Breast Cancer Treatment-Completion: Can an Integrative Medicine Center Play a Role?

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DISSERTATION

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Dedication

This dissertation is dedicated to my late father who came with his family to this country from Austria in pursuit of the American Dream. His academic and professional success came through hard work and imagination, just as this dissertation was completed with hard work and imagination. I also dedicate this dissertation to my children, Liliana, Erika, and Franklin, for whom I wish a life filled with adventure as they pursue their dreams. You inspire me to work hard for a better world. Your wonder at the newness of life brings joy to me every day.

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ABSTRACT

Introduction: The survival of women with breast cancer depends on treatment-completion. We explored factors that promote treatment-completion and reduce aromatase inhibitor (AI) medication switching. We evaluated the effect of any Integrative Medicine (IM) clinic use on those outcomes.

Methods: Means, frequencies, modified Poisson regression analysis, and propensity score analysis were used to examine three samples of women with hormone receptor-positive breast cancer treated with taxane chemotherapy or hormone therapy between 1/1/2009-12/31/2019 at MD Anderson Cancer Center. Treatment-completion was defined as a relative dose-intensity(RDI) of ≥85% for chemotherapy, or ≥54 months with a hormone therapy prescription; AI switching was also assessed.

Sample: There were 508, 3764, and 2253 women in the chemotherapy, hormone therapy, and AI switching samples, respectively.

Results: We found that 53.1% of patients completed chemotherapy, 64.3% of patients completed hormone therapy, and 68.8% of patients took just one AI medication. Less pain (RR, 0.97; 95%CI, 0.95 to 0.98; $p<0.001$) and SF-12 PCS (RR 1.03; 95%CI: 1.02 to 1.05; $p<0.001$) were associated with increase probability of hormone therapy treatment-completion in bivariate analysis. Differences between IM clinic users and non-users were not statistically significant among the samples.

Discussion: Many women did not complete treatment. Two quality-of-life measures were related to hormone therapy treatment-completion. Treatment-completion of IM clinic users were not different from non-users. Some predictors of treatment-completion are changeable and warrant a central focus during treatment. Future research should include more IM treatments (e.g., 8 acupuncture treatments) for the inclusion criteria.

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CHAPTER 1 INTRODUCTION

Cancer is one of the most common illnesses in the United States with an estimated 1,898,160 new cancer cases, and more than 608,570 cancer-related deaths forecast to occur in 2021 (Siegel et al., 2021). Breast cancer is the most prevalent type of cancer among women and new breast cancers are expected to be 30% of all female cancer diagnoses in 2020 (Siegel et al., 2021). In addition, mortality attributed to breast cancer is expected to be 15% of all cancer deaths (Siegel et al., 2021). Untreated breast cancer often results in death within three years (Johnstone et al., 2000), while the 5-year survival rate for treated breast cancer is 90% (Siegel et al., 2021). Despite the longstanding findings on the importance of undergoing all cancer treatments as prescribed by oncologists (Hortobagyi et al., 1983), a sizable proportion of people do not complete their cancer treatment (Wagner et al., 2018), whether it is chemotherapy (Knisely et al., 2018), or hormone therapy (Hershman et al., 2011).

Receiving less than the optimal amount of cancer treatment is linked to increased risk of death. Cespedes Feliciano et al. (2020) found a 30% increased risk of death (hazard ratio (HR), 1.30; 95% confidence interval (CI), 1.02-1.65) among women whose relative dose intensity for their chemotherapy was less than 85%. Discontinuation of adjuvant endocrine therapy within 12 months significantly increased the risk of cancer-specific mortality (HR, 2.76; 95% CI, 1.74-4.38) (Farias & Du, 2017b). Hershman et al. (2011) found the 10-year survival to be 80.7% for women who continued their hormone therapy medication compared to 73.6% for women who discontinued early ($p < 0.001$). This demonstrates why breast cancer treatment-completion is critical.

This dissertation study examined treatment-completion for a sample of women treated at MD Anderson Cancer Center. Treatment-completion for chemotherapy is defined here as receiving at least 85% of the prescribed dose of all chemotherapy medications in the allotted time of treatment. Receiving less than 85% of chemotherapy medication in the prescribed timeframe is linked to significantly worse outcomes (Barcenas et al., 2012; Budman et al., 1998). Treatment-completion for hormone therapy in this study means receiving at least 54 months (close to the 60 months recommended) of hormone therapy medication. Worse outcomes are associated with receiving significantly less than the five-year recommended guidelines (Chirgwin et al., 2016; National Cancer Institute, 2011; National Comprehensive Cancer Network, 2019). The term treatment-completion is defined as an endpoint that results from medication taking persistence, and treatment-incompletion is an endpoint that results from medication taking discontinuation.

There is a growing body of evidence documenting the prevalence of treatment incompletion. One study from the University of Virginia Hospital investigating treatment-incompletion among women with breast cancer, found that 26% did not complete their chemotherapy treatment (Knisely et al., 2018). Completing hormone therapy to treat breast cancer is more often studied than chemotherapy treatment-completion, with findings frequently noting high treatment-incompletion rates (Guedes et al., 2017; Lash et al., 2006; Wagner et al., 2018). One study of women with health insurance in Northern California found that 31% of study participants discontinued their hormone therapy medication before completing treatment (Hershman et al., 2011). Another study of low-income Medicaid Insured women in North Carolina found 20% of the sample discontinued their hormone therapy medication within the first year of the five-year treatment (Kimmick et al., 2009).

Furthermore, a meta-analysis found hormone therapy discontinuation rates to range from 31% to 73% (Murphy et al., 2012), while a qualitative analysis descriptively characterized the many factors affecting hormone therapy persistence (Lambert et al., 2018). Cancer treatment-completion is so important that it affects life and death: as hormone therapy completion rates decrease, cancer mortality rates increase (Farias & Du, 2017b; Hershman et al., 2011).

Synopsis of Breast Cancer Treatment

When a person is diagnosed with breast cancer, they choose a plan to treat the cancer. Most women undergo surgery to remove the tumor (National Comprehensive Cancer Network, 2019). In some instances, multimodal chemotherapy is prescribed, either provided before (neoadjuvant) or after (adjuvant) surgery. Depending on the type of chemotherapy, an individual dose or cycle is given weekly, every 2 weeks, or every 3 weeks for up to 6 months, and all of the doses/cycles together is considered a course of chemotherapy (National Comprehensive Cancer Network, 2019). In addition to surgery and chemotherapy, radiation therapy can treat the breast after surgery and chemotherapy (National Comprehensive Cancer Network, 2019). Depending on the type of cancer, a patient may be prescribed hormone therapy for a total of five years or more, which is prescribed during or after the other cancer treatments listed above (National Comprehensive Cancer Network, 2019). Both estrogen receptor-positive (ER+) and progesterone-receptor positive (PR+) breast cancers are hormone-receptor positive (HR+) breast cancers (National Comprehensive Cancer Network, 2019). HR+ refers to both ER+ and PR+ breast cancers in this study. Finally, these treatments can be prescribed individually, all together, or in any combination (National Comprehensive Cancer Network, 2019).

Treatment-completion

What does treatment persistence, discontinuation, and completion mean? These terms describe following the instructions given by medical providers such as doctors and nurses regarding the frequency of taking the medication, the timing of medication taking, and the dosage received. Here, medication taking persistence is defined as the time from the beginning of a treatment until its ending (Cramer et al., 2008). Persistence ends when discontinuation of medication taking behavior begins (Fernandez Ortega et al., 2011). Chemotherapy treatment-completion is defined as receiving ≥ 85% of the prescribed chemotherapy medication over the prescribed time determined at the beginning of treatment, and it is measured as relative dose intensity (RDI) (Ferreira Filho et al., 2002). RDI is determined by calculating the actual chemotherapy dose delivered to a patient across all chemotherapy cycles over the actual time, and then that is divided by the planned dose delivered over the prescribed time decided upon at the beginning of treatment (Bonadonna & Valagussa, 1981; Budman et al., 1998; Ferreira Filho et al., 2002). Hormone therapy cancer treatment-completion is frequently defined as a patient taking the medication daily for at least five years (National Cancer Institute, 2011; National Comprehensive Cancer Network, 2019). This dissertation examined treatment-completion, and related terms of persistence and discontinuation, of taxane chemotherapies, and hormone therapies.

