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Cancer survivors and survivorship care: Provider expectations, post-treatment health services, and patient reported outcomes

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Erin Elizabeth Hahn

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ABSTRACT OF THE DISSERTATION

Cancer survivors and survivorship care: Provider expectations, post-treatment health services, and patient reported outcomes

by

Erin Elizabeth Hahn

Doctor of Philosophy in Health Services

University of California, Los Angeles, 2013

Professor Patricia A. Ganz, Chair

The population of cancer survivors in the United States is currently estimated to be close to 14 million. Cancer survivors are at risk for a variety of physical and mental health deficits related to their disease and treatments. Most cancer survivors receive excellent care during their active cancer treatment (surgery, radiation, chemotherapy) but can feel lost and overwhelmed when entering the post-treatment phase of care. Research has shown that cancer survivors do not always receive optimal post-treatment care and preventative services.

This dissertation consists of three studies that explore issues in cancer survivorship care: 1) the use of guideline-recommended post-treatment health services in breast cancer survivors; 2) provider expectations and perceptions of breast cancer post-treatment care delivery; and 3) the prevalence of post-traumatic stress symptoms in cancer survivors and associated risk factors. This research used multiple data sources to explore these issues, including health insurance

claims data, medical record abstraction, qualitative interview data, and patient-reported outcomes. Several methodologies were employed to analyze these data, including qualitative data analysis, multi-level modeling, elaboration models, multivariate linear and logistic regression models, and Kaplan-Meier estimates.

This research found that there are persistent gaps in survivorship care delivery. First, breast cancer survivors treated and followed at an academic medical center did not consistently receive guideline-recommended post-treatment care, and patients in this sample commonly received non-recommended care that has not been shown to provide benefit and could potentially be harmful. Second, oncology and primary care providers perceive many barriers to providing high-quality care in the post-treatment care period, most importantly lack of care coordination within oncology and across specialties. Finally, a sub-set of cancer survivors followed in a clinical survivorship program was found to have persistent post-traumatic stress symptoms.

These results demonstrate the importance of organized survivorship care delivery programs that would ensure high-quality patient care for this unique population. Findings suggest that post-treatment care delivery is a complex, multi-level process with many potential targets for improvement in quality of care. These studies demonstrate the pressing need for improving survivorship care coordination in order to deliver guideline concordant care. In addition, the persistent psychological effects of cancer and cancer treatment require continued research into effectively identifying and treating those at risk for ongoing distress. Future research should focus on multi-level interventions targeting system-, provider-, and patient-level factors.

The dissertation of Erin Elizabeth Hahn is approved.

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For Harold

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Chapter 1:

Introduction to the dissertation

This dissertation consists of three studies that explore issues in post-treatment cancer survivorship care. This research addresses the following topics: 1) use of guideline-recommended post-treatment health services in breast cancer survivors; 2) provider expectations and perceptions of breast cancer post-treatment care delivery; and 3) the prevalence of post-traumatic stress symptoms in cancer survivors and associated risk factors. This chapter provides an overview of cancer survivorship and the role of survivorship care within the cancer care trajectory, including the development and use of survivorship care guidelines. It concludes with a statement of the dissertation aims and hypotheses and a brief description of each of the three studies that make up this research.

1.1 Cancer survivorship: a distinct phase of care within the cancer care continuum

Due to improvements in cancer screening, prevention, and treatments, cancer patients are living longer than before. The number of cancer survivors in the United States is estimated to be nearly 14 million.[1] In addition, the aging population in the U.S. will contribute to the ranks of survivors as cancer is predominantly a disease of those 65 years and older.[2] A landmark 2006 report on cancer survivorship from the Institute of Medicine (IOM), *From Cancer Patient to Cancer Survivor: Lost in Transition*, describes the substantial consequences of cancer and gaps in post-treatment care that currently exist for cancer survivors.[3] By clearly illustrating these issues, the report spurred interest in delivering high-quality, appropriate care to this unique patient population. Since this report, there has been investment in developing post-treatment

cancer survivorship clinics and services that target the unique concerns and needs of cancer survivors within both academic and community cancer centers.

Survivorship is a recognized discrete phase of the cancer experience as described by Fitzhugh Mullan, MD in 1986: "An evolution from the phase of extended survival into a period when the activity of the disease or the likelihood of its return is sufficiently small that the cancer can now be considered permanently arrested."(pg. 272)[4] Although there are several definitions of cancer survivors, it is generally accepted that "survivorship" can begin during treatment or immediate after the cessation of active treatment (chemotherapy, radiation, surgery). The definition of cancer survivor from the National Coalition for Cancer Survivorship, which has been adopted by the National Cancer Institute Office of Cancer Survivorship (OCS), includes family and caregivers: "An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and caregivers are also impacted by the survivorship experience and are therefore included in this definition." (http://cancercontrol.cancer.gov/ocs/definitions) The definition used by the IOM is slightly narrower: "The period following first diagnosis and treatment and prior to the development of a recurrence of cancer or death." (pg. 19)[3]

1.2 Long-term and late effects of cancer and cancer treatments

Although cancer survivors are living longer than ever before, the complex, multi-modal treatments they receive may lead to physical and psychosocial long-term and late effects.[5-8]. There is a substantial body of work on the long-term and late effects of breast, colorectal, lung, and prostate cancer as well as gynecologic and hematologic cancers. These studies have shown that cancer survivors are at risk of numerous serious physical sequelae of treatment such as

chronic fatigue, cardiomyopathy, second malignancies, chronic pain, menopausal symptoms, lymphedema, cognitive deficits, sexual dysfunction, and infertility.[9,10,11-28] Cancer survivors have also been found to be at risk for depression, anxiety, post-traumatic stress disorder, and impaired social functioning.[13,29-32] Reviews of cancer-related fatigue, psychosocial issues, and health-related quality of life show that cancer survivors can have significant health deficits related to their cancer experience that persist over time.[26,33-37]

1.3 Survivorship care guidelines

A critical issue in survivorship care is use of appropriate services during the post-treatment care phase. Significant over- and underuse of preventive services and surveillance care for post-treatment cancer patients has been documented.[38-43] Post-treatment surveillance care for cancer survivors is inconsistent, with some recommended services being under-utilized, such as mammograms for detection of breast cancer recurrence or new primary cancer,[43] and some non-recommended services being over-utilized, such as advanced imaging for surveillance of early stage cancer survivors.[44] There are consensus and/or evidence-based guidelines for post-treatment surveillance care of common cancers (breast, colorectal, lung, prostate) from the American Society of Clinical Oncology (ASCO)[45,46] and the National Comprehensive Cancer Network (NCCN)[47] that are designed to help address this problem. The ASCO guidelines for surveillance of early stage breast cancer patients are based on expert panel review of available evidence on breast cancer follow-up care, with the overarching goal of providing patients and providers concise, evidence-based procedures for post-treatment care. These guidelines include recommendations for post-treatment surveillance care, such as annual mammograms, as well as non-recommended surveillance care, such as use of advanced imaging services and biomarker

tests. The ASCO breast cancer surveillance guidelines have been reviewed and updated several times over the past 15 years.[45,48-50]

It is important that cancer survivors receive evidence-based recommended care for screening and prevention. This population has already experienced at least one significant health event and can be at increased risk for developing new health problems.[5,8,51] It is equally important not to expose cancer survivors to unnecessary risks, such as high-intensity imaging tests that have been shown to have little value in prolonging life or providing other benefit to cancer survivors.[52] These unnecessary services can cause significant harms: exposure to radiation from imaging services, such as computed tomography tests,[53] false positive results that can lead to further, more invasive testing, [54] and increased patient anxiety.[54] It is critical to assess adherence to guidelines to determine if cancer survivors are receiving appropriate care.

1.4 Cancer survivorship care

Given the predicted growth in the number of survivors and the potential for serious and persistent health-related issues, an organized, evidence-based system of care is needed. The IOM report noted that "the transition from active treatment to post-treatment care is critical to long-term health. If care is not planned and coordinated, cancer survivors are left without knowledge of their heightened risks and a follow-up plan of action." (pg. 1)[3] Work from the IOM,[3,55,56] the Centers for Disease Control and Prevention (CDC), and the OCS demonstrate the ongoing need for the establishment of best practices and effective interventions for cancer survivors.[57-64] Survivorship care is expected to provide coordination for post-treatment care focusing on cancer surveillance, general health and wellness counseling (such as nutrition, physical activity, alcohol use, and smoking cessation), psychosocial care (depression, anxiety, family needs, employment),

and long-term and late effects monitoring and management. As defined by McCabe, adult survivorship care is a programmed care-delivery approach utilizing the evidence as it evolves.[65]

There are several recommended models of survivorship care delivery, including dedicated survivorship clinics with physician- or nurse-led teams, shared-care models between oncology and primary care, and the use of survivorship care plans to coordinate post-treatment care.[55,66-68] No single model has been identified as the definitive practice for delivering survivorship care. In order to create successful guideline-adherent survivorship programs it is important to include the oncology and primary care provider perspective on care delivery. The identification and exploration of practice norms, provider motivations, and barriers to providing high-quality survivorship care can provide insight into developing effective programs that will deliver appropriate care to these patients.

In addition to addressing physical health care needs of cancer survivors, their psychosocial needs are an important component of survivorship care. As noted in the IOM report, many patients who are transitioning to the post-treatment phase of survivorship feel unexpectedly vulnerable.[3] In this new phase of care, survivors are faced with new fears and anxieties, such as fear of recurrence and anxiety about the future, and some may face persistent or exacerbated depressive symptoms.[3] Some survivors may experience feelings of grief about what has happened to them and may have trouble adjusting to physical compromises or other changes in health status. The identification and treatment of psychosocial issues in cancer patients and survivors is sub-optimal.[56] Efficiently identifying and addressing psychosocial distress early in the survivorship phase is an essential element of high-quality survivorship care.

1.5 Dissertation Aims

This dissertation explores the following questions relevant to cancer survivorship care: 1) What proportion of breast cancer survivors treated and followed at an academic medical center are receiving guideline-recommended post-treatment care services? 2) What are provider expectations and perceptions of post-treatment breast cancer care delivered within academic health care settings? 3) What proportion of cancer survivors report post-traumatic stress symptoms related to their cancer, and what factors are associated with reporting post-traumatic stress? Multiple data sets were used to address these questions, including qualitative interview data, administrative claims data, medical record review, and patient-reported survey data. The following section provides a brief overview of the purpose of each study in the dissertation.

1.5.1 Overview: Use of post-treatment health services in breast cancer survivors (Study 1)

The purpose of this study was to estimate the proportion of post-treatment breast cancer survivors receiving ASCO guideline recommended and non-recommended surveillance services in a sample of breast cancer patients treated and followed at an academic medical center. This study used a combination of administrative data from health insurance claims and medical record abstraction. Claims data provided information on service utilization, such as service type and date of service. Imaging services were categorized into surveillance or diagnostic use based on detailed medical record abstraction.

1.5.2 Overview: Provider perceptions and expectations of post-treatment care delivery (Study 2)

The second study explored oncology and primary care provider perceptions and expectations of post-treatment survivorship care for breast cancer patients. This was an exploratory study with no stated a priori hypotheses. The study used qualitative interview data

collected from providers at five different academic medical centers. A qualitative method was chosen to allow providers to describe in their own words their current practices, expectations, and perceptions of survivorship care delivery, with the goal of better understanding provider behavior during the post-treatment phase of the cancer care trajectory.

1.5.3 Overview: The prevalence of post-traumatic stress symptoms and associated risk factors in cancer survivors treated at an academic medical center (Study 3)

The third study determined the prevalence of post-traumatic stress symptoms in a heterogeneous sample of cancer survivors who received a consultation from a survivorship care program at a comprehensive cancer center. It was hypothesized that both demographic (gender, age) and psychosocial status (depression, perceived social support) would be associated with post-traumatic stress in this sample. The study used patient reported survey data from the Cancer Survivor Registry, which was developed by investigators at the UCLA-LIVESTRONG™ Survivorship Center of Excellence as a resource to advance knowledge about the long-term and late effects of cancer treatment. The study included an exploration of the Impact of Cancer scale as a correlate of post-traumatic stress symptoms to determine which survivorship issues may be influencing persistent symptoms.

1.6 Contributions of research

This dissertation contributes to the growing field of cancer survivorship in several ways. First, this research focuses on use of guideline-recommended post-treatment health services and includes a determination of reason for the service (surveillance versus diagnostic). This provides needed information on the actual prevalence of surveillance services in this population. Few previous studies of guideline adherence have examined medical records to evaluate the reasons

for the use of non-recommended services and whether they are needed. Secondly, this research explores the provider perspective on the challenges of post-treatment care delivery. Work from several federal agencies has called for the development and implementation of clinical survivorship programs.[61,63,64] Understanding the provider perspective is crucial in order to create successful survivorship programs that providers would feel comfortable integrating into everyday clinical practice. Finally, this research includes a study of post-traumatic stress symptoms in cancer survivors. Early identification and treatment of psychosocial issues in cancer patients and survivors is a priority area identified by the IOM.[56] Results of these three studies can directly inform the development of cancer survivorship programs and provides new information on this unique patient population.

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CHAPTER 2:

Use of imaging and biomarker tests for post-treatment care of early stage breast cancer survivors (Study 1)

2.1 Abstract

Background: The American Society of Clinical Oncology (ASCO) recently released a "Top Five" list of opportunities to improve the quality of cancer care. Item four on the list advises against using advanced imaging and biomarkers for surveillance in breast cancer patients treated with curative intent. We examined concordance with ASCO follow-up care guidelines for breast cancer survivors treated at an academic medical center.

Methods: Claims data and medical records were reviewed and abstracted for early stage breast cancer survivors starting one year post diagnosis. A trained abstractor classified imaging tests as diagnostic or surveillance. Proportions and frequencies were generated for receipt of services. Multilevel logistic regression was used to estimate factors associated with receiving recommended and non-recommended services and biomarker tests.

Results: Records were available for 258 patients. Mean age at diagnosis was 58 (SD 13), mean time since diagnosis was 6 years (SD 2), 71% were stage 0/1. Only 47% of the sample received a mammogram within one year of diagnosis. Fifty-five percent of the sample received at least one non-recommended imaging service for surveillance purposes. Eighty percent of the sample received at least one non-recommended biomarker test. Regression results indicate that main

treating physician, advanced disease stage, younger age at diagnosis, and greater number of years since diagnosis were associated with receiving non-recommended services for surveillance.

Conclusions: Use of non-recommended services for surveillance occurs frequently among early stage survivors. There are opportunities to increase use of guideline concordant post-treatment care for breast cancer survivors.

2.2 Introduction

There are approximately 3 million breast cancer survivors in the United States.[1] Mortality from breast cancer continues to decline due to improvements in screening and treatment, and the majority of breast cancer patients are diagnosed with early stage disease and can expect to have extended disease-free survival.[2] Having survived their disease, most patients enter into a prolonged post-treatment phase of care, where the value of active surveillance testing for cancer recurrence has a limited evidence base. Several studies, including a Cochrane systematic review, have found little utility for high intensity breast cancer surveillance programs.[3-7] Evidence-based guidelines for post-treatment surveillance care of breast cancer patients from the American Society of Clinical Oncology (ASCO)[5,12,13,14] include explicit recommendations for post-treatment care as well as non-recommended surveillance services, such as use of advanced imaging services and biomarker tests.[5] In addition, ASCO recently released a "Top Five" list as part of the Choosing Wisely® campaign, an initiative of the American Board of Internal Medicine.[15] This campaign aims to promote clinical care that is well supported by evidence, has beneficial effects on patient health by improving treatment and/or reducing risks, and, where possible, reduces costs of care.[16] The ASCO Top Five list advises against routine recurrence surveillance testing in early stage breast cancer survivors who have completed curative treatment, and discourages use of advanced imaging tests (positron emission tomography (PET), computerized tomography (CT) and radionuclide bone scans) and biomarker tests (carcinoembryonic antigen (CEA), cancer antigen (CA) 15-3, CA 27.29, CA 125).[15] Despite these guidelines, the literature reflects a reliance on biomarker tests and advanced imaging for surveillance of breast cancer survivors, with increasing use of imaging services over time.[8-11,17]

The purpose of this study was to estimate the proportion of post-treatment breast cancer survivors receiving ASCO recommended and non-recommended surveillance services in a sample of patients treated and followed at an academic medical center. We sought to determine how frequently post-treatment breast cancer patients received biomarker tests and imaging studies, and whether the latter were ordered for diagnostic or surveillance purposes. We also identified whether or not patients received mammographic surveillance as recommended by ASCO guidelines, since other studies have indicated poor adherence to this recommendation.

