SYMPTOMS IN EARLY AND LONG-TERM BREAST CANCER SURVIVORS WHO HAVE COMPLETED PRIMARY THERAPY

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SYMPTOMS IN EARLY AND LONG-TERM BREAST CANCER SURVIVORS
WHO HAVE COMPLETED PRIMARY THERAPY

A DISSERTATION
SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN NURSING

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT HOUSTON
SCHOOL OF NURSING
BY
FAITH STRUNK MSN, FNP-BC, AOCNP

DECEMBER, 2013
The University of Texas Health Science Center at Houston
School of Nursing
Houston, Texas

To the Dean for the School of Nursing:

I am submitting a dissertation written by Faith Strunk and entitled "Symptoms in Early and Long Term Breast Cancer Survivors Who Have Completed Primary Therapy." I have examined the final copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Nursing.

Geri L. Wood PhD, RN, FAAN
Committee Chair

We have read this dissertation and recommend its acceptance:

Accepted

Dean for the School of Nursing
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To my husband and daughter, who agreed to my beginning the doctoral program, without knowing what they were in for, and having continued to support me throughout.

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Special thanks go to the patients, nurses, physicians, and staff of the Nellie B. Connally Breast Center and the Breast Medical Oncology Department for their willingness to participate and support my research.
Abstract

Faith A. Strunk, MSN, FNP-BC, AOCNP

Symptoms in Early and Long-Term Breast Cancer Survivors
Who Have Completed Primary Therapy

December 2013

Background:
Many breast cancer survivors continue to have single or multiple symptoms after they have completed primary cancer therapy. The quantifiable, subjective experience of multiple symptoms and their impact is defined as symptom burden. Previous research has focused on symptoms during primary therapy or shortly after completion.

Objective:
The objectives of this study were to determine whether symptom burden differed between survivor status (early/long-term) and/or endocrine or hormonal adjuvant therapy use. We hypothesized that there would be no difference in the symptoms expressed between early and long-term survivors.

Methods:
In this cross-sectional study, data were collected on 133 survivors, using the M. D. Anderson Symptom Inventory, Karnofsky Performance Status, Charlson Comorbidity Index and a demographic/health history form to assess study variables.
Results:
Patients who were prescribed endocrine or hormonal therapy had higher symptom severity scores than those women who did not receive these therapies. There were no differences in symptom burden and symptom interference between early- and long-term survivors, and whether or not they took adjuvant therapy. As functional status increased, the patients' symptoms scores decreased. Comorbidities did not impact the symptom scores.

Conclusions: Breast cancer survivors, both early and long-term, continue to experience symptoms, but those taking hormonal or endocrine therapy experienced higher symptom severity. Understanding the connections in early and late survivorship between symptoms, cancer therapy, comorbidities and functional status may result in improved symptom management and outcomes for breast cancer survivors.

Key Words:
Breast cancer, survivor, symptoms, symptom burden, symptom interference, M.D. Anderson Symptom Inventory (MDASI), Karnofsky Performance Scale (KPS), Charlson Comorbidity Index (CCI)
Summary of the Study

This dissertation consists of the dissertation proposal which includes the specific aims, background and significance, research design and methods, research subject risk and protection, literature cited and appendixes, in the format of a Public Health Service Grant (PHS 398) and a manuscript entitled “Symptoms in Early and Long-term Breast Cancer Survivors Who Have Completed Primary Therapy” which presents the primary findings of the current research study. The study was approved by the University of Texas M. D. Anderson Cancer Center Institutional Review Board (IRB) (Appendix A) the Institutional Review Board at the University of Texas Health Science Center at Houston and the Committee for the Protection of Human Subjects, (Appendix B, Appendix C).

The overall objective of this research was to identify and compare the symptoms experienced by early (less than 3 years post completion of primary therapy) and long-term (3 through 5 years post completion of primary therapy) breast cancer survivors based on whether or not they are taking adjuvant hormonal or endocrine therapy. This study also explored the associations between functional status, symptom burden and comorbidities as assessed by the Karnofsky Performance Status (KPS) (Appendix G), the M. D. Anderson Symptom Inventory (MDASI) (Appendix F), and the Charlson Comorbidity Index (CCI) (Appendix H).

The study was conducted in the Nellie B. Connally Breast Center at the University of Texas M. D. Anderson Cancer Center. One hundred thirty four
participants were recruited, signed informed consent, and completed the study forms; one later withdrew consent.

Descriptive statistics were used to assess the distributional characteristics and demographics across survivor status and hormonal therapy use. Symptom burden and interference were calculated. Chi-square, Fisher's exact test and t-test were conducted to evaluate whether the characteristics differed by survivor status or use of adjuvant hormonal or endocrine therapy. A 2-way ANOVA was conducted to evaluate differences in symptom burden, symptom interference and burden/interference of individual symptoms.

Eligible patients were identified from daily reviews of 28 clinicians' clinic schedules and were scheduled on the research recruitment schedule (Appendix K). To facilitate the recruitment process the following techniques were used: visiting all clinicians that had eligible patients at the start of each clinic day and alerting them which specific patients at which times were eligible for the study, then revisiting several times during the day to provide a reminder. In addition, each clinician's clinic nurse was notified of the potential participant(s) and requested to let the investigator know when this patient was seen. To address the space constraint issues, the investigator arrived before clinic hours started, to request a room in which to administer the questionnaires, as the clinicians were concerned with maintaining patient schedules.

In order to track time from primary treatment, receipt of endocrine or hormonal therapy, and stage of disease to ensure equitable distribution of participant population, the investigator developed a subject log by stage form
(Appendix J). Patients were stratified by months post treatment; 0-36 months and 37-60 months, for clarity, rather than less than 3 years and 3-6 years.

A minor change to the protocol procedure was made for clarification of completion of the demographic history form, allowing the investigator or participant to complete it rather than participant only.

An additional three participants were planned to be recruited because two recruited earlier were actually early rather than long-term survivors and one participant withdrew consent after completing the forms. All but one planned type of participant was recruited; the investigator was unable to recruit one stage III, long-term survivor not on adjuvant hormonal or endocrine therapy. A total of 134 participants were recruited and the data from 133 analyzed.

The primary findings of the research study are presented in the manuscript "Symptoms in Early and Long-term Breast Cancer Survivors Who Have Completed Primary Therapy" (Manuscript A). Demographic and clinical characteristics were well balanced between survivor status and adjuvant therapy, by design. There was no difference in symptoms between early and long-term survivors, although those on adjuvant hormonal or endocrine therapy had higher symptom severity.

The appendixes A-P contain the following materials: the M. D. Anderson Institutional Review Board Approval letter, the UT Centralized IRB Review form, The Committee for the Protection of Human Subjects, the Institutional Review Board at the University of Texas Health Science Center confirmation letter for
agreement to rely on MDACC reviewing IRB, the letter of support from the Department of Breast Medical Oncology chairman, the demographic data collection form, the M. D. Anderson Symptom Inventory, the Karnofsky Performance Status, the Charlson Comorbidity Index, the documents developed and used in the collection of data, (subject log, subject log by stage, recruitment schedule), certificate of human subjects protection training, permission to use the Charlson Comorbidity Index, permission to use the MDASI, the M. D. Anderson Cancer Center study protocol, and the curriculum vitae.
Proposal

Significant Aims

Breast cancer is the most common cancer in women in the United States, with approximately 2.9 million survivors as of February 2013 (American Cancer Society, 2013). Usual treatment for women with invasive breast cancer includes chemotherapy and/or biotherapy, surgery, and/or radiation followed by adjuvant hormonal therapy, if hormone receptor positive disease.

The cancer and/or its treatment often cause multiple symptoms in survivors. These symptoms may also be related to other noncancer comorbidities, noncancer related medications or even other symptoms (Barsevick, Dudley, Beck, & Whitmer, 2005; Honea, Brant, & Beck, 2007; Kenefick, 2006). Symptoms may persist and can lead to reducing the dose or discontinuing treatment early which may affect long term survival (Bonadonna et al., 2005; Bonadonna, Valagussa, Moliternia, Zambetti, & Brambilla, 1995; Cleeland, 2007). Persistent symptoms also affect the survivors' quality of life.

Understanding the connections between symptoms, cancer therapy, comorbidities and functional status may result in improved symptom management and outcomes for breast cancer survivors. This study will evaluate the impact of functional status, cancer therapy, and comorbidities on the symptoms expressed in early (up to 3 years) and long-term (years 3 through 5) breast cancer survivors, who have completed primary therapy (surgery, chemotherapy or biotherapy, with or without radiation) and compare the symptoms between those taking hormonal therapy and those not taking hormonal therapy.
Historically, the literature has addressed the survivors’ symptoms during their primary therapy or shortly thereafter. But no studies have identified and compared the symptoms experienced by early and longer term breast cancer survivors based on whether or not they are taking adjuvant hormonal therapy. This study will identify symptoms that continue to be a problem in survivors who have completed primary therapy. This proposed study is significant because establishing this baseline will help to develop and pilot interventions that can be tested and used effectively in this population.

**Primary objectives.**

1. To determine whether symptom burden differs between early survivors (less than 3 years post-primary therapy) and long-term survivors (3 to less than 6 years post-therapy, inclusive).

2. To determine whether symptom burden differs between women who take endocrine or hormonal adjuvant therapy and those who do not.

**Secondary objectives.**

1. To determine, whether the effect of time post-treatment and endocrine or hormonal adjuvant therapy has an additive effect upon symptom burden or whether it has a synergistic or antagonistic effect upon symptom burden.

2. To determine whether symptom interference differs between early survivors and long-term survivors and between those
who do and do not take adjuvant endocrine or hormonal therapy, as well as to determine if time post-treatment and use of adjuvant endocrine or hormonal therapy have an additive or interactive effect upon symptom interference.

3. To determine if differences in individual symptom severity and interference exist between early and long-term survivors, with and without the use of adjuvant endocrine or hormonal therapy.

**Exploratory objective.**

To determine whether functional status and comorbidities affect symptom severity and interference.

**Background and Significance**

Breast cancer is the most common cancer in women in the United States (excluding skin cancer); 1 in 8 women will develop it during her lifetime (American Cancer Society, 2013). Overall women treated for breast cancer have an 89% survival rate after 5 years and 75% after 15 years with an estimated 2.9 million breast cancer survivors in the United States as of February 2013 (American Cancer Society, 2013). The number of all cancer survivors is projected to grow by 3% per year (Maddams et al., 2009). The breast cancer population is no exception; due to improvements in cancer care, earlier diagnosis and treatment larger numbers of women are living longer and cancer-free after diagnosis and treatment. Many survivors, once having completed primary therapy (surgery, chemotherapy/biotherapy, and/or radiation) continue to have
long-lasting symptoms, single or multiple (Barsevick, 2007; Cleeland, 2007; Janz et al., 2007; Rosedale & Fu, 2010). The experience of multiple symptoms has been identified as symptom burden (Burkett & Cleeland, 2007; Gapstur, 2007; Gill, Chakraborty & Selby, 2012). Symptom burden is defined as the subjective, quantifiable prevalence, frequency and severity of symptoms and encompasses the patient's perception of the impact of symptoms (Cleeland, 2007; Gapstur, 2007).

The experience of symptoms in survivors has been evaluated, but much of the literature has been focused on symptoms and supportive care during primary therapy (Chung, Cimprich, Janz, & Mills-Wisneski, 2009). Some studies have concentrated on the early survivorship periods; beginning at the end of primary therapy up until 27 months after completing primary therapy (Brant et al., 2011; Ganz, Kwan, Stanton, Bower, & Belin, 2011; Janz et al., 2007; Park, Bae, Jung, & Kim, 2011; Penttinen et al., 2010; Thompson, 2007; Yi, Swartz & Reyes-Gibby, 2011). These studies have found symptoms related to primary therapy with an impaired quality of life related to these reported symptoms (Bower, 2009; Dahl, Nesvold, Reinertsen, & Fossa, 2011; Janz et al., 2007; Park et al., 2011). The symptoms most frequently cited in the aforementioned studies included pain, fatigue or lack of energy, difficulty sleeping, arm pain and lymphedema, breast symptoms, feeling irritable or nervous, menopausal symptoms, weight changes, nausea, depression, and cognitive dysfunction. A number of studies have focused on a specific symptom, such as pain (Lundstedt et al., 2012; Mao et al., 2009; Rief, Bardwell, & Dimsdale, 2011), lymphedema (Armer & Stewart, 2010;
Meeske et al., 2009; Smoot et al., 2010), fatigue (Bower et al., 2008; Bower, Ganz, Irwin, Arevalo, & Cole, 2011; Thompson, 2007) or menopausal symptoms (Leining et al., 2006; Loibl, Lintermans, Dieudonne, & Neven, 2011; Ruddy et al., 2011). Cancer related fatigue was identified by 21% of both the 1-5 year and 5-10 year survivors (Bower et al., 2008). Sleep disturbances, fatigue and pain persisted in Hartl et al.'s (2003) study of survivors evaluated at an average of 4.2 years.

