI-II sum scores to identify and compare potential covariates due to depressive symptoms that may impact results, in participants with anastrozole treatment and controls, prior to treatment being administered. Scores could range from 0-63, with ***higher scores indicating more severe depression***. There was no significant difference in the scores for anastrozole group (M= 6.29, SD= 6.62) and control group (M=5.25, SD=5.83) conditions; t(269)= 1.37, p= .135 (Table 7). The results suggest that prior to treatment, there were no significant differences related to depression between the anastrozole group and the control group.

A t-test was conducted for the BPI sum scores to identify and compare potential covariates due to pain that may impact results, in participants with anastrozole treatment and controls, prior to treatment being administered. Scores could range from 0-70, with ***higher scores indicating more severe pain***. There was a significant difference in the scores for anastrozole group (M= 11.73, SD= 16.00) and control group (M=5.21, SD=12.30) conditions; t(269)= 3.79, p= .001 (Table 7). The results suggest that prior to treatment, there were significant differences related to pain between the anastrozole group and the control group.

A t-test was conducted for the POMS-fatigue/inertia sum scores to identify and compare potential covariates due to fatigue that may impact results, in participants with anastrozole treatment and controls, prior to treatment being administered. Scores could range from 0-28, with ***higher scores indicating increased fatigue***. There was no significant difference in the scores for anastrozole group (M= 5.33, SD= 5.18) and control group (M=5.78, SD=5.39) conditions; t(259)= -.381, p= .729 (Table 7). The results suggest that prior to treatment, there were no significant differences related to fatigue between the anastrozole group and the control group.

Table 7. Comparison of anastrozole and control groups prior to treatment

	Anastrozole			Control			
Variable, (Total score)	n	M	SD	n	M	SD	p-value***
PAOFI							
Memory (0-54)	123*	8.02	5.39	135**	8.25	4.94	.724
Lang/Comm (0-48)	123*	5.93	5.44	135**	5.80	4.52	.691
Use of Hands (0-12)	123*	1.21	1.37	135**	1.76	1.90	.051
Sens-Percep (0-18)	123*	0.62	1.11	135**	1.06	1.77	.081
Higher Level Cogn/Int Functioning (0-54)	123*	4.01	4.65	135**	3.76	4.50	.639
SF-36 – ***work items*** (7-35)	121	26.92	6.62	139	31.25	5.30	.001
BDI-II (0-63)	128	6.29	6.62	143	5.25	5.83	.135
BPI (0-70)	128	11.73	16.00	143	5.21	12.30	.001
POMS–fatigue/inertia (0-28)	122	5.33	5.18	139	5.78	5.39	.729

*2 missing data
**1 missing data
***Anastrozole group vs. Control group

3.3 HYPOTHESIS 2

Hypothesis 2: Postmenopausal women with breast cancer receiving anastrozole treatment self-report (a) higher numbers and (b) greater severity of work problems as compared to the control group, at pre-treatment, 6 months, and 18 months post initial treatment.

3.3.1 Patient Assessment of Own Function Inventory (PAOFI)

A 2 x 3 mixed analysis of variance was performed on the Patient Assessment of Own Function Inventory (PAOFI) sub-scales' sum scores, to examine functional limitations as a function of time and anastrozole treatment. The within-subjects independent variable was time with 3 levels (pre-treatment, 6 months post initial treatment, and 18 months post initial treatment). The between-subjects independent variable was treatment with 2 levels (anastrozole treatment and controls with no breast cancer nor treatment). Prior to running statistics, the data were restructured in SPSS to produce workable data for the necessary analysis. The PAOFI sub-scale scores were categorized by six assessment output domains: memory, language and communication, use of hands, sensory-perceptual, higher level cognitive and intellectual functions. The participants were measured on the POAFI at pre-treatment, 6 months post treatment, and 18 months post treatment. Assumptions of sphericity, normality, homogeneity of variance and covariance and determination of significant differences were established for each domain individually and reported respectively. The means, standard deviations, and standard

errors of the anastrozole group's PAOFI scores are reported in Table 8 and the control group's PAOFI scores are reported in Table 9.

Table 8. PAOFI Subscales – mean, standard deviation, and standard error of functional limitations by time for anastrozole group

Anastrozole Group **PAOFI subscales**	n	*M*	SD	SE
Memory				
Pre-treatment	42	6.50	4.11	.746
6 mo.	42	9.14	7.32	.972
18 mo.	42	9.02	7.14	.949
Language & Communication				
Pre-treatment	42	4.10	4.01	.675
6 mo.	42	6.14	5.74	.772
18 mo.	42	6.50	5.77	.809
Use of Hands				
Pre-treatment	42	1.14	1.35	.291
6 mo.	42	1.62	1.79	.294
18 mo.	42	1.81	1.78	.289
Sensory-Perception				
Pre-treatment	42	0.50	1.15	.277
6 mo.	42	1.33	2.17	.295
18 mo.	42	1.52	2.51	.347
Higher Level Cognitive & Intellectual Functions				
Pre-treatment	41	2.46	3.51	.661
6 mo.	41	4.29	6.06	.863
18 mo.	41	5.27	6.85	.913

Table 9. PAOFI Subscales – mean, standard deviation, and standard error of functional limitations by time for control group.

Control Group PAOFI subscales	n	*M*	SD	SE
Memory				
Pre-treatment	56	8.32	5.31	.646
6 mo.	56	7.71	5.41	.842
18 mo.	56	6.80	5.29	.822
Language & Communication				
Pre-treatment	56	5.40	4.62	.584
6 mo.	56	4.97	4.34	.668
18 mo.	56	4.75	4.81	.701
Use of Hands				
Pre-treatment	56	2.25	2.20	.252
6 mo.	56	1.95	1.99	.255
18 mo.	56	1.55	1.93	.250
Sensory-Perception				
Pre-treatment	56	1.48	2.16	.240
6 mo.	56	1.09	1.69	.255
18 mo.	56	1.13	2.04	.301
Higher Level Cognitive & Intellectual Functions				
Pre-*treatment*	56	3.95	4.69	.566
6 mo.	56	3.91	5.10	.738
18 mo.	56	3.79	4.98	.781

PAOFI – Memory. The assumption of homogeneity of covariance was not met, Box's *M* = 47.47, $F(6, 54012.242) = 7.635$, $p = .001$ ($\alpha = .001$), Mauchly's $W = .962$. Since the data violated the assumption, the within-subjects values were reported based on the Greenhouse-Geisser correction. Sphericity for within-subjects effects was met, Mauchly's W = .96, X^2 (2) = 3.63, p = .162. All other assumptions were met. There was no significant difference on the

PAOFI memory sum scores over the period of time examined within-subjects, $F(1.93, 185.05) = 2.15$, $p = 0.121$, $\eta^2 = .022$ and there were no significant differences between-subjects, $F(1, 96) = .343$, $p = 0.559$, $\eta^2 = .004$. The result of the PAOFI – *Memory* sum scores for both groups, over time, is displayed in Figure 2. Note: the time points 1, 2, and 3 represent pre-treatment, 6 months post-treatment, and 18-months post-treatment respectively.

