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Symptoms Experienced By Post-Menopausal Breast Cancer Survivors On Aromatase Inhibitors: A Secondary Analysis Of Baseline Data

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SYMPTOMS EXPERIENCED BY POST-MENOPAUSAL BREAST CANCER SURVIVORS ON AROMATASE INHIBITORS: A SECONDARY ANALYSIS OF BASELINE DATA

Master’s Thesis
Submitted to the Faculty
Yale University School of Nursing

In Partial Fulfillment
of the Requirements for the Degree
Master of Science in Nursing

May N. Cao
May 20, 2013
This Master’s Thesis is accepted in partial fulfillment of the requirements for the degree Master of Science in Nursing.

M. Tish Knobf, PhD, RN, FAAN

Date: May 13, 2013
SYMPTOM EXPERIENCE

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Date: May 13, 2013

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SYMPTOM EXPERIENCE

Abstract

SYMPTOMS EXPERIENCED BY POST-MENOPAUSAL BREAST CANCER SURVIVORS ON AROMATASE INHIBITORS: A SECONDARY ANALYSIS OF BASELINE DATA

Background: Endocrine therapy for breast cancer with Aromatase Inhibitors (AI) is designed to reduce risk of recurrence and improve survival. AI therapy is associated with a variety of symptoms including musculoskeletal complaints, which have contributed to discontinuation of treatment. It is significantly important to explore the symptom profile of AIs that contribute to patients’ quality of life and adherence behavior. Objective: The purpose of the study was a secondary analysis exploring the symptom profile of post-menopausal breast cancer survivors on AIs. Methods: Data were collected from self-reported demographic and medical forms from 36 women on AIs identified in the primary study. Symptoms were identified using the Breast Cancer Prevention Trial Symptom Checklist (BCPT-SCL) and mean severity distress scores were calculated for each symptom. Results: The most frequently reported symptoms were musculoskeletal and vasomotor specifically joint pain (75%), hot flashes (75%), general aches and pains (75%), and muscle stiffness (69.4%). The highest reported mean severity distress score was unhappiness with body image. Conclusions: There is no confirmed etiology or established evidence based management for musculoskeletal complaints related to AI use. Future studies are needed to further understand AI-related musculoskeletal symptoms in order to develop interventions to improve symptom management and symptom distress.
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CHAPTER I

Statement of the Problem

Women with post-menopausal breast cancer often undergo adjuvant endocrine therapy for hormone-responsive breast cancer. Aromatase inhibitors (AI) have become an alternative to Tamoxifen for women with estrogen receptor positive (ER+) breast cancer to decrease breast cancer recurrence. ER+ breast cancer grows in response to the hormone estrogen, and in post-menopausal women estrogen production happens in the peripheral tissues controlled by the enzyme aromatase that converts androgens into estrogens (Crew et. al, 2007). The AI targeted therapy blocks this conversion, which in turn causes estrogen depletion in the body.

However, AI therapy has a symptom profile that may decrease quality of life. Adverse symptoms include hot flashes, night sweats, musculoskeletal joint pain, fatigue, and bone loss (Freedman & Winer, 2010). The higher prevalence and incidences of these adverse symptoms in patients undergoing AI therapy may be related to the efficacy of AIs decreasing estrogen concentration (Dent et. al, 2011). The treatment-related adverse effects may jeopardize the reported disease free survival benefit due to adherence to AI therapy.

The purpose of the study was a secondary analysis exploring the symptom profile of post-menopausal breast cancer survivors on aromatase inhibitors at baseline prior to participating in a 12-month randomized control trial comparing supervised aerobic-resistance exercise to a home based control group. Identifying the critical symptoms responsible for decreasing quality of life in breast cancer survivors on AI therapy will help improve the clinical decision-making model to maximize symptom management and
minimize symptom occurrence. These data may provide insight into the AI symptom profile and explore the severity associated with symptom presentation in post-menopausal breast cancer survivors on AI adjuvant therapy.