Several studies have had contradictory findings. Castellon et al. (2004) found that cognitive dysfunction symptomatically abated in the 12-24 months after adjuvant chemotherapy. Jim et al. (2009) found significant differences in cognitive functioning and cognitive impairment between women who had received chemotherapy or radiation compared to healthy matched controls after 6 months. In a 2004 review, Tannock, Ahles, Ganz and van Dann found durable cognitive effects in 9 to 75% of patients, although the higher percentages were seen in those evaluated in a closer time frame with chemotherapy. However, in their study of longer term survivors (5 - 15 years), Klein et al. (2011) found an improvement in all symptoms except cognitive functioning and insomnia. The discrepancies among the findings may be related to the variability in primary therapy over time, pre-existing comorbidities or the use of adjuvant endocrine or hormonal therapy.

The proposed study will address the symptoms experienced by both early survivors (less than 3 years after completion of primary therapy) and long-term survivors (years 3-5 after completion of primary therapy). Symptoms may be
caused by comorbid illnesses or acute injuries, related to the disease itself or may be caused by treatments, in which case they are called side effects or toxicities (Cleeland, 2007). The framework of Symptom Burden (Cleeland, 2007; Gapstur, 2007) is the conceptual framework chosen for this study. Symptom burden has been described as the subjective counterpart to tumor burden (Cleeland & Reyes-Gibby, 2002) as well as the sum of the severity and impact of symptoms (Cleeland, 2007). It affects multiple patient outcomes, including survival, functional status and quality of life (Gapstur, 2007). Symptom burden is active, and changes over time, as patients undergo therapy or experience exacerbations or remissions of their disease (Vig & Pearlman, 2003). In this framework, symptoms related to therapy often are viewed as complicating post treatment recovery (Cleeland, 2007; Cleeland & Reyes-Gibby, 2002).

In this study, we will assess functional status, comorbidities and the experience of symptom burden. This study also will explore the association of comorbidities and symptoms expressed by early and long-term survivors. The evaluation of concurrent comorbidities is warranted because comorbidities have been related to symptom severity (Kurtz, Kurtz, Stommel, Given, & Given, 1999). This study will also address the associations between functional status and symptoms related to adjuvant endocrine or hormonal therapy.

Historically, the literature has addressed the symptoms of survivors during their primary therapy or shortly thereafter. But no studies have identified and compared the symptoms experienced by early and long-term breast cancer survivors related to the use of adjuvant endocrine or hormonal therapy.
Innovation

This study is innovative in that it will identify symptoms that potentially continue to be a problem for survivors who have completed primary therapy. This study will compare symptoms experienced among women taking adjuvant endocrine or hormonal therapy and those not taking endocrine or hormonal therapy, in early (less than 3 years after completion of primary therapy) and long-term (years 3 through completion of year 5 post primary therapy).

Research Design and Methods

Design.

This study utilized an exploratory cross-sectional study design.

Sample and setting.

The sample for this cross-sectional design study will be drawn from adult female patients in the Nellie B. Connally Breast Center at the University of Texas M. D. Anderson Cancer Center, an academic, comprehensive cancer center. M. D. Anderson is the largest institution in the University of Texas system, with 631 inpatient beds and 1,281,489 outpatient visits in 2012. The Nellie B. Connally Breast Center served over 4,720 new patients and consultations with over 33,000 follow-up visits in 2012. Non-English speaking women will be recruited through appropriate translation with the assistance of the language assistance office. Potential participants will be approached at the time of their scheduled routine clinic visit after approval by their clinic physician. One hundred twenty eight participants will be recruited; 64 for each arm.
Study participants must be an adult female survivor of invasive breast cancer, without clinical evidence of disease and have completed primary therapy (surgery, chemotherapy/biotherapy, and radiation). She may be continuing adjuvant hormonal therapy. She may be non-English speaking. Participants may not be diagnosed with noninvasive, metastatic, inflammatory, or recurrent breast cancer and may not be currently receiving chemotherapy or biotherapy. We plan to enroll 33 early survivors who have not received adjuvant endocrine or hormonal therapy, 33 early survivors who have received (or are currently receiving) adjuvant endocrine or hormonal therapy, 33 long-term survivors who have not received adjuvant endocrine or hormonal therapy, and 33 long-term survivors who have received (or are currently receiving) adjuvant endocrine or hormonal therapy. We will stratify the participants by stage so that 1/3 of each group will have had Stage I cancer, 1/3 will have had Stage II cancer and 1/3 will have had Stage III cancer. We expect that approximately 80% of breast cancer patients will have used adjuvant endocrine or hormonal therapy, and that the pool of early-term survivors will be larger than the pool of late-term survivors.

**Instruments.**

*M. D. Anderson Symptom Inventory (MDASI).* The MDASI is "a brief measure of the severity and impact of cancer-related symptoms" (Cleeland et al., 2000, p.1634) over the previous 24 hours and is completed by the breast cancer survivor. It contains 13 core symptoms: fatigue, sleep disturbance, pain, drowsiness, poor appetite, nausea, vomiting shortness of breath, numbness, difficulty remembering, dry mouth,
distress and sadness using a 0 (not present)-10 (as bad as you can imagine) numerical rating scale. Six additional items describe how much the symptoms have interfered with the patient's life during the past 24 hours using a 0 (did not interfere) – 10 (interfered completely) numerical scale: general activity, mood, work (including work around the house), relations with other people, walking and enjoyment of life. The patient completes the MDASI over 5-7 minutes. The MDASI has demonstrated internal consistency (reliability) with a coefficient alpha of 0.82 and validity established with factor analysis in many different studies (Paice, 2004). The MDASI has been psychometrically and linguistically validated in nine languages and linguistically validated in another 14 in addition to English. The MDASI will be used to evaluate symptoms over the previous week, rather than 24 hours. (Appendix F)

Karnofsky Performance Status (KPS). The KPS is a clinician-completed scale. It allows patients to be classified based on their degree of functional impairment, with a scale from 0 (dead) to 100 (normal, no complaints, no evidence of disease) (Schag, Heinrich, & Ganz, 1984). It is further subgrouped into three groups:

A. Able to carry on normal activity and to work no special care is needed (80-100),

B. Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed (50-70)
C. Unable to care for self. Requires equivalence of institutional or hospital care. Disease may be progressing rapidly (0 to 40).

In this study, the KPS will measure functional status. The KPS has shown reliability and validity previously with Cronbach’s alpha of .97 and construct validity demonstrated with a p<0.001 (Mor, Laliberte, Morris, & Wiemann, 1984; Schag et al., 1984.) (Appendix G).

**The Charlson Comorbidity Index (CCI).** The CCI will measure comorbidities. The CCI is an investigator completed index that measures 17 clinical conditions that are weighted to assess the effect of the conditions on the patient’s prognosis (Charlson, Pompei, Ales, & MacKenzie, 1987). Item scores range from 1 to 6 for each item and are based on the relative risk for each. Scores range from 0 to 34, with higher scores signifying greater comorbidity. An adjustment will be made to address all participants beginning with a score of 2, given because they all have cancer. It has established reliability with clinical conditions, including cancer (Hall, Ramachandran, Narayan, Jani, & Vijayakumar, 2004) (Appendix H).

**Demographic/health history questionnaire.** The demographic questionnaire includes age, educational status, race/ethnicity, primary language spoken, menstrual status (premenopausal- still having periods, perimenopausal- usual pattern of periods is altered, and postmenopausal- no periods for one year or more), work status (employed or not), co-
morbidity (Have you been diagnosed by a healthcare provider with any chronic medical condition—if so please list. If yes, has this condition limited your current daily activities?) (Appendix E). Treatment history was obtained from the medical record by the investigator (date and type of surgery (segmental mastectomy vs. mastectomy), type of lymph node surgery if any, (sentinel node biopsy or axillary node dissection), chemotherapy/biotherapy (anthracycline, taxane, non-anthracycline and/or trastuzumab), radiation, and adjuvant hormonal treatments (tamoxifen, toremifene or aromatase inhibitors).

Data Collection Procedures.

Study participants will be identified, consented and enrolled at the time of routine follow-up outpatient clinic visit to the Nellie B. Connally Breast Center. The health history/demographic questionnaire and the MDASI will be completed by the participant once enrolled. Data collection will take approximately 10 - 15 minutes. The principal investigator will determine the Karnofsky score and review the treatment history from the electronic medical record.

Analysis.

Assuming that 64 patients are enrolled in each arm, we will have 80% power to detect a difference of medium effect size equivalent to half a standard deviation in a 5% significance test for acceptable levels of type one and type two error. Descriptive statistics will be used to assess the distributional characteristics and demographics across survivor status and hormonal therapy use. Symptom burden and interference will be calculated separately, as
recommended by the MDASI User Guide. Chi-squared, Fisher's exact test and t-test will be conducted to evaluate whether the characteristics differed by survivor status or use of adjuvant hormonal or endocrine therapy. A 2-way ANOVA will be conducted to evaluate differences in symptom burden, symptom interference and burden/interference of individual symptoms. Finally, we will add Karnofsky Performance Status and the Charlson Comorbidity Index to our models to evaluate impact of functional status and comorbidities upon symptoms. All models will contain terms for stage of disease to account for stratification on that factor, as well as a term for age to adjust for the effects of age upon symptom severity and interference.

Limitations.

There are several potential limitations. Participants will be recruited from the Nellie B. Connally Breast Center, while there for a routine visit, and therefore will not be randomly selected. Inclusion will be dependent on the participants' willingness to participate. Previous studies in this facility have been conducted with primarily Caucasian, middle class, well-educated participants and may not be generalizable to minorities or other groups. Because this study is performed at one Cancer Center, the results may not be generalizable to other patients in other centers.

A pilot study will precede the planned dissertation research study and will allow the researcher to identify study limitations and problems, in order to address them. Even with these possible limitations, this study will provide new information
about symptoms that will be used to design later longitudinal and intervention studies.

**Alternative Approach.**

An alternative approach to studying the identified variables would be a prospective longitudinal study. The use of a cross-sectional design was chosen because of the need to gather preliminary data; a later longitudinal cohort study is planned to evaluate the symptoms in a cohort beginning at 1 year post diagnosis through 5 years, to evaluate which symptoms persist throughout the 5 years.

**Protection of Human Subjects**

All consenting members of the research team will undergo institutional review board training as required by the University of Texas M. D. Anderson Cancer Center including a 4 hour institutional course and a 1-hour electronic IRB review module required by the University of Texas MD Anderson Cancer Center. The Institutional Review Board at The University of Texas MD Anderson Cancer Center will review and approve all consenting materials, including the attached draft of the informed consent template, prior to use in consenting study participants. Reciprocal approval will be obtained from the University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects.

Potential study subjects will be consented at the time of the routine follow up visit. Risks associated with participation in the study will be outlined in the informed consent and reviewed with potential subjects by the consenting member of the research team. Potential participants will be reassured that non-
participation will not impact their care. Potential risks of study participation are minimal as the study will consist of completion of questionnaires and data collection from the medical record.

Consent documents, in addition to study data will be maintained in a locked file in the Principal Investigator's office and any electronic templates will be password protected on an institutional computer. Finally, continual oversight for the ethical procedures of the proposed study will be provided by the institutional IRB in the form of spontaneous auditing of consenting and data collection materials.

**Women and Minorities Inclusion**

All female adult breast cancer survivors attending a follow up visit to the Nellie B. Connally Breast Center will be approached to participate in this study. The racial composition of this patient cohort includes individuals of predominantly Caucasian, middle eastern and Hispanic descent. Non-English speaking survivors will be approached through the use of a translator in order to broaden the inclusion of minorities. Women and minority patients are recipients of breast cancer treatment and as such will be invited to participate in the study and included to the degree which they consent to participate.
Literature Cited


A Cross-Sectional Assessment of Symptoms in Early- and Long-Term Breast Cancer Survivors

Running title: Symptoms: Breast Cancer Survivors

Authors: Faith Strunk, PhD, RN, FNP, AOCNP, Assistant Professor at The University of Texas Health Science Center School of Nursing; Geri LoBiondo-Wood, PhD, RN, FAAN, Professor at The University of Texas Health Science Center School of Nursing; Terri Armstrong, PhD, RN, FAAN, Professor at The University of Texas Health Science Center School Of Nursing; Richard Theriault, DO, Professor at The University of Texas MD Anderson Cancer Center; and Bryan Fellman MS, Research Statistical Analyst in Biostatistics at The University of Texas MD Anderson Cancer Center.