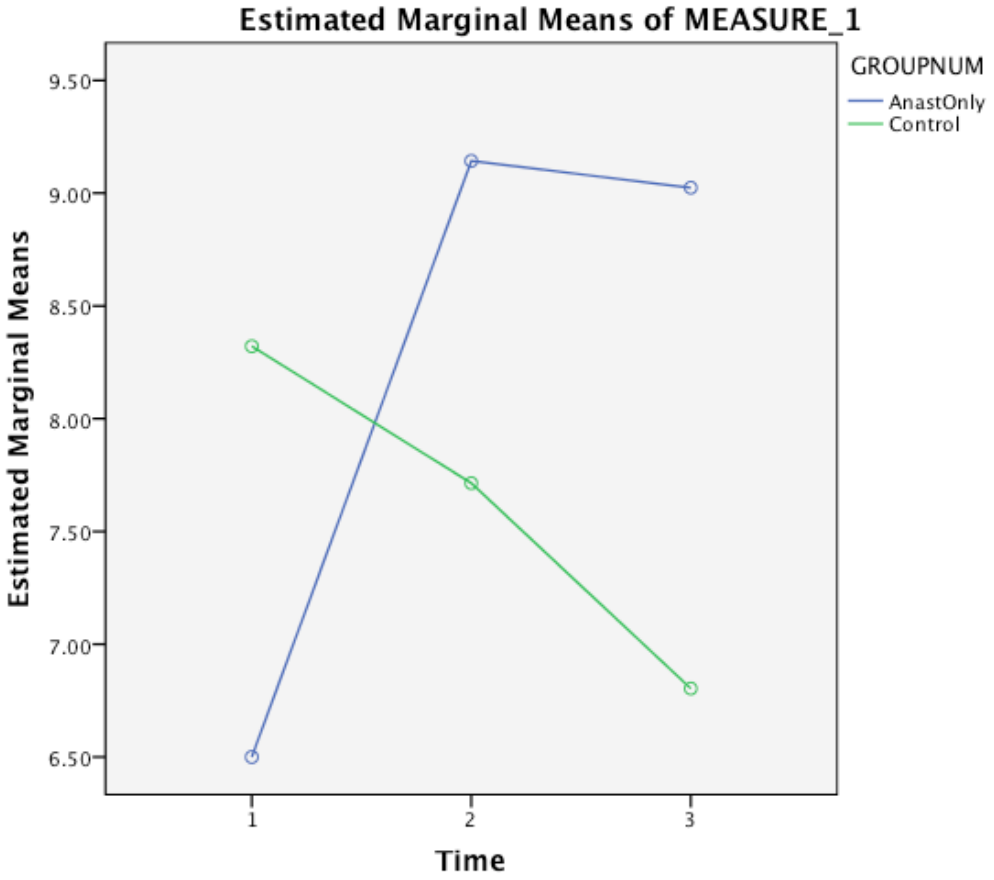


Figure 2. PAOFI – *Memory* sum scores at pre-treatment, 6 months, and 18 months

PAOFI - Language & Communication. The assumption of homogeneity of variance and covariance were met, Box's $M = 14.093$, $F(6, 54012.242) = 2.267$, $p = .034$ ($\alpha = .001$), Mauchly's $W = .971$. Sphericity for within-subjects effects was met, Mauchly's $W = .971$, $X^2 (2) = 2.785$, $p = .248$. The assumption of normality was also met. All other assumptions were

met. There was no significant difference on the PAOFI *language and communication* sum scores over the period of time examined within-subjects, $F(2, 192) = 2.704$, $p = 0.069$, $\eta^2 = 0.027$, and there was no significant difference between-subjects, $F(1, 96) = .382$, $p = 0.538$, $\eta^2 = 0.004$. The result of the PAOFI – *Language & Communication* sum scores for both groups, over time, is displayed in Figure 3. Note: the time points 1, 2, and 3 represent pre-treatment, 6 months post-treatment, and 18-months post-treatment respectively.

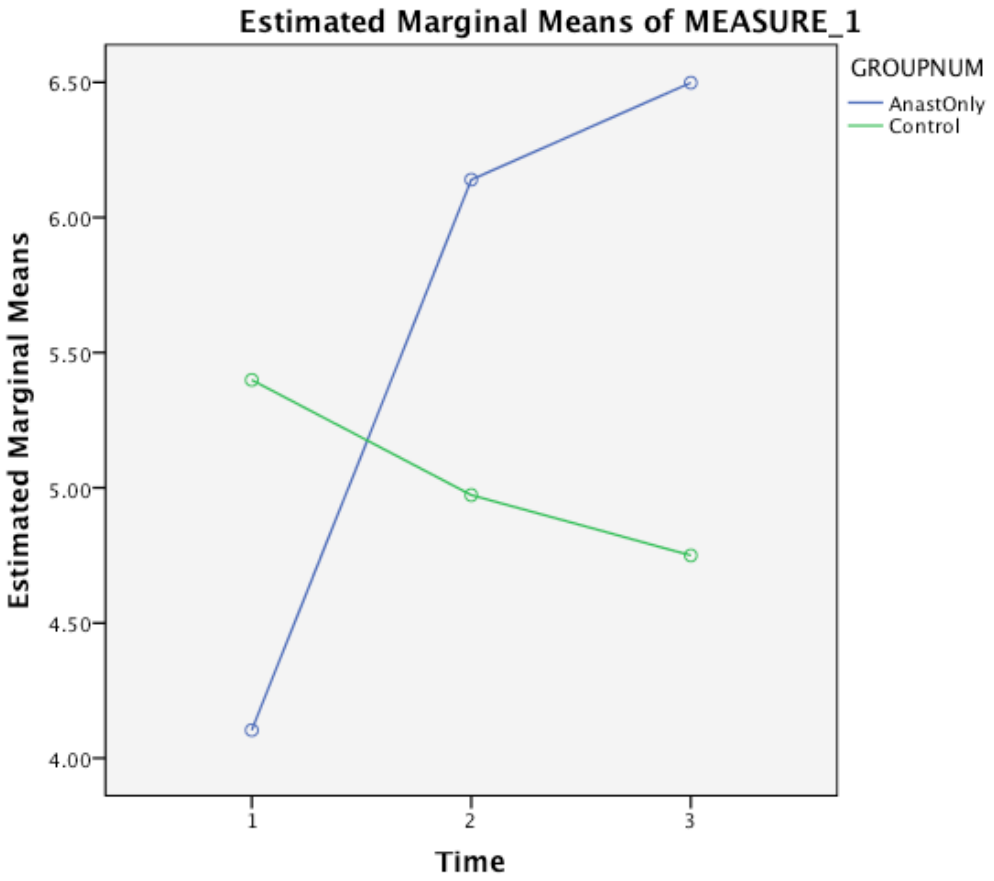


Figure 3. PAOFI – *Language & Communication* sum scores at pre-treatment, 6 months, and 18 months

PAOFI - Use of Hands. The assumption of homogeneity of variance and covariance were met, Box's $M = 11.987$, $F(6, 54012.242) = 1.928$, $p = .072$ ($\alpha = .001$), Mauchly's $W = .982$. Sphericity for within-subjects effects was met, Mauchly's W = .982, X^2 (2) = 1.753, p =

.416. The assumption of normality was also met. All other assumptions were met. There was no significant difference on the PAOFI *use of hands* sum scores over the period of time examined within-subjects, F(2, 192) = .167, p = 0.846, η^2 = .002, and no significant difference between-subjects, $F(1, 96) = 1.531$, $p = 0.219$, $\eta^2 = .016$. The result of the PAOFI – *Use of Hands* sum scores for both groups, over time, is displayed in Figure 4. Note: the time points 1, 2, and 3 represent pre-treatment, 6 months post-treatment, and 18-months post-treatment respectively.