Factors Related to Treatment-completion

The importance of taking cancer medicine has sparked research exploring the factors associated with breast cancer treatment-completion. Examples of demographic factors that have been found to be associated with treatment-completion include an age younger than 50 related to early discontinuation (Hadji et al., 2013; Huiart et al., 2012), being married

associated with higher rates of treatment-completion (Hershman et al., 2010; Reyes et al., 2016), and being white race correlated with greater rates of treatment-completion (Odds Ratio (OR), 3.65; 95% CI, 1.30–10.30) (Knisely et al., 2018). Examples of medical factors that have been found to be correlated with treatment-completion/incompletion are not receiving chemotherapy (Hershman et al., 2010; Kemp et al., 2014), not receiving surgery (Kemp et al., 2014), receiving treatment in a general practitioner practice (Hadji et al., 2013), and being prescribed a taxane chemotherapy medication (Henry et al., 2012). These findings suggest that treatment-completion is complex, and many factors may promote and/or hinder treatment-completion.

Many cancer patients experience symptoms or pain from cancer, and/or side effects from cancer treatment, and these negative experiences are frequently correlated with treatment discontinuation (Chim et al., 2013; Speck et al., 2013; Wagner et al., 2018). One recent study found that 45% of women reported experiencing severe or very severe treatment-related toxicity from chemotherapy (Friese et al., 2017). These effects may be individual or occur in clusters (Miaskowski et al., 2006), with wide ranges of frequency for symptoms like pain (29-67%), sadness (48-79%), sleep problems (54-78%) and fatigue (48-90%) (Browall et al., 2016), and are important data for oncologists, because cancer-related side effects are correlated with treatment discontinuation (Lash et al., 2006; Nabieva, Kellner, et al., 2018; Wagner et al., 2018).

Rates of breast cancer chemotherapy treatment-completion among health-insured women have been found to be as low as 74% (Knisely et al., 2018), while Barcenas et al. (2012) found much higher rates of treatment-completion (83.5%). Speck et al. (2013) found that 24.5% of the participants in their study received a reduced amount of chemotherapy

medication to treat their non-metastatic breast cancer, because they were suffering from a treatment-related side-effect called peripheral neuropathy (nerve pain in the arms and legs). This resulted in a lower chemotherapy RDI over the entire course of treatment, and the total amount of medication received was significantly lower than among individuals who did not receive a dose adjustment (Speck et al., 2013). Worse outcomes are correlated with receiving a lower RDI of chemotherapy medication than initially planned at the beginning of treatment (Bonadonna et al., 1995; Early Breast Cancer Trialists' Collaborative Group, 2005; Sandy & Della-Fiorentina, 2013).

The importance of taking the full amount of chemotherapy medication cannot be overstated. Completing treatment is correlated with fewer difficulties associated with having cancer, and fewer cancer treatment-related side effects (Yee et al., 2017); less illness-burden from cancer, combined with fewer treatment-related side effects, often result in higher cancer survival rates (Zhang et al., 2018). Chemotherapy treatment-incompletion is related to low emotional social support and poor body image (Reyes et al., 2016), and having anxiety or depression (Neugut et al., 2016), while treatment-completion was correlated with moderate to high-intensity physical exercise in an intervention study about the role of physical activity on treatment-completion (van Waart et al., 2015). Treating the whole person, including symptoms could improve chemotherapy treatment-completion.

Discontinuation of hormone therapy increases over time (Ayres et al., 2014). Hershman et al. (2011) found that 31% of health insured women prematurely discontinued their hormone therapy before the prescribed end date. Study participants who do not complete treatment experience greater mortality (Farias & Du, 2017b; Hershman et al., 2011). Similar results were found in Canada, where 32% discontinued within four years of

starting aromatase inhibitor's (AI's) (Wagner et al., 2018). The daily challenge to consistently take medication over the course of five years is hard, with musculoskeletal symptoms (Henry et al., 2012; Kadakia et al., 2016), hormone therapy medication toxicities (Moscetti et al., 2015), and having more comorbidities (Owusu et al., 2008), among the factors correlated with hormone therapy treatment-incompletion.

Hormone Therapy Medication Switching

Many women switch hormone therapy medication early in treatment due to side effects. Switching hormone therapy medications in the first year of treatment was linked to early treatment discontinuation (HR, 1.50; 95% CI, 1.23 to 1.83) (He et al., 2015), and supported the findings of other research that identified medication switching as a factor linked to non-adherence and early discontinuation (Murphy et al., 2012). Another study found hormone therapy medication switching significantly associated with a lower medication-possession-ratio (95% CI, 5.4 to 9.4) (a key indication of non-adherence) (Trabulsi et al., 2014). Better understanding the role of hormone therapy medication switching on treatment-completion is needed.

Complementary, Alternative, and Integrative Medicine

Complementary and alternative medicine (CAM) might help people better complete their breast cancer treatment. CAM has been a part of National Cancer Institute (NCI) funded research since the 1940's (National Cancer Institute, 2018). CAM is defined as "Any medical system, practice, or product that is not thought of as standard (medical) care" (National Cancer Institute, 2012a). Standard medical care is treatment widely used by health care professionals (National Cancer Institute, 2019), and the standard medical care treatments discussed here are chemotherapy and hormone therapy. Complementary medicine (CM) is a

non-standard cancer treatment that occurs in conjunction with usual cancer treatment, whereas alternative medicine is a non-standard cancer treatment that is used instead of usual cancer treatment (National Cancer Institute, 2012a) and is beyond the scope of this study. Integrative medicine (IM) is a subset of CM and is defined here as only the complementary treatments that have a history of demonstrable evidence of safety and benefit to people with cancer to support standard cancer treatments (National Cancer Institute, 2012a) and is the focus of this study.

IM is increasingly incorporated into cancer treatment (Boon et al., 2007), is used by nearly 80% of cancer survivors (John et al., 2016), and was most frequently used by women with breast cancer-86.5% in 2002 (Patterson et al., 2002) and 93% in 2016 (Luo & Asher, 2016). IM is often used after diagnosis and during active cancer treatment (Luo & Asher, 2016). IM has successfully reduced the negative effects of cancer and cancer treatment, including reductions in anxiety and depression (Goyal et al., 2014; Wurtzen et al., 2013), dry mouth (Pfister et al., 2010), pain (Cramer, Lauche, Haller, et al., 2013; Cramer, Lauche, Hohmann, et al., 2013; Goyal et al., 2014; Mao et al., 2014; Pfister et al., 2010), nausea and vomiting (Garcia et al., 2013), and fatigue (Chandwani et al., 2014; Taso et al., 2014). Given the benefit to patients by reducing disease/treatment effects, integrative medicine treatments, in conjunction with current best practices of cancer treatment, could improve treatment-completion rates.

Many different treatments fall under the IM umbrella including alternative medical systems (e.g. Traditional Chinese medicine or Ayurveda), exercise therapies, mind-body interventions, and nutrition counseling (National Cancer Institute, 2012b). Some treatments address symptoms and factors that have been empirically connected to breast cancer

treatment-completion. Mao et al. (2014) found acupuncture, an integrative medical treatment, produced lasting reduction of arthralgia (joint pain) among women with breast cancer receiving AI's. Arthralgia is a treatment side effect correlated with treatment discontinuation (Moscetti et al., 2015). Although prescribed to treat factors associated with treatment discontinuation, few studies have included treatment-completion findings while examining IM treatments.

Lifestyle interventions, defined here as being made up of multiple IM categories (frequently diet, exercise, and mind-body interventions), have been well received by cancer patients (Arun et al., 2017). One study reducing caloric intake and increasing regular exercise found lower levels of depression, and better immune functioning (Saxton et al., 2014), both of which are associated with treatment-completion. Lifestyle interventions consistently produce improvements in health related quality-of-life for women with breast cancer (Goodwin et al., 2014; Kenzik et al., 2015; Travier et al., 2014) and reduce stress (Courneya et al., 2014). One lifestyle study, designed to improve healthy behaviors and reduce stress, found that participants received chemotherapy medication with greater RDI, with less dispersion across time, less treatment discontinuation, and less loss to follow-up, compared to a randomly assigned assessment only group (Andersen et al., 2004). A different randomized controlled trial, comparing a lifestyle intervention employing moderate to high-intensity exercise program that included supervision, with a low-intensity in-home intervention, and a standard care group, among breast and colon cancer patients without serious physical, mental or cognitive problems, found that both exercise groups were less likely to need a dose adjustment/reduction during chemotherapy treatment (van Waart et al., 2015), and were a clear indicator that IM interventions could be correlated with treatment-

completion. These findings are supported by a similar randomized controlled trial (RCT) that found an exercise intervention resulted in a greater RDI of chemotherapy medication for the exercise group, among women treated with recurrent ovarian cancer (Mizrahi et al., 2015). Lifestyle changes focused on diet, exercise, and stress appear promising in their potential to aid treatment-completion and improved outcomes.