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Abstract

Background

Many breast cancer survivors continue to have single or multiple symptoms after they have completed primary cancer therapy. The quantifiable, subjective experience of multiple symptoms and their impact is defined as symptom burden. Previous research has focused on symptoms during primary therapy or shortly after completion of treatment.

Objectives

Our study objectives were to determine whether symptom burden differed according to survivor status (early as opposed to long-term survival) and/or use of endocrine or hormonal adjuvant therapy. We hypothesized that there would be no difference in the symptoms expressed among early- and long-term survivors.

Methods

In this cross-sectional study, data were collected on 133 survivors, using the MD Anderson Symptom Inventory, Karnofsky Performance Status, Charlson Comorbidity Index and a demographic/health history form to assess study variables.

Results

Patients who were prescribed endocrine or hormonal therapy had higher symptom severity scores than did women who did not receive these therapies.
No differences were noted in symptom burden and symptom interference between early- and long-term survivors or whether or not they had taken adjuvant therapy. As functional status increased, the patients' symptoms scores decreased. Comorbidities did not impact the symptom scores.

Conclusions

Breast cancer survivors continue to experience symptoms, but symptoms are more severe among those taking hormonal or endocrine therapy. Understanding the relationship between symptoms, cancer therapy, comorbidities, and functional status in early versus late survivorship may improve symptom management and outcomes for breast cancer survivors.

Key Words

Breast cancer, survivor, symptoms, symptom interference, M. D. Anderson Symptom Inventory (MDASI), Karnofsky Performance Status (KPS), Charlson Comorbidity Index (CCI)

Breast cancer is the most common cancer (excluding skin cancer) among women in the United States; one in eight women will develop the disease (American Cancer Society, 2013). Overall, women treated for breast cancer have an 89% survival rate after 5 years and a 75% survival rate after 15 years (American Cancer Society, 2013). In 2006, the number of breast cancer survivors was estimated to be 2.6 million. By 2009 they numbered 2.7 million and as of 2012 there are over 2.9 million (American Cancer Society, 2013; National
Cancer Institute, 2012). Earlier diagnosis and treatment and improvements in cancer care have enabled more women with breast cancer to live longer lives and, for many, cancer-free.

Many survivors who have completed their primary treatment (surgery, chemotherapy/biotherapy, and/or radiation therapy) may continue taking hormonal therapy. Once primary treatment is over, survivors expect their symptoms to subside. Unfortunately many breast cancer survivors continue to have long-lasting symptoms related to their cancer and/or its treatment (Barsevick, 2007; Cleeland, 2007; Janz et al., 2007; Rosedale and Fu, 2010).

Multiple symptoms that persist are known as symptom burden (Burkett and Cleeland, 2007; Gapstur, 2007; Gill, Chakraborty, and Selby, 2012). Symptom burden is the subjective, quantifiable prevalence, frequency, and severity of symptoms and encompasses the patient’s perception of the symptoms’ impact (Cleeland, 2007; Gapstur, 2007).

Symptom burden has been evaluated, but much of the research has focused on symptoms and supportive care during primary therapy (Chung, Cimprich, Janz, and Mills-Wisnesky, 2009). However, several studies have concentrated on the early survivorship periods—beginning and continuing through the first 27 months following completion of primary therapy (Brant et al., 2011; Ganz, Kwan, Stanton, Bower, and Belin, 2011; Janz et al., 2007; Park, Bae, Jung, and Kim, 2011; Penttinen et al., 2010; Thompson, 2007; Yi, Swartz and Reyes-Gibby, 2011). Findings suggest that symptoms related to primary therapy contribute to impaired quality of life (Bower, 2009; Dahl, Nesvold,
Reinertsen, and Fossa, 2011; Janz et al., 2007; Park et al., 2011). The symptoms most frequently cited in the aforementioned studies include pain, fatigue or lack of energy, difficulty sleeping, arm pain and lymphedema, breast symptoms, feeling irritable or nervous, menopausal symptoms, weight changes, nausea, depression, and cognitive dysfunction.

A number of studies have focused on a specific symptom, such as pain (Lundstedt et al., 2012; Mao et al., 2009; Rief, Bardwell, and Dimsdaile, 2011), lymphedema (Armer and Stewart, 2010; Meeske et al., 2009; Smoot et al., 2010), fatigue (Bower et al., 2008; Bower, Ganz, Irwin, Arevalo, and Cole, 2011; Thompson, 2007) or menopausal symptoms (Leining et al., 2006; Loibl, Lintermans, Dieudonné, and Neven, 2011; Ruddy et al., 2011). Other studies have explored longer-term issues. For example, the incidence of lymphedema was found to persist and/or increase over five years (Armer and Stewart, 2010; Norman et al., 2009). Cancer-related fatigue was cited by 21% of both the 1- to 5-year survivors and the 5- to 10-year survivors (Bower et al., 2008). Sleep disturbances, fatigue, and pain had persisted in survivors evaluated at an average of 4.2 years (Hartl et al., 2003).

Several studies have yielded contradictory findings. For example, the results of one study suggested that cognitive dysfunction abated in the 12 to 24 months after adjuvant chemotherapy (Castellon et al., 2004). Jim et al. (2009), however, found significant differences in cognitive functioning and cognitive impairment after six months among women who had received chemotherapy or radiation therapy compared to healthy matched controls. Tannock et al.'s 2004
review found durable cognitive effects in 9 to 75% of patients, although the higher percentages were observed among those evaluated closer to completion of chemotherapy. However, in a study of longer-term survivors (5 to 15 years), Klein et al. (2011) found an improvement in all symptoms except cognitive functioning and insomnia. The discrepancies among these findings may be attributable to variability in primary therapy over time, pre-existing comorbidities, or use of adjuvant endocrine or hormonal therapy.

The likelihood of poor health was much higher among those who had another comorbid condition (Elliott et al., 2011). Other studies have excluded participants who had an additional significant chronic illness (Thompson, 2007). Functional status has been addressed in previous studies and low functional status is associated with poorer quality of life (Penttinen et al., 2010).

Symptoms may arise from comorbid illnesses or acute injuries related to the disease itself, or they may be attributable to cancer treatment and manifested in the form of side effects or toxicities (Cleeland, 2007). Symptom burden (Cleeland, 2007; Gapstur, 2007) is the conceptual framework chosen for this study. Symptom burden has been described as the subjective counterpart to tumor burden (Cleeland and Reyes-Gibby, 2002) and as the sum of the severity and impact of symptoms (Cleeland, 2007). Symptom burden affects multiple patient outcomes, including survival, functional status, and quality of life (Gapstur, 2007). Symptom burden is active and changes over time as patients undergo treatment or experience exacerbations or remissions of their disease (Vig and Pearlman, 2003). In this framework, symptoms related to treatment
often are viewed as complicating post-treatment recovery (Cleeland, 2007; Cleeland and Reyes-Gibby, 2002).

Historically, the symptoms of survivors during primary therapy or shortly thereafter have been addressed in the literature. But no studies have identified and compared the symptoms related to the use of adjuvant endocrine or hormonal therapy that are experienced by early- and long-term breast cancer survivors.

The primary objective of this study was to determine whether symptom burden differed by survivor status (early versus long-term) and/or the use of endocrine or hormonal therapy. We hypothesized that no difference would be seen in the symptoms expressed among early- and long-term survivors.

This study also explored the association of comorbidities and symptoms expressed by early- and long-term survivors. Evaluation of concurrent comorbidities was warranted because comorbidities have been associated with symptom severity (Kurtz, Kurtz, Stommel et al.1999). This study also addressed the associations between functional status and symptoms related to adjuvant endocrine or hormonal therapy.

**Materials and Methods**

**Study design**

The study design was exploratory and cross-sectional. Institutional Review Board approval was obtained, and all subjects provided informed consent.
Setting

The study was conducted at the Nellie B. Connally Breast Center at The University of Texas MD Anderson Cancer Center, an academic, comprehensive cancer center. MD Anderson is the largest institution in The University of Texas system, with 631 inpatient beds and 1,281,489 outpatient visits in 2012. The Nellie B. Connally Breast Center served more than 4,720 new patients and consultation visits, and conducted more than 33,000 follow-up visits in 2012.

Study Participants

The participants were adult women who had completed primary treatment for breast cancer (surgery, chemotherapy/biotherapy, and/or radiation) as many as six years earlier and were receiving follow-up care at the Breast Center. Non-English speaking women were recruited with the assistance of the MD Anderson’s Language Assistance office. Exclusion criteria included diagnosis of non-invasive, metastatic, inflammatory, or recurrent breast cancer or current active treatment with chemotherapy or biotherapy. Participants could be taking adjuvant hormonal or endocrine therapy. The patients were consecutively recruited as they presented to the Breast Center for a routine follow-up visit and were stratified by time (early: 0 to 36 months after primary treatment versus long-term: 37 to 60 months after primary treatment), disease stage (I, II, or III), and whether or not they were taking adjuvant hormonal or endocrine therapy.
Sample Size

Using a 2 x 2 factor analysis model, with 33 survivors per cell (long/short-term survival by adjuvant endocrine therapy), we had 80% power to detect a one-unit difference in mean symptom burden scores through the use of adjuvant endocrine therapy. This translates into a standard deviation among means of 0.5. We also had more than 95% power to detect a two-unit difference between early- and long-term survivors—the same as a 1.0 standard deviation among means—and to detect a 1.12 standard deviation among means for the interaction effect. All testing was 2-sided, using a 5% level of statistical significance. A subject standard deviation of 2.0 was used to calculate power, based upon findings by Cleeland (2007). Because we had two primary objectives (the main effect of short/long-term survival and the effect of adjuvant endocrine/hormonal therapy), we had a 10% chance of falsely rejecting at least one of our primary hypotheses.

Data Collection Procedures

Study participants were identified, gave their informed consent, and were enrolled during their routine follow-up outpatient clinic visit to the Breast Center. Once enrolled, each participant completed the MD Anderson Symptom Inventory (MDASI). The principal investigator determined each patient’s Karnofsky score, completed the demographic and health history questionnaire with the participant, and extracted the treatment history from the electronic medical record.
Instruments

**Demographic/health history questionnaire.** The demographic/health history questionnaire includes age, educational status, race/ethnicity, primary language spoken, menstrual status, work status, comorbidities, treatment history, and use of any adjuvant hormonal therapy.

**MD Anderson Symptom Inventory (MDASI).** The MDASI was used to measure symptom severity, interference, and burden. The MDASI is a 19-item self-report measure of the severity and impact of cancer-related symptoms (Cleeland et al, 2000). It addresses 13 core symptoms: fatigue, sleep disturbance, pain, drowsiness, poor appetite, nausea, vomiting, shortness of breath, numbness, difficulty remembering, dry mouth, distress, and sadness using a numerical rating scale of 0 (not present) to 10 (as bad as you can imagine). Six additional items address how much the symptoms have interfered with the patient’s life during the past 24 hours, using a numerical scale of 0 (did not interfere) to 10 (interfered completely) regarding general activity, mood, work (including work around the house), relations with other people, walking, and enjoyment of life. Symptoms may be categorized as 0-4 mild, 5-6 moderate, and 7 or above severe; ratings of 5 or higher indicate a moderate-to-severe symptom that significantly impairs daily functioning (Mendoza et al., 2013). The MDASI takes approximately 5 to 7 minutes to complete. The inventory has demonstrated internal consistency (reliability) with a coefficient alpha of 0.82, and its validity has been established with factor analysis (Paice, 2004) in many different studies. The MDASI has been psychometrically and linguistically validated in nine
languages and linguistically validated in another 14 languages in addition to English. The MDASI was used to evaluate symptoms over the previous week, rather than 24 hours. Internal consistency of the MDASI for this study was measured by Cronbach's alpha = 0.91.

**Charlson Comorbidity Index (CCI).** The CCI was used to measure comorbidities. The CCI is an investigator-completed index that measures 17 clinical conditions that are weighted to assess the effect of the conditions on the patient's prognosis (Charlson, Pompei, Ales, and MacKenzie, 1987). Item scores range from 1 to 6 for each item and are based on the relative risk for each. Scores range from 0 to 34, with higher scores signifying greater comorbidity. One of the ten comorbidity items on the CCI is cancer, thus each subject began with a score of two. The CCI has an established reliability with clinical conditions, including cancer (Hall, Ramachandran, Narayan, Jani, and Vijayakumar, 2004).