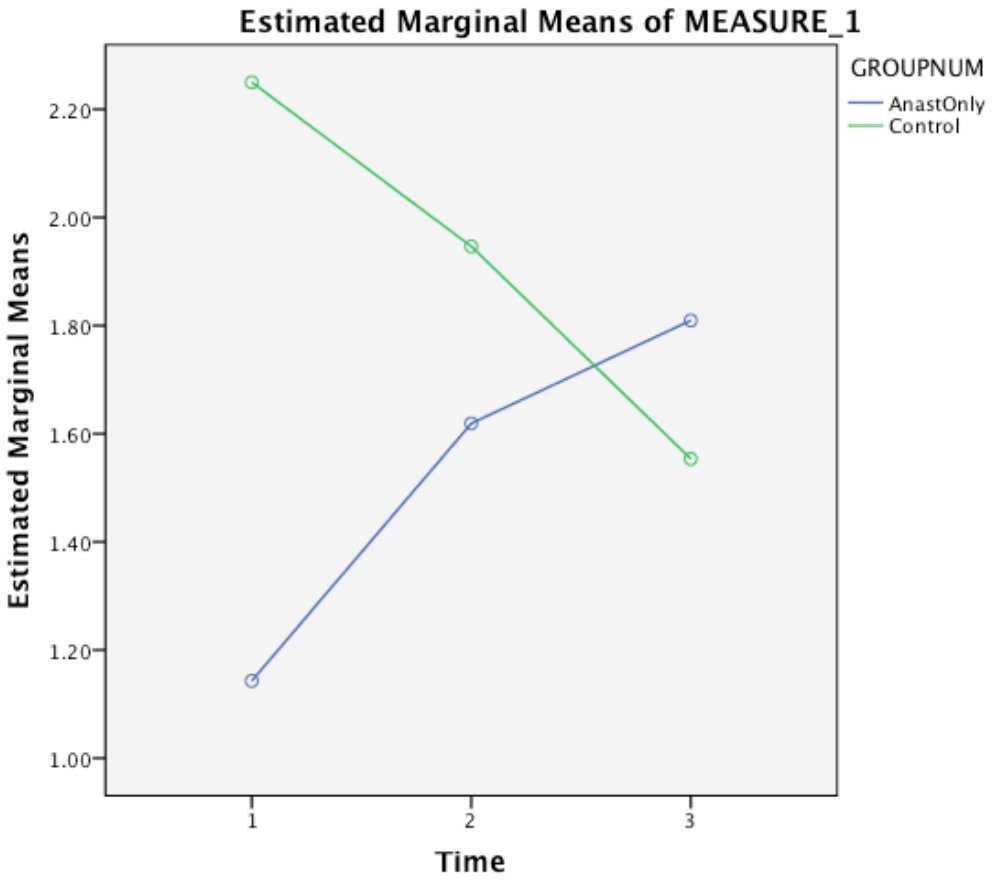


Figure 4. PAOFI – *Use of Hands* sum scores at pre-treatment, 6 months, and 18 months

PAOFI - Sensory-Perceptual. The assumption of homogeneity of covariance was not met, Box's $M = 36.752$, $F(6, 54012.242) = 5.911$, $p = .001$ ($\alpha = .001$), Mauchly's $W = .942$.

Since the data violated the assumption, the within-subjects values were reported based on the Greenhouse-Geisser correction. Sphericity for within-subjects effects was met, Mauchly's W = .942, X^2 (2) = 5.702, p = .058. All other assumptions were met. There was no significant difference on the PAOFI *sensory-perceptual* sum scores over the period of time examined within-subjects, $F(1.89, 181.43) = 1.609$, $p = .204$, $\eta^2 = .016$, and no significant differences between-subjects, $F(1, 96) = .108$, $p = .743$, $\eta^2 = .001$. The result of the PAOFI – *Sensory-Perceptual* sum scores for both groups, over time, is displayed in Figure 5. Note: the time points 1, 2, and 3 represent pre-treatment, 6 months post-treatment, and 18-months post-treatment respectively.

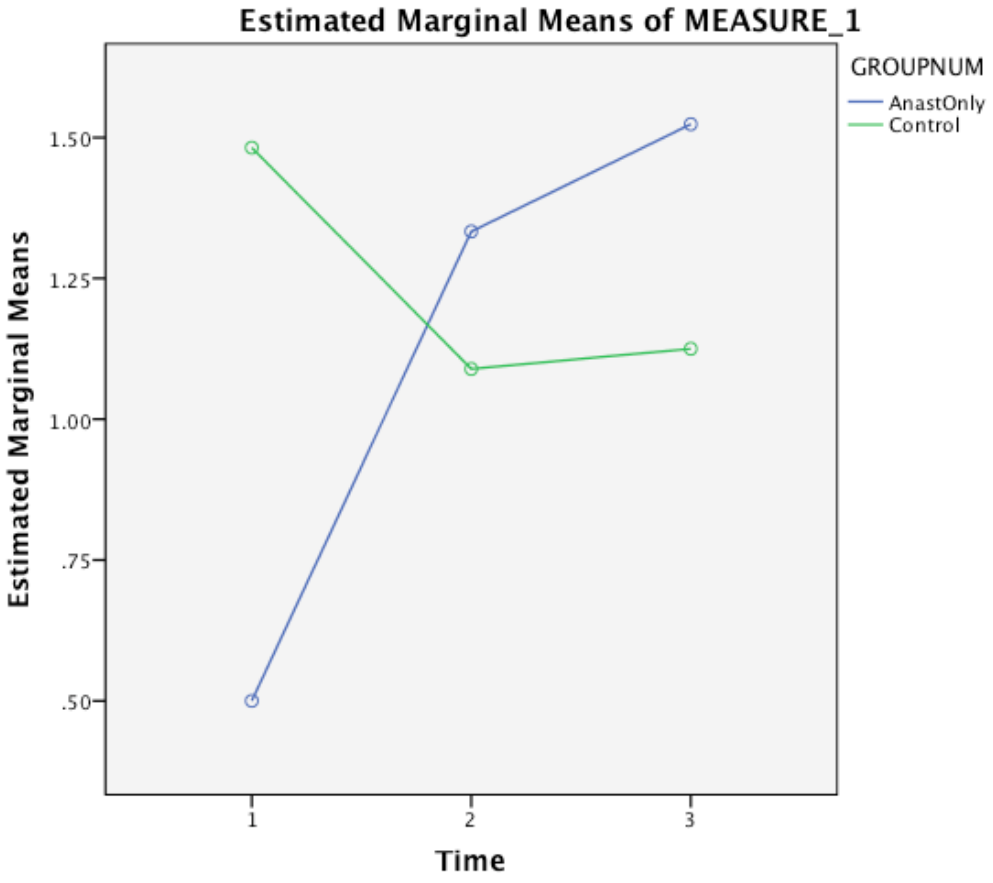


Figure 5. PAOFI – *Sensory-Perceptual* sum scores at pre-treatment, 6 months, and 18 months

PAOFI - Higher Level of Cognitive & Intellectual Function. The assumption of homogeneity of covariance was not met, Box's M = 35.610, $F(6, 51137.465) = 5.724$, p = .001 (α = .001), Mauchly's W = .956. Since the data violated the assumption, the within-subjects values were reported based on the Greenhouse-Geisser correction. Sphericity for within-subjects effects was met, Mauchly's W = .956, X^2 (2) = 4.269, p = .118. The assumption of normality was also met. All other assumptions were met. There was a significant difference on the PAOFI *higher level of cognitive & intellectual function* sum scores over the period of time examined within-subjects, $F(1.92, 181.92) = 4.639$, p = .012, η^2 = .047. There were no significant differences determined between-subjects, $F(1, 95) = .018$, p = .894, η^2 = .001.

Post hoc pairwise comparisons were performed using the Bonferroni adjustment to find the pattern of differences of functional limitations of the anastrozole group overtime. The participants reported significantly more functional limitations at 18 months post initial treatment as compared to before beginning treatment, p = .012. There were no other significant differences. The result of the PAOFI – *Higher Level of Cognitive & Intellectual Function* sum scores for both groups, over time, is displayed in Figure 6. Note: the time points 1, 2, and 3 represent pre-treatment, 6 months post-treatment, and 18-months post-treatment respectively.