Among women with breast cancer, mind-body interventions (i.e., meditation, yoga) have also successfully reduced anxiety and depression (Dhruva et al., 2012; Wurtzen et al., 2013), stress and fatigue (Bower et al., 2012; Hoffman et al., 2012), symptom burden (Dhruva et al., 2012; Goyal et al., 2014), increased cognitive function (Milbury et al., 2013), and improved sleep quality (Dhruva et al., 2012). Yoga reduces inflammation at the cellular level, one of the hallmarks of cancer (Bower et al., 2014; Kiecolt-Glaser et al., 2014). Qigong, another mind-body practice benefits breast cancer patients by reducing depression and fatigue (Chen et al., 2013). Mind-body treatments target many symptoms correlated with treatment-completion, which could further improve outcomes. One possible mechanism is through the reduction of symptom burden among cancer patients. Although mind-body interventions frequently get prescribed to treat symptoms associated with standard cancer treatment, scant research has explored whether IM practices affect standard cancer treatment-completion. And, even though most women with breast cancer engage in some type of IM treatment during or after their initial treatment including lifestyle changes, acupuncture, and/or mind-body practices, little research has examined the association between IM use and treatment-completion. Therefore, the specific aims of this study were:

1. To identify demographic, clinical, and treatment factors (e.g., distress, pain, quality of life age at diagnosis, marital status, race/ethnicity, socioeconomic position, disease stage,

and treatments received), associated with breast cancer treatment-completion (chemotherapy and hormone therapy), and Aromatase Inhibitor medication switching in women with non-metastatic breast cancer.

2. To determine whether women treated for non-metastatic breast cancer who receive Integrative Medicine Center (IMC) treatments have higher chemotherapy and hormone therapy treatment-completion rates, and less hormone therapy medication switching, compared with a propensity score analysis balanced sample of women treated for breast cancer who did not receive IMC clinic services.

CHAPTER 2 LITERATURE REVIEW

This chapter reviews the relevant research on treatment-completion and AI medication switching. The chapter begins with a description of the breast cancer therapies that are determined to best treat different breast cancer diagnoses. The chapter describes treatment-completion, operationalizes treatment-completion for the present study, and lays out some of the barriers patients face in completing breast cancer treatment. A conceptual model, based on Williams' (1990) multiple factors model to describe phenomena correlated with treatment-completion is presented and shown in Figure 2.1. Integrative medicine (IM), and similar terms are defined and relevant research utilizing IM previously correlated with treatment-completion is reviewed, but only in relation to the IM services that were available to patients as a part of this study.

Breast Cancer Treatment

Breast cancers have been classified based on whether they are in situ verses invasive, and a diagnosis of the breast cancer cells includes whether or not cell growth depends on the presence of hormone receptors (HR) (American Cancer Society, 2019d). Human epidermal growth factor receptor-2 (HER2) is a protein that, in higher numbers on the breast cancer cells, can increase the growth and spread of the cancer cells (American Cancer Society, 2019d). Invasive breast cancer is diagnosed in 81% female breast cancer diagnoses, while 73% of all breast cancers are HR+/HER2-, 12% are HR-/HER2-, 11% are HR+/HER2+, and 4% are HR-/HER2+ (American Cancer Society, 2019a). Breast cancer is also defined by how much it has spread in the body, with not spread outside of the breast (local) comprising 64% of breast cancers, spread to the lymph nodes (regional) comprising 27% of breast

cancers, and spread to other parts of the body (distant) comprising 6% of breast cancers (American Cancer Society, 2019a).

Treatment of hormone receptor positive (HR+) breast cancer varies widely, too, depending on the stage (0 – IV), or extent, of breast cancer (American Cancer Society, 2019b). For HR+ breast cancer, hormone therapy is recommended as the standard-of-care by most doctors, and it can be started at the beginning of treatment (American Cancer Society, 2019b). Stage 0 breast cancer is treated with breast conserving surgery (BCS), or simple mastectomy (American Cancer Society, 2019c). Generally, with stage I breast cancer, surgery, often BCS, is the primary treatment, and is followed by radiation therapy (American Cancer Society, 2019b). If in stage I breast cancer, the tumor size is > 1 cm, then chemotherapy is usually recommended, but there are instances when chemotherapy is recommended for tumors ≤ 1 cm (American Cancer Society, 2019b). Treating stage II cancers can involve a number of surgeries, ranging from BCS to mastectomy, and is followed by radiation therapy (American Cancer Society, 2019b). Sometimes chemotherapy is administered before surgery, called neoadjuvant chemotherapy. If chemotherapy is needed after surgery, called adjuvant chemotherapy, it occurs before radiation therapy (American Cancer Society, 2019b). When treating stage III cancers, the tumor is > 5 cm or is found growing into tissue (e.g. muscle, skin) (American Cancer Society, 2019b). Neoadjuvant chemotherapy is frequently administered in this situation, but sometimes surgery occurs first (American Cancer Society, 2019b). If neoadjuvant chemotherapy is not administered for stage III breast cancers, adjuvant chemotherapy and radiation therapy follow the surgery (American Cancer Society, 2019b). Stage IV breast cancers, having spread to other parts of the body, are treated with systemic therapy, which often includes both hormone therapy and

chemotherapy, as well as other types of treatments (American Cancer Society, 2018). Taxane chemotherapies are a class of agents used in several combinations of chemotherapy agents and are a standard chemotherapy for women with breast cancer (i.e., cyclophosphamide, doxorubicin; dose-dense cyclophosphamide, dose-dense doxorubicin, paclitaxel; cyclophosphamide, doxorubicin, and paclitaxel; cyclophosphamide, doxorubicin, fluorouracil, paclitaxel; cyclophosphamide, doxorubicin, dose-dense paclitaxel) (Estevez et al., 2007).

Operationalizing Treatment-Completion

Chemotherapy treatment-completion has been defined as the number of cycles planned compared to the number of cycles completed (Reyes et al., 2016). However, chemotherapy treatment-completion is not settled science. Neugut et al. (2016) define early discontinuation as receiving < 80% of prescribed cycles decided upon at the time of the initial treatment plan. However, treatment-incompletion will be defined here as receiving < 85% relative dose intensity (RDI) of prescribed therapies, because the higher and more concentrated the dose is, up to a point, the better survival outcomes are (Qi et al., 2020). RDI is calculated by determining the total amount of chemotherapy medication doses delivered across all the cycles, divided by the dose decided upon at the beginning of treatment. Altwairgi et al. (2015) argue that standards for reporting compliance to chemotherapy medication are needed when reporting on outcomes of randomly controlled trials (RCT's).

Women with HR+ breast cancer are prescribed oral hormone blocking medication, taken daily for at least five years (60 months), as the standard of care (National Comprehensive Cancer Network, 2016). Persistence is important given that discontinuation of hormone therapy is associated with increased breast cancer mortality (Chirgwin et al.,

2016; Hershman et al., 2011). Definitions for discontinuation of hormone therapy prior to completion of the five years prescription period vary. Chirgwin et al. (2016) have defined taking hormone blocking medication for a minimum of 54 consecutive months out of 60 as treatment-completion. Farias and Du (2017b) describe a 120-day gap in the supply of hormone therapy medication, while He et al. (2015), defined discontinuation as a study participant exceeding 180 days between refilling their hormone therapy medication. Others defined discontinuation as exceeding three months from the last hormone therapy refill (Huiart et al., 2012). Hadji et al. (2013) defined discontinuation as missing ≥ 90 days before restarting their hormone therapy medication or initiating a different hormone blocking medication, however restarting ≤ 90 days after stopping, or beginning to take new medication ≤ 90 days after stopping their prior hormone blocking medication, was deemed persistent. Here, like Chirgwin et al. (2016), treatment-incompletion is defined as receiving a prescription for AI hormone therapy medication for < 54 months. Although less than the guideline defined 60 months of treatment, it is in line with treatments available for analysis.