**Karnofsky Performance Status (KPS).** Patients' functional status was measured with the Karnofsky Performance Status. The KPS is a clinician- or investigator-completed scale that classifies patients according to their degree of functional impairment on a scale from 0 (deceased) to 100 (normal, no complaints, no evidence of disease) (Schag, Heinrich, and Ganz, 1984). The KPS is further divided into three subgroups: A) Able to carry on normal activity and to work, with no special care needed (80-100), B) unable to work, able to live at home and care for most personal needs, varying amounts of assistance needed (50-70), and C) Unable to care for self, requires equivalent of institutional
or hospital care; disease may be progressing rapidly (0-40). The KPS has shown reliability and validity previously with a Cronbach’s alpha of 0.97 and construct validity demonstrated with a $p<0.001$ (Mor, Laliberte, Morris, and Wiemann, 1984; Schag et al., 1984).

**Statistical Analysis**

The objectives of this study were to determine whether symptom burden differed between survivor status (early/long-term) and/or endocrine or hormonal adjuvant therapy use. Early survivors were defined as those who had finished primary treatment fewer than three years or 36 months prior to the date of the survey. Long-term survivors were defined as those who had finished their primary treatment at least three years, but less than six years (37 to 60 months), before the date of the survey.

Descriptive statistics were used to assess the distributional characteristics and demographics of the study population across survivor status and use of hormonal therapy. Chi-squared, Fisher’s exact test, and $t$-test were conducted to determine whether these characteristics differed by survivor status as well as by the presence or absence of current adjuvant endocrine or hormonal therapy. Symptom burden and interference were calculated separately according to the prorated score recommended by the M. D. Anderson Symptom Inventory User Guide.

A two-way ANOVA model was conducted to evaluate differences in symptom burden, symptom interference, and burden/interference of individual symptoms. We conducted another set of ANOVA models with the KPS and the
Charlson Comorbidity Index (CCI) to evaluate the impact of functional status and comorbidities on symptoms. A third two-way ANOVA model was used to evaluate differences in the individual MDASI items by survivor status and hormone therapy treatment. All models contain terms for stage to account for stratification on that factor, as well as age for the effects of age upon symptom severity and interference. The interaction between the two factors was tested in all models but was dropped if the term was non-significant. Cronbach's alpha was used to measure the internal consistency of MDASI with severity (α = 0.84), interference (α = 0.88), and overall MDASI (α = 0.91).

Results

A total of 141 patients were sequentially approached to participate in the study over a period of four months; 134 agreed to participate. Individuals who chose not to participate did so primarily because of time constraints. One individual withdrew her consent, leaving 133 study participants.

Patients and Disease Demographics

Patient characteristics, both demographic and disease-related, were well balanced between survival status and use of adjuvant therapy (Table 1). Subjects were predominantly white, non-Hispanic (65.4%), English-speaking (89.5%), married (72.7%), had a high school education (30.8%), and were a mean age of 56 (range, 30.5-83.0) The majority had estrogen receptor–positive (58.6%), Her2/neu–negative (80.5%) disease. Disease stage was stratified by
design, with equal numbers of stage I, II, and III in both arms (early and long-term). The majority had received chemotherapy (74.2% taxane, 68.3% anthracycline, and 9.8% other), but only 19.5% received trastuzumab. More women had undergone modified radical or total mastectomy (56.4%) than segmental mastectomy (45.9%). About half had undergone sentinel lymph node biopsy only (48.9%), half (51.1%) had axillary node dissection, and 78.2% of participants received adjuvant radiation therapy.

**Primary Treatment History**

In general, treatment history among early- and long-term survivors was not statistically significant, except for taxane chemotherapy and adjuvant therapy. Early survivors were more likely to have been treated with taxanes than were long-term survivors (82.8% vs. 66.2%; \( p=0.0289 \)). In addition, women who were not on adjuvant therapy were more likely to have received primary treatment with taxanes (87.7% vs. 61.2%; \( p=0.0005 \)). Receipt of anthracycline chemotherapy did not differ among early- vs. long-term survivors. The type of breast and axillary surgery was not statistically significant for these groups. Women who received adjuvant therapy were more likely to have received radiation therapy (\( p=0.0426 \)).

**MDASI Results**

Summary statistics for all the MDASI items are shown in Table 2. The frequency of reported symptoms and their severity/interference are shown in Table 3. No statistical evidence for a relationship between comorbidities and MDASI scores was observed; however, this patient population had few
comorbidities as indicated by the low CCI scores in general. As the Karnofsky Performance scores increased, MDASI scores decreased but not significantly, indicating that individuals with greater performance status had lower symptom severity.

**Symptom frequency and severity**

All but five of the women reported experiencing at least one symptom. Most women (81.2%) endorsed five or more symptoms. The majority of symptoms were in the mild to moderate categories, although 44% of women scored at least one symptom in the severe range (7 or higher). Fatigue was the most commonly reported symptom, whereas sleep disturbance was rated highest in severity.

**Symptom severity and survivor status**

Survivor status did not significantly impact the MDASI scores, and no significant difference was noted between early or long-term survivors in relation to reports of symptom severity. The interaction term between survivor status and adjuvant endocrine or hormonal therapy use was non-significant in all models, indicating no differences in symptom burden and interference between early and long-term survivors, regardless of adjuvant therapy use.

**Symptom severity and adjuvant therapy use**

Patients who had endocrine or hormonal therapy had higher symptom severity scores than did the women who did not, as reflected in the MDASI scores ($\mu = 29.1$ vs. $\mu = 22.0$; $p = 0.0250$)
Symptom severity and Karnofsky Performance Status

Karnofsky Performance Status was significantly related to pain ($p = 0.0004$), fatigue ($p = 0.0217$), sleep ($p = 0.0249$), distress ($p = 0.0040$), remembering things ($p = 0.0292$), and numbness ($p = 0.0195$), with lower KPS scores being related to higher symptom severity.

Symptom Severity and Charlson Comorbidity Index

The Charlson Comorbidity Index was significantly related only to symptoms of nausea ($p = 0.0000$) and vomiting ($p = 0.0050$).

Discussion

This study sought to examine the occurrence of symptom burden in early and long-term survivors with or without endocrine or hormonal adjuvant therapy use. Data suggested few statistically significant relationships between and among study variables. However, as would be expected for women taking adjuvant endocrine or hormonal therapy, these survivors had significantly higher symptom severity scores than did the women who did not receive these therapies. This finding may be attributable to the side effects of the hormonal or endocrine adjuvant therapies, including hot flashes, fatigue, insomnia, or headaches (Bowles, et al., 2012). Pain is another commonly reported symptom (Dunn & Gotay, 2013). Although clinicians discuss with their patients that the symptoms related to hormonal or endocrine therapy may improve over time, no
significant differences are seen in the scores of early versus long-term survivors who receive these therapies. The assumption was that closer to primary treatment, the survivor would experience certain symptoms that would resolve over time, although other symptoms might persist. Therefore, from clinical experience, we expected that long-term survivors would have fewer symptoms overall. However, our results suggest that women continue to experience multiple symptoms after treatment completion. Few studies have evaluated symptoms five years after diagnosis (Koch et al., 2013), when routine follow-up care has ended. This emphasizes the need to continue to assess symptom burden throughout the cancer treatment trajectory.

The median age of the participants was 56, which is lower than the median age of 61 for breast cancer diagnosis in the United States (American Cancer Society, 2013). It is unclear why our participants were younger. It may be that younger women are referred to our institution more often or that younger women tend to participate in research studies, but this finding reflects the literature, which often reveals a younger median age (Bower et al., 2006; Broeckel, Thors, Jacobsen, Small, and Cox, 2002; Carlson, Campbell, Garland and Grossman, 2007; Eversley et al., 2005; Otte, Carpenter, Russell, Bigatti, and Champion, 2010). The younger age of our patients may affect the symptoms expressed; as in previous studies, older women tended to minimize and attribute any symptoms they had to aging (Heidrich, Egan, Hengudomsub, and Randolph, 2006; Rooland and Heidrich, 2011; Royer, Phelan, and Heidrich, 2009)
Women with more symptoms have poorer functional status, whereas women with fewer symptoms have higher functional status scores. Our study bolstered these findings; as the Karnofsky Performance scale increased (nearer to 100 or normal function), the MDASI scores decreased (i.e., fewer symptoms or lower symptom burden). All study participants had completed primary therapy and were without evidence of disease, and they all scored at least an 80 on the KPS scale, which indicates the ability to carry on normal activity and to work.

Multiple studies have noted the most prevalent symptoms in breast cancer survivors to be pain, fatigue, disturbed sleep, cognitive problems, and mood (Dodd, Cho, Cooper, and Miaskowski, 2010). Our study had similar findings (Table 3), with the top five symptoms reported as fatigue, remembering things, disturbed sleep, pain, and feeling drowsy, although our study participants reported mood complaints less often. Vomiting was the least frequently reported symptom, as would be expected of women who had completed primary therapy. One unexpected finding was how often these survivors reported dry mouth. Dry mouth is not a symptom that is often reported as a concern in the clinical setting. In general, most survivors reported mild to moderate symptoms.

These data suggest persistence of mild to moderate symptom burden following breast cancer treatment regardless of survivor status. Statistically significant findings suggesting increased symptom severity for women receiving adjuvant endocrine or hormonal therapies identify a clinical opportunity to assess which symptoms develop at what point in time as a means of further addressing those symptoms and developing interventions. Moreover, for patients who
require more than the current five years of adjuvant therapy with hormonal or endocrine agents, this study identifies the need for attentive assessment of continued symptoms longer into survivorship for this population. Although few statistically significant relationships were found between and among other study variables, the impact of adjuvant therapy on female breast cancer patients' post-treatment symptom severity offers valuable insight for clinical practice.

**Strengths and Limitations**

One of the strengths of this study was the emergence of evidence indicating that symptom burden persists for women treated for breast cancer in both an early and long-term survivorship time frame. This finding adds to the existing literature related to symptom burden during and immediately following treatment. Moreover, symptom burden may be exacerbated by prolonged endocrine or hormonal adjuvant therapy. These findings inform clinical practice, which focuses on evaluating and managing symptom burden throughout survivorship, even after the completion of primary therapy.

This study had several limitations. Because this was a cross-sectional study, the duration of the symptoms could not be evaluated. Sampling bias may have occurred as participants were recruited from the Breast Center while they were there for a routine visit and therefore were not randomly selected. In addition, because this study was performed at only one cancer center, the results may not be generalizable to patients in other centers. Moreover, the majority of women in this study were married, white, non-Hispanic, employed full-time, high
school graduates—demographics that are not reflective of national data and may not be generalizable to minorities or other groups. Women of other races or ethnic groups may experience different symptoms. In addition, male breast cancer survivors were excluded from this study, are underrepresented in the literature, and may also experience different symptoms.

**Research Implications**

Although the number of participants who reported severe symptoms was low, most survivors reported at least one symptom (96%), and the majority of survivors in this study reported five or more. The most common, severe, and distressing symptoms need further evaluation. Longitudinal studies that compare survivors to healthy women are needed in order to characterize symptom incidence and persistence over time. Further research should be directed toward assessing the long-term impact of symptoms and evaluation of symptom distress. In addition, studies that comprise participants who reflect the age of the U. S. breast cancer population are needed, as are studies with minority populations that can provide insight into the symptom experiences of breast cancer survivors who are minorities.

**Clinical Implications**

Clinicians who care for breast cancer survivors need to be aware that the majority of these survivors, whether early or long-term, have symptoms, and that those who are on adjuvant hormonal or endocrine therapy experience greater symptom severity. Although most women in this study did not have significant
distress, assessment of the presence and severity of symptoms should be a routine part of oncology care. Clinicians can then provide anticipatory guidance and inform survivors about the persistence of symptoms. This will enable survivors to anticipate symptoms and will encourage development of programs to assist survivors in dealing with symptoms more effectively.

Conclusions

We conducted this study to evaluate symptoms experienced by breast cancer survivors who completed primary therapy. From clinical experience, we expected symptoms to lessen over time, and surmised that long-term survivors would have fewer symptoms. Our analysis revealed that both early and long-term survivors had symptoms, but those taking adjuvant endocrine or hormonal therapy experienced greater symptom severity, whether early- or long-term. Establishing this baseline will help to develop pilot interventions that can be tested and used effectively in this population. Understanding the connections among symptoms, cancer therapy, comorbidities, and functional status may result in improved symptom management and outcomes for breast cancer survivors.