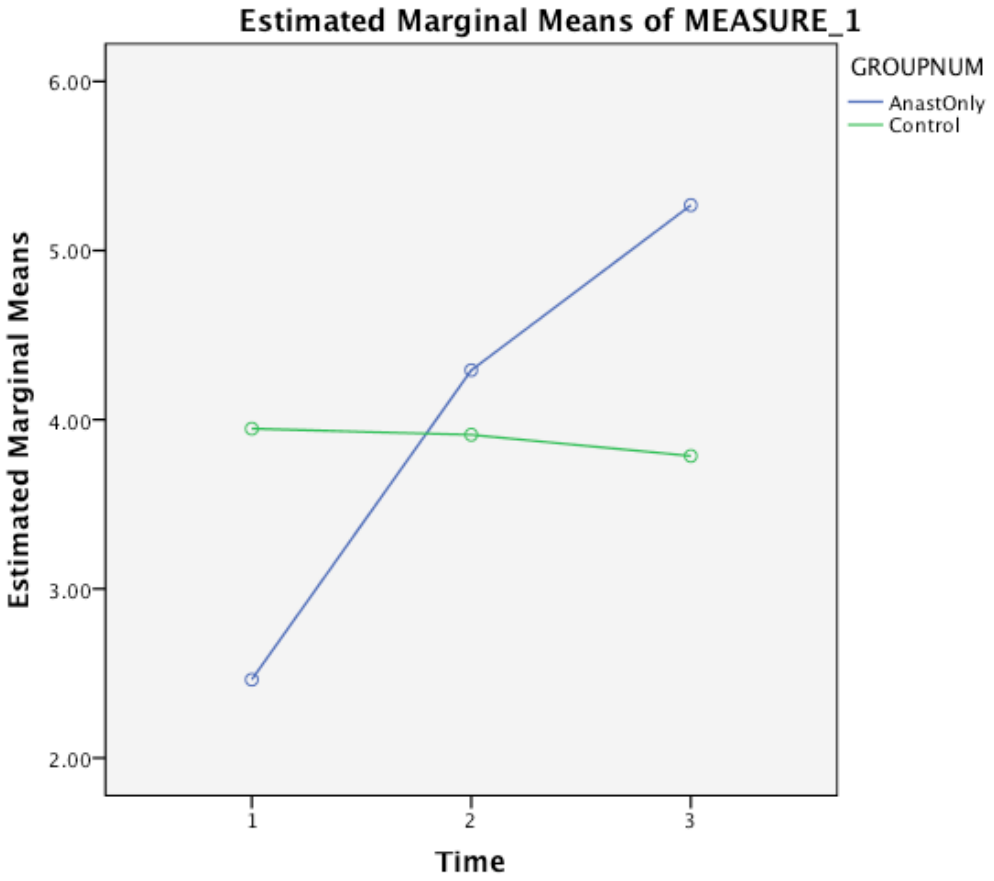


Figure 6. PAOFI – *Higher Level of Cognitive & Intellectual Function* sum scores at pre-treatment, 6 months, and 18 months

3.3.2 Medical Outcomes Study Short Form 36 Health Survey (SF-36) *work items*

A 2 x 3 mixed analysis of variance was performed on the Medical Outcomes Study Short Form 36 Health Survey (SF-36) *work items* sum scores, to examine work problems as a function of time and anastrozole treatment. The within-subjects independent variable was time with 3 levels (pre-treatment, 6 months post initial treatment, and 18 months post initial treatment). The between-subjects independent variable was treatment with 2 levels (anastrozole treatment and controls with no breast cancer nor treatment). Prior to running statistics, the data was restructured

in SPSS to produce workable data for the necessary analysis. The participants were measured on the SF-36–*work items* at pre-treatment, 6 months post treatment, and 18 months post treatment. The means, standard deviations, and standard errors of the anastrozole group and control group's SF-36–*work items* scores were reported in Table 10.

The assumption of homogeneity of variance and covariance were met, Box's M = 21.463, $F(6, 56884.708) = 3.454$, $p = .002$ ($\alpha = .001$), Mauchly's $W = .921$. Sphericity for within-subjects effects was not met, Mauchly's W = .921, X^2 (2) = 7.86, $p = .020$. Since the data violated the assumption, the within-subjects values were reported based on the Greenhouse-Geisser correction. All other assumptions were met. There was no significant difference on the SF-36–*work items* scores over the period of time examined within-subjects, F(1.854, 179.864) = 1.20, $p = .301$, $\eta^2 = .012$, but there was a significant difference between-subjects, $F(1, 97) = 12.205$, $p = .001$, $\eta^2 = .112$.

Table 10. SF-36 *work items* – mean, standard deviation, and standard error of work problems by time for anastrozole group and control group.

SF-36 *work items*	n	*M*	SD	SE
Anastrozole Group				
Pre-treatment	43	26.79	6.15	.939
6 mo.	43	28.00	6.72	1.024
18 mo.	43	28.53	7.02	1.070
Control Group				
Pre-treatment	56	31.36	5.16	.689
6 mo.	56	31.20	5.06	.677
18 mo.	56	31.21	4.67	.624

3.4 HYPOTHESIS 3

Hypothesis 3: Postmenopausal women with breast cancer receiving anastrozole will self-report (a) higher numbers and (b) greater severity of work problems over time.

3.4.1 Follow-up Health Questionnaire

Qualitative analysis of repeated measures was used to study frequency and severity of work problems, self-reported by the participants as results of the Follow-up Health Questionnaire. Results were examined at 6 months and 18 months post initial anastrozole treatment. The Follow-up Health Questionnaire included 6 "yes" or "no" questions, each requesting open-ended detail when appropriate. Of the six items, the results from the question, "Have you had any other significant changes in life since our last meeting," were found to be most applicable for this study and therefore were incorporated in the results for hypothesis #3. As the other questionnaire items mostly pertained to health related concerns, this question remained open for potential reports of work related issues. Only the anastrozole group's results were assessed, in line with the aims of the hypothesis. Multiple participants reported more than one change; therefore *change 1* and *change 2* define potentially two changes for several participants. Not all participants who reported one change also reported a second change. Not all changes related to work and not all participants identified a significant life change since the previous meeting.

The original data of reported changes were listed verbatim by the participants' response to the open-ended questions. For this study, the responses were then examined individually to identify responses related to work. At that point, each response was then categorized into work-

related groupings or variables that were similar in nature, such as a positive work change (i.e. new job) or negative work change (i.e. lost job), as described in table 11.

At 6 months, 73 participants who received anastrozole treatment completed the questionnaire. Of those individuals 38.4% (n= 28) reported that they had experienced a significant life change and 61.6% (n= 45) reported to have *not* experienced a significant life change. At 18 months post anastrozole treatment, 45 participants completed the questionnaire with 42.2% (n= 19) responding *yes* and 57.8% (n= 26) responding *no* to experiencing a significant life change. Furthermore, only the open-ended, self-reported responses provided by the subjects were considered in analysis. Both positive and negative reports of work related situations were studied. The responses were categorized by common themes and included: (a) working again/new job/additional job responsibilities/ working two jobs to help finances; (b) retired/semi-retired (spouse and/or participant); (c) had to decrease work hours due to fatigue secondary to treatment; (d) lost job/stress at work/looking for new job/gave up job, can't do anymore/work hours cut back/less pay due to shift change. Table 11 reflects the reported changes, related to work, by number and percentage at 6 months and 18 months. The (%) represents the percent of work-related changes out of the total number of *yes* responses in that time domain and change report category (change 1 or 2).

The total number of individuals who stated that *yes* they had experienced a significant life change, are represented at the bottom of table 11. The highest number of reported changes in work is 4 total changes, at both 6 month and 18 months. In the case of this study, the changes are determined to be positive as the individuals reported working again, new job, additional job responsibilities, or working two jobs, which assumes more cognitive and physical demands, therefore rejecting the hypothesis that reports of work problems would increase overtime.

Table 11. Changes Reported on Follow-up Health Questionnaire – Anastrozole Group

	6 months				18 months			
	Change 1		Change 2		Change 1		Change 2	
Work-related Variables	n	(%)	n	(%)	n	(%)	n	(%)
Working again/new job/additional job responsibilities/working two jobs to help finances	4	(5.5)	1	(1.4)	4	(8.9)	1	(0.8)
Retired/semi-retired (spouse and/or participant)	1	(1.4)	0	(0.0)	2	(4.4)	1	(0.8)
Had to decrease work hours due to fatigue secondary to treatment	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Lost job/stress at work/looking for new job/gave up job can`t do anymore/work hours cut back/less pay due to shift change	2	(2.7)	1	(1.4)	2	(4.4)	1	(0.8)
Total work-related changes reported	7		2		8		4	
Total life changes reported	28		7		19		9	

3.5 EXPLORATORY ANALYSIS

3.5.1 Brief Pain Inventory (BPI)

Given the results of the hypotheses, specifically hypothesis 1, pain was identified as a confounding variable as the anastrozole and control groups were significantly different on the BPI measure at baseline. Women with breast cancer taking aromatase inhibitors have been documented experiencing higher incidences of joint pain, as opposed to some other types of treatment (Crew et al., 2007). Given that pain may have been a confounding variable throughout

the study, exploratory analysis was completed to investigate whether pain remained constant or changed for the groups after treatment.