2.3 Methods

2.3.1 Identification of sample

Breast cancer survivors were identified within an academic medical center using an administrative data algorithm based on Current Procedural Terminology (CPT) and International Classification of Diseases (ICD) codes (Appendix 2.1). The algorithm was applied to administrative claims data for the interval between 2001 and 2009. This time interval was chosen to allow for sufficient follow-up time after diagnosis and treatment for examination of post-treatment surveillance care. This study received Institutional Review Board approval for all activities (UCLA IRB# 10-000279).

2.3.2 Eligibility

All patients met the following eligibility criteria: female non-metastatic (stage 0-IIIA) breast cancer diagnosed between January 1, 2001 and June 30, 2009; 21 years of age and older at the time of diagnosis; no evidence of cancer recurrence or new primary cancer (any type) within the surveillance time frame, and no evidence of previous cancers; and at least two years of administrative and medical records in order to assess use of post-treatment services.

2.3.3 Data sources

We obtained data from administrative claims and medical record abstraction. Variables obtained from administrative data included insurance type, date of birth, breast cancer diagnosis date, and imaging service and biomarker test occurrences by date of test. Variables obtained from medical record data included stage of disease, treatments received, and main treating physician, either a medical oncologist or breast surgeon. A research assistant was trained to perform the medical record abstractions. The training and abstractions were overseen by the study principal investigator and a research nurse practitioner. We captured imaging service and biomarker test data for this protocol starting one year after the date of diagnosis to avoid capturing services performed as part of the diagnostic workup or possibly related to treatment complications during active treatment. There was an average of 5 years of surveillance data available per patient (range 2-10 years).

2.3.4 Variables

The dependent variables were receipt of services: mammograms, imaging (chest and abdominal CT, chest and abdominal MRI, abdominal ultrasound, chest x-ray, radionuclide bone scan, PET scan), and biomarker tests (CEA, CA 27.29, CA 125, CA 15-3). Independent variables were age at diagnosis, time since diagnosis (years from date of diagnosis to November 1, 2011), cancer stage (stage 0/1 or stage 2/3A), treatment type (mastectomy/lumpectomy, chemotherapy, radiation), insurance type (health maintenance organization (HMO), preferred provider organization (PPO), Medicare fee-for-service), and main treating physician (assigned a unique identification number). Twenty-two main treating physicians were identified. For patients treated with surgery only, the breast surgeon was considered the main treating physician. For all other patients, the medical oncologist with the majority of patient visits was considered the main

treating physician. The medical oncologist was classified as the main treating physician for 90% of the sample. Insurance type was assigned based on the insurer covering the majority of services and visits during the surveillance timeframe, based on the charges billed to the patient's insurance company. Patients enrolled in Medicare Advantage plans were categorized with the HMO group.

2.3.5 Diagnostic versus surveillance status determination for imaging tests

We coded diagnostic versus surveillance use of post-treatment imaging services by medical record abstraction and review. We reviewed the entire medical record available from the academic medical center. Based on the strategy developed by Cooper et al,[18] the abstractor categorized imaging services into three categories: 1) surveillance in absence of signs or symptoms suggestive of recurrence; 2) diagnostic with signs or symptoms suggestive of recurrence, metastatic disease, or other disease or problem; or 3) indeterminate with no associated physician note. Categorization was based on the physician note associated with the service and the associated ICD codes used for health insurance billing. Physician notes that contained an active statement describing routine follow-up care with an imaging service were categorized as surveillance. The lack of a definitive statement of a new symptom or problem was also considered reason to categorize an imaging service as surveillance. However, it is possible that some of the imaging services classified as surveillance were, in fact, ordered for a diagnostic reason that was not recorded in the medical record or reflected in the associated ICD code. This categorization strategy may have resulted in overestimation of surveillance imaging services. Services with associated notes describing a new symptom or problem were categorized as diagnostic. The 4% of services initially categorized as indeterminate due to missing physician notes were reviewed during group meetings that included the research assistant, research nurse

practitioner, and the principal investigator. After discussion and review, consensus was reached on categorization of diagnostic or surveillance for the services initially categorized as indeterminate. The majority of indeterminate services were categorized as surveillance based on an associated ICD code indicating breast cancer (e.g., 174.xx). Our categorization approach was conservative: imaging services initially classified as diagnostic remained so throughout the surveillance timeframe, even though the subsequent follow-up could have been surveillance. A random sample of 15% of the records was also abstracted by the research nurse practitioner as a second coder comparison. A kappa statistic comparing the classification of surveillance versus diagnostic was calculated to measure agreement between the two sets of abstractions, yielding a k=0.72 ("substantial" agreement).[19]

2.3.6 Data Analysis

All analyses were performed using Stata (version 12.0) software. Means, ranges, and percentages were generated to summarize patient demographics and cancer disease and treatment characteristics. Proportions and frequencies were generated for receipt of ASCO guideline recommended and non-recommended services. Time to receipt of first mammogram for eligible patients was estimated using Kaplan-Meier estimates. Use of surveillance versus diagnostic imaging services was examined with proportions. Multilevel logistic regression with a random effect for main treating physician was used to estimate the unique association of independent variables with receiving recommended and non-recommended imaging services and biomarker tests. A multilevel model was used in order to account for the clustering of patients within the main treating physician variable.

2.4 Results

2.4.1 Study Sample

The study sample included 258 survivors after excluding 126 (Appendix 2.2). The most common reason for exclusion was less than two years of surveillance time at the academic medical center. Many patients were initially treated at the center, but then switched their care to a provider outside the academic health system. The mean age of the sample was 58 years (standard deviation (SD) 13) and the mean time since diagnosis was 6 years (SD 2) (Table 2.1). The majority had stage 0/1 disease and was treated with lumpectomy and radiation. Fifty-nine percent were enrolled in a HMO insurance plan. Three physicians were identified as the main treating physician for more than half of the sample.

2.4.2 Use of imaging and biomarker tests

Overall, 83% of the sample received at least one mammogram during the post-treatment period of observation. The length of time to the first mammogram for all eligible patients after cessation of active treatment (assumed to be 12 months after the date of diagnosis) is shown in Figure 2.1. Those with bilateral mastectomy were excluded (n=19). Forty-seven percent of the sample received the first mammogram within a year of cessation of active treatment, and 67% of the sample received the first mammogram within two years. Of the 120 patients who had a first mammogram within one year of cessation of active treatment, 56 (47%) had a second mammogram within the next year (Table 2.2). We explored whether insurance status influenced the percentage receiving a follow-up mammogram within the first year post-treatment: 52% of HMO-insured patients received a mammogram within the first year versus 40% of those with PPO or Medicare insurance (p=0.05, data not shown).

Sixty-seven percent of the sample received at least one non-recommended imaging service. The most common non-recommended imaging service was chest x-ray, with 45% of the sample receiving at least one (Table 2.3). Thirty percent of the sample received at least one breast MRI, and 20% received at least one chest CT. Eighty percent of the sample received at least one non-recommended biomarker test. Seventy-seven percent of the sample received at least one CEA test, and 77% of the sample received at least one CA 27.29. The majority of CEA and CA 27.29 tests were performed within the first two years after cessation of active treatment (Figure 2.2). Sixteen percent of all CEA and CA 27.29 tests were performed 5 or more years after active treatment ended. CA-125 and CA 15-3 tests were used less commonly, with 18% and 5% receiving at least one of each test, respectively.

2.4.3 Surveillance versus diagnostic use of imaging services

Fifty-five percent of the sample received at least one non-recommended imaging service that was classified as surveillance. Four imaging services were classified as surveillance the majority of the time: 79 abdominal CTs (61%), 128 breast MRIs (82%), 79 chest CTs (57%), and 72 PET scans (93%) (Table 2.3). Only 28% of chest x-rays, the most commonly used imaging service, were classified as surveillance. The majority of abdominal MRI, abdominal ultrasound, and bone scans were classified as diagnostic. Out of all non-recommended imaging services captured, 48% (514 out of 1082) were classified as surveillance.

2.4.4 Variables associated with receiving imaging services and biomarker tests

Stage of disease, age at diagnosis, and years since diagnosis were significantly associated with receiving a non-recommended imaging service that was classified as surveillance (Table 2.4). The odds of receiving a non-recommended imaging service classified as surveillance were 2.70 times higher for those who had stage 2 or stage 3A disease than for those who had stage 0

or stage 1 disease (p=0.01). Younger age at diagnosis was associated with higher odds of receiving a non-recommended imaging service classified as surveillance, with a one-year increase in age at diagnosis associated with a 3% decrease in the odds of receiving a non-recommended imaging service classified as surveillance (OR=0.97, p=0.05). A one-year increase in years since diagnosis was associated with a 23% increase in the odds of receiving a non-recommended imaging service classified as surveillance (OR=1.23, p=0.02). Main treating physician was also important in explaining variation in receipt of non-recommended imaging services. The intraclass correlation (rho) for main treating physician was 0.19 and significantly different than zero, meaning that 19% of the variance in receiving a non-recommended imaging service classified as surveillance was accounted for by the main treating physician.

Radiation, age at diagnosis, and insurance type were all significantly associated with receiving a mammogram. The odds of receiving a mammogram were 1.98 times higher for those who received radiation than for those who did not (p=0.08), and the odds of receiving a mammogram for those with Medicare fee-for-service insurance were 8.99 times higher than those with HMO insurance (p<0.001). A one-year increase in age at diagnosis resulted in a 6% decrease in the odds of receiving a mammogram (OR=0.94, p=0.001). Main treating physician was also important in explaining variation in receipt of mammograms. The intraclass correlation was 0.22 and significantly different than zero, meaning that 22% of the variance in receiving a mammogram was accounted for by the main treating physician.

Stage and years since diagnosis were significantly associated with receiving non-recommended biomarker tests (CEA, CA 15-3, CA 27.29, and CA 125). The odds of receiving a non-recommended biomarker test for those with stage 2 or stage 3A disease were 4.24 times higher than those with stage 0 or stage 1 disease, (p=0.04), and a one-year increase in years since

diagnosis was associated with a 42% increase in the odds of receiving a non-recommended biomarker test (p=0.006). Main treating physician was also important in explaining variation in receipt of non-recommended biomarker tests. The intraclass correlation for main treating physician was 0.56 and significantly different than zero, meaning that 56% of the variance in receiving a non-recommended biomarker test was accounted for by the main treating physician.

2.5 Discussion

We examined use of ASCO recommended and non-recommended post-treatment services in a group of breast cancer survivors treated and followed at an academic medical center. Only 47% of the sample received a recommended mammogram in the first year after cessation of active treatment, which falls well short of the ASCO recommendation of one mammogram one year after the initial diagnostic mammogram. However, some patients may have received mammograms outside of the academic medical center, leading to an overestimation of the length of time to the first mammogram. HMO-insured patients in the sample had a slightly higher percentage of mammograms by the end of the first year than PPO and Medicare insured patients (data not shown), although both groups are well below the ASCO recommendation. However, our overall mammogram findings are similar to other studies. A study using the Surveillance, Epidemiology, and End Results registry linked to Medicare claims to examine use of annual mammograms in a cohort of breast cancer survivors found that only 62% received annual mammograms.[20] Other studies have reported rates of annual mammograms for breast cancer survivors from 50%-80%.[11,21-23] We also found that non-recommended imaging services were used frequently, particularly chest x-ray, with almost half of the sample receiving at least one. Non-recommended biomarker tests were also commonly used, particularly CEA and CA 27.29.

Importantly, we were able to categorize the non-recommended imaging services as surveillance or diagnostic using medical record abstraction. The majority of published studies examining adherence to breast cancer surveillance guidelines used administrative data only.[9,11,24] A 2006 study characterized post-treatment care in cancer survivors as surveillance or diagnostic using medical record abstraction.[18] The results showed that 49% of imaging services for breast cancer survivors were used for surveillance only. In our study, 48% of all imaging services were classified as surveillance. PET scans were almost uniformly classified as surveillance (93%), and breast MRIs (82%) and abdominal CTs (61%) were classified as surveillance the majority of the time. These services were routinely ordered with 55% of the sample receiving at least one non-recommended imaging test classified as surveillance, despite the evidence showing little to no benefit of aggressive post-treatment surveillance programs.[4,5,7] However, this may be an overestimation of services ordered for surveillance. Our classification scheme assigned imaging services that lacked a definitive statement of a new symptom or problem as surveillance, potentially miss-classifying services that were in fact diagnostic. Most imaging services did have an associated note that contained an active statement of surveillance or diagnosis of a new symptom or problem, but some associated notes were vague, leading to uncertainty regarding classification.

The variables associated with receipt of a non-recommended imaging service for surveillance purposes show that ordering these services is influenced by a diverse set of factors (Table 2.4). For patients with higher stage disease and younger age at diagnosis, physicians and patients may elect a more aggressive surveillance approach with the hope of identifying recurrent or new disease early, although available evidence does not support this approach. The main treating physician was significant in each of the three models, accounting for 19%, 22%, and

56% of the variance in receiving a non-recommended imaging service for surveillance, receiving a mammogram, and receiving a non-recommended biomarker test, respectively. This finding suggests that appropriate feedback to individual physicians about their utilization patterns could influence subsequent adherence to guidelines. Patient demand for services may also play a role in these findings.

This study has several limitations. First, this is a relatively small sample of patients treated and followed at a single academic center. This allowed us to do detailed medical record abstractions, providing important data on use of post-treatment services. However, this limits the generalizability of our findings. Other types of institutions may have very different practices and customs for post-treatment follow-up care, although several larger studies have found poor adherence to post-treatment guidelines for cancer patients generally.[8,11,18,25] Second, imaging services initially classified as diagnostic remained so throughout the surveillance timeframe, a conservative approach that potentially underestimates the number of surveillance services. Even using this conservative approach we found a high percentage of imaging services were used for surveillance purposes. Third, we used data solely from one academic medical center and did not seek outside records. Patients may have received care elsewhere, which could have led to underestimation of appropriate and inappropriate services. Our examination of the sample by insurance group shows that even HMO-insured patients who can be expected to receive all of their care within the academic medical center did not all receive mammograms within the first year after diagnosis, suggesting that underuse of recommended services is a systematic problem. Finally, we had limited patient-level variables. Potentially important demographic variables and patient awareness/desire for post-treatment care were not available from our data sources.

In conclusion, our findings show a high rate of non-recommended testing and underuse of mammographic screening in early-stage breast cancer survivors treated and followed at an academic medical center. These patterns were observed in a setting where individual physicians do not have a financial incentive for ordering tests and services, and should have access to evidence-based guidelines to direct follow-up care. This suggests that the ordering of non-recommended services is a complex process driven by multiple factors, only some of which were captured in this study. Overuse of post-treatment services is a persistent problem with potentially serious impacts: false positive results that may lead to use of unnecessary invasive procedures, financial costs, and heightened patient anxiety. As the population of breast cancer survivors continues to grow, it will be of even greater importance to base post-treatment care decisions on available evidence and guidelines.