CHAPTER II

Review of the Literature

For post-menopausal breast cancer women undergoing adjuvant endocrine therapy, Tamoxifen and AIs have showed a marked reduction in breast cancer morbidity and mortality (Cigler & Gross, 2007). There have been recent findings that AIs may even be more effective at lowering recurrence rates compared to Tamoxifen (Dowsett et al., 2010). With established disease-free benefits, it is of significant importance to explore the symptom toxicities of AIs that may lower patients’ quality of life and adherence behavior.

AI Symptom Profile. Aromatase inhibitors are an integral part of standard adjuvant hormone therapy for estrogen receptor-positive breast cancer that is generally well tolerated in patients. However, there have been certain symptoms that self-reportedly lower quality of life in patients undergoing this particular therapy. Table 1, identifies the symptoms that are associated with AI treatment. Common side effects include musculoskeletal symptoms, changes in cognitive function, vasomotor and atrophic vaginal symptoms and loss of bone mass (Dent et al., 2011). A 6-month cohort study of 100 breast cancer patients initiating AI treatment (compared to a healthy cancer-free control group of similarly aged women) found that the participants undergoing AI treatment reported a significant increase in symptoms from baseline to follow-up that
SYMPTOM EXPERIENCE

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Medical Center</th>
<th>Other Centers</th>
<th>Patient/Provider Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Medical Center 1</td>
<td>Medical Center 2</td>
<td>Patient experience 1</td>
</tr>
<tr>
<td></td>
<td>Medical Center 3</td>
<td>Medical Center 4</td>
<td>Patient experience 2</td>
</tr>
</tbody>
</table>

- **Fatigue**: Often reported as a side effect of cancer treatments.
- **Patient Experience**: Can vary widely among patients.

**Table 1:** Symptom Profile of Aromatase Inhibitors (AI)
SYMPTOM EXPERIENCE

included: hot flushes, night sweats, dyspareunia, alopecia, forgetfulness, depression, and sleep difficulties (Gallicchio et al., 2011). Women undergoing menopause characteristically experience vasomotor symptoms, vaginal atrophy, skeletal, psychological, and sexual dysfunctions. With the dramatic fall of estrogen levels in post-menopausal women, AIs may exacerbate estrogen deprivation that leads to their particular symptom profile (Burstein, 2007).

The most prevalent and troublesome AI reported toxicity is musculoskeletal symptoms including arthralgia (Coleman et al., 2008). Crew and colleagues carried out a cross-sectional survey of 200 breast cancer patients, where 47% reported AI-related joint pain and 44% reported AI-related joint stiffness. Post-menopausal women often experience joint and skeletal pain as part of the natural aging process (Felson & Cummings, 2005). Data suggest that joint pains are uniquely associated with AI use with 47% of patients attributing the cause of their current arthralgia to AI therapy and 74% recognized the onset of arthralgia within 3 months of starting treatment (Mao et al., 2009). Henry and colleagues (2008) found 44 out of 100 participants in their study qualified for referral to rheumatology associated with AI therapy and 13% discontinued AI treatment due to rheumatologic toxicity. The areas most commonly affected by AI-related arthralgia include in descending order: hands, knees, hips, lower back, and shoulders (Donnellan et al., 2001). In the same study, 5% discontinued Anastrozole (third generation AI) due to the severity of their symptom and discontinuation lead to the resolution of their arthralgia.

Variables Associated with AI Symptom Experience. The etiology behind AI symptom toxicities is largely unknown and certain variables associated with the
development of AI-related symptoms have not been clearly established. However, there are some data that reported that particular groups had a higher propensity for developing AI-related symptoms. Mao and colleagues (2009) performed a cross-sectional survey and reported an inverse relationship to the length of time since cessation of menses to onset of reported AI-related arthralgia. In a multiple regression analysis, obese participants with a BMI between 25 to 30 kg/m2 and participants who received Tamoxifen therapy had an inverse relationship with reported AI-joint symptoms (Crew et al., 2007).