A 2 x 3 mixed analysis of variance was performed on the Brief Pain Inventory (BPI) sum scores, to examine reported pain as a function of time and anastrozole treatment. The within-subjects independent variable was time with 3 levels (pre-treatment, 6 months post initial treatment, and 18 months post initial treatment). The between-subjects independent variable was treatment with 2 levels (anastrozole treatment and controls with no breast cancer nor treatment). Prior to running statistics, the data was restructured in SPSS to produce workable data for the necessary analysis. The participants were measured on the BPI at pre-treatment, 6 months post treatment, and 18 months post treatment. The means, standard deviations, and standard errors of the anastrozole group and control group's BPI scores were reported in Table 12.

The assumption of homogeneity of variance and covariance were met, Box's M = 8.025, $F(6, 59126.136) = 1.293$, $p = .256$ ($\alpha = .001$), Mauchly's $W = .989$. Sphericity for within-subjects effects was also met, Mauchly's W = .989, X^2 (2) = 1.133, p = .567. All other assumptions were met. There was no significant difference on the BPI scores over the period of time examined within-subjects, F(2, 204) = .650, $p = .523$, $\eta^2 = .006$, but there was a significant difference between-subjects, $F(1, 102) = 5.941$, $p = .017$, $\eta^2 = .055$. This difference is displayed graphically in Figure 7. Note: time points 1, 2, and 3 represent pre-treatment, 6 months post-treatment, and 18 months post-treatment, respectively.

Table 12. BPI – mean, standard deviation, and standard error of pain by time for anastrozole group and control group.

BPI	n	*M*	SD	SE
Anastrozole Group				
Pre-treatment	44	11.14	15.05	2.28
6 mo.	44	12.71	15.94	2.44
18 mo.	44	15.91	17.47	2.28
Control Group				
Pre-treatment	60	7.17	15.22	1.96
6 mo.	60	8.18	16.34	2.09
18 mo.	60	5.38	13.18	1.95

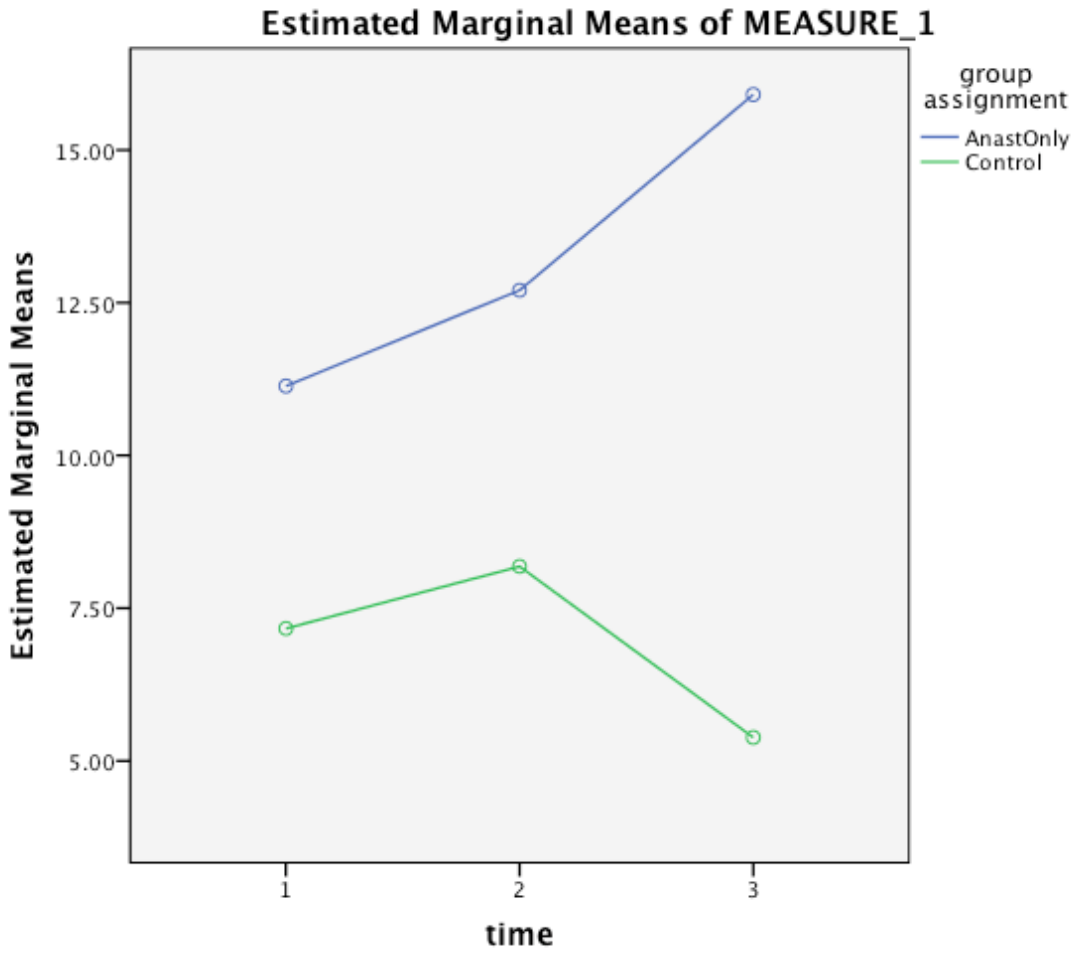


Figure 7. BPI sum scores at pre-treatment, 6 months, and 18 months

4.0 DISCUSSION

Self-reported data provides perspective of the individual experiencing the condition and the individual's understanding of resulting manifestations due to the condition. This study aimed to examine self-reported work problems after anastrozole treatment in postmenopausal women with breast cancer. In this study it was found that overall, the anastrozole group reported more work problems than the control group overtime. Pain emerged as a confounding variable that supports reason for further investigation of the effects and role of pain due to breast cancer and/or treatment, specifically as it pertains to work performance.

4.1 HYPOTHESIS 1

Hypothesis 1 proposed that *postmenopausal women with breast cancer self-report (a) higher numbers and (b) greater severity of work problems as compared with the control group, at baseline, prior to treatment*.

The PAOFI subscales, SF-36 –*work items*, BDI-II, BPI, and POMS-fatigue/inertia sum scores were evaluated to investigate the participants' perceived limitations to their individual ability to function. Among all five subscales of the PAOFI, there were no significant differences between the breast cancer (anastrozole) group and the control group, rejecting the null hypothesis

for this measure and proposing that statistically there were no major differences between the amount and severity of functional limitations between the groups at baseline for that measure. The SF-36–*work items* supported the hypothesis and showed a significant difference between the anastrozole and control groups ($p < .001$). The means of the groups displayed overall lower scores for the anastozole group, which suggests that the women with breast cancer reported more limitations to functional ability related to work. Limitations for the anastrozole group at baseline may be due to effects of the breast cancer such as symptoms of pain, nausea, or changes in body function, or result of surgery.

To consider other physiological factors that may affect work performance, the BDI-II, POMS-fatigue/inertia, and BPI were used to uncover any potential covariates or confounding factors at baseline. The BDI-II and the POMS-fatigue/inertia measures produced no significant results and rejected the hypothesis in the case of these two measures. Alternatively, the results of the BPI produced a significant difference ($p < .001$), and by comparing groups' means implies that women with breast cancer report more pain compared to controls, prior to administration of treatment (Table 7). The report of pain seemed rational as breast cancer has tendency to be painful for many women. For this reason, the exploratory analysis of BPI data overtime was later run to investigate potential increases of pain overtime and the pain differences between the groups overtime (see below in section 4.4).

To address hypothesis 1 in summary, at baseline prior to anastrozole treatment, women with breast cancer reported higher numbers of work problems and greater physical pain than controls. Unexpectedly though, while women with breast cancer reported more functional problems with working, they did not significantly differ from the control group on reports of individual assessment of their own functioning (memory, language and communication, use of

hands, sensory-perceptual ability, higher level of cognitive and intellectual functioning), as assessed by the PAOFI subscales. Additionally, based on findings, women with breast cancer and controls had similar levels of depression and fatigue prior to treatment.