Chapter 2 Figures and Tables

Table 2.1: Patient demographics and cancer disease and treatment characteristics, N=258

Characteristic	Number	%
Age at diagnosis, years		
Mean	58	
Standard deviation	13	
Range	[28, 95]	
Years from diagnosis date to November 1, 2011		
Mean	6	
Standard deviation	2	
Range	[2, 10]	
Disease stage		
Stage 0 or 1	182	71
Stage 2 or 3A	76	30
Lumpectomy		
Yes	187	72
No	71	28
Mastectomy		
Yes	71	28
No	187	72
Chemotherapy		
Yes	104	40
No	154	60
Radiation		
Yes	188	73
No	70	27
Insurance type		
HMO	151	59
PPO	37	14
Medicare	70	27
Main treating physician		
Provider 1	24	9
Provider 2	67	26
Provider 4	39	15
Provider 5	25	10
Provider 6	6	2
Provider 7	34	13
Provider 8	7	3
Provider 9	9	4
Provider 10	5	2
Provider 11	5	2
Provider 13	17	7
Other*	20	8

*Other includes providers with less than 3 patients

Table 2.2: Number of mammograms received by years after cessation of active treatment

Time Interval: Years after treatment cessation	**Patients in interval**	**Patients that received a mammogram** (% of total sample in interval)
1	258	120 (47%)
2	243	115 (47%)
3	217	127 (59%)
4	174	105 (60%)
5	121	55 (46%)

Table 2.3: Use of non-recommended imaging services and biomarker tests starting one year post-diagnosis including percent of imaging services used for surveillance
N=258

Imaging service or biomarker test	Percent of sample that received at least one (number)	Total service count	Percent surveillance out of total service count (number)
Abdominal CT	19% (48)	129	61% (79)
Abdominal MRI	4% (11)	21	39% (8)
Abdominal ultrasound	15% (37)	53	13% (7)
Bone scan	17% (44)	64	26% (17)
Breast MRI	30% (77)	156	82% (128)
Chest CT	20% (52)	139	57% (79)
Chest x-ray	45% (114)	443	28% (124)
PET scan	12% (31)	77	93% (72)
CA 15-3	5% (14)	30	-
CA 125	18% (46)	91	-
CA 27.29	77% (199)	1661	-
CEA	77% (198)	1518	-

Abbreviations:
CT: Computed tomography
MRI: Magnetic resonance imaging
PET: Positron emission tomography
CA: Cancer antigen
CEA: Carcinoembryonic antigen

Table 2.4: Multilevel logistic regression with random effects for the main treating physician: Model 1) received any non-recommended imaging service determined to be for surveillance purposes (computed tomography scan, magnetic resonance imaging, ultrasound, bone scan, positron emission tomography scan); Model 2) received any post-treatment mammogram; and Model 3) received any non-recommended biomarker test: carcinoembryonic antigen (CEA), cancer antigen (CA) 15-3, CA 27.29, and CA 125 tests. The group variable is the main treating physician.
N=258

Model 1: Received any non-recommended imaging service for surveillance				
Variable	**Odds ratio**	**Standard error**	**p-value**	**95% confidence interval**
Mastectomy	1.97	0.89	0.13	[0.81, 4.76]
Radiation	1.77	0.76	0.19	[0.76, 4.12]
Chemotherapy	1.34	0.34	0.24	[0.82, 2.18]
Stage 2/3A	2.70	1.04	0.01	[1.27, 5.74]
Age at diagnosis	0.97	0.02	0.05	[0.93, 0.99]
PPO insurance	0.55	0.28	0.23	[0.20, 1.48]
Medicare	0.79	0.37	0.61	[0.31, 1.97]
Years since diagnosis	1.23	0.11	0.02	[1.03, 1.46]
Sigma_u	0.89	0.29		[0.47, 1.68]
Intraclass correlation (rho)*	0.19	0.10		[0.06, 0.46]
Likelihood ratio test: rho=0	chibar2(01)=17.33 Prob >=chibar2 = 0.000			
Model 2: Received any post-treatment mammogram				
Variable	**Odds ratio**	**Standard error**	**p-value**	**95% confidence interval**
Mastectomy	0.88	0.36	0.76	[0.39, 1.97]
Radiation	1.98	0.78	0.08	[0.92, 4.30]
Chemotherapy	0.93	0.22	0.77	[0.59, 1.48]
Stage 2/3A	1.17	0.46	0.69	[0.54, 2.52]
Age at diagnosis	0.94	0.02	0.001	[0.91,0.98]
PPO insurance	1.21	0.59	0.70	[0.46,3.16]
Medicare	8.99	4.82	0.000	[3.14, 25.72]
Years since diagnosis	1.06	0.09	0.51	[0.89, 1.26]
Sigma_u	0.97	0.36		[0.47, 2.01]
Intraclass correlation (rho)*	0.22	0.13		[0.06, 0.56]
Likelihood ratio test: rho=0	chibar2(01)=10.18 Prob >=chibar2 = 0.001			
Model 3: Received any non-recommended biomarker test				
Variable	**Odds ratio**	**Standard error**	**p-value**	**95% confidence interval**
Mastectomy	1.27	0.79	0.70	[0.38, 4.28]
Radiation	0.94	0.54	0.91	[0.30, 2.93]
Chemotherapy	1.59	0.50	0.14	[0.86, 2.93]
Stage 2/3A	4.24	2.93	0.04	[1.10, 16.43]
Age at diagnosis	1.02	0.03	0.43	[0.97, 1.07]
PPO insurance	1.17	0.78	0.82	[0.31, 4.35]
Medicare	0.99	0.67	0.99	[0.26, 3.75]
Years since diagnosis	1.42	0.18	0.006	[1.11, 1.83]
Sigma_u	2.04	0.59		[1.16, 3.59]
Intraclass correlation (rho)*	0.56	0.14		[0.29, 0.80]
Likelihood ratio test: rho=0	chibar2(01)=33.11 Prob >=chibar2 = 0.000			

Reference groups: Lumpectomy, HMO insurance, stage 0/1 disease
*The intraclass correlation (rho) is the amount of variance in the outcome accounted for by the group variable (main treating physician)

Figure 2.1: Kaplan-Meier estimate of time to first mammogram for eligible patients N=239

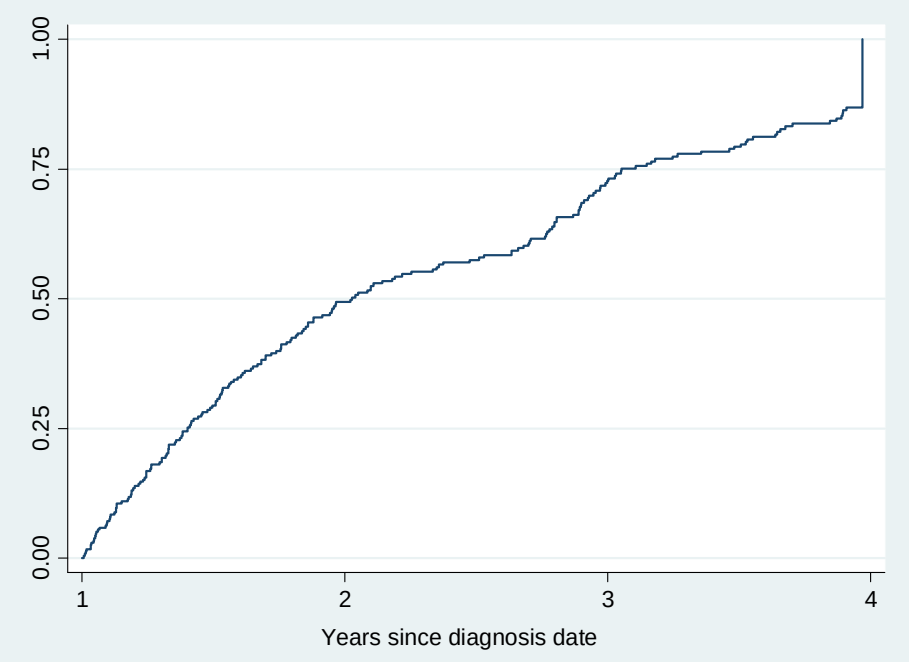
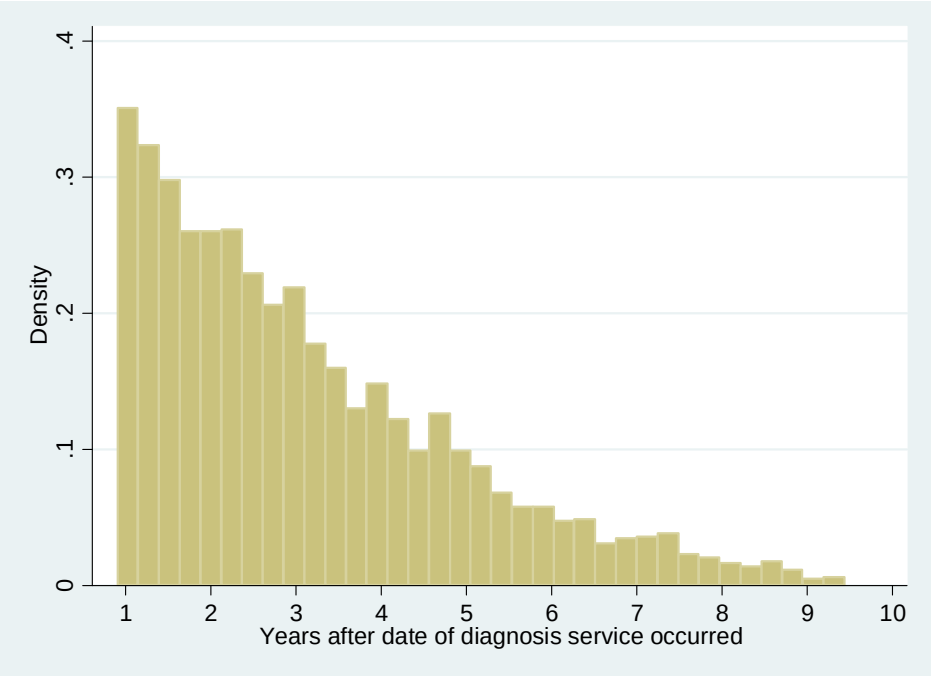


Figure 2.2: Number of years since diagnosis date that carcinoembryonic antigen (CEA) and cancer antigen (CA) 27.29 tests occurred
N=258



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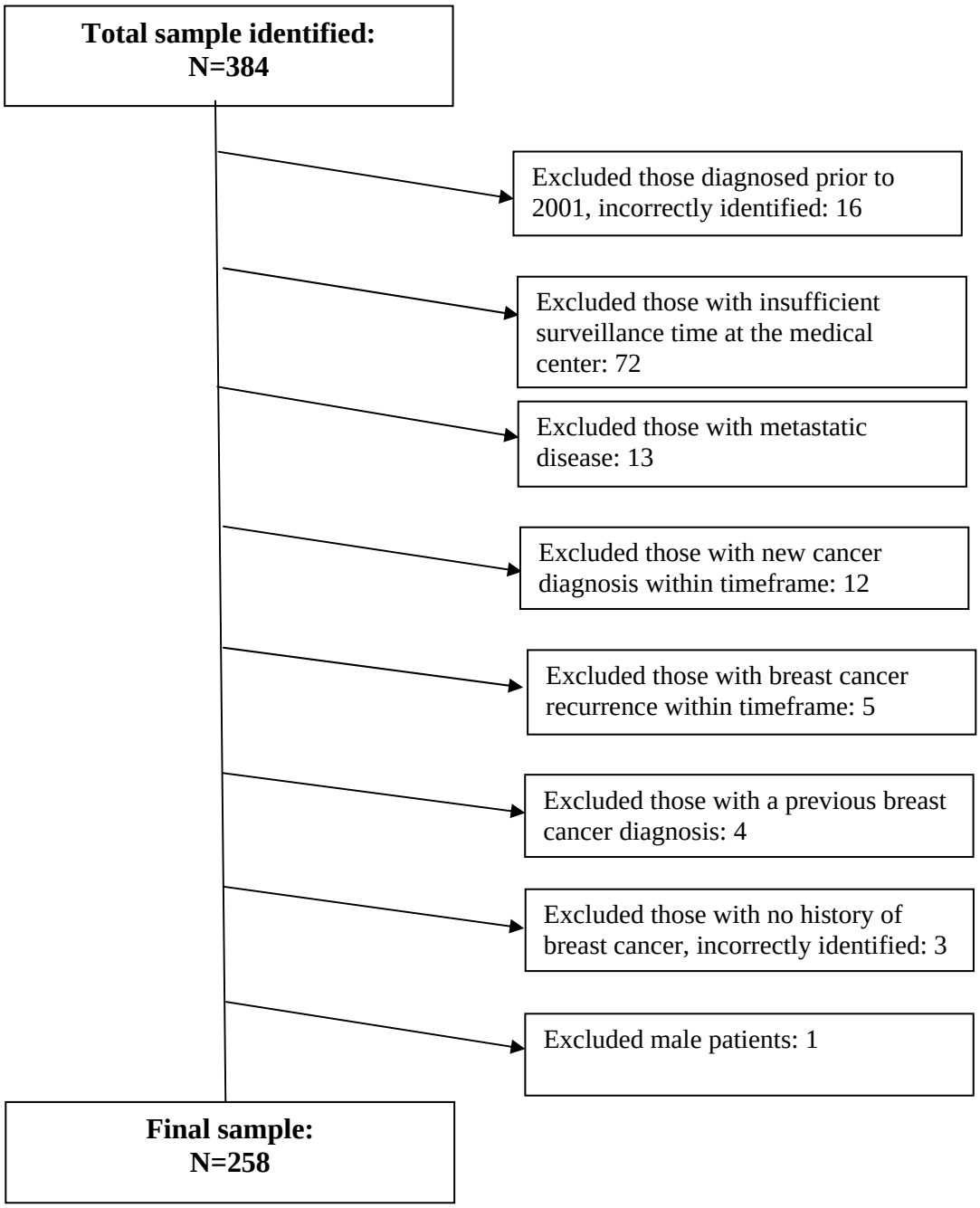
Appendix 2.1

Current procedural terminology (CPT) and International Classification of Disease (ICD) codes to be used in identifying surveillance testing based on American Society of Clinical Oncology (ASCO) breast surveillance guidelines

	Test	CPT Code	ICD-9 Code
Recommended	Mammogram, film	76090-76092	V76.11 V76.12 (screening) 87.37
	Mammogram, digital	G0202 G0204 G0206	V76.11 V76.12 (screening) 87.37
Non-Recommended Services	Bone scan	78300-78320 78399	92.14 (radioisotope bone scan)
	Liver/abdominal ultrasound	76700, 76705	88.76 (diagnostic ultrasound)
	Chest x-ray	71010-71035	87.44 (routine) 87.49 (other)
	Chest CT	71250, 71260 71270, 71275 (CT thorax w/ and w/o contrast)	87.41 (CT thorax) 87.42 (other tomography thorax)
	Abdominal CT	74150-74175 (CT of abdomen w/ and w/out contrast)	88.01 (CT abdomen)
	Chest MRI	71550, 71551 (MRI chest w and w/out contrast) 71552, 71555 (MRA chest w/ and w/out contrast)	88.92 (MRI, chest and myocardium)
	Abdominal MRI	74181-74185 (MRI /MRA abdomen w/ and w/out contrast)	88.97 (MRI other)
	FDG-PET scan	78811-78816	
	Breast MRI	77058 (unilateral) 77059 (bilateral) HCPCS C8903-08	174.0 - 175.9 (malig) V10.3 (pers hx breast) 233.0 (carc in situ) V76.10 (spec screen) V76.19 (other screen)
	Biomarkers: CEA CA-125 CA 15-3 CA 27.29	 82378 (carcinoembryonic antigen), 86149, 86151 86316 86300 86300	

Appendix 2.2: Exclusion cascade



CHAPTER 3:
Provider perceptions and expectations of breast cancer post-treatment care (Study 2)

3.1 Abstract

Purpose: The Athena Breast Health Network collaboration is a University of California system-wide project initiated with the intent to drive innovation in breast cancer prevention, screening and treatment. This qualitative research examines provider perceptions and expectations of post-treatment breast cancer care across five Network sites with the goal of better understanding provider behavior during the post-treatment phase of the cancer care trajectory.

Methods: Investigators at each site conducted semi-structured interviews with oncology specialists and primary care providers (PCPs). Interviews used case study examples and open- and closed-ended questions on the delivery of post-treatment breast cancer care. Informant responses were manually recorded by the interviewer, compiled in a database, then coded and analyzed using NVivo 9 software.