Due to the five-year duration of hormone therapy prescription (National Comprehensive Cancer Network, 2016), and in-home, self-administered, oral delivery of the medication, measuring medication-taking behaviors can be challenging (Ziller et al., 2009). The present study, like Ziller et al. (2009), uses data from a single hospital's electronic medical record, and is similar to the work of Moscetti et al. (2015) exploring hormone therapy discontinuation among women with breast cancer. Data included medication prescribing information regarding the chemotherapy dose amount and date delivered, as well as the number of hormone therapy prescriptions and refills given to study participants. From these data we calculated the relative dose intensity and the extent hormone therapy treatment-

completion. Other data included domains of factors that are described in detail in the next section. Measuring in-home, self-administered adherence to hormone blockage medication was beyond the scope of this study.

Treatment-Completion

Abiding by long-term treatments is a well-known problem (Owens et al., 1975; Wilholm, 1980), and has been identified for those with a variety of chronic conditions like organ transplant recipients (Nevins et al., 2017) and persons with diabetes (Edelman & Polonsky, 2017). Evidence of high rates of treatment-incompletion among women with curable breast cancer has also existed for a long time (Hortobagyi et al., 1983), even among women where inaction would likely result in death within three years (Johnstone et al., 2000). Treatment-incompletion continues to be a problem during chemotherapy (Knisely et al., 2018; Usiskin et al., 2021), even though it is known that receiving ≥ 85% RDI is related to better overall survival (HR = 2.04; 95% CI 1.13, 3.70; p = 0.02) (Qi et al., 2020). Similarly, hormone therapy completion is a problem for many with Wagner et al. (2018) reporting 32% of participants discontinued within four years, and literature reviews reporting discontinuation rates ranging from 12-73% (Ayres et al., 2014).

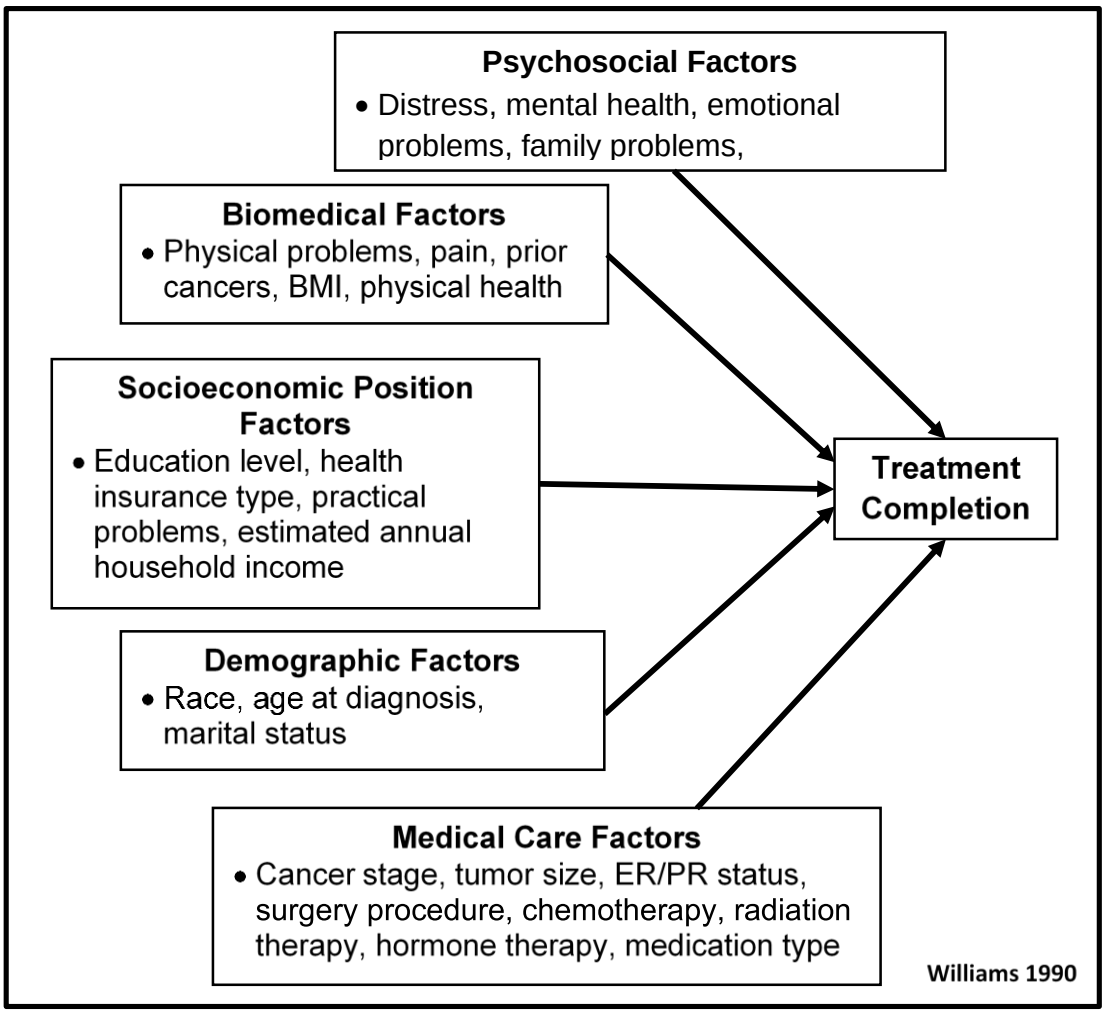
Williams' Multiple Factors Conceptual Model

The World Health Organization (WHO) identifies five main factors that influence palliative cancer-care specific treatment adherence, including socioeconomic-related factors, health care team/health system-related factors, condition-related factors, therapy-related factors, and patient-related factors (World Health Organization, 2003). However, the WHO model only describes adherence to palliative cancer care (with end of life expected to occur within the next six months), and not the completion of prescribed cancer treatment intended

to cure the person of cancer (World Health Organization, 2003). The WHO model could not be used to explain treatment-completion in this study, because it was limited to palliative cancer care rather than curative cancer care.

Given the complexity of cancer treatment, let alone human behavior, a theoretical model that may help organize the factors associated with treatment-incompletion/completion is one that accounts for multiple domains of factors affecting health and incorporates multiple factors when predicting patient medical decisions related to cancer diagnosis and treatment (Williams, 1990). The Williams conceptual framework was designed to explain differences in health outcomes for people with a lower socioeconomic position (SEP) compared to those with a higher SEP (Williams, 1990). This framework has informed research on race and SEP as factors affecting health (D'Anna et al., 2010; Wiltshire et al., 2009). The model is adapted here so that breast cancer treatment-completion is the primary outcome that may be influenced by the different factors that make up Williams' (1990) conceptual framework. The factors organizing this model are psychosocial factors, biomedical factors, socioeconomic factors, demographic factors, and medical care factors (Figure 2.1) (Williams, 1990). The model depicts socioeconomic position (SEP) as central in health and health care. This study considers similar factors. Psychosocial factors include health related behaviors from stress reduction to positive health behaviors like eating well, abstaining from smoking, and reduced alcohol consumption (Williams, 1990).

Figure 2.1 Adapted Williams Multiple Factor Conceptual Model



Socioeconomic position factors include annual household income, education level and health insurance. Biomedical factors include genetic-related differences like hormone receptor positive tumors, which are easier to treat than triple negative tumors (Wang & Du, 2015; Williams, 1990). Other biomedical factors include co-occurring conditions (Williams, 1990). Examples of demographic factors include race/ethnicity, age, domestic partnership status (e.g., married, widowed, divorced, single, etc.), and caring for children in the home (Williams, 1990). Williams (1990) describes medical care factors as treatment to improve health, however in the present study medical care factors are those that relate to the type of cancer treatment that may affect treatment-completion (chemotherapy and hormone therapy). Side-effects to cancer treatment were included in the medical care factors category.

These five factors result in an individualized level of breast cancer treatment-completion. Assessing the factors that are correlated with a patients' ability to complete their prescribed therapies may provide information critical to intervening in strategic ways that improve breast cancer treatment-completion. Below is a selective review of the relevant literature to describe the many factors affecting breast cancer treatment-completion, which includes incompletion, persistence, and discontinuation. These five factors, psychosocial factors, biomedical factors, socioeconomic position factors, demographic factors, and medical care factors, are ordered as depicted in Williams' (1990) model.