As mentioned previously, women treated for breast cancer, in various positions and types of occupations, commonly experience job loss, demotion, unwanted changes in tasks, problems with the employer and co-workers, personal changes in attitudes to work and diminished physical capacity (Brisson et al., 1999). Multiple factors may be contributing to the women's perceptions of work problems. The PAOFI is a self-report tool. An objective measure of physical and cognitive abilities or limitations to function would properly supplement the PAOFI to confirm accurate report of limitations. Also, attitudes or possible discrimination from others, not directly captured in the measures used in this study, have potential to highly impact work performance and work satisfaction. Furthermore, an individual's meaning of the value of work may also be changed as values often shift and other life factors take priority when cancer is diagnosed. Work may not be of the greatest importance currently, therefore possible lack of effort at work and chance of an increase in the individual's perceived work problems.

4.2 HYPOTHESIS 2

Hypothesis 2 proposed that *postmenopausal women with breast cancer receiving anastrozole treatment self-report (a) higher numbers and (b) greater severity of work problems as compared to the control group, at pre-treatment, 6 months, and 18 months post initial treatment.*

The PAOFI subscales data and SF-36 data were independently analyzed to examine functional limitations (PAOFI) and work problems (SF-36), to identify potential variances within-subjects and between-subjects. Analytical testing revealed that there were no significant differences within-subjects nor between-subjects for the PAOFI subscale measures of *memory*, *language and communication,* and *sensory-perceptual* functioning. A significant difference was identified within-subjects on the PAOFI *higher level of cognitive & intellectual function* subscale (p= .012); there was no significant difference between-subjects. Further analysis recognized that the greatest difference in report of functional limitations was between baseline and 18 months post anastrozole treatment. This implies that the cognitive/intellectual effects of treatment diminish overtime. While some studies support cognitive impairment due to treatment, the work of Buwalda and Schagen (2013) suggests that there is little evidence that aromatase inhibitors have a lasting detrimental effect on cognitive performance in breast cancer patients.

The SF-36–*work items* results demonstrated the presence of significant differences between the anastrozole group and the control group overtime but not within-subjects. The anastrozole group reported more physical and emotional problems related to work. These findings are supported by a substantial amount of literature on work-related issues hypothesized to be due to breast cancer treatment (Villaverde et al., 2008; Moran, Short, & Hollenbeak, 2011; Brisson et al., 1999)

The SF-36–*work items* results supported hypothesis 2, indicating that postmenopausal women with breast cancer do report higher frequencies of work problems over time as compared to the control group (p= .001). The within-subjects results produced by the PAOFI *higher level of cognitive & intellectual function* subscale may better support hypothesis 3 as it simply addresses women experiencing greater functional limitations over time as compared to

themselves at different time points. Cognitive limitations due to anastrozole treatment were studied by Calvio, Peugeot, Bruns, Todd, and Feuerstein (2010) and results of the study were analogous with the results produced by the SF-36 measure. Interestingly, their discussion included that fatigue and job stress presented the strongest correlation of work problems. Fatigue due to anastrozole treatment may be an avenue of study that can contribute to the overall understanding of the effects of anastrozole but were not directly examined in this study.

4.3 HYPOTHESIS 3

Hypothesis 3 proposed that *postmenopausal women with breast cancer will self-report (a) higher numbers and (b) greater severity of work problems over time.*

The Follow-up Health Questionnaire was implemented to qualitatively assess work problems overtime in just the anastrozole group, in addition to other open-ended comments, both positive and negative, about work that the participants provided. While the PAOFI *higher level of cognitive & intellectual function* subscale indirectly supports hypothesis 3 by addressing limitations to function, it was determined that there is not sufficient enough evidence to strongly support hypothesis 3. Only minimal numbers of reported work problems were reported in the data, and were too small to analyze statistically. Nonetheless, the qualitative data shows (Table 10) that while both positive and negative changes occurred, majority of changes were negative or unfavorable, assuming that the loss of a job or stress at work would be considered unfavorable. Negative work changes have potential of being the result of the effects and symptoms of breast

cancer or its treatment, attitudes or discrimination of co-workers, supervisors, and employers, or personal factors of the individual coping with the condition.

4.4 EXPLORATORY ANALYSIS - PAIN

Pain emerged as a potential confounding variable at baseline and between subjects overtime. The anastrozole group reported significantly higher levels of pain throughout the study as compared to the control group. These findings suggest, similarly to the literature, that pain is commonly a side effect of aromatase inhibitor treatment and/or a symptom of breast cancer. More specific to the current study, with the understanding that pain was present throughout the data collection, did the effects of pain compromise other variables in the study such as perception of work limitations, fatigue, or cognitive functioning? Naturally, with increased pain, humans feel less physically capable as opposed to when there is less pain present. Further studies are recommended for the degree of pain caused by breast cancer and aromatase inhibitor treatments, pain related to work performance, and the effects of pain on self-report assessments.

4.5 LIMITATIONS

In this study self-reported data was used for all measures. Obvious concerns of poor validity and reliability were taken into consideration upon data analysis. Although self-reported information is of great value, implementing an objective data measure in addition to the current measures would be ideal to compliment the subjective information the patients provided.

Although the design of the study succeeded in providing knowledge of frequency of work performance limitations, once the data was being assessed, it was clear that the measures failed to capture the level of severity of the work problems (example: job loss is more severe than a demotion). The measures posed a problem in gathering this data because there was a lack of data and specific questions to directly reflect the severity component. Varieties of work problems were lumped together in the data and not available to distinguish between each type of work problem. To correct this, a measure would either be researched or developed to adjust and directly assess work content and intensity, ranking work changes or problems on a well-developed and standardized severity scale.

Pain may also be moderating perception of function and self-report data, potentially interfering with reliable self-report, and should be adjusted for in future studies. The combination of poor reliability of self-reported data and affective factors may compound the unreliability and potentially negate the use of self-reported data as a reliable measure.

On the Follow-up Health Questionnaire, in addition to the low number of reported work problems, ranking the severity of work problems was determined to be unwarranted due to insignificant numbers and lack of data to directly reflect the severity component. Simply based on numbers, the work changes by category for the anastrozole group overall presented to be more positive than negative as double the amount of women reported a positive work increase as opposed to the other category of work changes who reported work loss. A more robust tool would be necessary to capture the true effect.

There are significant differences between groups in work problems for the SF-36–*work items* measure. Equally, it was expected that the PAOFI would also present functional limitations, as limitations to function would likely be the cause of the work problem. Unless

however, this would occur if the work problems were due to another outstanding factor that a significant number of women in the anastrozole group were experiencing, not directly associated with functional abilities captured by the PAOFI. Such impacts may be the typical aging process, economic situation, attitudes toward women with breast cancer or breast cancer survivors. This would imply different measures would be more appropriate depending on the identification of the specific factors potentially affecting the study outcomes. Further investigation and studies would be recommended.

Furthermore, the study was limited by the demographic disposition of the sample. The sample consisted of predominantly white American women and a portion of African American women. No other racial or ethnic groups were represented. A more diverse demographic population, specifically racial/ethnic diversity would be ideal for a normally distributed sample.

4.6 FUTURE STUDIES

The purpose of this study was to examine the effects of the anastrozole breast cancer treatment, as it relates to the individuals' abilities to function at work. Ideal next steps in research would include identifying specific work problems to promote analyzing the impact in specific work contexts in future studies. Job analysis and workplace analysis would improve the understanding of job and workplace demands and how the individual can function optimally in that role and what supports may be necessary for success. This would enhance the current knowledge of the impact of anastrozole treatment on work performance.

Agreeing with Steiner, et al. (2004), it would be beneficial to develop a model to properly assess work problems due to breast cancer treatment. Potentially taking a closer look at

contextual factors including personal factors such as ethnicity and socioeconomic status, affective functioning, coping strategies and environmental factors such as support system, economic impact, and attitudes.