Results: There were 39 key informants across the sites: 14 medical oncologists, 7 radiation oncologists, 11 surgeons, 3 oncology nurses, and 4 PCPs. Care coordination was a major unprompted theme identified in the interviews. There was a perceived need for greater care coordination across institutions in order to improve delivery of post-treatment health care services and a need for greater care coordination within oncology, particularly to help avoid duplication of follow-up care and services. Participants expect frequent follow-up visits and to

use biomarker tests and advanced imaging services as part of routine surveillance care. Implementing survivorship care programs was perceived as a way to improve care delivery.

Conclusions: These results identify a need for increased focus on care coordination during the post-treatment phase of breast cancer care within the UC system, and the potential for system and provider level interventions that could help increase coordination of post-treatment care.

Implications for Cancer Survivors: Breast cancer survivors do not always receive evidence-based care. This research helps to better understand what motivates provider behavior during the post-treatment phase and lays a foundation for targeted interventions to increase adherence to evidence-based recommendations.

3.2 Introduction

The number of individuals living with a personal history of cancer is increasing. In 1971 an estimated 3 million persons were living five years beyond a cancer diagnosis. As of 2012, it is estimated that there are almost 14 million survivors in the United States, with about one fourth of these breast cancer survivors.[1] With approximately 1.6 million individuals expected to be diagnosed with cancer in 2012, the provision of care for survivors already poses an important healthcare challenge, and there is increasing interest in improving the quality of post-treatment care of cancer survivors.[2] Survivorship care, especially with regard to coordination of post-treatment care, is now a national priority, well-described in the 2006 Institute of Medicine (IOM) report, *From Cancer Patient to Cancer Survivor: Lost in Transition*.[3] There is concern that cancer survivors may not receive optimal post-treatment care within our fragmented health care system. The IOM report notes that "…the transition from active treatment to post-treatment care is critical to long-term health. If care is not planned and coordinated, cancer survivors are left without knowledge of their heightened risks and a follow-up plan of action."[3] The University of California (UC) Athena Breast Health Network collaboration is a large scale, UC system-wide project initiated with the intent to drive innovation in breast cancer prevention, screening, treatment, and survivorship care. This paper describes research on provider perceptions and expectations of breast cancer post-treatment care within the UC system as part of the overarching Athena project. The purpose of this study was to determine real-world expectations and perceptions of providers involved in the delivery of post-treatment care to breast cancer patients, and to identify themes that may lead to a deeper understanding of provider behaviors and care delivery during this phase of the cancer care trajectory.

3.3 Background

It has been shown that there can be significant over- and underuse of both preventive services and surveillance care for post-treatment cancer patients.[4-9] There are evidence-based guidelines for post-treatment care of breast cancer from the American Society of Clinical Oncology (ASCO) [10] and the National Comprehensive Cancer Network (NCCN) [11] that are designed to help address this problem. These guidelines include recommendations for use of post-treatment surveillance care, such as mammograms for breast cancer survivors, as well as non-recommended surveillance care, such as use of most imaging services. In addition, ASCO recently released a "Top Five" list as part of the Choosing Wisely® campaign, an initiative of the American Board of Internal Medicine.[12] This campaign aims to promote clinical care that is well supported by evidence, has beneficial effects on patient health by improving treatment and/or reducing risks, and, where possible, reduces costs of care.[13] The ASCO Top Five list advises against routine recurrence surveillance testing in breast cancer survivors who have completed curative treatment, and discourages use of advanced imaging tests (positron emission tomography (PET), computerized tomography (CT) and radionuclide bone scans) and blood tests for biomarkers (CEA, CA 15-3, CA 27-29).[12]

Prudent use of these guidelines may help to reduce the use unnecessary services within oncology. However, the literature shows that adherence to guideline recommendations for cancer survivors has been less than optimal.[7,14] Additionally, it can be difficult for researchers examining the question of adherence to post-treatment guidelines to determine whether use of services is driven by symptoms and physical findings, or if these services are used in routine post-treatment surveillance.[4,6,9] Duplicative tests and services may be influenced by lack of care coordination for cancer survivors (e.g., lack of a common medical record among providers), as

well as patient expectations and anxiety about cancer recurrence. Other important components that may drive patterns of post-treatment care are provider expectations and preferences, the focus of this research.

Given the increasing numbers of cancer survivors [2] and the research showing that high-intensity surveillance does not benefit early stage breast cancer survivors,[10,15] it is important to understand what is driving the current post-treatment practice patterns that show overutilization of non-recommended services. We conducted a study using provider interviews and patient surveys at the five UC Cancer Centers participating in Athena (UC San Diego, UC Irvine, UC Los Angeles, UC San Francisco, and UC Davis) to examine how different tertiary cancer centers provide post-treatment breast survivorship care and how well the existing models of care at each site facilitate adherence to guideline recommendations for surveillance and management of common post-treatment symptoms. A qualitative method was chosen to allow providers to describe *in their own words* what their current practices, expectations, and perceptions are of post-treatment care delivery. This approach allowed us to identify and develop themes that arose from the data, an approach recommended for this type of health services research [16] and one that allows exploration of the perspectives of those involved in the delivery of breast cancer post-treatment care. This approach is more commonly called "generic qualitative research."[17,18] By examining these themes, we hoped to identify patterns of care delivery for this common cancer, as well as a deeper understanding of what is motivating provider behavior during the post-treatment phase of the cancer care trajectory. Our assumptions regarding post-treatment care delivery were based on the available literature, which shows that guideline adherence is poor but does not provide information on why this care is not guideline concordant. We viewed this qualitative information as being essential for the development of future interventions designed to

motivate providers to increase adherence to evidence-based recommendations. Our generic approach was chosen to allow us to uncover and explore potential issues in quality of care and care delivery and to have our research process shape the collection of data.

3.4 Methods

3.4.1 Setting and participants

The University of California has five National Cancer Institute (NCI) designated comprehensive cancer centers, each of a separate campus. As part of the Athena project, providers involved in caring for post-treatment breast cancer patients were identified at each of these centers. Provider identification was carried out by the site-affiliated Principal Investigator (PI). A broad sample of provider types was sought in line with maximum variation sampling theory, which attempts to capture main themes or ideas that appear across a small but varied sample.[19] Provider types targeted for the study included medical oncologists, radiation oncologists, surgeons, primary care physicians (internal medicine, family medicine, gynecology), and oncology nurses, who were viewed as opinion leaders and were directly involved in the care of many breast cancer patients at each institution. Providers were eligible to participate if they were employed and actively engaged in providing post-treatment care to breast cancer patients at the UC site at the time of the interview. Providers were invited to participate by the site PI via an electronic invitation with email follow-up. Each site had a target of 5 to 10 participants. All study activities were approved using a UC-wide Institutional Review Board (IRB) Memorandum of Understanding (MOU) with UC Los Angeles as the lead IRB (UCLA IRB #10-000867).

3.4.2 Data collection

In-depth semi-structured interviews were conducted in person or over the telephone using an interview guide developed by a committee of investigators from each site knowledgeable about the treatment and follow-up surveillance of breast cancer patients. The interview script focused on patterns of follow-up care, symptom management, and institutional challenges and included open-ended questions with ad-hoc probes as well case vignettes (Appendix 3.1). The case vignettes were developed through a consensus process by the five site PIs: two medical oncologists, one breast surgeon, and two health services/cancer control researchers. The case vignettes described three different breast cancer patients with distinctive recurrence risk profiles that might influence follow-up patterns (Table 3.1). After presentation of each patient vignette, the key informant clinician was asked about the frequency of follow-up visits for the patient, the types of tests and/or procedures used for follow-up care, and the inclusion of other providers in follow-up care. Each interview took between 30-75 minutes to complete. Interviews were transcribed by the interviewers and oral informed consent was obtained from each participant at the start of the interview.

3.4.3 Data analysis

Qualitative data analysis followed the constant comparative method (CCM) as described by Glaser [20] and thematic analysis as described by Morse and Field.[21] CCM employs a data coding strategy that references new text coded in a particular category to previously coded text in that category, aiding in the recognition and development of the theoretical properties and themes in the data. While CCM arises out of Grounded Theory research, it is not used exclusively for Grounded Theory.[22] CCM has applications within other research frameworks, such as thematic analysis, and was chosen in order to allow for the development of meaningful themes within the

interview data, a method that is appropriate given our stated goal of exploring the perspectives of those involved in the delivery of post-treatment breast cancer care.[23] All transcribed interview data was entered into NVivo 9 data management software (QSR International, Cambridge, MA) to assist with coding and theme development. Two independent coders, a nurse practitioner and a health services researcher, analyzed the transcribed data. The initial interview transcript was read several times prior to initiation of coding. The primary coder then developed a detailed categorization scheme of themes, sub-themes, and relationships based on the interview content. Subsequent interviews were read and coded with reference to the prior coding scheme. Frequent comparisons between the two coders ensured coding consistency and adherence to theme constructs. Discrepancies in coding were discussed at meetings between the two coders, with differences in theme identification resolved by consensus. We did not engage in respondent validation, but we did attempt to gather a wide range of perspectives. Twenty-seven distinct themes emerged from the data. Cohen's kappa was calculated to measure initial inter-coder reliability. This report highlights the most prevalent themes in the data.

3.5 Results

3.5.1 Study sample

There were 39 key informants across the five participating sites: 14 medical oncologists, 7 radiation oncologists, 11 surgeons, 3 oncology nurses, and 4 primary care practitioners (PCPs). The mean number of years of employment within the UC health care system was 10.4 years (SD 6.8, minimum=1, maximum=30). Cohen's kappa for inter-coder reliability equaled 0.77.

3.5.2 Themes and findings

Care coordination

Across all sites, care coordination was a major unprompted theme identified in the interviews. The concept of coordination had over 100 discrete mentions across the 39 interviews. The broad theme of coordination had relationships with the majority of other themes identified in the data as shown in the concept map (Figure 3.1). The concept map is a visual representation of the data that shows the relationships between themes and subthemes that were identified from the coded data. Three distinct coordination themes emerged from the data: shared care between oncology and primary care, care coordination across the institution, and care coordination within oncology.

Shared care between oncology and primary care was perceived as a positive method of post-treatment care for breast cancer survivors by most participants:

"Medical oncologist and PCP share care in the post-treatment phase--co-manage for first 5 years. After 5 years, PCP dominates."

"PCP providers excellent to share care with; good model."

"Oncologist and PCP co-manage, based on history of chemo; followed for several years by medical oncologist."

A minority of participants expressed doubt that PCPs wanted to carry out shared-care responsibilities during the post-treatment phase.

"Most PCPs prefer not to be involved in oncology post-treatment care."

"It can be difficult to communicate [with PCPs] during post-treatment…and sometimes patients are on inappropriate medications from PCP and I direct patients to stop or change meds."

"PC [primary care] physicians don't deal with breast issues."

"Sometimes PCP doesn't respond or provide any feedback."

A perceived need for greater care coordination across the institution in order to improve delivery of post-treatment health care services was evident throughout the interviews.

"[We need] more integrated care and communication with PCPs, other specialists, and complementary medicine docs. Minimize repetitive visits between specialists."

"[We need] an integrated EMR, need to have better communication and ability to flag records. Improved patient communication of symptoms to MDs--a patient portal…cancer care and support are decentralized."

"I'd like to see coordinated effort with respect to psychosocial care, use of survivorship care plans…[and] more organized follow-up."

"Improvements would be…streamlining after care issues; improved communication with medical oncology; access to care plans and other services."

There was also a perceived need for greater care coordination within oncology, particularly to help avoid duplication of follow-up care and services. The responses demonstrate wide variability among provider types and participating sites.

"To improve care [we need] better communication among oncology specialists; burden is on patient—there is no coordination. Multidisciplinary care is desirable."

"I would like to see coordinated scheduling of appointments; help to avoid duplication [of services]."

"Oncology follow-up is not systematic, intervals not regularized. [Follow-up can] depend on the medical oncologist and/or surgeon; if dismissed by surgeon or oncologist, radiation oncologist may follow more frequently."

"[We need] better communication with oncology, role delineation. Survivorship plans of care could help with this."

"Rad onc, med onc, and surg onc should alternate visits for follow-up."

Use of imaging and biomarker tests as expected part of routine post-treatment care

Participants were asked open-ended questions about types of routine follow-up services for post-treatment patients based on the three case vignettes. Almost all participants expected to use biomarker tests as a routine part of post-treatment care. Few participants clearly articulated why they ordered specific tests and/or services, although some indicated that they generally repeated tests and services that had been ordered before. For example, discussion of PET scans used in routine follow-up care demonstrated that providers expect to order a PET scan if one has been done before, for any reason:

"PET CT as follow-up…[because] staging with scans at diagnosis often done."

"I will do a PET CT, if done at baseline, will repeat; ad hoc patterns [for imaging]."

"PET CTs are done after treatment, it's expected."

The informants also perceived problems with coordination of imaging in post-treatment care:

"Imaging, mammography, I do whatever screening is necessary...need to make sure it is getting done."

"Unclear who takes responsibility for ordering imaging."

Ways to improve delivery of post-treatment care

These providers indicated that structured post-treatment clinical services would improve their ability to deliver care, such as survivorship clinics or a dedicated survivorship clinician

(e.g., nurse practitioner, physician assistant). Use of survivorship care plans and/or treatment summaries was identified as a sub-theme of structured post-treatment care. These themes have a strong relationship to the theme of care coordination, with many responses cross-categorized into both themes.

"We need to offer post-treatment care to everyone in an organized way."

"An improvement would be physician extenders to focus on survivorship population."

"*Increase support personnel; offer post-treatment care to everyone."*

"A goal—a multidisciplinary clinic for breast cancer survivors with hem/onc clinicians, pain management, psych…would have consultations."

"[Patients] start redefining life after treatment, they aren't the same person. We have to help [them] redefine self and relationships and find a new normal."

"We need survivorship clinic for post-treatment care."

"Creation of survivorship plans [would improve ability to provide post-treatment care]."

3.6 Discussion

Findings from this qualitative study illustrate some of the ongoing issues in providing high-quality post-treatment care to breast cancer survivors. By gaining insight into the perceptions and expectations of providers involved in post-treatment care delivery, we sought to gain an understanding of some of the drivers of provider behavior. Based on these findings, care coordination is a critical missing element of post-treatment care delivery. This theme demonstrates both the strengths and weaknesses of post-treatment care delivery across the five centers. The theme of shared care between primary and oncology care demonstrates both an expectation and perception of coordinating care across specialties as an important aspect of post-

treatment breast cancer care. Engaging in shared-care between oncology and primary care has been shown to result in improved general health care and cancer surveillance for breast cancer survivors.[24,25] However, many participants identified a lack of coordination within oncology as a problem, specifically the inability to coordinate follow-up visits across oncology specialists. The lack of awareness and knowledge of how other members of the oncology team are following post-treatment patients is a serious hindrance to care coordination, and is described as sometimes leading to duplication of visits, tests, and other services. The providers in this study feel that care should be coordinated throughout the oncology team and with primary care, but have no simple mechanism for doing so within their institutions.

Our study participants reported use of biomarker tests and imaging as part of routine post-treatment care. The literature shows that some ASCO and NCCN guideline-recommended services are being under-utilized, such as mammograms for detection of recurrence or new primary breast cancer in breast cancer survivors.[8,9] Conversely, some non-recommended services have been shown to be over-utilized, such as biomarker testing and chest and/or abdominal imaging.[6,14,26] These non-recommended services have not been shown to be associated with significant differences in survival or quality of life, yet use of these services persists in breast cancer post-treatment care.[10] A recent study found that 40% of women treated for early stage (I-II) breast cancer had at least one non-recommended imaging test (computerized tomography scan, bone scan, breast MRI, PET) during the surveillance care interval.[14] Use of advanced imaging services such as breast MRI and PET scans are also not recommended according to the ASCO guidelines and "Top Five" list. [10,12]

It remains somewhat unclear why oncology providers in our study reported routinely using non-recommended imaging tests as part of breast cancer surveillance care. Few reasons are

given for use of these services other than indicating that if a service had been used once it would most likely be used again, as with the PET scans. Coordination was again an important element in use of imaging and other services. The participants perceived that gaps in their knowledge of what other providers were ordering could lead to confusion and potentially duplication of services.