Funding Sources

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Conflicts of interest Disclosure

No conflicts of interest to disclose.
References


Table 1

Demographics by survivor status and endocrine/hormonal therapy

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**Demographics by survivor status and endocrine/hormonal therapy**

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<td>Chemoanthracycline</td>
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<td>75.4</td>
<td>42</td>
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<td>MRM or total mastectomy</td>
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<td>27</td>
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<td>31</td>
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<td>38</td>
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<td>SLN only</td>
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<td>31</td>
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<td>50.0</td>
<td>34</td>
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<tr>
<td>AND</td>
<td>No</td>
<td>31</td>
<td>47.7</td>
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<td>34</td>
<td>52.3</td>
<td>34</td>
<td>50.0</td>
<td>31</td>
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</table>
Table 2

Summary statistics for the MDASI

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
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<tr>
<td><strong>Core symptoms</strong></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Pain</td>
<td>133</td>
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<td>2.8</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Fatigue</td>
<td>132</td>
<td>3.4</td>
<td>2.5</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Nausea</td>
<td>132</td>
<td>0.5</td>
<td>1.7</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Sleep</td>
<td>131</td>
<td>3.3</td>
<td>3.0</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Distress</td>
<td>133</td>
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<td>2.8</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Shortness of breath</td>
<td>133</td>
<td>1.0</td>
<td>1.9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Remembering things</td>
<td>132</td>
<td>2.8</td>
<td>2.7</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Lack of appetite</td>
<td>133</td>
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<td>1.7</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Drowsy</td>
<td>133</td>
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<td>2.6</td>
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<tr>
<td>Dry mouth</td>
<td>132</td>
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<td>0</td>
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</tr>
<tr>
<td>Sad</td>
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<td>2.7</td>
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<td>10</td>
</tr>
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<td>Vomiting</td>
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<td>0.6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Numbness</td>
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<td><strong>Interference items</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General activity</td>
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<td>0</td>
<td>10</td>
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<td>Walking</td>
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Note. Cronbach’s alpha’s for Severity (0.84), Interference (0.88), MDASI (0.91)
Table 3
Symptom frequency, Percentage reported moderate/severe and the average symptom severity/interference score

<table>
<thead>
<tr>
<th>Variable</th>
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<th>% Mod/Sev</th>
<th>Mean</th>
<th>SD</th>
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<tr>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Pain</td>
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<tr>
<td>Fatigue</td>
<td>113</td>
<td>39</td>
<td>4.0</td>
<td>2.3</td>
</tr>
<tr>
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<td>17</td>
<td>47</td>
<td>4.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Sleep</td>
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<td>Distress</td>
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<td>33</td>
<td>3.8</td>
<td>2.6</td>
</tr>
<tr>
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<td>44</td>
<td>27</td>
<td>3.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Remembering things</td>
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<td>34</td>
<td>3.6</td>
<td>2.5</td>
</tr>
<tr>
<td>Lack of appetite</td>
<td>32</td>
<td>25</td>
<td>3.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Drowsy</td>
<td>92</td>
<td>34</td>
<td>3.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>59</td>
<td>22</td>
<td>3.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Sad</td>
<td>78</td>
<td>36</td>
<td>3.7</td>
<td>2.6</td>
</tr>
<tr>
<td>Vomiting</td>
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<td>25</td>
<td>3.0</td>
<td>2.2</td>
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<tr>
<td>Numbness</td>
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<td>3.7</td>
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<td><strong>Interference Items</strong></td>
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<td>General activity</td>
<td>78</td>
<td>32</td>
<td>3.5</td>
<td>2.2</td>
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<tr>
<td>Mood</td>
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<td>26</td>
<td>3.1</td>
<td>2.4</td>
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<td>Work</td>
<td>81</td>
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<td>2.5</td>
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<tr>
<td>Relations</td>
<td>49</td>
<td>20</td>
<td>2.6</td>
<td>2.0</td>
</tr>
<tr>
<td>Walking</td>
<td>67</td>
<td>40</td>
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<td>2.5</td>
</tr>
<tr>
<td>Enjoyment of life</td>
<td>60</td>
<td>28</td>
<td>3.1</td>
<td>2.2</td>
</tr>
</tbody>
</table>
Appendix A

M. D. Anderson Institutional Review Board Approval Letter
To: Faith A. Strunk
From: Veronica Roberts
CC: Diana L. Urbauer, Geri Wood, LaTonia R. Okadigwe, OPR Protocol Activations
MDACC Protocol ID #: 2012-0909
Protocol Title: Symptoms in Early and Long-term Breast Cancer Survivors Who Have Completed Primary Therapy
Version: 03
Subject: Contingencies Met - Protocol 2012-0909

On 11/14/2012 the Institutional Review Board 4 committee, chair, or designee granted approval to the above named and numbered protocol since the contingencies outlined by the IRB 4 on 11/09/2012 have been met.

It was noted that the protocol, informed consent documents (ICDs) and/or the Waivers of ICD and Authorization are satisfactory and in compliance with federal and institutional guidelines. No participants may be entered on this protocol until it has been officially activated by OPR.

In keeping with the requirements outlined in 45CFR46.109(e) and 21 CFR56.109(f), the IRB shall conduct continuing review of all protocols at intervals appropriate to the degree of risk, but not less than once per year.

You are responsible for promptly reporting to the IRB:

- any severe adverse events;
- any death while patient is on study;
- any unanticipated problems involving risks to subjects or others;
- any proposed changes in the research activity (changes may not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects).

To activate this study, please compose and send a "Request for Activation" memo in PDOL.

The existing Informed Consent and/or Waivers of Informed Consent and Authorization cannot be used until the protocol is Activated.
If a Material Transfer Agreement (MTA) is required, it must be obtained prior to Activation.

In the event of any questions or concerns, please contact the sender of this message at (713) 792-2933.

Veronica Roberts 11/18/2012 04:23:37 PM

This is a representation of an electronic record that was signed and dated electronically and this page is the manifestation of the electronic signature and date:

Veronica Roberts
11/18/2012 04:23:20 PM
IRB 4 Chair Designee
FWA #: 00000363
OHRP IRB Registration Number: IRB 4 IRB00005015
Appendix B

UT Centralized IRB Review Form
Information for the Overall Principal Investigator - In addition to submitting an application to your organization's IRB (designated the "Reviewing IRB"), an "Intent to Submit for Centralized Review" form must be submitted to the IRB office at each participating organization.

Information for the Site Principal Investigator - The purpose of this form is to request centralized review at your organization (designated the "Relying Organization"). This request will be considered by your organization and a decision made on a case-by-case basis. The IRB office from your organization will forward the final decision to the Reviewing IRB.

If your organization agrees to Centralized IRB Review, you will be required to submit additional materials in accordance with local policy. The review of local issues by your organization is a separate process from the IRB approval being sought by the Overall PI. Reminder: you are not authorized to initiate research at your organization until both processes are completed: 1) the study is approved by the Reviewing IRB and an approval letter is issued, and 2) the local policy issues have been resolved and an activation letter has been issued by your Organization.

<table>
<thead>
<tr>
<th>Study Title:</th>
<th>Symptom in Early and Long Term Breast Cancer Survivors who have Completed Primary Treatment</th>
</tr>
</thead>
</table>

Name and Address of Site Principal Investigator (PI):

- Site PI's Name (Last Name, First Name, MI):
- Department: [Select Department]
- PI's Telephone#: [Number]
- PI's Cell or Pager Number: [Number]
- PI's e-mail address: [Email]
- PI's FAX Number: [Number]

Name of the Overall Principal Investigator (PI):

- Overall PI's Name (Last Name, First Name, MI): [Name]
- Organization: [Organization]

3. Which University of Texas Participating Organization will serve as the Reviewing IRB?

Select only one

- UT at Arlington (UTA)
- UT Austin (UT Austin)
- UT Brownsville
- UT at Dallas (UTD)
- UT at El Paso (UTEP)
- UT Pan American
- UT Permian Basin
- UT San Antonio (UTSA)
- UT Southwestern

4. Which University of Texas Participating Organizations will be engaged in this research?

<table>
<thead>
<tr>
<th>Column A - Participating Organizations</th>
<th>Column B - Institutions affiliated with the participating organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Select the Participating Organization(s) that will be engaged in the research</td>
<td>Insert the institutions affiliated with the participating organization that will also be engaged in the research</td>
</tr>
<tr>
<td>UT Tyler</td>
<td>UT Southwestern</td>
</tr>
</tbody>
</table>

**FOR IRB OFFICE USE ONLY**

1. Select the appropriate Organization

2. The Investigator's Intention to include this organization as part of the Centralized IRB Review by the IRB designated in Item 3 is:

   [ ] Acceptable  [ ] Not Acceptable

3. Notification Preference – the Reviewing IRB must notify this institution of approvals and study closure using the following method(s):

   [ ] send a copy of the IRB letter  [ ] send a monthly statement of listing the protocols approved in the previous month

   [ ] send a weekly statement of listing the protocols approved in the previous week  [ ] send an copy of the IRB letter to the Site PI at this organization who is then responsible to provide this information to the Institution

4. Federalwide Assurance Information – select the applicable statement(s):

   [ ] The box that applies Subpart A to all research is checked

   [ ] The box that applies Subparts B, C, and D to all research is checked

5. Verification that Reviewing IRB is listed on FWA

   [ ] The IRB designated in Item 3 above is listed on this institution's Federalwide Assurance

   [ ] The IRB designated in Item 3 above is also listed on the Federalwide Assurance for each affiliated institution listed in Item 4, Column B

6. Signature of the Official Authorized by Organization:

   [Signature]

   [Date: 12-12-12]

   Aman U. Buzdar, M.D.
Appendix C

CPHS IRB UTHSC Confirmation Letter
TO: Faith Strunk  
UT- H - SN - Nursing  
FROM: Cynthia Edmonds, MLA  
IRB Coordinator  
Office of Research Support Committees  
DATE: January 16, 2013  
RE: HSC - SN - 12 - 0880  
Symptoms in Early and Long-term Breast Cancer Survivors  
Reference Number: 091363  

Dear Ms. Strunk,  

This is a confirmation letter that the Committee for the Protection of Human Subjects (CPHS), the Institutional Review Board at the University of Texas Health Science Center at Houston, has received all the applicable documents for the above referenced protocol. The CPHS agrees to rely on the reviewing IRB, MD Anderson Cancer Center, which granted approval on November 9, 2012. It is your responsibility to maintain approval with the MDACC IRB and renew your protocol per their schedule.  

Please feel free to contact the Committee for the Protection of Human Subjects (CPHS) at 713-500-7943 if you have any additional questions or concerns.
Appendix D

Letter of Support
December 12, 2012

Faith A. Strunk, MSN, RN, FNP
The University of Texas Health Science Center School of Nursing
6901 Bertner Avenue
Houston, TX 77030

RE: Letter of Support - Symptoms in Early and Long-term Breast Cancer Survivors Who Have Completed Primary Therapy 2012-0909

Ms. Strunk:

This letter acknowledges your interest in conducting the above study in the Nellie B. Connolly Breast Center at the University of Texas M D Anderson Cancer Center. I believe your study will make valuable and important contributions, and we look forward to supporting you and your research, which involves 132 participants from the Breast Center.

I thank you for the opportunity to work with you on this study. Our patients depend upon exciting and quality research like this to give them hope.

Sincerely yours,

Vicente Valero, M.D., F.A.C.P.
Chairman Ad-Interim
Professor of Medicine

VVC / bmc
Appendix E

Demographic/Health History Form
Demographic Form

1. Birth date: Month__Day_____Year____

2. Participant's marital status (at present):
   Married/Partnered  □  Separated  □
   Divorced  □  Single, living with another adult  □
   Widowed  □  Single, living alone  □

3. Race:
   Asian or Pacific Islander  □  Hispanic  □
   Black Non-Hispanic  □  White Non-Hispanic  □
   Native American or Alaskan  □  Other (Specify)  □
   Native  □

4. Primary language spoken:__

5. Education (Mark only the highest completed):
   High School  □  Associate  □
   Bachelors  □  Masters  □
   PhD  □  Technical School  □
   Other___

6. Job status (check the one that best describes your status):
   Employed outside the home, fulltime  □  Unemployed  □
   Employed outside the home, part time  □  Retired  □
   Disabled due to illness  □  Work at home  □

7. Menstrual status (check the one that best describes your status):
   Premenstrual (still having periods)  □
   Perimenopausal (usual pattern of periods is altered)  □
   Postmenopausal (no periods for one year or more)  □

8. Other health problems: Have you been diagnosed by a health care provider with any chronic medical conditions? Please list them below. If yes, has this condition limited your current daily activities?

______________________________________________________________________________________________
Appendix F

M.D. Anderson Symptom Inventory
M. D. Anderson Symptom Inventory (MDASI) Core Items

Part I. How severe are your symptoms?

People with cancer frequently have symptoms that are caused by their disease or by their treatment. We ask you to rate how severe the following symptoms have been in the last 24 hours. Please fill in the circle below from 0 (symptom has not been present) to 10 (the symptom was as bad as you can imagine it could be) for each item.