Patients treated with prior taxane chemotherapy were reported to be at a significantly higher risk for developing AI-related joint pain and stiffness (Crew et al., 2007; Henry et al., 2012). Levels of Vitamin D may also be a factor for AI symptom emergence with women more likely to report no disability from joint pain who had high Vitamin D levels compared to those with lower levels (Khan et al., 2009). Participants younger than 55 years of age and those with pre-existing pain at baseline are associated with a higher AI discontinuation rate (Henry et al., 2012).

AI endocrine therapy assists in the depletion of estrogen levels in the body, the hormone responsible for ER+ breast cancer to occur. Therefore, it has been hypothesized that the adverse effect profile is largely due to estrogen deprivation that drive menopausal type symptoms. Interestingly, Cuzick and colleagues (2008) explored the mechanism behind endocrine hormone therapy with related toxicities as a marker for treatment efficacy in the ATAC trial (comparison between Anastrozole alone or in combination with Tamoxifen). They found that over 30% of women reported vasomotor and joint symptoms during the first 3 months of therapy, and subsequently had lower recurrence than those who did not report any of these symptoms at 3 months of follow up (Cuzick et...
al., 2008). The results suggest an association between early symptom appearances with drug therapeutic effects.

Although none of these reported findings are absolute predictors associated with AI-related symptoms, the efficacy of these drugs to reduce disease recurrence is well established and further research to identify these symptoms will help improve clinical symptom management. The purpose of this study is to provide insight into the AI symptom profile and explore the severity of reported symptoms in post-menopausal breast cancer survivors on AI adjuvant therapy.

**Study Aims**

1. To identify the symptoms of post-menopausal breast cancer survivors currently on AI adjuvant therapy who are enrolled in the primary study at the time of enrollment.

2. To describe the severity of the identified symptoms of post-menopausal breast cancer survivors currently on AI adjuvant therapy who are enrolled in the primary study at the time of enrollment.

**Conceptual and Operational Definition**

**Symptom.** A subjective evidence of disease or physical disturbance, *broadly:* something that indicates the presence of bodily disorder.

The Breast Cancer Prevention Trial Symptom Checklist (BCPT-SCL) (See Appendix A) was used to measure this variable. Scores on this Likert-type scale range from a 0 (not at all) to a 4 (extremely). The original instrument indicated a response for presence of symptom as a yes or no. For this study 0 will indicate no (absence of symptom) and severity scores from 1 to 4 will indicate yes (presence of symptom). The
original instrument was created for the Tamoxifen Prevention Trial (Ganz et al., 1995); however, the symptoms assessed are related to menopause and hormonal therapies that produce menopausal type symptoms, which will be appropriate for all subjects in this study.

CHAPTER III
Methods

Research Design

The primary study is a randomized control trial comparing an endurance-resistance exercise intervention group to a health promotion control group over a 12-month period of time. The exercise intervention-experimental group participated in a supervised endurance-resistance component 3 times a week, and an additional recommended 30-minute aerobic exercise most other days of the week. The health promotion control group received recommendations for moderate intensity physical activity most days of the week.

A total of 154 women diagnosed with breast cancer, gynecologic cancers, colorectal cancers, and lymphoma were enrolled to examine the effects of an endurance-resistive exercise intervention on bone mass, body composition, metabolic factors, and functional status over time. The goal of the original study was to improve physiological health outcomes in an at-risk early post-menopausal cancer survivor population.

The women were recruited through the Yale–New Haven Hospital and Saint Raphael Tumor Registries with HIC approval. Each patient’s physician was contacted to request permission to reach out to the patient. Once permission was granted, a letter was sent to each woman inviting participation in the study. Recruitment was also done through flyers in community practices and in community settings.
The statistician used a block method to randomly assign participants into the exercise intervention group and the health promotion group.