Additionally, observational studies of work performance including job analysis and vocational assessment prior to breast cancer treatment and post treatment may render more valid outcomes and initiate ideas for intervention and possibly work accommodations if necessary, to mitigate the potential negative impacts on work performance.

4.7 IMPLICATIONS FOR HEALTH & REHABILITATION PROFESSIONALS

Analyzing the impact of anastrozole treatment in specific work contexts will supplement the current available literature. The results of this study suggest that multiple factors may be affecting work performance in addition to anastrozole treatment, specifically pain. Consideration of pain management, therapy, or alternative breast cancer treatment should be thoroughly discussed prior to treatment decision-making.

Knowing that more individuals with breast cancer are surviving and are continuing to work or returning to work, in addition to being aware that treatment effects and residual symptoms are often present, this population is likely in need of vocational rehabilitation support and services. While breast cancer does not have an instant cure, these women should likewise not be expected to return to their routine lives and work at optimal performance. Counseling and vocational services would be advantageous for this population to utilize as returning to work is a process and requires adjustment. A rehabilitation counselor could provide knowledge of and advocacy for work accommodations and modifications to assist the individual in working toward

successful function at work. As many aspects of breast cancer and its treatments are disabling, it would be worthwhile to advocate for funding and support to view cancer as a disability.

Health and rehabilitation professionals are recommended to evaluate the needs of the individual with breast cancer, especially as it pertains to treatment options, in a broader perspective by adopting a holistic approach and thoroughly assessing the contextual factors of the individual including personal, social, and environmental factors, including value of work and work performance. Supplemental information such as information provided by the individual's support system, may be incorporated to gather a more global understanding of function and impacts due to treatment or other factors.

5.0 CONCLUSION

As more women are living longer after breast cancer treatment and are returning to or maintaining jobs and careers, assessing impacts of breast cancer treatments on work performance is critical to guide future treatment decision making and rehabilitative interventions. Limitations in higher-level cognitive and intellectual functions were identified to be affected by the anastrozole treatment, but no other functional limitations exhibited significant changes. Results of this study suggest that anastrozole treatment may decrease work performance or increase work problems. As work performance would be assumed to be dictated by functional abilities, it remains unclear if anaztrozole treatment is directly impacting work limitations or if it may be working in conjunction with additional contextual factors, such as external barrios, or personal factors. Pain emerged as a confounding variable throughout the study, as the anastrozole group consistently reported more pain than the control group.

Through future clinical practice and research, if significant patterns of additional factors are identified, it may prove beneficial to return to this research and correct for covariates or other impacting factors and incorporate additional measures that objectify work performance outcomes. Future studies are needed to explore work performance related to anastrozole treatment. Additional research findings may update current information related to function at work, to add to the ICF core sets for breast cancer, ultimately assisting in the treatment decision

making, vocational rehabilitation service delivery and improving quality of life and work satisfaction of breast cancer survivors.

APPENDIX A

STUDY DESIGN GRAPHICAL REPRESENTATION

WORK PERFORMANCE LIMITATIONS POST ANASTROZOLE TREATMENT FOR WOMEN WITH BREAST CANCER (PRO14010224)

Background

Breast Cancer & Treatment

- Estimated 232,340 new cases of breast cancer diagnosed in U.S. women; 29% of newly diagnosed cancers in U.S. women (American Cancer Society, 2013).
- Aromatase inhibitors, including anastrozole, are anti-estrogen agents that have proven efficacy for adjuvant therapy in post menopausal women with breast cancer (Nabholtz, 2008, Rinaldi, 2013)

Adjuvant treatment effects

- Trends toward worse cognitive function among women exposed to an aromatase inhibitor have been studied (Nattinger, et. al., 2013).
- Anastrozole treatment, may have negative effects on cognitive functioning (Bender et. al., 2007, Nattinger et al., 2013). Cognitive impairments contribute to the likelihood of increased work problems. Theoretically, anastrozole treatment may increase the likelihood of work problems.

Work Limitations

- Work → central component of most individuals' lives.
- Work after cancer is highly desirable for individuals on a person, social, and economic level, ultimately contributing to quality of life, dignity, self-esteem, and purpose (Steiner et al., 2004).
- Common self-reported concerns → job loss, demotion, unwanted changes in tasks, problems with the employer and co-workers, personal changes in attitudes to work and diminished physical capacity (Brisson et al., 1999)

Primary Study: Anastrozole Use In Menopausal Women (AIM) study (R01CA107408)
Principal Investigator: Dr. Catherine M. Bender
Funded by: National Institutes of Health

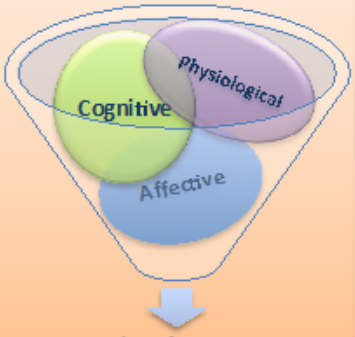
Problem Statement

Higher percentages of breast cancer survivors are returning to work and/or continuing to maintain employment after treatment. The literature suggests that adjuvant therapy, specifically anastrozole, may have negative affects on cognitive functioning. Cognitive impairments contribute to the likelihood of increased work problems.

Objectives

→Examine work problems through a critical analysis of self-reported data of women receiving anastrozole treatment.

→Identify potential work performance limitations after receiving anastrozole treatment as compared with controls.



Hypotheses

→Postmenopausal women with breast cancer self-report (a) higher numbers and (b) greater severity of work problems as compared with the control group, at baseline, prior to treatment.

→Postmenopausal women with breast cancer receiving anastrozole treatment self-report (a) higher numbers and (b) greater severity of work problems as compared to the control group, at pre-treatment, 6 months, and 18 months post initial treatment.

→ Postmenopausal women with breast cancer receiving anastrozole will self-report (a) higher numbers and (b) greater severity of work problems over time.

Taylor Popelas, 2014
University of Pittsburgh, School of Health & Rehabilitation Sciences, Department of Rehabilitation Science & Technology,
Rehabilitation Counseling

Methods

Study Design

Retrospective analysis of data, collected longitudinally

Participants

Postmenopausal women with breast cancer, who received anastrozole treatment and controls.

Inclusion	Exclusion
Female; < 75yo; postmenopausal	Hospitalization for psych. Illness within past 2 years
English speaking; >8y of education	Prior diagnosis of neurologic illness

Measures

Intervention
Anastrozole treatment

-Demographics
-Patient Assessment of Own Functioning Inventory (PAOFI)
-Medical Outcomes Study Short Form-36 (MOS SF-36) *work item s*
-Beck's Depression Inventory-II (BDI-II)
-Profile of Mood States (POMS-fatigue/inertia subscales)
-Brief Pain Inventory (BPI)

Baseline

18 mo.
-PAOFI
-MOS SF-36 *work item s*
-Follow-up Health Questionnaire

6 mo.
-PAOFI
-MOS SF-36 *work item s*
-Follow-up Health Questionnaire

Data Analyses

- Repeated measures ANOVA
- T-tests
- Qualitative analysis

BIBLIOGRAPHY

American Cancer Society. *Breast Cancer Facts & Figures 2013-2014.* Atlanta, GA: American Cancer Society, Inc. 2013.

American Cancer Society. *Cancer Facts & Figures 2013.* Atlanta, GA: American Cancer Society; 2013.

Bennett, B., Goldstein, D., Lloyd, A., Davenport, T., & Hickie, I. (2004). "Fatigue and psychological distress--exploring the relationship in women treated for breast cancer." *Eur J Cancer 40*(11), 1689-95. *PubMed*. Web. 8 Dec. 2013.

Bell, M.J., Terhorst, L., Bender, C.M. (2013). Psychometric analysis of the patient assessment of own functioning inventory in women with breast cancer. *Journal of Nursing Measurement*, *21*(2*)*, 320-334.

Beck, A.T., Steer, R.A., & Brown, G.K. (1996). Beck Depression Inventory-II manual [Written questionnaire]. San Antonio, TX: Psychological Corporation.