Psychosocial Factors. Psychosocial factors affecting treatment-completion include both person-centered, such as individual level factors like health behaviors and mental health, as well as family/social support system factors like feeling supported or aided by others (Williams, 1990). Importantly, one study found that receiving ≥ 85% RDI of chemotherapy was significantly correlated with baseline distress ($r = 0.243$) among African American

women with breast cancer (Yee et al., 2017). Additionally, worsening mood was associated with greater AI treatment discontinuation (HR, 2.77; 95% CI, 2.72-2.81) for women with early stage breast cancer (Kadakia et al., 2016). Surprisingly, depression was protective against early treatment discontinuation (HR, 0.92; 95% CI, 0.87–0.97) among German women with breast cancer treated in a general practice or gynecological practice (Hadji et al., 2013), and these findings are supported by a literature review that noted similar findings in other research (Van Liew et al., 2014). However, other research of women with breast cancer found that having depressive symptoms was positively correlated with hormone therapy discontinuation (adjusted $R^2 = 0.10$, $P < 0.001$) (Stanton et al., 2014). He et al. (2015) found a significant relationship between taking antidepressants in the first year of hormone therapy and early discontinuation over the next four years (HR, 1.22; 95% CI, 1.06 to 1.40). This dissertation study used available quality of life and distress scores to assess similar variables and their relation to treatment-completion.

Biomedical Factors. Examples of biomedical factors include the specific type of cancer, the prognosis and comorbidities that affect treatment-completion, as well as the overall health of a person at the time of diagnosis. Having worse physical functioning at baseline was correlated with higher rates of chemotherapy discontinuation due to toxicity (OR 20.15; 95% CI, 9.48-42.83), or treatment refusal (OR 8.32; 95% CI, 3.81-18.14), than being the most physically fit among women in Germany age 25-71 (Eichler et al., 2017). More comorbidities were related to a significantly greater likelihood of early hormone therapy discontinuation (HR, 1.52; 95% CI, 1.18 to 1.95) in studies of older breast cancer patients (Owusu et al., 2008). Contrary to the above findings, having more comorbid diseases was correlated with

reduced risk of hormone therapy treatment-discontinuation (HR, 0.81; 95% CI, 0.75–0.86) among women over 70 in a multicenter study among German women (Hadji et al., 2013). Having more comorbidities prior to a breast cancer diagnosis predicted early hormone therapy treatment discontinuation (HR, 1.35; 95% CI, 1.03 to 1.76) among Swedish women diagnosed between 2001 and 2010 (He et al., 2015). Poor sleep quality prior to initiating hormone therapy was correlated with early hormone therapy discontinuation (59.0% vs. 42.9%; OR=1.91, 95% CI 1.26–2.89; p=0.002) (Kidwell et al., 2014). Furthermore, the use of antidepressants, pain medication (HR, 1.33; 95% CI, 1.16 to 1.52), gastrointestinal drugs (HR, 1.25; 95% CI, 1.08 to 1.43), or sedatives/hypnotics (HR, 1.24; 95% CI, 1.07 to 1.43) one year before a breast cancer diagnosis was correlated with greater levels of adjuvant hormone therapy discontinuation (He et al., 2015). Given the importance of comorbidities on treatment-completion, this study used indirect comorbidity measures to assess biomedical factors related to treatment-completion.

Socioeconomic Position Factors. Socioeconomic position factors include income, employment status, and possessing health insurance to pay for care. One study of women from high, medium, and low socioeconomic positions, treated in the Atlanta area, who were less than 100% adherent to intravenous chemotherapy, found these women were significantly different than the participants who completed 100% of their chemotherapy in that they had lower odds of having health insurance (OR, 0.121; p = .016) (Wells et al., 2015). Among the same sample described earlier in this paragraph, completers of adjuvant chemotherapy had significantly higher income than those who did not complete their intravenous chemotherapy (Wells et al., 2015). Out-of-pocket-

costs were associated with lower adjuvant endocrine therapy treatment adherence among a national sample of women 65 and older on Medicare (Farias & Du, 2017a), building on prior work by Kimmick et al. (2015), who found 14.4% of their sample missed doses because of the cost of the medicine. Additionally, Farias and Du (2017b) found that disparities in adherence to adjuvant endocrine therapy could be explained by differences in socioeconomic position and out-of-pocket costs among women 65 and older using Medicare. Having insurance is critical to receiving cancer treatment, as Liu et al. (2013) found 91% of women with health insurance were still taking their hormone therapy medication at three years, versus 56% of women without health insurance who were still taking their hormone therapy medication at three years (adjusted OR = 0.12, p = 0.001). For this dissertation, health insurance fell into the category of SEP, because cancer care is a billed service (Parman, 2013), and education level as a proxy to measure SEP, is a strategy employed and supported by other social science research (Galobardes et al., 2006). In addition, this dissertation used the median household-income of the census tract of study participants' home addresses as an added measure to approximate study participants household-income.

Demographic Factors. As stated above, demographic factors including age, race/ethnicity, relationship status, and menopausal status, have all been correlated with treatment-completion. For example, white race was associated with greater likelihood of completing neoadjuvant chemotherapy, compared to nonwhites (76% to 50%) (OR 3.65, p=.014), among 124 women with breast cancer treated in North Carolina between 2009 and 2016 (Knisely et al., 2018). For women in another sample, being over age 70 was associated with endocrine therapy discontinuation in a multisite sample of

postmenopausal women (Nabieva, Kellner, et al., 2018), while another study found being older was associated with early hormone therapy discontinuation (Owusu et al., 2008). He et al. (2015) found that both the very young (< 40 years; HR, 1.39; 95% CI, 1.08 to 1.78) and the very old (≥ 65 years; HR, 1.15; 95% CI, 1.03 to 1.28) were at greater risk of hormone therapy discontinuation among a sample of Swedish women diagnosed with breast cancer, duplicating prior research with similar findings (Hadji et al., 2013).

Medical Care Factors. Examples of medical care factors that affect persistence include the type of cancer treatment, such as having received a taxane-containing chemotherapy (HR, 1.9; 95% CI, 0.99 to 3.6; p = .048) (Henry et al., 2012). He et al. (2015) found that a history receiving hormone replacement therapy at baseline was associated with adjuvant hormone therapy discontinuation (HR, 1.27; 95% CI, 1.08 to 1.49). Furthermore, taking drugs to relieve symptoms predicted early hormone therapy discontinuation (He et al., 2015). However, Kemp et al. (2014) found that, in a population-based study that included people 45 and older in New South Wales, Australia, women, who didn't undergo chemotherapy (HR = 1.4, 95% CI = 1.1-1.8), or have a mastectomy (HR = 1.5, 95% CI = 1.2-1.8), were at greater risk of discontinuing endocrine therapy, which is counter to the findings listed above.

In other studies, the quality of medical care or communication between patient and physician has been linked with treatment-completion (Kimmick et al., 2015; Liu et al., 2013). Given the nature of the secondary data used in this study, it was not possible to include measures of patient provider communication and a few other variables identified in prior literature. Examples of medical care factors associated with

neoadjuvant chemotherapy discontinuation include toxicities affecting the gastrointestinal system, and the neurological system (Knisely et al., 2018). Additionally, febrile neutropenia-related toxicities (fever and low number of neutrophils in the blood) (National Cancer Institute, nd) have been associated with adjuvant chemotherapy dose delay, dose reduction, and/or early discontinuation among women in the United Kingdom diagnosed with early breast cancer between 2006 and 2012 (Adjogatse et al., 2014). Furthermore, taxane-containing chemotherapies have been associated with peripheral neuropathy, febrile neutropenia, and pain (Kim et al., 2011).

There is substantially more evidence showing the effects of medical care factors on treatment-completion/incompletion of hormone blocking therapies than there is on chemotherapy treatments. For instance, receiving treatment in a university hospital is associated with hormone therapy non-adherence ($p = 0.014$) (Pourcelot et al., 2018). One study found that women treated in a gynecological practice experienced less risk of discontinuing Tamoxifen or other AI's than women treated for breast cancer in a general practice (HR = 0.52, 95% CI: 0.45–0.60, $p < 0.0001$) (Jacob et al., 2016), which supported similar findings of prior research (Hadji et al., 2013).