Sample

From the 154 women participating in the primary study, 36 women with breast cancer were identified who were currently on AI adjuvant endocrine therapy. These participants on AI therapy are the focus of the secondary analysis exploring their symptom profile at the time of enrollment. Data were also collected on demographics (e.g. age, ethnicity, educational level, employment status, and occupation), and clinical variables (e.g. hormone receptor +/-; surgery only; surgery and chemotherapy only; surgery and radiation only; surgery and chemotherapy and radiation).

Data Collection

In the primary study, patients completed a self-reported Demographic and Medical Data Form at baseline before starting the intervention and the Breast Cancer Prevention Trial Symptom Checklist (BCPT-SCL).

Variables

Demographic variables. The following are the demographic variables as self-reported by participants on the Demographic and Medical Data Form under the Demographics section (See Appendix B) in the parent study and the level of measurement of each variable.

Age. Age in chronological years. Level of measurement: interval.

Ethnicity. Self-reported ethnic identity. Level of measurement: nominal.

Education level. High School Graduate; Trade or Technical School; Some College; College Graduate; Graduate School. Level of measurement: ordinal.
**Employment status.** Full-time; Part-time; Retired; Temporarily not Employed.

Level of measurement: nominal.

**Clinical variables.** The following are the clinical variables as self-reported by participants on the Demographic and Medical Data Form under the Cancer/Medical Data section (See Appendix B) in the parent study and the level of measurement of each variable.

**Hormone receptor.** Estrogen receptor positive or negative; Progesterone receptor positive or negative; Her-2/neu positive or negative. Level of measurement: nominal.

**Primary treatment types.** Surgery only; surgery and chemotherapy only; surgery and radiation only; surgery and chemotherapy and radiation. Level of measurement: nominal.

**Number of symptoms.** As reported by the BCPT-SCL. For Study Aim 1, we used each item of the 42 items of the BCPT-SCL individually. Level of measurement: interval.

**Severity of symptoms.** As reported by the BCPT-SCL. For Study Aim 2, the mean severity scores are calculated for each reported symptom (range = 1-4). The higher the number, the more severe that particular symptom experience is to the participants reported. Level of measurement: interval.

**Data Analysis**

**Sample.** The demographic and clinical characteristics of the sample were described using frequencies and measures of central tendency and dispersion, depending on the level of measurement of the variable.
**Study Aim 1.** Each of the 42 items on the BCPT-SCL was described using frequencies of those who reported having the symptom and measures of central tendency and dispersion for each item of the BCPT-SCL.

**Study Aim 2.** Of the 42 items identified on the BCPT-SCL, we used the mean value to describe the severity of each symptom identified.

**Ethical Considerations**

Permission to conduct this study was obtained by the parent study through the Yale University Human Investigations Committee, protocol number 0801003383, granted on July 2007 - 2013.

**CHAPTER IV**

**Results**

**Demographic Characteristics**

The demographic and clinical characteristics were analyzed with the descriptive statistics package of SAS v 9.2. The demographic characteristics are described in Table 2. The average age was 57.9 years (SD 7.09, range = 39-75); ethnicity was mostly white (86.5%), the majority had a graduate degree (36.1%), and almost half worked full time (51.4%).

| Table 2. Demographic characteristics of subjects (N=36) |
|-----------------|--------|------|
| Characteristics | Mean   | SD   | Frequency (%) |
| Age (years)     | 58     | 7.14 |                |
| Ethnicity       |        |      |                |
| White           | 32     | (88.8)|                |
| Black or African| 2      | (5.6)|                |
| Other           | 2      | (5.6)|                |
| Education level |        |      |                |
| High school/ trade school | 6  | (17.1)|                |
| Some college    | 8      | (22.9)|                |
| College graduate| 9      | (25.7)|                |
| Graduate school | 12     | (34.3)|                |
| Employment status|     |      |                |
| Full-time       | 18     | (50) |                |
| Part-time       | 8      | (22.2)|                |
| Retired         | 6      | (16.7)|                |
| Temp employed   | 4      | (11.1)|                |
Medical Characteristics