<table>
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<th></th>
<th>Not Present</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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</thead>
<tbody>
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<td>O</td>
<td>O</td>
<td>O</td>
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<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>2. Your fatigue (tiredness) at its WORST?</td>
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<td>O</td>
<td>O</td>
<td>O</td>
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<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>3. Your nausea at its WORST?</td>
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<td>O</td>
<td>O</td>
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<td>4. Your disturbed sleep at its WORST?</td>
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<td>5. Your feelings of being distressed (upset) at its WORST?</td>
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<td>6. Your shortness of breath at its WORST?</td>
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<tr>
<td>7. Your problem with remembering things at its WORST?</td>
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<td>O</td>
<td>O</td>
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<tr>
<td>8. Your problem with lack of appetite at its WORST?</td>
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<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<td>9. Your feeling drowsy (sleepy) at its WORST?</td>
<td>O</td>
<td>O</td>
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<td>O</td>
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<td>10. Your having a dry mouth at its WORST?</td>
<td>O</td>
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</tbody>
</table>
11. Your feeling sad at its WORST? | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10
---|---|---|---|---|---|---|---|---|---|---|---
| O | O | O | O | O | O | O | O | O | O | O

12. Your vomiting at its WORST? | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10
---|---|---|---|---|---|---|---|---|---|---|---
| O | O | O | O | O | O | O | O | O | O | O

13. Your numbness or tingling at its WORST? | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10
---|---|---|---|---|---|---|---|---|---|---|---
| O | O | O | O | O | O | O | O | O | O | O

### Part II. How have your symptoms interfered with your life?

Symptoms frequently interfere with how we feel and function. How much have your symptoms interfered with the following items in the last 24 hours:

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<tr>
<th>Item</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tr>
<td>15. Mood?</td>
<td>O</td>
<td>O</td>
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<td>O</td>
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<tr>
<td>16. Work (including work around the house)?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<tr>
<td>17. Relations with other people?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<tr>
<td>18. Walking?</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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</table>
Appendix G

Karnofsky Performance Scale
# KARNOFSKY PERFORMANCE SCALE

**Description**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Normal, no complaints, no evidence of disease</td>
</tr>
<tr>
<td>90</td>
<td>Able to carry on normal activity; minor signs or symptoms of disease</td>
</tr>
<tr>
<td>80</td>
<td>Normal activity with effort; some signs or symptoms of disease</td>
</tr>
<tr>
<td>70</td>
<td>Cares for self, unable to carry on normal activity or to do active work</td>
</tr>
<tr>
<td>60</td>
<td>Requires occasional assistance, but is able to care for most of his/her needs</td>
</tr>
<tr>
<td>50</td>
<td>Requires considerable assistance and frequent medical care</td>
</tr>
<tr>
<td>40</td>
<td>Disabled, requires special care and assistance</td>
</tr>
<tr>
<td>30</td>
<td>Severely disabled, hospitalization indicated. Death not imminent</td>
</tr>
<tr>
<td>20</td>
<td>Very sick, hospitalization indicated. Death not imminent</td>
</tr>
<tr>
<td>10</td>
<td>Moribund, fatal processes progressing rapidly</td>
</tr>
<tr>
<td>0</td>
<td>Dead</td>
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Appendix H

Charlson Comorbidity Index
<table>
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<tr>
<th>Weight</th>
<th>Condition</th>
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<td>1</td>
<td>Myocardial infarct</td>
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<tr>
<td></td>
<td>Congestive heart failure</td>
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<tr>
<td></td>
<td>Peripheral vascular disease</td>
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<tr>
<td></td>
<td>Cerebrovascular disease</td>
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<tr>
<td></td>
<td>Dementia</td>
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<td></td>
<td>Chronic pulmonary disease</td>
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<tr>
<td></td>
<td>Ulcer disease</td>
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<td></td>
<td>Mid liver disease</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
</tr>
<tr>
<td>2</td>
<td>Hemiplegia</td>
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<tr>
<td></td>
<td>Moderate or severe renal disease</td>
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<tr>
<td></td>
<td>Diabetes with end-organ damage</td>
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<tr>
<td></td>
<td>Any tumor</td>
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<tr>
<td></td>
<td>Leukemia</td>
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<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td>3</td>
<td>Moderate or severe liver disease</td>
</tr>
<tr>
<td>6</td>
<td>Metastatic solid tumor</td>
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Appendix I

Subject Log
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<th>ACCESSION #</th>
<th>DATE ENROLLED</th>
<th>STAGE TNM &amp;</th>
<th>RECEPTOR STATUS</th>
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Appendix J

Subject Log by Stage
### SUBJECT LOG BY STAGE

#### PROTOCOL 2012-0909

<table>
<thead>
<tr>
<th>YES Adjuvant Hormonal/Endocrine Tx</th>
<th>Early (1-3 YRS) 0-36 mos</th>
<th>NO Adjuvant Hormonal/Endocrine Tx</th>
<th>EARLY (1-3 YRS) 0-36 mos</th>
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Appendix K

Recruitment Schedule
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</table>
Appendix L

Certificate of Human Subjects Protection Training
CERTIFICATE OF COMPLETION

is hereby granted to

Faith A. Strunk

Name

to certify satisfactory completion of the

Human Subjects Protection Training 2009 Refresher Course

on

March 04, 2009

Signature

Susan Trisbee

[Signature]
MD Anderson Cancer Center

CERTIFICATE OF COMPLETION

is hereby granted to

Faith A. Strunk

Name

to certify satisfactory completion of the
IRB Review for Non-exempt Human Subject Research

on

June 14, 2011

Signature

Jan Yungelas
Appendix M

Permission to use the Charlson Comorbidity Index
---Original Message---
From: Mary E. Charlson, MD [mailto:mecharl@med.cornell.edu]
Sent: Friday, September 21, 2012 2:29 PM
To: Strunk, Faith A
Subject: RE: permission for use of Charlson Comorbidity Index

Good Afternoon,

You may use the index for your study.

Best,
Mary Charlson

From: Strunk, Faith A [Faith.A.Strunk@uth.tmc.edu]
Sent: Thursday, September 20, 2012 3:23 PM
To: Mary E. Charlson, MD
Subject: permission for use of Charlson Comorbidity Index

Dear Dr. Charlson,

I am Faith Strunk, a doctoral student at the University of Texas- Houston, Health Science Center School of Nursing. I am currently planning a pilot study that is looking at symptoms in breast cancer patients who have completed primary therapy (surgery, chemotherapy/biotherapy and radiation) and the effects of time post-therapy and adjuvant endocrine therapy. I am also exploring the effects of functional status and comorbidities on symptom severity and interference. Acknowledging the reliability, validity and applicability to my study population, I am writing to request your permission to use the Charlson Comorbidity Index in my study.


Thank you for your time,

Faith A. Strunk
doctoral student
University of Texas- Houston Health Science Center School of Nursing
cell: 713-382-7204
Appendix N

Permission to use the MDASI
-----Original Message-----
From: symptomresearch
Sent: Tuesday, October 16, 2012 4:49 PM
To: Strunk, Faith A
Cc: symptomresearch
Subject: RE: Order Form for Pain Research Group Assessment Tools

I have attached the MDASI-core as you requested. Please let me know if you have any questions. Thank you for your interest in the MDASI.

The email that is sent with the tool is the authorization letter for all the non-funded academic research or educational purpose.

Best regards,

Nazim Ali

-----Original Message-----
From: Faith Strunk [mailto:fastrunk@mdanderson.org]
Sent: Friday, October 12, 2012 1:45 PM
To: symptomresearch
Subject: Order Form for Pain Research Group Assessment Tools

Order Form for Pain Research Group Symptom Assessment Tools

Assessment Tool: M. D. Anderson Symptom Inventory (core MDASI)

Psychometrically validated language(s): Chinese - Simplified, English, Filipino, French, Greek, Japanese, Korean, Russian

Linguistically validated language(s):
Afrikaans, Arabic, Dutch, German, Hebrew, Hindi, Italian, Portuguese - Brazil, Portuguese - Portugal, Spanish, Swedish, Turkish, Vietnamese

Purpose: Non-funded academic research

Study Type: Descriptive study or survey

Detailed description:
Much of the survivorship symptom literature has focused on symptoms and supportive care during primary therapy, few studies have looked at breast cancer survivors much further than 2 years after completing primary therapy, and those that have, have contradictory results. Pain, fatigue, and sleep disturbances are most often found. This study will address
the symptoms experienced by early (less than 3 years after completion of primary therapy) and longer term survivors (years 3-5 after completion of primary therapy). We will assess functional status, comorbidities and the experience of symptom burden expressed by the survivors. We will identify and compare the symptoms experienced by early and long-term breast cancer survivors related to the use of adjuvant endocrine therapy.

Study ID: Symptoms in early and long-term survivors of breast cancer who have completed primary therapy

Disease Type: Invasive breast cancer, stages I-III

Mailing Address:

-----------------------------------
First Name: Faith
Last Name: Strunk
Title:  
Company: MDACC
Department: Breast Medical Oncology
Address: 1515 Holcombe Blvd Unit 1354
City: Houston
State: TX
Country: United States
ZIP Code: 77030
Telephone: 713-563-0774
Fax: 713-563-0908
E-mail: fastrunk@mdanderson.org

Billing Address: Same as Mailing Address
Appendix O

The M. D. Anderson Cancer Center Protocol 2012-0909
1.0 Background

Breast cancer is the most common cancer in women in the United States (excluding skin cancer); one in 8 women will develop it during her lifetime (American Cancer Society, 2011). Overall women treated for breast cancer have an 89% survival rate after 5 years and 75% after 15 years. The National Cancer Institute has estimated that there were approximately 2.7 million breast cancer survivors in the United States as of January 2009 (2011). The number of all cancer survivors is projected to grow by 3% per year (Maddams, et al., 2009). The breast cancer population is no exception; due to improvements in cancer care, earlier diagnosis and treatment larger numbers of women are living longer and cancer-free after diagnosis and treatment. Many survivors, once having completed primary therapy (surgery, chemotherapy/biotherapy, and/or radiation) continue to have long-lasting symptoms, single or multiple (Barsevick, 2007; Cleeland, 2007; Janz, et al., 2007; Rosedale & Fu, 2010). The experience of multiple symptoms has been identified as symptom burden (Burkett & Cleeland, 2007; Gapstur, 2007; Gill, Chakraborty & Selby, 2012). Symptom burden is defined as the subjective, quantifiable prevalence, frequency and severity of symptoms and encompasses the patient's perception of the impact of symptoms (Cleeland, 2007; Gapstur, 2007).

The experience of symptoms in survivors has been evaluated, but much of the literature has been focused on symptoms and supportive care during primary therapy (Chung, et al., 2009). Some studies have concentrated on the early survivorship periods; beginning at the end of primary therapy up until 27 months after completing primary therapy (Janz, et al., 2007, Thompson, 2007, Park, Bae, Jung & Kim, 2011. Penttinen, et al., 2010, Brant, et al., 2011, Yi, Swartz and Reyes-Gibby, 2011, Ganz, Kwan, Stanton, Bower and Belin, 2011). These studies have found symptoms related to primary therapy with an impaired quality of life related to these reported symptoms (Janz, et al., 2007, Park, et al., 2011, Bower, 2008, Dahl, Nesvold, Reinertsen, & Fossa, 2011). The symptoms most frequently cited in the aforementioned studies included pain, fatigue or lack of energy, difficulty sleeping, arm pain and lymphedema, breast symptoms, feeling irritable or nervous, menopausal symptoms, weight changes, nausea, depression, and cognitive dysfunction. A number of studies have focused on a specific symptom, such as pain (Mao, et al., 2009, Lundstedt, et al., 2012, Rief, et al., 2011), lymphedema (Armer & Stewart, 2010, Meeske, et al., 2009, Smoott, et al. 2010), fatigue (Bower, et al, 2008, Bower, et al., 2011, Thompson, 2007) or menopausal symptoms (Leining, et al., 2006, Loibl, Lintermans, Dieudonne, & Neven, 2011, Ruddy, et al., 2011). Cancer related fatigue was identified by 21% of both the 1-5 year and 5-10 year survivors (Bower, et al., 2008). Sleep disturbances, fatigue and pain persisted in Hartl et al.'s study of survivors evaluated at an average of 4.2 years (2003).

Several studies have had contradictory findings. Castellon, et al. found that cognitive dysfunction symptomatically abated in the 12-24 months after adjuvant chemotherapy (2004). Jim, et al., (2009) found significant differences between women who had received chemotherapy or radiation compared to healthy matched controls after 6 months. Tannock, Ahles, Ganz and van Dann's 2004 review found durable cognitive effects in 9 to 75% of
patients, although the higher percentages were seen in those evaluated in a closer time frame with chemotherapy. However, in their study of longer term survivors (5 - 15 years), Klein et al. (2011) found an improvement in all symptoms except cognitive functioning and insomnia. The discrepancies among the findings may be related to the variability in primary therapy over time, pre-existing comorbidities or the use of adjuvant endocrine or hormonal therapy.