One frequent reason cited for hormone blocking medication treatment discontinuation is drug related side effects (Henry et al., 2012; Liu et al., 2013; Nabieva, Kellner, et al., 2018), including treatment side effects at the beginning of endocrine therapy (Nabieva, Fehm, et al., 2018; Wagner et al., 2018). Henry et al. (2012) found that medication side-effects were reported as a reason for discontinuation among 79% of the participants who discontinued hormone therapy in a multisite study

of mostly white women. These findings were backed up by a recent study where 73.5% of all those who discontinued hormone therapy did so because of treatment-related side effects (Nabieva, Kellner, et al., 2018). There is a broad literature base that found many different side effects associated with hormone therapy treatment discontinuation due to toxicities like various manifestations of pain in the form of arthralgia (Moscetti et al., 2015), and musculoskeletal symptoms (Henry et al., 2012; Kadakia et al., 2016; Nabieva, Fehm, et al., 2018). Bluethmann et al. (2017) also found that menopausal symptoms affected treatment discontinuation, and Kemp et al. (2014) found hot flashes were connected to treatment discontinuation (HR = 2.1, 95% CI = 1.3-3.3). Furthermore, sleep disorders are correlated with hormone therapy discontinuation (HR 1.95; 95% CI, 1.41–2.70) (Nabieva, Fehm, et al., 2018). The above factors connected to treatment discontinuation could not be directly measured in this study, despite consistent findings of their correlation with treatment-completion.

Hormone Therapy Medication Switching

Recent research defines non-adherence as changing anti-hormone medication, despite the change coming at the direction of the oncologist (Saha et al., 2017). Hormone therapy medication switching has been linked to non-adherence and early discontinuation (Murphy et al., 2012). Changing hormone blocking medication was associated with treatment discontinuation (HR, 1.50; 95% CI, 1.23 to 1.83) among a sample of Swedish women (He et al., 2015). Another study found hormone therapy medication switching associated with a lower medication-possession-ratio (95% CI 5.4, 9.4) (a key indication of non-adherence) (Trabulsi et al., 2014). Hormone therapy medication switching was included in the analyses of the present dissertation for the

purposes of measuring another form of treatment-completion that is impacted by the challenges the cancer patients face when trying to complete treatment.

As indicated above, many different forces are related to treatment-incompletion and often relate to hardship experienced by people affected by cancer. This study examined if having fewer of the problems experienced by people with breast cancer will be related to better treatment-completion, and hypothesized that resolving some of the problems experienced by people with breast cancer, through treatment in the IMC, would be related to better treatment-completion. Integrative approaches to cancer care specifically target the challenges that people with cancer face due to both their symptoms, and their cancer treatment (MD Anderson Cancer Center, 2018a).

Integrative Medicine

Complementary medicine is a non-standard cancer treatment that occurs in conjunction with standard cancer treatment (National Center for Complementary and Integrative Health, 2018), such as receiving acupuncture to treat nausea and vomiting symptoms due to chemotherapy (Widgren & Enblom, 2017). Alternative medicine is a non-standard medical treatment that replaces a standard western medical treatment (National Center for Complementary and Integrative Health, 2018). Integrative medicine differs from complementary medicine by coordinating care that is comprehensive across types of treatments and providers (National Center for Complementary and Integrative Health, 2018). For cancer, integrative medicine clinical services aim to treat anxiety and stress, and emotional health, as well as mental, and physical health (MD Anderson Cancer Center, 2018a). Complementary medicine treatments might help people better complete their breast cancer treatment. Complementary medicine has been a part of National Cancer Institute

(NCI) funded research since the 1940's. Complementary medicine can be defined as "Any medical system, practice, or product that is not thought of as standard (medical) care" (National Cancer Institute, 2012a). Standard medical care is treatment widely used by health care professionals (National Cancer Institute, nd). The standard medical care treatments that are the focus of this study are chemotherapy and hormone therapy. Integrative medicine employs complementary medicine practices to augment or support standard cancer treatments that have a history of demonstrable evidence of safety and benefit to people with cancer (Lyman et al., 2018; National Cancer Institute, 2012a), and may help people struggling with symptoms associated with treatment-incompletion (e.g. pain) (Hershman et al., 2018). Because alternative medicine is a non-standard cancer treatment that is used instead of modern cancer treatment (National Cancer Institute, 2012a), and there is overwhelming evidence that standard cancer care improves outcomes, (Johnstone et al., 2000; Siegel et al., 2018), alternative medicine treatments were not explored in this study. It should be noted that others have found that complementary medicine is not always helpful to breast cancer treatment, because those using complementary and alternative modalities were more likely to discontinue hormone therapy early (HR = 3.2; 95%CI: 1.5-6.9) (Huiart et al. 2013). In contrast, integrative medicine services are now recommended as part of guideline-driven care for breast cancer patients to help manage symptoms and could lead to lower levels of treatment-incompletion (Lyman et al., 2018). As stated above, many different treatments make up integrative medicine (IM). There are clinical practice guidelines outlining evidence-based treatments for breast cancer using IM (Greenlee et al., 2017). At MD Anderson Cancer Center, treatments that serve the patient population include massage, psychology (counseling), acupuncture, meditation or yoga (individual or group), music

therapy (individual or group), physical therapy/exercise counseling, dietary counseling, and physician consultations (MD Anderson Cancer Center, 2018a).

Massage

Oncology Massage, designed specifically for cancer patients, began in 2007 (Society for Oncology Massage, nd). Primary benefits of oncology massage center on symptom-management. One meta-analysis found massage was associated with a small reduction in fatigue (standardized mean difference (SMD) -0.61, 95 % CI -1.09,-0.13; p = 0.01) (Pan et al., 2014), as well as significant reductions in pain (SMD -0.33; 95 % CI, -0.69, -0.03; p = 0.07). Another found that oncology massage reduced anxiety (Greenlee et al., 2017; Lee et al., 2016). Massage is also recommended for treating those with a depressed mood (Dion et al., 2016; Greenlee et al., 2017). A third meta-analysis found that massage reduced surgery related pain and general pain (Lee et al., 2015). Pain, for example, is linked with AI treatment discontinuation (HR, 2.09; 95% CI, 1.14-3.80, p = 0.016) (Chim et al., 2013).

Psychology (Counseling)

Psychological treatment for difficulties due to the physical and psychosocial effects of having breast cancer through counseling/therapy has an extensive history (Johannsen et al., 2016; Timothy et al., 1979). One such treatment is cognitive behavioral therapy (CBT) (Cully & Teten, 2008; Daniels, 2015). CBT interventions have helped alleviate sleep problems in 46.2% of the sample (Irwin et al., 2017), fatigue (Effect Size = 0.64) (Heckler et al., 2016), and depression (Effect Size = −0.87) (Xiao et al., 2017) among women with breast cancer. Motivational interviewing was found to help diet and exercise behaviors (Sheppard et al., 2016). Mindfulness-based

interventions (Wurtzen et al., 2013), like mindfulness-based stress reduction (Greenlee et al., 2017), can help treat anxiety and/or depression. Being anxious or having a depressed mood has been connected to an increased risk of non-adherence (Bender et al., 2014).

Acupuncture

Acupuncture is a form of traditional Chinese medicine that locates multiple points on the body believed to have greater bioelectrical conductance and reduced resistance, and then inserts multiple sterile needles made of solid stainless steel into the identified points (Garcia, 2011; National Center for Complementary and Integrative Health, 2017). Research has found acupuncture reduces menopausal symptoms among woman with breast cancer (Mean difference = -3.28; 95% CI:-5.75, -0.80; p = 0.009) (Chien et al., 2017), which was associated with hormone therapy discontinuation in other research (Bluethmann et al., 2017; Kemp et al., 2014). Research on acupuncture found reduced joint pain caused by AI medication/HR+ breast cancer treatment (weighted mean difference: -3.81; 95% CI: -5.15 to -2.47) (Chen et al., 2017), and reduced general pain (Lee et al., 2016). Another study combining acupuncture and reflexology found reduced peripheral neuropathy among study participants (Ben-Horin et al., 2017). Furthermore, Garland et al. (2017) found that electro-acupuncture improved sleep quality and efficiency among breast cancer survivors with hot flashes, 70% of whom were actively taking hormone blocking medication. Acupuncture also alleviated fatigue (Greenlee et al., 2017; Lee et al., 2016). One multicenter RCT found that acupuncture combined with enhanced self-care reduced hot flashes, while acupuncture study participants reported higher quality of life among several domains of

functioning (Lesi et al., 2016). Among women with breast cancer, acupuncture was effective in reducing chemotherapy induced nausea and vomiting (Greenlee et al., 2017; Shen et al., 2000). Nausea and vomiting were connected to reduced likelihood of hormone therapy adherence among women in the United Kingdom (Schoffski et al., 2017).