Bender, C.M., Sereika, S.M., Ryan, C.M., Brufsky, A.M., Puhalla, S., & Berga, S.L. (2013). Does lifetime exposure to hormones predict pretreatment cognitive function in women before adjuvant therapy for breast cancer? *Menopause*, *20*(9*)*, 905-913.

Bender, C.M., Sereika, S.M., Brufsky, A.M., Ryan, C.M., Vogel, V.G., Rastogi, P., Cohen, S.M., Casillo, F.E. and Berga, S.L. (2007). Memory impairments with adjuvant anastrozole versus tamoxifen in women with early-stage breast cancer. *Menopause, 14*, 995-8.

Brach, M., Cieza, A., Stucki, G., Fu¨ßl, M., Cole, A., Ellerin, B., Fialka-Moser, V., Kostanjsek, N., & Melvin, J. (2004). ICF core sets for breast cancer. *Journal for Rehabilitation Medicine*, *44*, 121-127. doi:10.1080/16501960410016811.

Brisson, C., Dubois, L., Fraser, A., Lauzier, S., Maunsell, E. (1999). Work problems after breast cancer: an exploratory qualitative study. *Psycho-oncology, 8*, 467-473.

Buwalda, B. & Schagen, S. B. (2013). Is basic research providing answers if adjuvant anti-estrogen treatment of breast cancer can induce cognitive impairment?. *Life sciences*. Retreived from http://www.biomedsearch.com/nih/basic-research-providing-answers-if/23353876.html. 8 Dec. 2013.

Calvio, L, Peugeot, M, Bruns, G, Todd, B, & Feuerstein, M. (2010). Measures of cognitive function and work in occupationally active breast cancer survivors. *Journal of Occupational and Environmental Medicine, 52*(2), 219-227.

Chelune, G.J., Heaton, R.K. & Lehman, R.A.W. (1986). Neuropsychological and personality correlates of patients' complaints of disability. *Advances in Clinical Neuropsychology.*

Cleeland, C.S. (1991). Brief Pain Inventory [Written questionnaire]. Houston, TX: Anderson Cancer Center.

Cleeland, C.S. (2009). *The brief pain inventory (BPI)*. Retrieved February 21, 2014, from http://www.mdanderson.org/education-and-research/departments-programs-and-labs/departments-and-divisions/symptom-research/symptom-assessment-tools/BPI_UserGuide.pdf.

Cooney, M., Galvin, R., Connolly, E., & Stokes, E. (2012). The international classification of functioning (ICF). *Disability and Rehabilitation,* 9, 740-748. doi:10.3109/09638288.2012.707742.

Crew, K.D., Greenlee, H., Capodice, J., Raptis, G., Brafman, L., Fuentes, D., Sierra, A., & Hershman, D.L. (2007). Prevalence of joint symptoms in postmenopausal women taking aromatase inhibitors for early-stage breast cancer. *Journal of Clinical Oncology, 25*(25), 3877-3883. doi: 10.1200/JCO.2007.10.7573

Curran, S. L., Andrykowski, M. A., & Studts, J. L. (1995). Short form of the profile of mood states (POMS-SF): Psychometric information. *Psychological Assessment, 7*(1), 80-83. doi:http://dx.doi.org/10.1037/1040-3590.7.1.80.

Dozois, D. J. A., Dobson, K. S., & Ahnberg, J. L. (1998). A psychometric evaluation of the beck depression Inventory–II. *Psychological Assessment, 10*(2), 83-89. doi:http://dx.doi.org/10.1037/1040-3590.10.2.83

Hartmann, L. C. (2012). *The Mayo Clinic breast cancer book.* Intercourse, PA: Good Books.

IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

Jenkins, V., Shilling, V., Fallowfield, L., Howell, A., & Hutton, S. (2004). Does hormone therapy for the treatment of breast cancer have a detrimental effect on memory and cognition? A pilot study. *Psycho-oncology, 13,*61-6.

Karki, A., Simonen, R., Malkia, E., & Selfe, J. (2005). Impairments, activity limitations and participation restrictions 6 and 12 months after breast cancer operation. *Journal for Rehabilitation Medicine, 37,* 180-188. doi:10.1080/16501970410024181.

McHorney, C.A., Ware, J.E., Rachel Lu, J.F., & Sherbourne, C.D. (1994). The MOS 36-Item short-form health survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. Medical Care *32*(1), 40-66.

McNair D., Lorr M., & Droppleman L.F (1981). EdITS Manual for the Profile of Mood States [Written questionnaire]. San Diego, CA: EdITS/Educational and Industrial Testing Service.

Moran, J. R., Short, P. F. & Hollenbeak, C. S. (2011). Long-term employment effects of surviving cancer. Journal of health economics, 30. Retreived from http://www.biomedsearch.com/nih/Long-term-employment-effects-surviving/21429606.html 12 Dec. 2013.

Nabholtz, J.M. (2008). Aromatase inhibitors in the management of early breast cancer. *European Journal of Surgical Oncology, 34*(11),1199-1207.

Nattinger, A.B., Pezzin, L.E., Restrepo, J.A., Durgerian, S., Malkin, M.G. and Rao, S.M (2013). Cognitive performance among breast cancer survivors treated with aromatase inhibitors. *Journal of Cancer Therapeutics and Research*, *2*(7). doi:10.7243/2049-7962-2-7.

Rinaldi, R.Z. (2013). Aromatase inhibitor adjuvant chemotherapy of breast cancer results in cancer therapy induced bone loss. *Current Osteoporosis Reports, 11,* 61-64.

Pullens, M.J.J., De Vries, J., Roukema, J.A.(2010). Subjective cognitive dysfunction in breast cancer patients: a systematic review. *Psycho-oncology, 19*, 1127-1138.

Schilder, C.M.T, Seynaeve, C., Linn, S.C., Boogerd, W., Beex, L.V.A.M., Gundy, C.M., Nortier, J.W.R., van de Velde, C.J.H., van Damn, F.S.A.M., and Schagen, S.B. (2012). Self-reported cognitive functioning in postmenopausal breast cancer patients before and during endocrine treatment: findings from the neuropsychological TEAM side-study. *Psycho-oncology, 21,* 479-487.

Steiner, J.F., Cavender, T.A., Main, D.S., & Bradley, C.J. (2004). Assessing the impact of cancer on work outcomes. *American Cancer Society, 101*(8), 1703-1711.

Szymanski, E., & Parker, R.M. (2010). "Work and disability: basic concepts." *Work and disability: contexts, issues, and strategies for enhancing employment outcomes for people with disabilities*. 3rd ed. Austin, Tex.: Pro-Ed, 2010. 1-15. Print.

Tchen, N., Juffs, H.G., Downie, F.P., Yi, Q., Hu, H., Chemerynsky, I., Clemons, M., Crump, M., Goss, P.E., Warr, D., Tweedale, M.E., & Tannock, I.F. (2003). Cognitive function, fatigue, and menopausal symptoms in women receiving adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology, 21*, 4175-4183.

Tiedtke, C., Rijk, A. D., de Casterlé, B. D., Christiaens, M., & Donceel, P. (2009). Experiences and concerns about 'returning to work' for women breast cancer survivors: a literature review. *Psycho-Oncology, 19*, 677-683.

Villaverde, M. R., Batlle, F.J., Yllan, V.A., Gordo, J.A.M., Sánchez, R.A., Valiente, S.J.B. & Baron, G.M. (2008). Employment in a cohort of breast cancer patients. Occupational medicine (Oxford, England), 58. Retreived from

http://www.biomedsearch.com/nih/Employment-in-cohort-breast-cancer/18667388.html. 8 Dec. 2013.

Ware, J.E., & Sherbourne, C.D (1992). The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care, 30*(6), 473-83.

Ware, J.E., Snow, K.K., Kosinski, M., & Gandek, B. (1993). SF-36® Health Survey Manual and Interpretation Guide [Written questionnaire]. Boston, MA: New England Medical Center, The Health Institute.

World Health Organization (2001). *International classification of functioning, disability, and health.* Geneva: World Health Organization.