The medical characteristics are represented in Table 3. All participants on AI therapy were estrogen receptor (ER) positive, while only 7.1% of participants were Her-2/neu (HER2) positive. The majority of women had breast conservation therapy with radiation therapy as part of their treatment. Almost one-third (30.6%) had complete mastectomies and a quarter of the women did not receive radiation treatment. Nearly half (52.8%) of the women received adjuvant chemotherapy and 47.2% did not.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone Receptor</td>
<td></td>
</tr>
<tr>
<td>Estrogen receptor +</td>
<td>28 (100)</td>
</tr>
<tr>
<td>Progesterone receptor +</td>
<td>23 (82.1)</td>
</tr>
<tr>
<td>Her-2/neu +</td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Breast Conservation</td>
<td>25 (69.4)</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>11 (30.6)</td>
</tr>
<tr>
<td>Radiation</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (75)</td>
</tr>
<tr>
<td>No</td>
<td>9 (25)</td>
</tr>
<tr>
<td>Adjuvant Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19 (52.8)</td>
</tr>
<tr>
<td>No</td>
<td>17 (47.2)</td>
</tr>
</tbody>
</table>

Symptom Profile

Of the 42 symptoms from the BCPT-SCL, the symptoms reported by ≥ 30% of participants and their mean severity scores are depicted in Table 4. The most frequently reported symptoms were joint pain (75%), hot flashes (75%), and general aches and pains (75%) followed by muscle stiffness (69.4%), unhappy with appearance (61.1%), breast sensitivity (61.1%), forgetfulness (61.1%), night sweats (58.3%), vaginal dryness (58.3%), and headaches (52.8%).

The highest reported mean severity score was unhappiness with body image (2.2) and the next top most frequently reported symptoms reflected mild to moderate mean severity distress scores were hot flashes (1.9), breast sensitivity (1.8), night sweats (1.8), joint pain (1.7), early awakening (1.7), forgetfulness (1.6), general aches and pains (1.5),
difficulty concentrating (1.5), pain with intercourse (1.5), social avoidance (1.5), short temper (1.5), and tendency to take naps (1.5).

The remaining 20 of 42 symptoms that were under the range were reported only by 8.1%-27% of participants and were associated with minimal symptom distress (mean severity scores of $< 1 \pm 0.8$).

Table 4. Symptoms Reported by $\geq 30\%$ of Participants and Mean Severity Scores*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>n (%) who reported 1-4 (presence of symptoms)</th>
<th>Mean Severity Score* range 1-4 (to the nearest tenths)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot flashes</td>
<td>27 (75.0)</td>
<td>1.9</td>
<td>1.17</td>
</tr>
<tr>
<td>Joint pain</td>
<td>27 (75.0)</td>
<td>1.7</td>
<td>0.90</td>
</tr>
<tr>
<td>General aches/pains</td>
<td>27 (75.0)</td>
<td>1.5</td>
<td>0.89</td>
</tr>
<tr>
<td>Muscle stiffness</td>
<td>25 (69.4)</td>
<td>1.4</td>
<td>0.70</td>
</tr>
<tr>
<td>Breast sensitivity</td>
<td>22 (61.1)</td>
<td>1.8</td>
<td>1.05</td>
</tr>
<tr>
<td>Unhappy with body</td>
<td>22 (61.1)</td>
<td>2.2</td>
<td>1.30</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>22 (61.1)</td>
<td>1.6</td>
<td>0.86</td>
</tr>
<tr>
<td>Vaginal dryness</td>
<td>21 (58.3)</td>
<td>1.4</td>
<td>1.02</td>
</tr>
<tr>
<td>Night sweats</td>
<td>21 (58.3)</td>
<td>1.8</td>
<td>1.22</td>
</tr>
<tr>
<td>Headaches</td>
<td>19 (52.8)</td>
<td>1.4</td>
<td>1.07</td>
</tr>
<tr>
<td>Early awakening</td>
<td>18 (50.0)</td>
<td>1.7</td>
<td>0.91</td>
</tr>
<tr>
<td>Numbness, tingling</td>
<td>17 (47.2)</td>
<td>1.4</td>
<td>1.17</td>
</tr>
<tr>
<td>Difficulty concentrating</td>
<td>15 (41.7)</td>
<td>1.5</td>
<td>1.06</td>
</tr>
<tr>
<td>Easily distracted</td>
<td>15 (41.7)</td>
<td>1.3</td>
<td>0.80</td>
</tr>
<tr>
<td>Tendency to take naps</td>
<td>14 (38.9)</td>
<td>1.5</td>
<td>0.94</td>
</tr>
<tr>
<td>Pain with intercourse</td>
<td>13 (36.1)</td>
<td>1.5</td>
<td>1.20</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12 (33.3)</td>
<td>0.9</td>
<td>0.79</td>
</tr>
<tr>
<td>Decrease bladder control</td>
<td>12 (33.3)</td>
<td>1.0</td>
<td>1.04</td>
</tr>
<tr>
<td>Short temper</td>
<td>12 (33.3)</td>
<td>1.5</td>
<td>1.09</td>
</tr>
<tr>
<td>Social avoidance</td>
<td>12 (33.3)</td>
<td>1.5</td>
<td>1.17</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (30.6)</td>
<td>0.8</td>
<td>0.98</td>
</tr>
<tr>
<td>Constipation</td>
<td>11 (30.6)</td>
<td>1.1</td>
<td>0.70</td>
</tr>
</tbody>
</table>