The majority of participants identified structured post-treatment clinical services as a way to improve care delivery. Based on the interview data, post-treatment survivorship care is largely unorganized within the five institutions. Providers perceive this as a barrier to coordinating care delivery for this population. The reported need for an organized system of post-treatment care underlines the major themes found in the data. Care coordination, frequency of follow-up, and use of non-recommended surveillance services could all be potentially improved with a structured system of post-treatment care that appropriately utilizes health information technology. For example, if providers were able to easily coordinate centralized appointment scheduling within the oncology treatment team (medical oncology, radiation oncology, surgery), it could help providers to organize post-treatment visits and potential decrease repetitive visits and services. Or, a post-treatment care program or provider could take the lead in organizing this phase of care, communicating with the oncology team as needed. However, there are practical barriers to implementing such strategies. For example, providers currently have a strong incentive to continue frequent follow-up visits based on fee-for-service reimbursement and the use of relative value units (RVUs) in provider salaries.

These results indicate that there are substantial opportunities for system and provider level interventions that could help to improve coordination post-treatment care. Knowledge translation (KT) or T3 translational research, defined as the incorporation of evidence-based

findings into clinical practice, is a complex process that requires organizational and provider buy-in.[27,28] A combination of KT/T3 strategies could be effective in helping post-treatment care providers to deliver evidence based care. For example, systems processes such as evidence-based computerized reminders combined with provider-level education and incentives, including individual provider audit with timely, customized feedback, may be an effective combined strategy to increase appropriate post-treatment care for breast cancer survivors.

This study used qualitative research methods to generate insights into post-treatment care delivery within the UC system and to explore provider expectations of care delivery. This methodology has its limitations, in that it is the opinions of a modest number of individual providers. However, those interviewed were among the institutional opinion leaders involved in the delivery of breast cancer care, and thus they likely reflect the general approach to post-treatment care delivery at these academic medical centers. The results demonstrate that there is significant room for improvement across the participating sites, and that organized survivorship care is still being developed within these five academic centers. We found that providers are engaging in shared-care between oncology and primary care during the post-treatment phase, but that overall care coordination within institutions and within oncology specialties could be improved. The recurrent theme of care coordination emphasizes the need for organized survivorship services within each institution. By illustrating the current state of post-treatment breast cancer care delivery these results can help to drive innovation and adaptation in cancer care delivery across the UC system as part of the UC Athena Network Breast Health Project and beyond. As our health care system moves toward using coordinated electronic medical records systems, opportunities to improve the organization and delivery of post-treatment cancer care will become more apparent.

Chapter 3 Figures and Tables

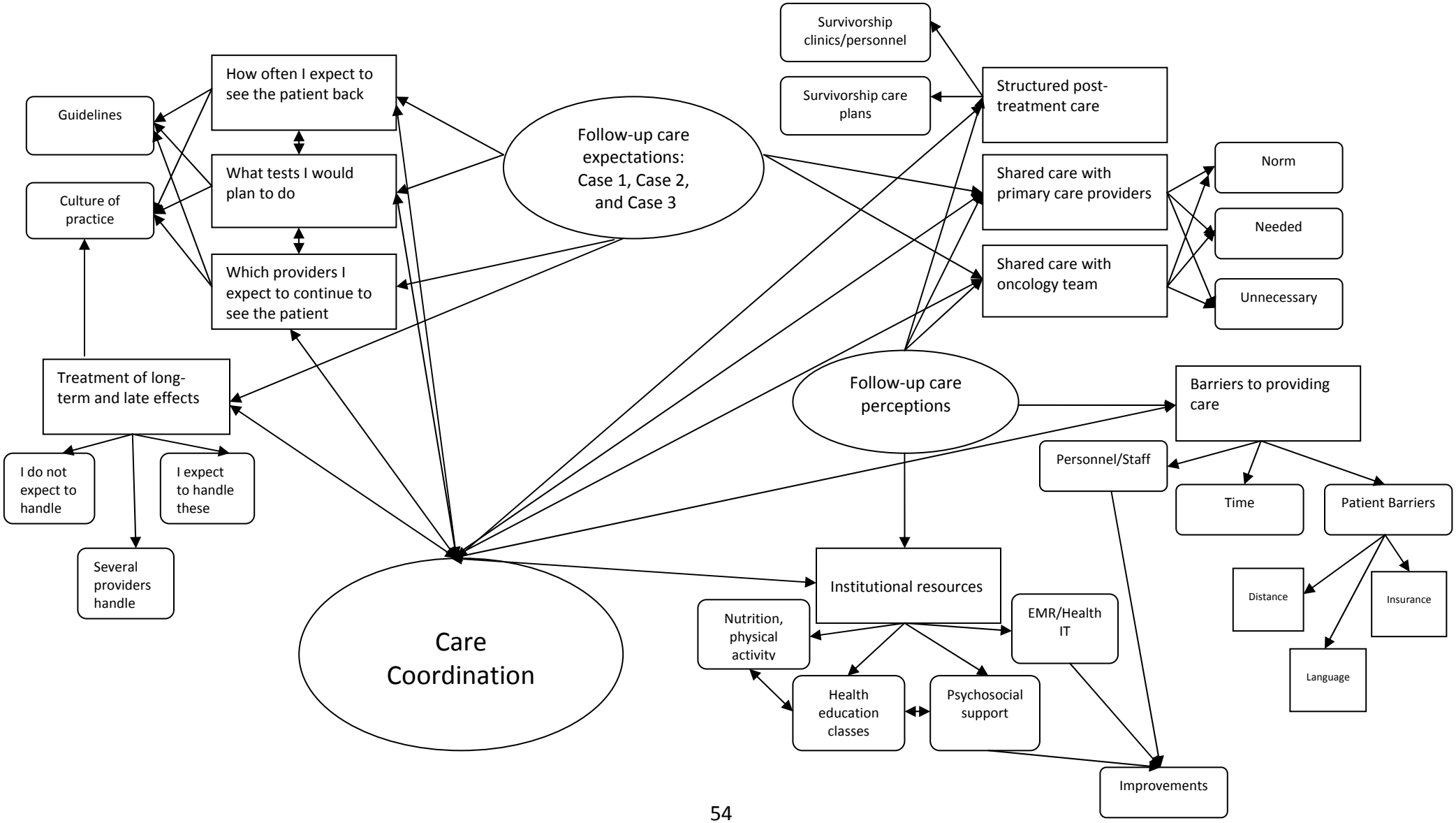
Table 3.1: Breast cancer case vignettes presented as part of participant interviews

	Low risk case	Medium risk case	High risk case
Age	67 years old	60 years old	41 years old
Menopausal status	Post-menopausal	Post-menopausal	Pre-menopausal
Tumor characteristics	1.2 cm, grade 2 IDC ER+/PR+/HER2- 0/2 + sentinel nodes	2.5 cm, grade 2 IDC ER+/PR-/HER2- 1/15 + lymph nodes	Locally advanced, high grade ER-/PR-/HER 2/12 + lymph nodes
Surgery	Lumpectomy with sentinel lymph node dissection	Lumpectomy with axillary lymph node dissection	Bilateral mastectomies with immediate reconstruction
Chemotherapy	No	Taxotere and Cytoxan	Neoadjuvent AC-Taxol
Radiation	Yes	Yes	No
Other therapies	Aromatase inhibitor	Aromatase inhibitor	No
Comorbid conditions	None	Hypertension; obesity; non-insulin dependent diabetes; moderate to severe DJD	None

Abbreviations:

IDC: Infiltrating ductal carcinoma
ER: Estrogen receptor
PR: Progesterone receptor
HER2: Human epidermal growth factor receptor 2
DJD: Degenerative joint disease
AC: Adriamycin and cyclophosphamide

Figure 3.1: Concept map of themes, sub-themes, and relationships discovered and coded from the interview data. The size and shape of the text box is related to the number of mentions in the data. Ovals indicate the highest number of mentions, followed by rectangles, then squares; larger shapes indicate more mentions than a smaller size of the same shape. For example, care coordination was mentioned the most of any theme so it is the largest oval. The next most common mentions are follow-up care perceptions related to the case vignettes, followed by follow-up care perceptions.



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Appendix 3.1 Script for oncology and primary care provider semi-structured interviews

INTERVIEW INTRODUCTION

As part of the University of California ATHENA Breast Health Network project, we are conducting an interview-based study with several oncology care providers at this and other UC medical centers to better understand how care is delivered to breast cancer patients after their active treatment is complete. This knowledge will help us identify successful and effective models of care within the academic setting that can be used to improve the care of women with breast cancer across the United States. We would like to use the information from this interview for both research and quality improvement purposes.

The following interview questions focus on post-treatment care for breast cancer patients.

Definition of post-treatment care: includes breast cancer surveillance follow-up, management of symptoms and late effects of cancer treatment, counseling regarding general health and wellness care for patients that have completed active treatment (chemotherapy, surgery, radiation), communication and coordination of care with primary care providers.

INTERVIEW QUESTIONS

The first part of the interview includes few background questions about you:

Organization: _____

Medical specialty: _____

Number of Years at Institution: _____

Delivery of Post-Treatment Care: *Medical domain*

In order to better understand the current processes of care at your institution for post-treatment breast cancer patients, I will present three case scenarios with varying degrees of severity for discussion. Please feel free to ask me to repeat case details.

1. *Can you describe the flow of post-treatment medical care for a low risk ER+ patient in your own practice; for example, a 67 year old post-menopausal woman with a 1.2 cm grade 2 IDC (ER+/PR+/HER2-) 0/2 SLN+ who underwent a lumpectomy/SLND and then radiation and who has started on an aromatase inhibitor.*

Probes: [Interviewer: ask if these topics are not covered in answer above]

- *How are these patients typically followed for breast cancer recurrence surveillance?*
- *What tests are usually done for this type of patient when treatment ends?*
- *Which providers are involved?*
- *How often do you see the patient?*

2. *Next, let's go over the flow of post-treatment care for an intermediate risk patient who is ER+ with multiple co-morbidities:*
   60 year old post-menopausal woman with a 2.5 cm grade 2 IDC (ER+/PR-/HER2-) with 1/15 LN+. Patient underwent lumpectomy with ALND followed by radiation, and then received Taxotere and Cytoxan x 4 cycles. Patient is an aromatase inhibitor and is obese and has hypertension, non-insulin dependent diabetes, and moderate to severe degenerative joint disease.

   Probes: [Interviewer: ask if these topics are not covered in answer above]

- *How are these patients typically followed for breast cancer recurrence surveillance?*

- *What tests are usually done for this type of patient when treatment ends?*

- *Which providers are involved?*

- *How often do you see the patient?*

3. *Finally, please describe the flow of care for a high risk ER- patient:*
   41 year old premenopausal woman with a locally advanced high grade ER-/PR-/HER- who received neoadjuvant chemotherapy consisting of AC-Taxol. The patient underwent bilateral mastectomies with immediate reconstruction and had 1.5 cm of residual IDC in the breast and 2/12 LN+ at the time of surgery.

   Probes: [Interviewer: ask if these topics are not covered in answer above]

- *How are these patients typically followed for breast cancer recurrence surveillance?*
- *What tests are usually done for this type of patient after treatment ends?*
- *Which providers are involved?*
- *How often do you see the patient?*

Now we have some general questions about post-treatment care for breast cancer patients:

4. *How are post-treatment breast cancer patients typically followed for <u>general health care</u>, e.g. preventive care, bone density, CRC screening?*

Sometimes post-treatment patients can have ongoing symptoms from their treatment. We are going to ask a few questions about management of common long term and late effects:

5. *How is ongoing fatigue handled for post-treatment patients?*

6. *How is sleep disruption handled for these patients?*

7. *Do you see many patients with ongoing pain?*

    a. *If yes, how do you care for these patients?*

    b. *Is a pain management program available for patient referral?*

8. *How is diagnosis and treatment of depression handled for these patients?*

9. *How often are long-term survivors (5-10+ years out) still being seen in your practice?*

10. *Do you see a need to free up space for newly diagnosed patients in your practice?*

11. *Have you heard about cancer treatment summaries or survivorship care plans?*

a. *If yes: Do you know if your breast cancer patients receive one?*

    i. *If yes: Who creates the summary?*

    ii. *At what point is it done (e.g., 6 months out, 12 months, variable)?*

    iii. *Who receives a copy of the care plan?*

12. *In your opinion, are general health and wellness topics, such as nutrition, physical activity, and weight management, part of general post-treatment care at your institution?*

    a. *If yes, how are these services delivered (e.g., classes, physician visits)?*

Delivery of Care*: Psychosocial domain*

1. *How is psychosocial care handled at your institution post-treatment, such as depression screening, support services and education?*

2. *Can you walk me through how you would refer one of your patients to these services?*

Systems of Care

1. *What would you like to see happen to improve your ability to provide optimal post-treatment care to breast cancer patients?*

2. *How do you communicate with the breast cancer patient's primary care provider?[Interviewer: if PCP interview, substitute oncology care provider]*

3. *What are some of the barriers to sharing care with the patient's PCP?* [*Interviewer: if PCP interview, substitute oncology care provider]*

4. *What are some barriers to providing post-treatment care to your patients, such as health insurance restrictions or limited English proficiency of patients?*

5. *Would you say that insurance status can impact the pattern of care for these patients?*

Population

1. *When in the course of breast cancer treatment should patients begin to receive post-treatment care?*

Thank you very much for participating in this interview.
Your input is very important to us!

UCLA IRB APPROVED: IRB #10-000867

CHAPTER 4:

The prevalence of post-traumatic stress symptoms and associated risk factors in cancer survivors treated at an academic medical center (Study 3)

4.1 Abstract

Objective: The purpose of this study was to determine the prevalence of clinically elevated post-traumatic stress symptoms in a group of cancer survivors and to investigate the relationship between these symptoms and various correlates, including the Impact of Cancer scale (IOC).

Methods: A one-time survey battery was administered to a sample of cancer survivors who were participating in an institutional registry of cancer survivors. The survey included standardized measures, including the PTSD Checklist-Civilian Version (PCL-C), the Impact of Cancer (IOC) Scale v.2, and the SF-36, among other measures related to the long-term and late effects of cancer treatment. Bivariate and multivariate analyses were performed to estimate the associations between PCLC-C and other variables. Regression analyses were conducted to examine factors associated with the continuous PCL-C score and three score cut-points: 30, 38, and 44.

Results: Responses were available from 162 cancer survivors. Mean age was 51 years (standard deviation (SD) 16); mean time since diagnosis was 11 years (SD 10). Twenty-five percent were diagnosed before the age of 18. The mean PCL-C score was 27 (SD 9, range 17-64); 29% of the sample scored 30 and above, 13% scored 38 and above, and 7% scored 44 and above. In a linear regression model, a one-unit increase in the IOC negative summary scale was associated with a

4.17 increase in total PCL-C score ($p<0.001$). Higher depressive symptoms ($p=0.003$), lower social support ($p=0.02$), less income ($p=0.03$), and being married ($p=0.04$) were also uniquely associated with higher PCL-C scores.

Conclusions: Elevated PTSD symptoms are a persistent problem for some cancer survivors. The negative impact summary scale of the IOC had a strong relationship with the endorsement of symptoms linked to PTSD. The prevalence of PTSD symptoms in this sample suggest that the PCL-C should be used to identify cancer survivors at risk for developing PTSD symptoms, and the IOC should be used to develop relevant interventions for this population.

4.2 Introduction

Post-traumatic stress disorder (PTSD) is a serious anxiety disorder that can affect those exposed to a traumatic event or stressor.[1] These stressors can include life-threatening illnesses such as cancer.[1] Cancer survivors are at risk for many physical and psychosocial long-term and late effects,[2-4] and the evaluation and treatment of PTSD is an important part of cancer survivorship care. Allostatic load—the physiological consequences of exposure to repeated or chronic stress—can be higher in individuals experiencing PTSD, highlighting the physical effects of PTSD and demonstrating the need to properly identify and treat this disorder.[5-7] Unfortunately, identification and treatment of PTSD and other psychosocial issues in cancer patients and survivors is sub-optimal.[8,9]

The literature on PTSD in cancer survivors is heterogeneous. A 2002 review of PTSD in cancer demonstrated that the estimated prevalence in cancer survivors varied from 2%-32%.[10] Recent studies of breast cancer survivors reflect this variability in estimated prevalence with reports of 2% and 20%, [11-13] and studies of other cancer types have also found variability in PTSD prevalence.[14-20] In contrast, the general population is estimated to have a lifetime prevalence of PTSD between 4% and 7%.[21-23] The findings of association of demographic, medical, and psychological variables with PTSD are mixed in cancer survivors, and the associations are not uniform across studies or disease groups (Table 4.1).