Physical Activity Consultation

Physical activity has benefits for everyone, including women with breast cancer undergoing cancer treatment (Fong et al., 2012) and a physical activity consultation sets goals, creates exercise plans, and helps patients learn how to be active during their treatment (The University of Texas MD Anderson Cancer Center, 2016). Benefits derived from physical activity that relate to oncologic treatment-completion have been documented. Exercise leads to significant reductions of adjuvant chemotherapy dose adjustments (OR, 0.26; 95% CI, 0.11 to 0.61; P = .002) (van Waart et al., 2015); however, there is no consensus within the scientific community (Courneya et al., 2013). Growing evidence suggests physical activity has some benefit to women with breast cancer by reducing fatigue (Espindula et al., 2017; Fong et al., 2012; Furmaniak et al., 2016; Galiano-Castillo et al., 2014; Hayes et al., 2013; Mishra et al., 2012; van Waart et al., 2015). Physical activity reduces depression (Fong et al., 2012) or depressed mood (Galiano-Castillo et al., 2014), and lowers anxiety (Lahart et al., 2018). Physical activity has been found to reduce treatment symptoms/side effects (Furmaniak et al., 2016), joint pain (Irwin et al., 2015), and general pain (Espindula et al., 2017; Forsythe et al., 2013; Irwin et al., 2015; Mishra et al., 2012; van Waart et al., 2015). As stated above, fatigue (Kidwell et al., 2014; Schoffski et al., 2017), anxiety and depression

(Bender et al., 2014; Van Liew et al., 2014), side effects (Lash et al., 2006), and pain (Chim et al., 2013) have all been connected to breast cancer treatment non-adherence.

Meditation

The positive effect of meditation on well-being is clear (Cohen, 2018). For women with breast cancer, meditation can alleviate depressive symptoms (Bower et al., 2015; Boyle et al., 2017; Greenlee et al., 2014; Johns et al., 2016), as well as anxiety (Greenlee et al., 2014; Johns et al., 2016). Furthermore, meditation related intervention studies found improvements in study participants by reducing fatigue ($p = 0.007$) in a diverse sample of women with stage 0-III breast cancer diagnosed before age 50 (Bower et al., 2015), and in a study of mostly white women diagnosed in the US between 2012-2013 (Johns et al., 2016). Fatigue was associated with chemotherapy discontinuation among mostly white women 65 and older (Ruddy et al., 2012), and baseline feelings of tiredness were correlated with hormone therapy discontinuation (Kidwell et al., 2014). Meditation even has a positive effect on pain (Johns et al., 2016), which is related to hormone therapy discontinuation (Henry et al., 2012).

Integrative Oncology Physician Consult

The consultation with the oncology physician provides guidance and feedback about questions about complementary treatments and integrative approaches to cancer care, (MD Anderson Cancer Center, 2018a). IM treatments are frequently recommended during the consult (MD Anderson Cancer Center, 2018a).

In summary, treatment-incompletion of standard-of-care breast cancer treatment continues to be a problem. Many factors influence a person's ability to complete their

chemotherapy, and AI treatments. Psychosocial, biomedical, socioeconomic, demographic, and medical factors are correlated with treatment-completion. Services provided at an IMC treat many of the factors, and their symptoms, associated with treatment incompletion. Yet little research has explored how well an attendee of an IMC is able to complete the standard-of-care treatment for hormone receptor positive breast cancer.

Because there is a lack of research on breast cancer treatment-completion at major cancer centers, and a shortage of research on breast cancer treatment-completion of IMC attendees, the aims of this study are, as stated in Chapter One, to identify the factors related to breast cancer treatment-completion and determine the association between receiving IMC services and breast cancer treatment-completion.

CHAPTER 3 METHODS

This chapter discusses the design and methodology of the present study. The purpose of this dissertation is two-fold: 1) explore factors associated with treatment-completion and hormone therapy medication switching among women treated for breast cancer and 2) examine the hypothesis that patients who receive Integrative Medicine Center (IMC) services complete treatment more often than a propensity score balanced comparison group. This study examined existing data collected from the electronic medical records of both the Integrative Medicine Clinic, whose REDCap database is in the Department of Palliative, Rehabilitative, and Integrative Medicine, and the Breast Cancer Management System (BCMS) database, which is in the Department of Breast Medical Oncology, both of which are located at MD Anderson Cancer Center. To test the hypotheses for Aim 1, missing values were replaced using the Markov chain Monte Carlo multiple imputation method. Then, analyses were carried out which included univariate descriptive statistics and bivariate generalized linear model (GLM) using a modified Poisson regression with robust error variance estimators to test for significant associations between individual variables and treatment-completion (Zou, 2004). This regression is useful for the analysis of non-normal data distributions that have only positive values (Zou, 2004). This was followed by conducting three multiple Poisson regressions to identify factors associated with treatment-completion while controlling for other factors. To test the hypothesis for Aim 2, a balanced comparison group of patients who did not receive IMC services was constructed with a covariate adjustment using propensity scores to compare to those who did receive IMC services, to determine if there was a difference in treatment-completion between the two groups.

Aim 1

Aim 1 is to identify demographic, clinical, and treatment factors (e.g., distress, pain, quality of life, age at diagnosis, marital status, race/ethnicity, socioeconomic position, disease stage, and treatments received), associated with breast cancer treatment-completion (chemotherapy and hormone therapy), and Aromatase Inhibitor medication switching in women with non-metastatic breast cancer.

Aim 1 Samples

The chemotherapy and hormone therapy samples were created using data from the Department of Breast Medical Oncology's Breast Cancer Management System (BCMS), the Integrative Medicine clinic, EPIC database, the Pharmacy database, Patient History database, and the Legacy database. Patients were included if they were women diagnosed with breast cancer at MD Anderson. Patients were excluded if they had metastatic breast cancer (stage IV) to exclude advanced disease. Those whose diagnosis and initial treatment dates were greater than 3 months apart were excluded to increase the chance that all treatments were received from MD Anderson rather than other facilities and thus were included in the data reviewed for this study. Patients were also only included if the cancer is hormone receptor-positive (HR+) to ensure a similar treatment trajectory that includes a 5-year hormone therapy prescription beginning at some point during treatment, and a human epidermal growth factor receptor 2-negative (HER2-) to reduce the number of different chemotherapy treatment plans a patient could receive to four different regiments for calculating the relative dose intensity (RDI). Finally, for chemotherapy treatment-completion: patients were included if they started a taxane-containing chemotherapy after 3/1/2016, and before 2/1/2019 (due to the average 6-month duration of chemotherapy treatment), because the start date relates to

the OneConnect electronic health record go-live date and the average six-month chemotherapy treatment duration for some treatment-plans. For hormone therapy treatment-completion: patients were included if they started a hormone therapy after 1/1/2009, and before 1/1/2014 (due to the prescribed 5-years of treatment), which is the earliest date that the IMC offered acupuncture as a service to patients. For hormone therapy medication switching: patients were included if they meet the above criteria for inclusion in the hormone therapy treatment-completion sample and were prescribed an aromatase inhibitor hormone therapy as the first hormone blocking medication.

Outcome Measures

Chemotherapy

The chemotherapy treatment-completion dependent variable is a dichotomous variable gauging taxane-containing chemotherapy completion measured at the end of treatment. Chemotherapy completion was assessed using the electronic medical record reporting the total chemotherapy dose administered. Treatment-incompletion (Table 3.1) was defined as receiving < 85% RDI of prescribed therapies (Bonadonna & Valagussa, 1981; Budman et al., 1998; Ferreira Filho et al., 2002). Chemotherapy treatment-completion was coded as 1 and incompletion coded as 0.

Dose intensity was calculated using the following formula:

"Dose intensity = Total dose received (mg/m2)/ (Actual time from the first to the last treatment + theoretical time of non-given cycles + one cycle time), where time is expressed in weeks (Ferreira Filho et al., 2002)."