**Conceptual Framework: Symptom Burden**

The proposed study will address the symptoms experienced by both early survivors (less than 3 years after completion of primary therapy) and longer term survivors (years 3 - 5 after completion of primary therapy). Symptoms may be caused by comorbid illnesses or acute injuries, related to the disease itself or may be caused by treatments, in which case they are called side effects or toxicities (Cleeland, 2007). The framework of Symptom Burden (Cleeland, 2007, Gapstur, 2007) is the conceptual framework chosen for this study. Symptom burden has been described as the subjective counterpart to tumor burden (Cleeland & Reyes-Gibby, 2002) as well as the sum of the severity and impact of symptoms (Cleeland, 2007). It affects multiple patient outcomes, including survival, functional status and quality of life. (Gapstur, 2007). Symptom burden is active, and changes over time, as patients undergo treatment or experience exacerbations or remissions of their disease (Vig & Pearlman, 2003). In this framework, symptoms related to treatment often are viewed as complicating post treatment recovery (Cleeland, 2007, Cleeland & Reyes-Gibby, 2002).

In this study, we will assess functional status, comorbidities and the experience of symptom burden. This study also will explore the association of comorbidities and symptoms expressed by early and long term survivors. The evaluation of concurrent comorbidities is warranted because as comorbidities have been related to symptom severity (Kurtz, et al, 1999). This study will also address the associations between functional status and symptoms related to adjuvant endocrine or hormonal therapy.

Historically, the literature has addressed the symptoms of survivors during their primary therapy or shortly thereafter. But no studies have identified and compared the symptoms experienced by early and long term breast cancer survivors related to the use of adjuvant endocrine or hormonal therapy.

2.0 Objectives

**Primary Objectives**

1. To determine whether symptom burden differs between early survivors (less than 3 years post-primary treatment) and long-term survivors (3 to less than 6 years post-treatment, inclusive).
2. To determine whether symptom burden differs between women who take endocrine or hormonal adjuvant therapy and those who do not.

**Secondary Objectives**
1. To determine, whether the effect of time post-treatment and endocrine or hormonal adjuvant therapy has an additive effect upon symptom burden or whether it has a synergistic or antagonistic effect upon symptom burden.

2. To determine whether symptom interference differs between early survivors and long-term survivors and between those who do and do not take adjuvant endocrine or hormonal therapy, as well as to determine if time post-treatment and use of adjuvant endocrine or hormonal therapy have an additive or interactive effect upon symptom interference.

3. To determine if differences in individual symptom severity and interference exist between early and long-term survivors, with and without the use of adjuvant endocrine or hormonal therapy.

**Exploratory Objective**

To determine whether functional status and comorbidities affect symptom severity and interference.

**3.0 Number of Patients**

We plan to enroll 33 early survivors who have not received adjuvant endocrine or hormonal therapy, 35 early survivors who have received (or are currently receiving) adjuvant endocrine or hormonal therapy, 33 long-term survivors who have not received adjuvant endocrine or hormonal therapy, and 33 long-term survivors who have received (or are currently receiving) adjuvant endocrine or hormonal therapy. Early survivors are those who finished primary treatment less than 3 years prior to the date of survey; long term survivors are those who finished their primary treatment at least 3 years prior to date of survey but less than 6 years prior to the date of survey.

We will stratify the participants by stage so that 1/3 of each group will have had Stage I cancer, 1/3 will have had Stage II cancer and 1/3 will have had Stage III cancer. We expect that approximately 80% of breast cancer patients will have used adjuvant endocrine or hormonal therapy, and that the pool of early-term survivors will be larger than the pool of late-term survivors. Therefore, we will accrue each survivor type until we meet minimum sample size requirements for the group; this means that enrollment in some groups and strata of the study might stop before enrollment in other groups. This may lead to biased results since not all women will be enrolled from the same time cohort, however, this is a pilot study to be used to plan a longitudinal study and therefore these results will be for hypothesis generation when planning a future study.

**4.0 Patient Eligibility**

**Inclusion criteria:**

Study participants must:

1. Be a woman 18 years of age or older.
2. Be a survivor with a diagnosis of invasive breast cancer who has no clinical evidence of disease.
3. Have completed primary therapy (surgery, chemotherapy/biotherapy, and
radiation) less than six years prior to study entry. She may continue to receive adjuvant endocrine or hormonal therapy including tamoxifen, toremifene, anastrazole, exemestane or letrozole.

4. May be non-English speaking.

**Exclusion criteria:**

1. Study participants may not be diagnosed with noninvasive, metastatic, inflammatory, or recurrent breast cancer.
2. Participants may not be receiving chemotherapy or biotherapy at time of enrollment.
3. Lack of approval of each participant’s physician. Physician’s will be approached by the investigator and asked if they feel the participant meets entry criteria prior to the subjects being approached for consideration of enrollment.
4. Pregnant women will be excluded.

**5.0 Instruments**

**MDASI**-The MDASI will be used to measure symptom severity, interference and burden. The MDASI is a 19-item self-report measure of the severity and impact of cancer-related symptoms (Cleeland et al, 2000). Respondents are asked to rate the severity of cancer-related symptoms (13 items) and their interference (6 items) with individual functioning. The global symptom severity and global interference scores measure the patient’s symptom burden. Validity has been tested using principle factor analysis with oblique rotation; reliability established with alphas ranging from 0.82-0.85 for the symptom items and 0.91 for the interference scale (Cleeland et al., 2000). The MDASI is available in multiple languages.

**The Karnofsky Performance Status (KPS)**-The KPS will be used to measure functional status. The KPS is a clinician or investigator completed scale that classifies patients based on their degree of functional impairment on a scale from 0(dead) to 100(normal, no complaints, no evidence of disease). (Schag, Heinrich and Ganz, 1984). It is further subgrouped into three groups: A. Able to carry on normal activity and to work, no special care needed, B. unable to work, able to live at home and care for most personal needs, varying amount of assistance needed and C. Unable to care for self, requires equivalent of institutional or hospital care; disease may be progressing rapidly. The KPS has shown reliability and validity previously with Cronbach’s alpha of 0.97 and construct validity demonstrated with a p<0.001(Mor, Laliberte, Morris & Wiemann, 1984, Schag et al., 1984).
The Charlson Comorbidity Index (CCI) - The CCI will measure comorbidities. The CCI is an investigator completed index that measures 17 clinical conditions that are weighted to assess the effect of the conditions on the patient’s prognosis. Item scores range from 1 to 6 for each item and are based on the relative risk for each. Scores range from 0 to 34, with higher scores signifying greater comorbidity. An adjustment will be made to address all participants beginning with a score of 2, given because they all have cancer. It has established reliability with clinical conditions, including cancer (Hall et al., 2004).

6.0 Data Collection Procedures

Enrollment: The investigator will check with the Nellie B. Connelly Breast center appointment desk for eligible patients based on inclusion criteria. Physicians will be contacted for permission to approach the patient.

Data Collection Procedures:
1. Review Breast Center appointment schedule for survivors less than 3 years after completion of primary therapy and those from 3 - 5 years.
2. Check with primary attending oncologist to ask if it would be permissible to approach the patients to seek their participation in a study on symptom assessment.
3. Once the patient is in a clinic exam room, knock on the door, introduce self as a researcher and ask if this is a good time to speak with the patient.
4. Explain the purpose of the study. The participant will complete a symptom instrument and either the participant or the investigator will complete the demographic history form. The expected time frame for completion is no more than 10-15 minutes. Ask if there any questions.
5. Once all questions have been addressed to the patient’s satisfaction, ask if they would agree to participate in the study.
6. Provide the consent and wait for the signature before proceeding.
7. Provide a copy of the demographic history form to the patient and ask them to complete it or the investigator will complete it.
8. The investigator will determine the functional status of the patient (Karnofsky score); gather information from the medical record to complete the Charlson Co-morbidity Index.
9. Provide a copy of the MDASI to the patient and explain the scoring.
10. If the patient wishes to stop before completing the instrument, thank them for their time and exit the room.
11. Ask the patient if they have any symptoms not listed on the MDASI to list them on the bottom of the MDASI.
12. Note the time the instrument was started and time completed.
13. Before placing the completed instruments in a plain unmarked envelope, review to check for missing data. If any data are missing, the investigator will review with the patient for an error in completing the instrument or a comprehension issue.
14. Each envelope containing completed instruments and consents will be kept in a locked cabinet, entered into Core and assigned a study number. Each patient will
be assigned a study number.
15. If the patient expresses distress, or rates any symptom 7 or higher, the researcher will contact their treating physician. The patient will also be instructed to contact their health care team.

7.0 Evaluation During Study

The primary researcher will track time from primary treatment and receipt of endocrine or hormonal therapy to ensure equitable distribution of participant populations. Descriptive data will be reviewed weekly to assess adequate representation of time since completion of primary therapy. The researcher will track estrogen or progesterone receptor status, as it may not be equitably distributed across different disease stages, in order to maintain a sample representative of each group.

8.0 Data Monitoring Plan

The investigator and dissertation chair will meet weekly to review progress. The primary investigator will review weekly to ensure adequate representation across stages and estrogen receptor status. Other committee members may attend as desired. All portions of the study being conducted, including any missing data, enrollment of subjects, adverse effects, data collection and protection strategies will be reviewed. This study is minimal risk, so study related adverse effects are not expected. Should any adverse effects occur, they will be investigated, logged, and reported to both the MD Anderson Cancer Center's IRB and the University of Texas Health Science Center (CPHS) within 48 hours of occurrence. This study is expected to be completed within one year. Progress of the study, a completed report, adverse event logs, certification of training requirements, HIPPA forms, and publications resulting from this study will be sent to the IRB and CPHS at the completion of the study and during any audits.

9.0 Protocol Monitoring Plan

Security Plan: Paper instruments will be coded and de-identified. The code list will be kept in the PI's office in a locked cabinet and not shared. All completed instruments will be placed in a brown envelope upon completion and stored in a locked file with no identifiers. Once the information is transferred into the computer, the file will be password protected. Once the study is completed, all paper data including the code list will be shredded.

Distress Plan: If the patient expresses distress, or rates any symptom 7 or higher, the researcher will contact their treating physician. The patient will also be instructed to contact their health care team.
10.0 Statistics

Using a 2x2 factorial design, we will have 80% power to detect a one-unit difference in mean symptom burden scores by use of adjuvant endocrine or hormonal therapy, which translates to a standard deviation among means of 0.5. Additionally, we have over 95% power to detect a 2-unit difference between early-term and long-term survivors, which is the same as a 1.0 standard deviation among means, and to detect a 1.12 standard deviation among means for the interaction effect. All testing will be 2-sided using a 5% level of statistical significance. A subject standard deviation of 2.0 was used to calculate power, based upon findings by Cleeland, et. al. (2000). Because we have two primary objectives, we will have a 10% chance of falsely rejecting at least one of our primary hypotheses.

Descriptive statistics will be used to assess the distributional characteristics and demographics of the study sample. Summary statistics and graphs will be used to examine symptom burden, as well as individual symptom severity and interference. Fisher’s exact tests and t-tests will be used to determine whether demographic and clinical baseline data are similar between short- and long-term survivors, as well as between those who had adjuvant endocrine or hormonal therapy and those who did not. Symptom burden and interference will be calculated separately, as recommended by the MDASI User Guide. We will use 2-way ANOVA models to evaluate differences in symptom burden, symptom interference and severity/interference of individual symptoms. Finally, we will add Karnofsky Performance Status and the Charlson Comorbidity Index to our models to evaluate impact of functional status and comorbidities upon symptoms. All models will contain terms for stage of disease to account for stratification on that factor, as well as a term for age to adjust for the effects of age upon symptom severity and interference.

Anticipated Problems and Alternate Strategies

Missing data: A single investigator will be collecting the data. The completed forms will be reviewed when collected. Any missing data will be discussed to ascertain an error in completing the instrument or a comprehension difficulty with an item. Percent of missing items will be calculated and is expected to be less than 1%. The MDASI User's Guide allows for calculation of severity and interference scores when not all items are answered. Its recommendations will be implemented when not all 19 items are answered.

11.0 References

Strunk, Faith


INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Symptoms in Early and Long-term Breast Cancer Survivors Who Have Completed Primary Therapy
2012-0909

Subtitle:

Study Chair: Faith A. Strunk

You are being asked to take part in this psychosocial research study at The University of Texas MD Anderson Cancer Center ("MD Anderson"). This consent form explains why this research study is being done and what your role will be if you choose to take part. This form also describes the possible risks connected with being in this study. After reviewing this information with the person responsible for your enrollment, you should know enough to be able to make an informed decision on whether you want to take part in the study.