* Mean severity rated from 1 (mild to slight distress); 2 (moderate); 3 (quite a bit); 4 (extremely)
CHAPTER V

Discussion

Post-menopausal breast cancer survivors who are hormone receptor positive are often put on adjuvant AI therapy that may have lasting toxicities effecting quality of life, as well as adherence to therapy. Previous literature has shown that the most prevalent and troublesome symptom experienced by patients on AIs were musculoskeletal in nature, especially arthralgia (Coleman et al., 2008). AI therapy may also exacerbate menopausal effects such as vasomotor symptoms related to further estrogen deprivation (Burstein, 2007). This study found similar results to Coleman and colleagues (2008) and Burstein’s (2007) studies where the most frequently reported symptom of the study population was joint pain ($n = 27$), hot flashes ($n = 27$), and general aches and pains ($n = 27$).

Interestingly the highest reported severity score in this study was related to body image due to unhappiness with their body’s appearance. Ganz and colleagues (2003) conducted a cohort study of 577 breast cancer survivors who were disease-free for a minimum of 2 years. They found that emotional distress was higher in younger women undergoing menopausal transition related to therapy. They also found one of the most prevalent complaints was being unhappy with their body at breast cancer diagnosis among all ages (range 25-51), and were not age group specific (Ganz et al., 2003). Of the 577 women in the study, 55.8% underwent a lumpectomy, 44.2% underwent a mastectomy, and the majority did not choose reconstruction surgery (Ganz et al., 2003).

In another study done by Ganz and colleagues (2004), breast cancer patients who received lumpectomy surgery without chemotherapy had the lowest reported rate of being unhappy with appearance (Ganz et al., 2004). One study found that concerns with
appearance correlating with weight gain had higher weight/appearance scale scores in women who had been treated with chemotherapy (Alfano et al., 2006). Emotional distress relating to body image in breast cancer patients can vary widely throughout their treatment course with possible factors including diagnosis of breast cancer, primary treatment, reconstruction, and adjuvant therapy that may effect their overall quality of life after completion of treatment.

In a recent study that looked at the effects of an exercise intervention on symptoms in breast cancer survivors, 62% of the sample were on endocrine therapy with hot flashes, joint pains, and muscle stiffness as the most reported symptoms (Knobf et al., 2013). Alfano and colleagues (2006) study, using a shortened version of the BCPT Symptom Checklist, found that 98% of their breast cancer population reported hormone-related symptom in the past year and the women who predominantly reported vasomotor symptoms had received chemotherapy treatment, Tamoxifen therapy, and were post-menopausal.