The Impact of Cancer (IOC) instrument was designed to measure both the positive and negative impacts of cancer.[24] Physical and mental health outcomes are related to the IOC, as shown in multiple settings and cancer survivor samples.[24-27] Although the positive IOC score (higher score means more positive impacts of cancer) has been strongly associated with post-traumatic growth and meaning,[26,28] less is known about the value of the negative IOC score as a

correlate of PTSD symptoms in cancer patients and survivors, although one study of long-term lymphoma survivors found a significant relationship between the IOC negative impact scale and PTSD symptoms.[29] The purpose of this study was to determine the prevalence of clinically significant PTSD symptoms in a heterogeneous group of cancer survivors, examine the associations of specific variables identified in the literature with PTSD in cancer survivors, and investigate the relationship between PTSD symptoms and the IOC scales.

4.3 Methods

4.3.1 Design and participants

The study sample for this investigation came from the Cancer Survivor Registry (CSR), which was developed by investigators at the UCLA-LIVESTRONG™ Survivorship Center of Excellence (COE) as a resource to advance knowledge about the long-term and late effects of cancer treatment. Participants in the CSR were recruited from the clinical programs of the COE. They were asked to complete a one-time survey that included self-report data on demographics, medical history, health behaviors, and physical and mental health. Cancer survivors seen in the COE survivorship clinics were invited by mailed invitation to participate in the CSR. They were eligible for the study if they were 18 years of age and older, had completed their active cancer treatment (surgery, chemotherapy, radiation), and were English-speaking. All cancer types were eligible. A questionnaire packet including the informed consent form was mailed to interested participants and the completed packet returned in a postage-paid envelope. There were no monetary incentives to participation. Institutional Review Board (IRB) approval was received for all study activities (UCLA IRB approval #10-001256).

4.3.2 Measures

Demographic and medical characteristics

Demographics include age, gender, race/ethnicity, education, income, and marital status. Cancer characteristics include cancer diagnosis type(s), cancer treatment(s) (surgery, chemotherapy, radiation), time since diagnosis, and age at diagnosis.

Psychosocial characteristics

Social support was measured with the ENRICHD Social Support Instrument (ESSI), a 7-item self-report instrument.[30] Responses were categorized into high support/low support based on total score, with those scoring 18 or less considered to have low social support, a standard score cut-point.[31] Depressive symptoms were measured using the Center for Epidemiologic Studies Depression instrument (CES-D), a widely used 20-item self-report instrument designed to measure depressive symptomatology in the general population.[32] Responses were categorized into depressed/not depressed based on total score; those scoring 16 or greater were categorized as depressed, a standard score cut-point. The physical (PCS) and mental (MCS) component summary scores from the RAND 36-Item Health Survey (SF-36 v.1) were used as indicators of health-related quality of life.[33] The PCS and MCS are weighted aggregations of the scores for the eight SF-36 subscales and are reported as continuous variables with respect to a mean of 50 and SD of 10 in the U.S. general population.

Post-traumatic stress

Patients completed a commonly used measure of PTSD in the civilian population, the PTSD Checklist-Civilian Version (PCL-C).[34] The PCL-C assesses symptoms in civilian populations using a 17-item self-report checklist. Each symptom is scored on a scale of 1 (low) to 5 (high) and the item scores are summed to a total that ranges from 17 to 85 points. Test-retest

correlation coefficients ranging from 0.68 to 0.92 and correlations with other established measures (e.g., the Clinician Administered PTSD Scale (CAPS), the Impact of Events Scale (IES)) of r>0.75 have been reported.[35-40] The sensitivity and specificity of the PCL-C varies by subgroup, creating some uncertainty regarding the optimal scoring cut-points. For example, a widely cited study by Blanchard et al showed that in adults who had experienced an acute trauma the optimal scoring cut-point to capture those with PTSD symptoms is 44,[35] a finding replicated by Ruggiero et al.[36] However, studies of women enrolled in an HMO insurance plan and older primary care patients have shown optimal cut-points of 30 and 37, respectively.[40,38] The current PCL-C scoring guidelines from the United States Department of Veterans Affairs recommend a civilian primary care cut-points of 30-38 for diagnosis of PTSD.[41] Our study examines the PCL-C score as a continuous outcome as well as the three PCL-C score cut-points based on the literature and the guidelines from the United States Department of Veterans Affairs: 30 and above, 38 and above, and 44 and above.

Impact of Cancer

The Impact of Cancer (IOC) scale was developed to measure the unique positive and negative consequences that are associated with being a cancer survivor.[24] The IOC version 2, which has been evaluated in survivors with different types of cancers, was used in this study. [26,42] The IOC has eight subscales measured by 37 items. There are four positive sub-scales (Health Awareness, Positive Self-Evaluation, Altruism/Empathy, and Meaning of Cancer) and four negative subscales (Appearance Concerns (AC), Body Change Concerns (BC), Life Interference (LI), and Worry (W)). These sub-scales are combined to create the positive impact scale score (PIS) and the negative impact scale score (NIS), respectively. Each negative item sub-scale is made up of either three (AC and BC) or seven questions (LI and W). Topics covered by the sub-

scales include energy and body performance (BC), body disfigurement and appearance (AC), isolation, uncertainty about the future, and cancer-related symptoms (LI), and concerns about cancer recurrence and general health (W). Respondents indicate item agreement using a five item categorical response scale with a range of 1 (low) to 5 (high). The NIS and PIS were used in the analyses as well as the four individual negative sub-scales. Correlations among the IOC v.2 subscales are reported elsewhere.[26]

4.3.3 Data analysis

Overall mean PCL-C scores for the sample were reported along with the percentage of the sample with scores equal to or above the three cut-point values. Bivariate analyses compared mean PCL-C scores for categorical variables using t-tests. Pearson correlations were calculated for the association between the PCL-C total score and continuous variables. The relationship between the PCL-C score, the IOC NIS, and the SF-36 MCS, was examined using an elaboration model.[43,44] This was performed because of the high correlation among these three measures. Elaboration models provide an opportunity to discover additional information about the relationship between the variables and outcome by quantifying the amount of variance in the outcome accounted for when a variable is added to the model.[43,44] The elaboration model uses a simple linear regression of the outcome and the focal independent variable, followed by a three-variable regression model with a second independent variable added to the model. We standardized the coefficient value to a unit variance to calculate the absolute difference in the focal independent variable coefficient value between the simple bivariate model and the three-variable model. This difference provides the exact percentage of the variance in the outcome accounted for by the addition of the third variable to the model, which provides a check of spuriousness.

Both multivariate linear and logistic regression models were used to identify variables associated with PCL-C scores. Linear regression was used for the continuous PCL-C score and logistic regression for the variant of the dependent variables created by dichotomizing PCL-C scores using the three score cut-points. A full model was compared to a parsimonious model using the likelihood ratio test to determine if there is any additional benefit of including the full set of variables compared to only those shown to be at least marginally significant in bivariate analyses ($p<0.10$). The IOC NIS sub-scales were included in separate regression analyses to explore the association of PCL-C scores and the individual IOC NIS sub-scales. All analyses were conducted using Stata version 12.1.

4.4 Results

4.4.1 Study sample

Of the 681 survivors who were invited by letter to join the CSR study, 241 (35%) indicated interest in participating. Of the 241 respondents, 166 (69%) returned the completed questionnaire and consent form; the other 75 were lost to follow-up and did not respond to telephone calls or letters from the study coordinator. Study respondents versus non-respondents were more likely to have been diagnosed as an adult than diagnosed as a child before the age of 18 (54% of those diagnosed as an adult responded vs. 17% of those diagnosed as a child, $p<0.001$). Respondents were also more likely to be female (42% of females responded vs. 19% of males, $p<0.001$) and white (39% white vs. 28% other race/ethnicity, $p=0.004$). The final study sample included 162 survivors after excluding four participants who did not complete the PTSD section of the questionnaire.

The sample characteristics are shown in Table 4.2. The mean age of the sample was 51 years (standard deviation (SD) 16 years) and the mean time since diagnosis was 11 years (SD 10 years). The mean age at diagnosis was 40 years (SD 20), and the range reflects the inclusion of childhood cancer survivors in the sample (range 0 to 78 years). Sixty percent of the sample were breast cancer survivors, 25% were survivors of childhood cancers diagnosed under the age of 18, and 8% were survivors of adult-onset hematologic cancer (leukemia/lymphoma). Twenty-five percent were survivors of childhood cancers diagnosed under the age of 18, and 27% of the sample were non-white. Twenty-four percent reported low social support based on the ESSI score and 27% were categorized as depressed based on the CES-D score. The mean scores of the SF-36 PCS and MCS were close to 2004-2005 general population means (population mean scores: PCS 49; MCS 54).[45] The mean IOC NIS was 2.74 (SD 0.77) and the mean IOC PIS was 3.83 (SD 0.64). The overall mean PCL-C score was 27 (SD 9) and 29% of the sample scored 30 and above, 13% scored 38 and above, and 7% scored 44 and above.

4.4.2 Bivariate associations of PCL-C total score with other variables

Bivariate associations between the PCL-C total score and other variables are listed in Table 4.3. None of the medical characteristic variables (treatment type, time since treatment, childhood cancer survivor, multiple cancer diagnoses) had significant associations with the PCL-C total score. Age, race/ethnicity, income, and marital status were significantly associated with the PCL-C total score. The psychosocial variables (social support, depressive symptoms, SF-36 PCS, SF-36 MCS, and the IOC NIS) were all statistically significantly associated with the PCL-C total score. The correlations of the PCL-C total score with the IOC NIS ($r=0.628$) and the SF-36 MCS ($r=-0.620$) were statistically significant at the $p<0.05$ level and large. In addition, the IOC NIS and SF-36 MCS ($r=-0.450$) correlated significantly at the $p<0.05$ level.

4.4.3 Elaboration Model

The addition of the SF-36 MCS beyond the simple bivariate regression model decreased the standardized IOC NIS coefficient by 30%, from 0.813 to 0.567. The addition of the SF-36 MCS variable increased the R^2 value from 0.40 to 0.54. Thus, the addition of the SF-36 MCS variable helps to explain a substantial amount of variance in the outcome (total PCL-C score) but the IOC NIS is still an important correlate.

4.4.4 Multivariate regression analyses

Table 4.4 lists the results of multiple linear regression for the total PCL-C score and logistic regression for the three PCL-C cut-points. The first model is the full multivariate linear regression model with all demographic and medical characteristic variables included. As seen with the bivariate relationships, only some of the demographic variables and none of the medical characteristic variables are significant in the full model (Model 1, Table 4.4). Lower income (less than $60,000 per year) and being married were significantly related to higher PCL-C scores (p=0.04 and p=0.05, respectively). In addition, depressive symptoms (p=0.005), lower SF-36 MCS scores (p=0.003), and IOC NIS (p<0.001) were significantly associated with higher PCL-C scores. High levels of social support were associated with lower PCL-C total scores (p=0.06). A parsimonious model with only the five psychosocial variables and three significantly related demographic variables (income, marital status, and race) was compared to the full model using a likelihood ratio test. The results (prob=0.9790) show that the parsimonious model is the optimal choice (Model 2, Table 4.4). In the parsimonious linear model, there were significant associations between the total PCL-C score and two demographic variables, lower income (p=0.03) and being married (p=0.04). Four of the five psychosocial variables are significant. Those categorized as depressed according to the CES-D have a PTSD total score 4.59 points

higher than those categorized as non-depressed (p=0.003). Those reporting high social support on the ESSI have PTSD total score 2.43 points lower than those reporting low social support (p=0.02). For every unit increase for the IOC NIS, there is a 4.17 increase in total PTSD score (p<0.001), and for every unit increase in the SF-36 MCS there is a 0.21 decrease in the PTSD total score. In summary, those who have lower income, are depressed, have low social support, score lower on the SF-36 MCS, and score higher on the IOC NIS are significantly more likely to have higher total PTSD scores.

Logistic regression models were used for the three PCL-C score cut-points to investigate if variables were consistently correlated with the outcome across the three scoring groups (Models 3-5, Table 4.4). The parsimonious model variables were used as described above. The SF 36 MCS and the IOC NIS were significant in each scoring group. The odds ratios for the IOC NIS are striking. For a one unit increase in the IOC NIS, the odds of being in the score of 30 or greater group increase by a factor of 14.21 (p<0.001). For the score of 38 or greater group, the odds increase by a factor of 7.81 (p=0.01), and for the score of 44 or greater group, the odds increase by a factor of 37.09 (p=0.008).

4.4.5 Exploration of Impact of Cancer negative sub-scales

We explored which subscales in the IOC NIS were significantly associated with the PCL-C. The four NIS sub-scales (AC, BC, LI, and W) were included as independent variables in a regression model. Two of the sub-scales, LI and W, were consistently significantly correlated across all four models, with odds ratios ranging from 1.37 to 27.80 (Table 4.5). It should be noted that the confidence intervals became quite large for the estimates in the PCL-C score cut-point groups of 38 and above and 44 and above. This indicates instability, in this case due to the small cell sizes for these two groups.

4.5 Discussion

This study examines PTSD symptoms in a sample of long-term cancer survivors, including an investigation of the relative contribution of variables identified in the literature as associated with PTSD symptoms, and an exploration of the relationship between endorsing PTSD symptoms and the Impact of Cancer scale. Two scoring methods for PTSD symptoms were examined, the total score for the PCL-C, and scoring cut-points. The overall prevalence of PTSD symptoms in this sample is similar to other study findings.[10,46] In our study, the mean PCL-C score was 27 (SD 9), and 29% of the sample scored 30 and above, 13% scored 38 and above, and 7% scored 44 and above. These results are interesting given that the mean time since diagnosis in this sample is eleven years, indicating that PTSD symptoms persist for several years for some survivors. Other studies have found that the prevalence of PTSD symptoms in cancer survivors can decline in the years after diagnosis and treatment but can persist over a long time interval.[47-49]

In this sample, demographic factors such as gender, education, and race were not significantly associated with PCL-C scores in bivariate and/or multivariate analyses. Only marital status and income were significant in the full multivariate regression model, and neither variable remained consistently significant in the scoring cut-point models. The PTSD literature has not shown a consistent pattern regarding demographic variables (Table 4.1). In the studies shown in Table 4.1, education was significant in five of ten studies that included education as a variable, and income was significant in three of six studies that included income as a variable. Cancer-specific variables such as cancer type, cancer stage, and treatment type tend to be non-significant in studies of PTSD symptoms and cancer survivors. In our study these and other

cancer-related variables (age at diagnosis, childhood cancer, multiple cancer diagnoses) were also found to be non-significant.

The comparison of the full and parsimonious models (Table 4.4, Models 1 and 2) shows that there is no difference in the explanation of variance between the full model, which includes six demographic variables (age, gender, race, education, income, and marital status),seven cancer characteristic variables (age at diagnosis, years since diagnosis, multiple diagnoses, childhood cancer diagnosis, chemotherapy, radiation, and surgery), plus the psychosocial variables, and the parsimonious model, which includes only three demographic variables (race, income, and marital status), no cancer characteristic variables, and the psychosocial variables (R^2=0.62 vs. R^2=0.62).

The psychosocial variables (depression, social support, SF-36 MCS, and IOC NIS) were significantly associated with PCL-C scores in the full and parsimonious linear models with the PCL-C score as a continuous outcome (Table 4.4). In the three score cut-point models, only the SF-36 MCS and the IOC NIS were significant at all three score cut-points. Use of the elaboration model allowed for an examination of spuriousness in the relationship between the PCL-C score, the IOC NIS, and the SF-36 MCS. The results indicate that the IOC NIS is an important correlate of PTSD symptoms even when including the SF-36 MCS in the model. The IOC NIS has high odds ratios (7.81 to 37.09) in all three cut-point models, indicating a substantial relationship with PCL-C scores.