You are being asked to take part in this study because you are a woman who has been treated for breast cancer and are receiving follow up care.

DESCRIPTION OF RESEARCH

2. PURPOSE OF STUDY

The goal of this research study is to learn what symptoms breast cancer survivors may be having after completing primary therapy (surgery, chemotherapy or biotherapy, and/or radiation). Researchers also want to learn how taking tamoxifen,
anastrazole, letrozole, or exemestane impacts the activities of daily living, time after primary therapy, and chronic illnesses.

3. DESCRIPTION OF STUDY

If you agree to take part in the study, you will complete a questionnaire about any symptoms you may be having after primary therapy. You will also complete a questionnaire that asks about your background such as age, employment, and any chronic illnesses that you may have.

The questionnaires should take a total of about 20 minutes to complete. If your questionnaires suggest that you are depressed, upset, or distressed, the researcher will let your clinic team know.

Length of Study
Your participation in this study will be over after you complete the second questionnaire.

This is an investigational study. There will be no cost to you for participating in this study.

Up to 135 participants will be enrolled in this study. All will take part at MD Anderson.

4. RISKS, SIDE EFFECTS, AND DISCOMFORTS TO PARTICIPANTS

You should discuss the risks of questionnaires with the study chair. The known risks are listed in this form, but they will vary from person to person. Some questions may make you feel upset or uncomfortable. You may refuse to answer any question. If you have concerns after completing the questionnaires, you are encouraged to contact the study researchers or staff.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen. All study data be stored in password-protected computers and/or locked file cabinets. There will be no personal identifying information connected to your questionnaire answers. The study data will be destroyed 5 years after the study has been published.

Researchers will take appropriate steps to keep your information private. However, there is no guarantee of absolute privacy.

This study may involve unpredictable risks to the participants.

NOT FOR USE IN CONSENTING PATIENTS
5. POTENTIAL BENEFITS

Future patients may benefit from what is learned. There are no benefits for you in this study.

6. ALTERNATE PROCEDURES OR TREATMENTS

You may choose not to take part in this study. You may seek help for any symptoms you may be having outside of this study by seeing your doctor.
Additional Information

7. You may ask the study chair any questions you have about this study. You may contact the study chair, Faith A. Strunk, at 713-563-0774. You may also contact the Chair of MD Anderson’s Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-2933 with any questions that have to do with this study or your rights as a study participant.

8. Your participation in this research study is strictly voluntary. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you withdraw from the study, data collected about you up to the time you withdrew may have to remain in the study database for inclusion in the data analysis. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

9. This study or your participation in it may be changed or stopped at any time by the study chair or the IRB of MD Anderson.

10. You will be informed of any new findings that might affect your willingness to continue taking part in the study.

11. MD Anderson will take appropriate steps to keep your personal health information private. However, there is no guarantee of absolute privacy. Health authorities, and the IRB of MD Anderson might review your record to collect data or to check that the research is being done safely and correctly. In some situations, health authorities could be required to reveal the names of participants.

12. MD Anderson may benefit from your participation and/or what is learned in this study.

STUDY COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson’s IRB at 713-792-2933 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Unless otherwise stated in this consent form, all of the costs linked with this study, which are not covered by other payers (health maintenance organization [HMO], health insurance company, etc.), will be your responsibility.
There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

**Authorization for Use and Disclosure of Protected Health Information:**

A. During the course of this study, the research team at MD Anderson will be collecting information about you that they may share with the parties named in Section E below.

B. If you refuse to provide authorization to disclose your protected health information, you will not be able to participate in this research study.

C. Your protected health information will be protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and it may be re-disclosed at some point.

D. All identifying information such as your name and address will be kept private. This information may be kept at MD Anderson forever. You will be assigned a code number so that your name will not be used. The research team at MD Anderson will be able to link the code number to your name. In some instances, in order to ensure the scientific value of the study, the parties named in Section E below will be able to view your study record but will not be permitted to copy any identifying information contained in your record.

E. The following parties may view your identifying information:

- Officials of the doctoral nursing program at the University of Texas - Houston Health Science Center School of Nursing
- The Office for Human Research Protections (OHRP) (a regulatory agency that oversees research in humans)
- The IRB of MD Anderson
- Officials of MD Anderson
- Study monitors who verify the accuracy of the information
- Individuals who put all the study information together in report form

F. You have the right to see and reproduce your records related to the research study, and ask for corrections, for as long as this information is held by the study chair and/or MD Anderson. However, in some studies, in order to ensure the scientific value of the study, participants are not able to view or reproduce their study records until the research has been completed with all participants in the study.

G. There is no expiration date for the use of your information as stated in this authorization. You may withdraw your authorization to share your protected health information.
information at any time in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP). You may contact the IRB Staff at 713-792-2933 with questions about how to find the NPP. If you withdraw your authorization, you will be removed from the study, and the study chair and staff will no longer use or disclose your protected health information in connection with this study, unless the study chair or staff needs to use or disclose some of your research-related personal health information to preserve the scientific value of the study. The parties listed in Section E above may use any study data that were collected before you canceled your authorization.

H. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
CONSENT/AUTHORIZATION

I understand the study. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

SIGNATURE OF PARTICIPANT  DATE

LEGAL AUTHORIZED REPRESENTATIVE (LAR)
The following signature line should only be filled out when the participant consents to take part in the study but does not have the capacity to legally sign this document on his or her own behalf.

SIGNATURE OF LAR  DATE

WITNESS TO CONSENT
I was present during the explanation of the research to be performed under Protocol 2012-0909.

SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR)  DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

PERSON OBTAINING CONSENT
I have discussed this psychosocial research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

SIGNATURE OF STUDY CHAIR  DATE

OR PERSON AUTHORIZED TO OBTAIN CONSENT
TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into __________________________ and assisted the people obtained and providing consent by translating all questions and responses during the consent process for this participant.

NAME OF TRANSLATOR __________________________ SIGNATURE OF TRANSLATOR __________________________ DATE __________________________

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION __________________________ DATE __________________________

(OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR)
Appendix P

Curriculum Vitae
Faith A. Strunk  
6901 Bertner Avenue, #606, Houston TX 77030  
713-500-2186/713-500-2171 fax  
faith.a.strunk@uth.tmc.edu

**EDUCATION**

PhD student  
University of Texas Health Science Center At Houston  
School of Nursing  
6901 Bertner Avenue  
Houston, TX 77030  
8/2010-present

MSN  
University of North Carolina  
105 Hanes Hall CB 2100  
Chapel Hill, NC 27599-2100  
12/30/1993

BS, Comp Studies: Info Sys Mgmt  
University of Maryland-European Division  
University Blvd at Adelphi Road  
College Park, MD 20742  
1/30/1987

BSN  
Arizona State University  
PO Box 870312  
Tempe, AZ 85287-0312  
5/18/1979

**LICENSURE & CERTIFICATION**

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**PROFESSIONAL EXPERIENCE**

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<td>Various military hospitals</td>
<td>Clinical Staff Nurse</td>
<td>5/1980-6/1989</td>
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McNeese State University, Lake Charles, LA  Adjunct Faculty  8/1994-5/1996
UTMB Correctional Managed Care CT Terrell Unit  Midlevel provider (Family Nurse Practitioner)  8/1999-12/2000
Angleton, TX 77515
UTMB Correctional Managed Care CT Terrell Unit  Family Nurse Practitioner  5/2004-present
1300 FM 655  Rosharon, TX 77583
UTMB Correctional Managed Care CT Terrell Unit  Family Nurse Practitioner  5/2004-present
1300 FM 655  Rosharon, TX 77583
University of Texas M. D. Anderson Cancer Center  Advanced Practice Nurse
Department of Breast Medical Oncology
1515 Holcombe Blvd Unit 1354
Houston, TX 77030

INTERNATIONAL EXPERIENCE

HONORS & AWARDS

Award  Awarding Organization  Date
M. D. Anderson Scholar for the University of Texas School of Nursing Accelerated Doctoral Program  University of Texas M. D. Anderson Cancer Center  8/2010-8/2013

GRANTS

Research Grants

None
Educational Grants

None

Other Funded Projects Including Contracts for Service

None

PUBLICATIONS

Peer Reviewed Publications

None

Non-Peer Reviewed Publications


Books & Chapters

None

Media & Other Creative Products

None

Peer Reviewed Abstracts

None

Other

None

PRESENTATIONS

International

Strunk, F. (10/2008) – Survivorship Issues and Strategies to Meet the Needs of Survivors, Chilean Oncology Nursing Society Annual Conference, Santiago, Chile, speaker, invited

National

None
Regional/State

09/06 – Breast Cancer: Risk Factors, New Treatment Options, and Symptom Management, Nurse Oncology Education Program, Laredo, Texas, speaker, invited

02/07 – Breast Cancer: Risk Factors, New Treatment Options, and Symptom Management, Nurse Oncology Education Program, Harlingen, Texas, speaker, invited

03/07 – Breast Cancer: Risk Factors, New Treatment Options, and Symptom Management, Nurse Oncology Education Program, Beaumont, Texas, speaker, invited

12/08 – Breast Cancer: Risk Factors and Breast Cancer: New Treatment Options and Symptom Management. Women's Health Update, Nurse Oncology Education Program, Austin, TX, speaker, invited

03/09 – Breast Cancer: Risk Factors and Breast Cancer: New Treatment Options and Symptom Management. Women's Health Update, Nurse Oncology Education Program, Bryan, TX, speaker, invited

12/10 -- Breast Cancer... What Do I Do When My Breast Cancer Patient Has This?, Care of the Cancer Patient, Nurse Oncology Education Program, Temple, Texas, speaker, invited

03/11 – Breast Cancer Double Check, SPARC program, Nurse Oncology Education Program, McAllen, Texas, speaker, invited

03/11 -- Breast Cancer, Well Women: Breast and Cervical Health, Nurse Oncology Education Program, Abilene, Texas, speaker, invited

04/11 – Breast Cancer, Well Women: Breast and Cervical Health, Nurse Oncology Education Program, Tyler, Texas, speaker, invited

05/12 – Breast Cancer: Risk Factors, Evaluation, and Treatment Options, Faculty Training Program, Nurse Oncology Education Program, Houston, Texas, speaker, invited

12/12 -- Update on Breast Cancer Treatment 2012, 2012 Texas Department of State Health Services Clinical Conference, Cardea, Austin, TX, speaker, invited

10/13 – The Joining Forces Initiative, Service Learning Opportunities and Nursing Students: An Innovative Program, Joining Forces to Restore Lives: Nursing Education and Research in Veterans Health, Tampa, FL, speaker, invited

Local

05/11 -- Breast Cancer, Faculty Training Program, Nurse Oncology Education Program, Houston, Texas

04/05 – 04/10 -- Breast Cancer; Cancer Care Course: Solid Tumor Day 1, quarterly lecture, Nursing Professional Development & Education, M. D. Anderson Cancer Center; Houston, Texas

05/05 – Breast Cancer, Faculty Training Program, Nurse Oncology Education Program, Houston, Texas

04/06 – Breast Cancer Update, Advanced Practice Nurses General Meeting, M. D. Anderson Cancer Center, Houston, Texas
PROFESSIONAL SERVICE

Consultations
None

Editorial Boards/Panels
None

Professional Service
None

Professional Memberships

Houston Chapter Oncology Nursing Society, member
Oncology Nursing Society, member
Sigma Theta Tau, member
Texas Nurse Practitioners, member

Institutional Service

Institution | Committee | Role | Inclusive Dates
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M. D. Anderson Cancer Center | APN Orientation Committee | Chair-elect | 9/1/2004-8/31/2005
 | | Chairman | 9/1/2005-8/31/2006
M. D. Anderson Cancer Center | APN Leadership Committee | Chair-elect | 9/1/2005-8/31/2006
 | | Chairman | 9/1/2006-8/31/2007
 | | Past-chair | 9/1/2007-8/31/2008
M. D. Anderson Cancer Center | APN Practice/Competency | member | 9/1/2008-8/31/2009
 | | Chair-elect | 9/1/2009-8/31/2010
University of Texas HSC School of Nursing | Joining Forces Committee | member | 2012-2013

Community Service

Organization | Committee | Role | Inclusive Dates
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Sacred Heart Co-Cathedral, Houston, TX various ministries |  | Leader | 9/2005-current
American Diabetes Association Diabetes Walk LaGrange, GA |  | Chairman | 1998

OPTIONAL APPENDICES

Courses Taught
None
List of Project/Thesis/Dissertation Advisees

None

OTHER