The findings of this study confirm the most prevalent distressing symptoms include musculoskeletal and vasomotor symptoms in breast cancer survivors on AI therapy.

**Limitations of the Study**

Limitations of this study include a small sample size and homogenous group of women. A larger sample size with a more heterogeneous group of women would increase reliability of observations. Other limitations include unknown time of diagnosis, unknown time of AI treatment initiation, and varying lengths of AI treatment times before starting the study.
Implications for Research

Further studies would benefit in exploring the association of symptoms and severity of symptoms with demographic and clinical variables reported by these breast cancer survivors on AI adjuvant therapy. The new results from the ATLAS trial comparing 5 years of adjuvant Tamoxifen versus 10 years has suggested that the latter can further decrease breast cancer recurrence and mortality in half (Davies et al., 2012). There is no current evidence that extended AI therapy past 5 years have similar effects to the results from the ATLAS trial. Previous studies have shown that Letrozole (third generation AI) may show greater benefit in patients with hormone positive tumors compared to Tamoxifen (Gross et al., 2007). Data suggests that using an AI for upfront monotherapy, sequential therapy 2-3 years after Tamoxifen, or extended therapy after 5 years of Tamoxifen reduced the recurrence of breast cancer compared to Tamoxifen for 5 years alone (Burstein et al., 2010). Future research with randomized clinical trials will give more insight on the efficacy of AIs used in extended therapy.

Implications for Practice

There is no confirmed etiology behind AI musculoskeletal symptoms, and evidence-based management for musculoskeletal complaints related to AI therapy have yet to be established. A thorough history and physical assessment of each patient will provide better insight in clinical management. A complete musculoskeletal assessment with consideration of NSAID or acetaminophen administration can help provide the best individualized care for patients (Park, Knobf, & Sutton, 2012). The efficacy of AIs to reduce recurrence of disease and mortality in breast cancer survivors emphasize the importance for future studies to assist in identifying AI-related symptom toxicities,
establishing management techniques, and minimizing symptom distress to improve adherence to AI therapy. Prospective studies identifying the critical symptoms and their associated variables responsible for decreasing quality of life in breast cancer survivors on AI therapy will help improve the clinical decision-making model to maximize symptom management and minimize symptom occurrence.
References


Appendix A

### BCPT-SCL

<table>
<thead>
<tr>
<th>Problem</th>
<th>In Past 4 Weeks?</th>
<th>Severity</th>
<th>Problem</th>
<th>In Past 4 Weeks?</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Headaches</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>17. Ringing in ears</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>3. Blind spots, fuzzy vision</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>18. General aches/pains</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>5. Vomiting</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>20. Chest pains</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>7. Constipation</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>22. Muscle stiffness</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>8. Difficulty w/ bladder control (when laughing or crying)</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>23. Difficulty breathing</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>9. Difficulty w/ bladder control (at other times)</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>24. Dry mouth</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>10. Vaginal discharge</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>25. Weight gain</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>11. Vaginal bleeding or spotting</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>26. Weight loss</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>12. Genital itching or irritation</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>27. Unhappy w/ the appearance of my body</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>14. Pain with intercourse</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>29. Feelings of suffocation</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>15. Cramps</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>30. Forgetfulness</td>
<td>☐ ☐ ☐ ☐ ☐</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

Every Day Problems During the Past Four Weeks

We are interested in knowing whether you have had any of the following problems during the **PAST FOUR WEEKS**. If you did not have the problem mark NO. If you did have the problem mark YES and then mark the number which best describes how much the problem bothered you.

0 = Not at All  1 = Slightly  2 = Moderately  3 = Quite a bit  4 = Extremely
Appendix A

Every Day Problems During the Past Four Weeks

We are interested in knowing whether you have had any of the following problems during the PAST FOUR WEEKS. If you did not have the problem mark NO. If you did have the problem mark YES and then mark the number which best describes how much the problem bothered you.