Our exploration of the IOC NIS subscales revealed that two of the four subscales, Life Interference (LI) and Worry (W), were consistent significant correlates of high PCL-C scores in each of the four regression models (Table 4.5). This is an important finding that should be replicated in future studies. Example items from these two subscales include: “I feel like cancer runs my life” (LI), “Having had cancer has made me feel like some people do not understand

me" (LI), "I feel like time in my life is running out" (W), and "Having had cancer makes me feel unsure about my future" (W). Our results are similar to recent findings by Smith et al who showed that the IOC NIS was strongly associated with PTSD symptoms in a longitudinal study of long-term survivors of non-Hodgkin's lymphoma.[29] Smith also found that three of the four IOC NIS sub-scales were significantly associated ($p<0.05$) with persistent PTSD symptoms: Life Interference, Worry, and Appearance Concerns.[29] The items included in the IOC NIS sub-scales are issues that could be addressed in survivorship care visits and within primary care as well as with referral to mental health professionals. The PCL-C could be an important tool for use in clinical practice to identify those at risk for developing sustained PTSD symptoms after cancer treatment.

This study has several limitations: a cross-sectional survey design, lack of comparison group, a sample of cancer survivors from only one academic medical center, and non-response bias. The cross-sectional design provides only a snapshot of this sample, which limits our ability to conclude that the presumed stressor, cancer, caused the outcome, PTSD symptoms. However, based on the literature and our study results which indicate that the IOC has a strong relationship with PTSD symptoms, it is reasonable to assume that PTSD symptoms followed the cancer diagnosis. Although the inclusion of a non-cancer comparison group would be useful, the estimates of PTSD in the general population provide a reference estimate. Our sample had higher prevalence of PTSD (7% to 29%, depending on scoring method) than is reported for the general population (4% to 7%).[23] Our sample is drawn from a single academic center, potentially limiting the generalizability of the results, although similar results regarding the relationship of PTSD symptoms and the IOC NIS have been reported.[29] Non-response bias is also a potential limitation. Responders were more likely to have been diagnosed with cancer as an adult versus

diagnosed as a child before the age of 18, more likely to be female, and more likely to be white. It is possible that these differences led to biased results. This is of particular concern with those diagnosed before the age of 18, as other studies have found an estimated prevalence of PTSD of 16-25% in adult survivors of childhood cancers.[16,50,51]

In conclusion, we used a standardized assessment tool for detection of PTSD symptoms, finding that this is a persistent problem for some cancer survivors. In addition, the negative impact summary scale of a widely used and evaluated cancer-specific survivorship questionnaire, the IOC, was found to have a strong relationship to endorsing PTSD symptoms. In particular, the study results indicate that the IOC NIS subscales of Life Interference and Worry are strongly associated with PTSD symptoms in this sample. The prevalence of PTSD symptoms in this sample suggest that the PCL-C should be used to identify cancer survivors at risk for developing PTSD symptoms, and the IOC should be used to develop relevant interventions for this population.

Chapter 4 Tables

Table 4.1: Correlates of risk factors in multivariate analysis for developing post-traumatic stress disorder symptoms after cancer

	Study author, year, cancer type, and sample size; significance at p<0.05 level					
Risk Factor	**Cordova et al 1995: Breast cancer (N=55)[52]**	**Alter et al 1996: Mixed disease (N=27)[53]**	**Andrykowski 1998: Breast cancer (N=82)[12]**	**DuHamel et al 2004: BMT/SCT survivors (N=236)[54]**	**Kangas et al 2005: Head, neck, lung (N=82)[19]**	**Rourke et al 2006: Adult survivors of childhood cancer (N=182)[16]**
Age at study	Significant	NS	-	Significant	NS	NS
Education	Significant	-	NS	NS	-	NS
Income	Significant	-	-	NS	-	-
Marital status	NS	-	-	NS	NS	NS
Race/ethnicity	-	-	-	NS	-	NS
Gender	-	-	-	NS	NS	Significant
Employment	-	-	-	NS	-	NS
Cancer type	-	NS	-	NS	-	NS
Cancer stage	NS	NS	Significant	-	-	-
Time since treatment	NS	NS	Significant	NS	-	NS
Age at diagnosis	-	-	NS	-	-	NS
Treatment type	NS	NS	NS	NS (BMT type)	NS	Significant
Cancer recurrence	-	-	-	-	-	-
Social support	-	-	Significant	-	-	-
Anxiety	-	-	-	-	NS	NS
Depression	-	-	-	-	NS	NS
Intrusive thoughts	-	-	-	-	NS	-

	Study author, year, cancer type, and sample size; significance at p<0.05 level					
Risk Factor	**Smith et al 2008: NHL (N=886)[14]**	**Stuber el al 2010: Adult survivors of childhood cancer (N=6542)[15]**	**Palgi et al 2010*: Gastric cancer (N=123)[18]**	**O'Connor et al 2011: Breast cancer (N=3343)[13]**	**Gonçalves et al 2011: Ovarian cancer (N=121)[49]**	**Vin-Raviv et al 2013: Breast cancer (N=1139)[55]**
Age at study	Significant	Significant	NS	Significant	Significant	-
Education	Significant	Significant	-	Significant	NS	NS
Income	NS	Significant	-	Significant	-	NS
Marital status	-	Significant	Significant	NS	NS	NS
Race/ethnicity	Significant	NS	-	NS	-	Significant
Gender		NS	Significant	-	-	-
Employment		Significant	-	Significant	NS	-
Cancer type	-	NS	-	-	-	-
Cancer stage	NS	-	NS	-	NS	NS
Time since treatment	Significant	-	-	-	NS	-
Age at diagnosis	-	-	-	-	-	Significant
Treatment type	NS	Significant	-	Significant	NS	NS
Cancer recurrence	NS	NS	-	-	-	-
Social support	Significant	-	Significant	-	-	-
Anxiety	-	-	-	-	-	-
Depression	-	-	Significant	-	-	-
Intrusive thoughts	-	-	-	-	-	-

*Bivariate analysis only

Abbreviations: NS: Non-significant; YA: Young adult; BMT: Bone marrow transplant; SCT: Stem cell transplant

Table 4.2: Demographic, medical, and psychosocial characteristics of sample, N=162

Variable	Number or percent
Age at enrollment	
Mean	51
SD	16
Range	[18, 88]
Gender	
Male	15%
Female	85%
Race/Ethnicity	
White	74%
Black (non-Hispanic)	3%
Asian (non-Hispanic)	9%
Latino/Hispanic	12%
Other (non-Hispanic)	3%
Years since diagnosis	11
Mean	10
SD	[1, 44]
Range	
Education	
Less than high school	2%
High school graduate/GED	1%
Some college	22%
College graduate	34%
Graduate degree	40%
Income (annual)	
Under $15,000	6%
$16,000-$30,000	7%
$31,000-$60,000	18%
$61,000-$100,000	21%
Over $100,000	48%
Marital status	
Married	55%
Living with partner	7%
Widowed	4%
Divorced	11%
Never married	22%
Age at diagnosis	
Mean	40
SD	20
Range	[0, 78]
Cancer type	
Breast	60%
Colorectal	1%
Lung	2%
Blood, adult (leukemia/lymphoma)	8%
Adult survivor of pediatric cancer	25%
Other	4%

More than one cancer diagnosis type (% yes)	20%
Cancer treatment	
Surgery	82%
Chemotherapy	70%
Radiation	75%
Low social support (ESSI) (% yes)	24%
Depression (CES-D score of 16 or above) (% yes)	27%
SF-36 PCS	
Mean	49
SD	10
Range	[15, 65]
SF-36 MCS	
Mean	49
SD	11
Range	[13, 66]
Impact of Cancer	
Negative Impact Scale (NIS)	
Mean	2.74
SD	0.77
Positive Impact Scale (PIS)	
Mean	3.84
SD	0.64
PCL-C total score (score 17-85)	
Mean	27
SD	9
Range	[17, 64]
PCL-C cut-points	
Scored 30 and above	29%
Scored 38 and above	13%
Scored 44 and above	7%

Abbreviations:

SD: Standard deviation

ESSI: ENRICHD Social Support Instrument

CES-D: Center for Epidemiologic Studies Depressive Symptoms instrument

SF-36 PCS: Physical Component Summary Score

SF-36 MCS: Mental Component Summary Score

PCL-C: Post-traumatic stress disorder Checklist-Civilian version

Table 4.3: Bivariate associations of demographics, medical characteristics, and psychosocial variables with post-traumatic stress disorder Checklist-Civilian version (PCL-C) total score

Variable	Number patients	*PCL-C Score* Mean	Standard Deviation	Correlation (r)	P-value
Age at enrollment, years				-0.168	0.03
Gender					
Male	25	26.2	8.6		0.60
Female	137	27.2	9.1		
Race					
White	119	25.9	7.8		0.008
Non-white	43	30.2	11.1		
Black	4	26.0	6.4		0.82
Asian	15	31.4	10.2		0.05
Hispanic/Latino	18	27.7	2.0		0.74
Other	6	37.2	16.9		0.005
Years since diagnosis				0.045	0.57
Education					
Less than high school	3	25.3	4.6		0.74
High school graduate/GED	2	18	1.4		0.16
Some college	36	27.3	8.8		0.84
College graduate	55	26.6	8.3		0.67
Graduate degree					
Income (annual)					
< $15,000	9	30.2	11.0		0.28
$16,000 - $29,999	11	27.7	8.9		0.80
$30,000 - $59,999	30	32.3	11.7		0.004
$60,000 - $99,999	32	25.3	7.4		0.23
>/= $100,000	78	25.2	7.5		0.01
Marital Status					
Married	91	26.6	9.3		0.50
Living with partner	12	23.8	8.2		0.19
Widowed	5	22.6	6.4		0.27
Divorced/separated	18	27.5	8.0		0.82
Never married	36	29.6	8.9		0.05
Age at diagnosis, years				-0.156	0.05
Breast cancer					
Yes	96	26.4	9.0		
No	66	27.9	9.1		0.31
Lung cancer					
Yes	3	33.3	13.6		
No	159	26.9	8.9		0.23
Blood, adult (leukemia/lymphoma)					
Yes	12	31.83	10.4		
No	150	26.7	8.8		0.07
Childhood cancer survivor					

Yes	40	27.8	9.0		
No	122	26.8	9.1		0.54
Multiple diagnoses					
Yes	32	28.0	9.6		0.52
No	132	26.8	8.9		
Chemotherapy					
Yes	113	27.8	9.1		0.13
No	49	25.4	8.8		
Radiation					
Yes	121	26.9	9.2		0.75
No	41	27.4	8.6		
Surgery					
Yes	132	26.8	8.9		0.51
No	30	28.0	9.8		
Social support (ESSI)					
High support	123	25.3	7.5		0.000
Low support	39	32.5	11.2		
Depressive symptom score (CES-D)					
Score less than 16	119	23.7	5.6		0.000
Score 16 and above	43	36.2	10.1		
SF-36 PCS				-0.374	0.000
SF-36 MCS				-0.620	0.000
IOC PIS				0.103	0.191
IOC NIS				0.628	0.000

Abbreviations:
ESSI: ENRICHD Social Support Instrument
CES-D: Center for Epidemiologic Studies Depressive Symptoms instrument
SF-36 PCS: Physical Component Summary Score
SF-36 MCS: Mental Component Summary Score
IOC PIS: Impact of Cancer Positive Impact Summary Score
IOC NIS: Impact of Cancer Negative Impact Summary Score

Table 4.4: Multivariate linear and logistic regression of post-traumatic stress disorder Checklist-Civilian version (PCL-C) scores, full and parsimonious models

Model 1: Full Model with Continuous PCL-C Score as Outcome (R^2=0.61)				
	Coefficient	Standard Error	P-value	95% Confidence Interval
Age at enrollment	-12.34	10.58	0.25	[-33.24, 8.57]
Gender	0.03	1.49	0.99	[-2.93, 2.99]
Non-white race	1.44	1.19	0.23	[-0.92, 3.81]
Years since diagnosis	12.39	10.58	0.24	[-8.53, 33.30]
Education				
< college degree	-0.05	1.43	0.97	[-2.88, 2.77]
College degree	-0.23	1.14	0.84	[-2.49, 2.03]
Annual Income				
< $60k	2.96	1.43	0.04	[0.12, 5.80]
< $99k	0.97	1.30	0.46	[-1.61, 3.55]
Married	2.24	1.16	0.05	[-0.05, 4.54]
Age at diagnosis	12.33	10.57	0.25	[-8.57, 33.22]
Childhood survivor	-0.28	2.58	0.92	[-5.38, 4.83]
Multiple diagnoses	-1.38	1.45	0.34	[-4.25, 1.48]
Chemotherapy	-0.00	1.15	0.99	[-2.27, 2.27]
Radiation	-0.70	1.18	0.55	[-3.04, 1.63]
Surgery	1.09	1.49	0.46	[-1.85, 4.04]
ESSI	-2.42	1.28	0.06	[-4.96, 0.11]
CES-D	4.48	1.59	0.005	[1.34, 7.62]
SF-36 MCS	-0.20	0.07	0.003	[-0.33, -0.07]
IOC PIS	1.06	0.81	0.19	[-0.53, 2.66]
IOC NIS	4.21	0.77	0.000	[2.69, 5.73]
Model 2: Parsimonious Model with Continuous PCL-C Score as Outcome (R^2=0.61)				
	Coefficient	Standard Error	P-value	95% Confidence Interval
Non-white race	1.31	1.11	0.24	[-0.90, 3.51]
Annual Income				
< $60k	2.75	1.27	0.03	[0.24, 5.25]
< $99k	0.83	1.24	0.51	[-1.62, 3.28]
Married	2.22	1.07	0.04	[0.11, 4.33]
ESSI	-2.44	1.16	0.04	[-4.73, -0.15]
CES-D	4.59	1.51	0.003	[1.6, 7.58]
SF-36 MCS	-0.21	0.06	0.001	[-0.33, -0.09]
IOC PIS	0.80	0.74	0.28	[-0.67, 2.26]
IOC NIS	4.17	0.72	0.00	[2.75, 5.59]
Likelihood ratio test of full model compared to parsimonious model: Prob > chi2 = 0.9790				
Model 3: Parsimonious Model with Bivariate PCL-C Score of 30 or Greater as Outcome (pseudo R^2=0.57)				
	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Non-white race	1.95	1.25	0.29	[0.56, 6.84]
Annual Income				

< $60k	1.61	1.22	0.53	[0.36, 7.09]
< $99k	1.07	0.88	0.93	[0.21, 5.40]
Married	1.03	0.67	0.96	[0.29, 3.70]
ESSI	0.16	0.10	0.005	[0.04, 0.58]
CES-D	3.35	2.73	0.14	[0.68, 16.57]
SF-36 MCS	0.91	0.04	0.03	[0.84, 0.99]
IOC PIS	3.07	1.59	0.03	[1.12, 8.47]
IOC NIS	14.21	8.94	0.000	[4.14, 48.75]
Model 4: Parsimonious Model with Bivariate PCL-C Score of 38 or Greater as Outcome (pseudo R^2=0.61)				
	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Non-white race	0.62	0.58	0.61	[0.10, 3.91]
Annual Income				
< $60k	21.97	25.40	0.008	[2.28, 211.82]
< $99k	0.57	0.80	0.69	[0.04, 8.94]
Married	3.39	3.07	0.18	[0.58, 19.97]
ESSI	0.81	0.75	0.83	[0.13, 5.00]
CES-D	5.52	5.88	0.11	[0.68, 44.52]
SF-36 MCS	0.89	0.05	0.03	[0.81, 0.99]
IOC PIS	2.98	2.13	0.13	[0.73, 12.10]
IOC NIS	7.81	6.24	0.01	[1.63, 37.38]
Model 5: Parsimonious Model with Bivariate PCL-C Score of 44 or Greater as Outcome (pseudo R^2=0.61)				
	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Non-white race	2.94	3.19	0.32	[0.35, 24.68]
Annual Income				
< $60k	27.29	37.61	0.02	[1.83, 403.37]
< $99k	0.86	1.67	0.94	[0.02, 39.37]
Married	24.02	31.93	0.02	[1.78, 325.02]
ESSI	2.89	3.92	0.43	[0.20, 41.12]
CES-D	1.18	1.52	0.90	[0.95, 14.68]
SF-36 MCS	0.90	0.05	0.07	[0.81, 1.01]
IOC PIS	6.27	6.29	0.08	[0.88, 44.86]
IOC NIS	37.09	50.88	0.008	[2.52, 545.46]

Reference groups: Annual income: $100k or greater; Education: Graduate degree
Abbreviations:
ESSI: ENRICHD Social Support Instrument
CES-D: Center for Epidemiologic Studies Depressive Symptoms instrument
SF-36 MCS: Mental Component Summary Score
IOC PIS: Impact of Cancer Positive Impact Summary Score
IOC NIS: Impact of Cancer Negative Impact Summary Score

Table 4.5: Examination of the associations of Impact of Cancer Negative Item Sub-Scales (NIS) (Appearance, Body Changes, Life Interference, and Worry) with the post traumatic stress disorder Checklist-Civilian version (PCL-C) in multivariate linear and logistic regression models

Model 1: Parsimonious Model with Continuous PCL-C Score as Outcome (R^2=0.65)				
	Coefficient	Standard Error	P-value	95% Confidence Interval
Non-white race	1.70	1.07	0.12	[-0.42, 3.82]
Annual Income				
< $60k	1.74	1.27	0.17	[-0.76, 4.24]
< $99k	0.03	1.21	0.98	[-2.36, 2.41]
Married	2.69	1.04	0.01	[0.65, 4.74]
ESSI	-2.37	1.11	0.03	[-4.56, -0.18]
CES-D	4.94	1.46	0.001	[2.05, 7.83]
SF-36 MCS	-0.19	0.06	0.002	[-0.31, -0.07]
IOC PIS	0.41	0.71	0.56	[-0.99, 1.82]
IOC NIS_ Appearance	-0.77	0.47	0.10	[-1.70, 0.16]
IOC NIS_ Body Changes	-0.17	0.54	0.75	[-1.24, 0.90]
IOC NIS_ Life Interference	3.96	0.74	0.000	[2.49, 5.42]
IOC NIS_ Worry	1.37	0.57	0.02	[0.23, 2.50]
Model 2: Parsimonious Model with Bivariate PCL-C Score of 30 or Greater as Outcome (pseudo R^2=0.61)				
	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Non-white race	1.90	1.31	0.35	[0.50, 7.30]
Annual Income				
< $60k	1.26	1.06	0.78	[0.24, 6.58]
< $99k	0.72	0.63	0.70	[0.13, 3.97]
Married	1.28	0.91	0.72	[0.32, 5.12]
ESSI	0.14	0.10	0.007	[0.03, 0.58]
CES-D	4.16	3.85	0.12	[0.68, 25.49]
SF-36 MCS	0.91	0.04	0.03	[0.83, 0.99]
IOC PIS	2.95	1.72	0.04	[0.94, 9.23]
IOC NIS_ Appearance	0.88	0.32	0.73	[0.44, 1.78]
IOC NIS_ Body Changes	1.12	0.39	0.75	[0.56, 2.22]
IOC NIS_ Life Interference	7.99	4.44	0.000	[2.69, 23.71]
IOC NIS_ Worry	2.18	0.90	0.05	[0.98, 4.89]
Model 3: Parsimonious Model with Bivariate PCL-C Score of 38 or Greater as Outcome (pseudo R^2=0.73)				
	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Non-white race	1.56	0.25	0.17	[0.21, 1.32]
Annual Income				
< $60k	34.18	56.32	0.03	[1.19, 38.56]
< $99k	0.35	0.61	0.55	[0.01, 11.01]
Married	7.10	8.82	0.11	[0.62, 80.97]

ESSI	6.66	9.88	0.20	[0.36, 122.22]
CES-D	41.20	74.06	0.04	[1.22, 139.25]
SF-36 MCS	0.87	0.06	0.03	[0.74, 0.98]
IOC PIS	5.37	5.58	0.11	[0.70, 41.19]
IOC NIS_ Appearance	0.53	0.24	0.17	[0.21, 1.32]
IOC NIS_ Body Changes	0.42	0.26	0.15	[0.13, 1.39]
IOC NIS_ Life Interference	27.80	34.49	0.007	[2.44, 316.28]
IOC NIS_ Worry	6.78	6.01	0.03	[1.19, 38.56]
Model 4: Parsimonious Model with Bivariate PCL-C Score of 44 or Greater as Outcome (pseudo R^2=0.70)				
	Odds Ratio	Standard Error	P-value	95% Confidence Interval
Non-white race	9.86	12.39	0.07	[0.84, 115.56]
Annual Income*	0.25	0.16	0.03	[0.07, 0.87]
Married	66.24	120.56	0.02	[1.87, 234.56]
ESSI	2.25	3.00	0.54	[0.17, 30.65]
CES-D	5.36	8.40	0.29	[0.28, 115.90]
SF-36 MCS	0.93	0.05	0.18	[0.83, 1.04]
IOC PIS	7.08	8.42	0.10	[0.69, 72.81]
IOC NIS_ Appearance	0.72	0.31	0.44	[.031, 1.67]
IOC NIS_ Body Changes	0.77	0.53	0.71	[0.20, 2.95]
IOC NIS_ Life Interference	5.24	4.38	0.05	[1.02, 27.01]
IOC NIS_ Worry	10.75	11.36	0.03	[1.35, 85.31]

*Cells too small to support inclusion of individual dummy variables for income

Abbreviations:

ESSI: ENRICHD Social Support Instrument

CES-D: Center for Epidemiologic Studies Depressive Symptoms instrument

SF-36 MCS: Mental Component Summary Score

IOC PIS: Impact of Cancer Positive Impact Summary Score

IOC NIS: Impact of Cancer Negative Impact Summary Score

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CHAPTER 5:

Conclusion of dissertation research

This dissertation explored issues related to post-treatment cancer survivorship care. Multiple data sources including interview data, administrative data, medical record abstraction, and patient reported outcome data were used to conduct the three studies that make up this dissertation: 1) use of guideline-recommended and non-recommended post-treatment health services in breast cancer survivors; 2) a qualitative exploration of oncology and primary care provider expectations and perceptions of breast cancer post-treatment care delivery; and 3) patient reported post-traumatic stress symptoms and the impact of cancer in a heterogeneous sample of cancer survivors. Several methodologies were employed to explore the data from these studies, including qualitative data analysis, multi-level modeling, elaboration models, and Kaplan-Meier estimates. This chapter briefly summarizes the findings from these three studies and reviews study limitations. A discussion of potential next steps and future research opportunities based on study findings concludes this chapter.

5.1 Use of post-treatment health services in breast cancer survivors: findings

Results from the first study of this dissertation show that breast cancer survivors treated and followed at an academic medical center are not consistently receiving ASCO guideline recommended mammograms.[1] Only 47% of the study sample received a mammogram within one year of cessation of active treatment. It is possible that some patients received mammograms elsewhere and the service was not captured in the study. However, only 52% of HMO-insured patients received a mammogram within the first year. HMO-insured patients generally receive

care at a single institution. The fact that the HMO-insured patients fell well short of the ASCO guideline indicates that this is a pervasive problem. Other studies of post-treatment use of mammograms have similar findings.[2-5]

While some patients in this sample did not receive appropriate post-treatment care, many patients received non-recommended post-treatment care. The ASCO guidelines specifically recommend against using imaging services, such as positron emission tomography (PET) and computerized tomography (CT) scans, and biomarker tests.[1] Use of these non-recommended services was common in this sample: 67% of the sample received at least one non-recommended imaging service, and 80% of the sample received at least one non-recommended biomarker test. Imaging services were categorized as surveillance or diagnostic based on medical record review. Fifty-five percent of the sample received at least one non-recommended imaging test that was classified as surveillance. Classification of surveillance was based on either an active statement of surveillance in the associated physician note or the lack of a definitive statement of a new symptom or problem. It should be noted that this strategy may have lead to the miss-classification of some imaging services and an overestimation of surveillance services. These non-recommended tests are not harmless. There are potential harms from radiation exposure, false positive and false negative results, and increased patient anxiety.[6,7] There are also financial costs of these non-recommended and potentially harmful services including patient costs, such as health insurance co-payments, and costs to the larger health care system.

Several variables were significantly associated with receiving non-recommended services in this sample, such as higher stage disease, and younger age at diagnosis. Main treating physician was consistently significant in models analyzing use of non-recommended imaging (19% of the variance), use of non-recommended biomarker tests (22% of the variance), and use

of mammograms (56% of the variance), meaning that some physicians had greater proclivity for use of these services than others. This finding suggests that understanding and influencing provider perception, behavior, and motivation could lead to increased adherence to guideline-recommended care for this population. This patient population has already had one significant health event, breast cancer, and it is critical to ensure that they receive evidence-based post-treatment screening and preventive care.

5.2 Provider perceptions and expectations of post-treatment breast cancer care delivery: findings

The second study of this dissertation examined the provider point of view regarding post-treatment care delivery for breast cancer patients. Interviews with oncology and primary care providers at five academic medical centers provided insight into some of the drivers of provider behavior during this phase of care. The results indicate that care coordination is a critical element during post-treatment care. Care coordination between primary and oncology care was frequently mentioned as the ideal method to deliver post-treatment care. Participants also identified the lack of care coordination within oncology specialties (medical oncology, radiation oncology, surgical oncology) as a significant problem. Participants reported that there was no simple way to communicate or coordinate care within or across specialties and lack of coordination was seen as a potential driver of use of unnecessary services.

Participants also reported the expectation of using non-recommended services (imaging, biomarker tests) as part of routine post-treatment care. The lack of care coordination was again cited as a potential reason; participants perceived gaps in their knowledge of what other providers were ordering that sometimes lead to confusion and potentially duplication of services,

and if a service had been ordered in the past it was likely to be ordered in the future, even if the indication for the service was unclear (e.g. PET scans). It is interesting to note that the expected course of post-treatment care delivery did not vary much based on the risk profiles of the three case vignettes presented to the providers as part of the interview process. These results indicate that providers perceive lack of care coordination as a major issue in post-treatment care delivery, and that combined strategies of systems- and provider-level interventions aimed at improving care coordination are needed.

5.3 The prevalence of post-traumatic stress symptoms and associated risk factors in cancer survivors treated at an academic medical center: findings

The final study of this dissertation examined post-traumatic stress symptoms in a sample of cancer survivors treated at an academic survivorship center. Study results show that between 7%-29% of the sample had Post-traumatic Stress Disorder Checklist-Civilian Version (PCL-C) scores indicating post-traumatic stress disorder (PTSD) symptoms, depending on the scoring method used. Examination of potential correlates of PTSD symptoms in this sample revealed that psychosocial variables (depression, social support, impact of cancer) explained more of the variance than demographic (e.g. gender, age) or cancer characteristic (e.g. stage, treatment type) variables, although income and marital status were significant in some of the models. The literature on PTSD and cancer survivors found inconsistent patterns of associations with PTSD.[8-11] The Impact of Cancer Scale, v.2 (IOC), emerged as an important correlate of PTSD symptoms in this sample. In particular, higher scores on two sub-scales of the negative impact summary scale, Life Interference and Worry, were highly associated with PCL-C scores indicating PTSD symptoms. This finding is concordant with a larger, longitudinal study of non-Hodgkin's

lymphoma survivors, which showed that the IOC NIS was significantly associated with persistent PTSD symptoms as measured by the PCL-C.[12] These results suggest that the PCL-C, which is a short, publically accessible screening tool, may be useful in clinical practice to identify those at risk for developing PTSD symptoms. Further research in this area is called for, ideally a longitudinal study of the IOC and PTSD symptoms in cancer survivors who have recently completed active treatment.

5.4 Limitations of this research

There are several limitations of this research to be acknowledged. Sample size is a potential limitation for two of the three studies. Study #1 used a convenience sample of 258 breast cancer patients treated and followed at an academic center, and study #3 used a sample of 162 cancer survivors treated at an academic survivorship center. The small sample sizes and single institution source limit statistical power, generalizability of the findings to other settings, and the ability to make inferences about study results. This is particularly noticeable in study #3, which uses three different score cut-points as outcomes. The third cut-point is extreme, and the resulting analysis relied on small cell sizes, resulting in large confidence intervals. However, these small sample sizes allow for in-depth exploration of data, such as the medical record abstraction conducted as part of study #1. Another potential problem for study #1 and study #3 is selection bias. The participants in these studies chose to obtain their cancer care at an academic medical center. Cancer patients cared for at an academic center may have different characteristics than those cared for at community-based centers, and these differences may bias the results. For example, it is possible that the participants in study #3 who chose to access post-treatment follow-up care at an academic survivorship center have more symptoms (e.g. long-

term and late effects) of their disease and treatment and are thus more likely to seek care at an academic center.

Generalizability of results is a potential limitation for all three studies. Studies #1 and #3 have samples from a single academic center, and while study #2 has a sample from five academic centers, all of the centers are part of the University of California system. The data obtained in these studies are only referable to the academic medical care setting and lack the community perspective, where the vast majority of cancer survivors are cared for. Each of these studies should be considered exploratory and hypothesis generating with the expectation that these results will be used to guide the development and implementation of more definitive research studies in other health systems with larger study samples. In addition, these preliminary findings may serve as a catalyst for implementation of quality improvement strategies to enhance the delivery of high quality care to the growing number of cancer survivors.

5.5 Implications for future research

Results from these three studies describe some of the challenges in delivery of high quality care to cancer survivors. Significant gaps in the delivery of guidelines concordant post-treatment care for breast cancer survivors were identified, including overuse of non-recommended services and underuse of mammograms. There is a lack of care coordination within oncology specialties and between oncology and primary care that health care providers perceive as a significant barrier to appropriate post-treatment care delivery. PTSD was identified in 7%-29% of cancer survivors, representing the persistent effects of cancer and cancer treatment that require assessment and intervention. These results indicate the need for future research in all three content areas.

The results of study #1 and study #2 suggest that improving post-treatment care delivery is a multi-level process with many potential intervention targets. Research on reducing the use of non-recommended services and increasing the use of recommended mammograms is inherently tied to provider perceptions and expectations of post-treatment care. Targeting only one aspect of this issue, such as providing electronic reminders to providers about use of mammograms, is not likely to be effective in changing outcomes. Based on the results of these studies, improving care *coordination* is a key part of improving care *delivery*. Thus research on combining systems- and provider-level intervention is needed to shed light on these issues. For example, a multi-level intervention strategy of organizational/systems care coordination efforts (e.g. common electronic records and scheduling systems, multi-discipline clinics) combined with provider-targeted interventions (e.g. provider education, feedback on individual performance) could be tested in an integrated health delivery system.

The persistent effects of cancer and cancer treatment require continued research into effectively identifying and treating those at risk for both physical and mental health issues. The potential to identify cancer survivors at risk for developing serious psychosocial effects such as PTSD should be explored further. Some of the issues identified in this research that may have an effect on the development of PTSD symptoms, such as the IOC negative item sub-scales with questions about worry about recurrence, uncertainty about the future, and feeling misunderstood, could be addressed in cancer survivorship programs, oncology and primary care visits, and with referral to mental health practitioners. Asking these questions and exploring these issues will provide the information needed to improve health care for cancer survivors.

5.6 Conclusion

Cancer survivorship care is an important part of the cancer care continuum. Due to continuing advances in screening and treatment, the population of cancer survivors will continue to grow. Cancer survivors are at risk for many long-term consequences of their disease and treatment, and caring for this patient population represents many challenges. Study findings suggest that post-treatment care for cancer survivors is frequently not evidence based, and that psychosocial issues are not always addressed. High-quality survivorship care programs should be designed to allow the provision of appropriate care in a systematic way to all cancer survivors. Using a combination of qualitative, administrative, medical record, and patient reported data, this research showed that there are persistent gaps in survivorship care. These mixed-source approaches (e.g., administrative plus quantitative data) could be used in larger study settings in the future to quantify baseline survivorship services. This research provides several targets for future research and actionable items for clinical practice.

5.7 References

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