<table>
<thead>
<tr>
<th>Problem</th>
<th>In Past 4 Weeks?</th>
<th>Severity</th>
<th>Problem</th>
<th>In Past 4 Weeks?</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>31. Excitability</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>38. Difficulty concentrating</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
<tr>
<td>32. Short Temper</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>39. Easily distracted</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
<tr>
<td>33. Tendency to take naps, stay in bed</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>40. Dizziness, faintness</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
<tr>
<td>34. Night Sweats</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>41. Numbness, tingling</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
<tr>
<td>35. Cold Sweats</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>42. Early awakening</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
<tr>
<td>36. Tendency toward accidents</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>43. Any other problems?</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
<tr>
<td>37. Avoidance of social affairs</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
<td>44. Other</td>
<td>☐ ☐</td>
<td>☐ ☐</td>
</tr>
</tbody>
</table>
Appendix B

Demographic and Medical Data Form

Demographics

1. Age________

2. Ethnic Group

   White____ Black____ Hispanic____ Asian____ Other____

3. Marital Status

   Never married___ Married___ Divorced/separated___ Widow___ Remarried___

4. Children

   Yes___ No___
   If yes, how many (and ages)__________________________________________

5. Home Life/Living

   Spouse___ Significant other___ other family members___ alone___

6. Level of school completed

   Grade school 1 2 3 4 5 6 7 8
   High School 1 2 3 4
   Technical School 1 2 3 4
   College 1 2 3 4
   Graduate School

7. Employment Status

   Full time___ Part time___ Retired___ Never employed___
   Temporarily not employed___ (not work related or illness related)
   Homemaker___ student___

8. Occupation


9. Income

   _$<$20,000 ___$20-40,000 ___$40,000-60,000  ___>$60,000
Appendix B

10. Smoking History
   Current__________ if yes, # cig/day _____# years smoked_____
   Past___________ if yes, # years
   Never__________

11. Alcohol Intake Yes_______ No________
   # drinks/day _______ or # drinks/week________

12. Prior treadmill use/experience______________________________

Cancer/Medical Data

Cancer Site
   1. breast
   2. ovarian
   3. cervical
   4. uterine
   5. lymphoma-non-Hodgkin’s
   6. lymphoma-Hodgkin’s
   7. colo-rectal

Primary/Local Treatment
1. Surgery Yes____ No_______
   If yes, describe________________________________________________________________________
   If yes, date____________________________________________________________________________

2. Radiation Therapy Yes____ No______
   If yes, primary____ post-operative _________________
   If yes, describe (site)_______________________________________________________________________
   If yes, dates____________________________________________________________________________

3. Chemotherapy Yes______ No_______
   If yes, describe________________________________________________________________________
   If yes, dates____________________________________________________________________________

4. Hormone Therapy Yes____ No________
   If yes,
   1. Tamoxifen
   2. Zoladex
   3. Arimedix
   4. Other (describe)________________________________________________________________________

   If yes, dates hormone therapy: __________ to ___________
Appendix B

5. Biologic Therapy  Yes__________  No__________
If yes, describe__________________________________________________________________________
If yes, dates______________________________________________________________________________

6. Hemoglobin/Hematocrit (most recent-give date)______________________________________________

7. Menopause data-pre treatment
   a. premenopausal (monthly menses)
   b. perimenopausal (irregular menses over 12 months)
   c. postmenopausal (specify # years)
   d. postmenopausal on HRT (specify # years HRT and date stopped)
   e. postmenopausal secondary to hysterectomy (specify ovaries removed or not and date)

8. Menopause status at study entry
   a. perimenopausal (irregular menses over 12 months)
   b. postmenopausal (specify # years)
   c. postmenopausal on HRT (specify # years HRT and date stopped)
   d. postmenopausal secondary to hysterectomy (specify ovaries removed or not and date)