The ratio between the delivered dose divided by the prescribed dose resulted in the RDI (Bonadonna & Valagussa, 1981; Budman et al., 1998; Ferreira Filho et al., 2002).

Hormone Therapy

The second dependent variable for Aim 1, hormone therapy treatment-completion, is a dichotomous variable gauging hormone therapy completion measured at the end of treatment. Hormone therapy completion was assessed using the electronic medical record reporting the total months of hormone therapy received. Treatment-incompletion (Table 3.1) was defined as receiving < 54 months of prescribed hormone therapy medication (Chirgwin et al., 2016). Hormone therapy treatment-completion was coded as 1 and incompletion coded as 0.

Switching Hormone Therapy Medication

The third dependent variable for Aim 1, aromatase inhibitor (AI) hormone therapy medication switching (Table 3.1), is defined as changing AI hormone therapy medication at any time before the < 54 months cutoff denoting hormone therapy treatment-completion (Chirgwin et al., 2016; Murphy et al., 2012). AI hormone therapy medication switching was assessed using the BCMS and Pharmacy databases reporting the type of AI hormone therapy medication received as the first hormone therapy medication. Switching hormone therapy medication was coded as 1 and not switching medication during treatment coded as 0.

Table 3-1 Dependent Variables

Dependent variables	How measured	Treatment-completion definition
Chemotherapy	Nominal y/n	receiving ≥ 85% RDI of prescribed taxane-containing chemotherapy medication
Hormone therapy	Nominal y/n	receiving ≥ 54 months of prescribed hormone medication
Switching AI hormone therapy medication	Nominal y/n	Switching within 54 months of prescribed hormone medication

Aim 1 Independent Variables

To identify factors related to treatment-completion of this sample, treatment-completion was compared using the following independent measures. All categorical independent variables were dummy coded for analysis.

Psychosocial Factors

Several variables were used to examine mental, emotional, and social elements that are hypothesized to affect treatment-completion within the chemotherapy sample (Table 3.2). Most psychosocial variables were only available for either the chemotherapy or the hormone therapy samples, most likely due to when patients received treatment, resulting in different measures in different samples. *Psychosocial Distress Screen:* Distress was assessed using the Distress Thermometer, which is one question measuring a patient's current level of distress on a 0 to 10-point scale (Ma et al., 2014) by asking how much distress a patient has been experiencing in the past week, which also includes today. *Family problems*, and *emotional problems* are two distinct questions that identified the respective problems using an open-ended format that asked patients to describe challenges they were facing currently. The problems listed were converted to a dichotomous variable (yes/no) for *family problems*, and *emotional problems* from the qualitative data using the following criteria:

- *Yes*: one or more problems listed
- *No*: no answer, or statement indicating no problems

Patient Health Questionnaire. Depression was assessed using the first two questions of the Patient Health Questionnaire (PHQ-2) to screen for depression (American Psychological Association, 2019) within the chemotherapy sample. The PHQ-2 has a sensitivity of 0.86, and specificity of 0.78 for major depression (Arroll et al., 2010). The questions ask if 'in the last two weeks' a person: (has) *little interest or pleasure in doing things;* and (is) *feeling down, depressed or hopeless* (Arroll et al., 2010). These PHQ-2 questions were answered with the following four discrete choices: *not at all, several days, more than half the days,* and *nearly every day,* and each answer scored 0-3 respectively (Arroll et al., 2010). The two answers were summed, ranging from 0-6, and in clinical settings a score of ≥2 indicates further depression assessment is needed (Arroll et al., 2010).

Medical Outcomes Study Short Form-12 (SF-12) Mental Component Summary. Health related quality of life within the hormone therapy sample was assessed using the Medical Outcomes Study Short Form 12-item (SF-12) scale; the SF-12 has a six-item sub-scale called the Mental Component Summary (MCS) (Ware et al., 1996). The internal consistency, measured using Cronbach's Alpha, was tested and appears valid among people with cancer ($\alpha MCS12=0.88$) (Bhandari et al., 2018). Hagell et al. (2017) recommended that raw scores of the SF-12 be used to assess quality of life rather than standardized scores. Therefore, raw scores were used.

Table 3-2 Psychosocial Factors

Psychosocial factors	How measured	Location/Note/Measurement instrument
Distress	Scale 1-10	Ambulatory Patient Needs Screening
Family problems	Nominal	Ambulatory Patient Needs Screening: Yes-problems reported/No-no problems reported
Emotional problems	Nominal	Ambulatory Patient Needs Screening: Yes-problems reported/No-no problems reported
Patient Health Questionnaire 2	Scale 0-6	Ambulatory Patient Needs Screening: (not at all, several days, more than half the days, and nearly every day)
SF-12 MCS	Scale 6-27	Patient History Database

Biomedical Factors

Medical related factors that the patient brings with them at the start of their cancer treatment were assessed in several different ways (Table 3.3). A list of *physical problems* identified by self-report among the chemotherapy sample during the A*mbulatory Patient Needs Screening* was an open-ended question that asked a patient to describe the physical challenges that they were currently facing. The *physical problems* listed were converted to a dichotomous variable (yes/no) for *physical problems* from the qualitative data using the following criteria:

- *Yes*: one or more problems listed
- *No*: no answer, or statement indicating no problems

Prior cancers is an ordered variable that counted the number of cancers a patient was diagnosed with prior to the cancer diagnosis that meets the inclusion criteria of the current study. Pain was measured on a 0 to 10 scale, and collected through the Patient History Database, which was available for the hormone therapy sample and the AI medication switching subset only. Pain was not available for the chemotherapy study participants. Body

Mass Index (BMI) was measured using the standard kg/m^2 method, which is recorded in the chart and used to calculate chemotherapy dose.

Medical Outcomes Study Short Form-12 (SF-12) Physical Component

Summary. Health related quality of life within the hormone therapy sample was assessed using the Medical Outcomes Study Short Form 12-item (SF-12) scale; the SF-12 has a six-item sub-scale called the Physical Component Summary (PCS) (Ware et al., 1996). The internal consistency, measured using Cronbach's Alpha, was tested and appears reliable among people with cancer ($\alpha PCS12=0.89$) (Bhandari et al., 2018). Hagell et al. (2017) recommended that raw scores of the SF-12 be used to assess quality of life rather than standardized scores. Therefore, raw scores were used.

Table 3-3 Biomedical Factors

Biomedical factors	How measured	Location/Note/Measurement instrument
Physical problems	Categorical	Ambulatory Patient Needs Screening: Yes-problems reported/No-no problems reported
Prior cancer	Ordinal	Number of cancers prior to the current cancer meeting inclusion criteria of this study
Pain Scale	Scale	Pain: 0-10
BMI	Scale	kg/m^2
SF-12 PCS	Scale 6-20	Patient History Database

Socioeconomic Position Factors

Socioeconomic position was measured in a few ways (Table 3.4). A list of *Practical Problems* (e.g. transportation difficulties, falling behind on household/medical bills, challenges securing childcare) were identified by self-report among the chemotherapy sample during the A*mbulatory Patient Needs Screening*, which was an open-ended question that asked a patient to describe the practical challenges that they were currently facing. The

practical problems listed were converted to a dichotomous variable (yes/no) for *practical problems* from the qualitative data using the following criteria:

- *Yes*: one or more problems listed
- *No*: no answer, or statement indicating no problems

Insurance type was collected during billing and was divided into the following four groups: 1) Medicaid; 2) Medicare; 3) managed care; and 4) Government/Embassy or Self-Pay.

Census tract median household income was calculated using the home address of the participant to identify the median household income of the census tract within which each patient residence is located. Each address was matched to the census tract number in which the address resides using the US Census Bureau census tract data (United States Census Bureau, nd). Median annual household income of census tracts was downloaded from the American Community Survey's 2017 5-year estimates (Social Explorer; U.S. Census Bureau, 2017).

Employment status was collected during treatment and divided into the following four groups: 1) Employed; 2) Not Working; 3) Retired; 4) Disabled/Student/Part Time.

Table 3-4 Socioeconomic Factors

Socioeconomic factors	How measured	Location/Note/Measurement instrument
Practical problems	Nominal	Ambulatory Patient Needs Screening: Yes-problems reported/No-no problems reported
Insurance type	Nominal	Medicaid, Medicare, managed care, government/embassy, or self-pay
Median census tract household income	Scale	Median household income using census tract data.
Employment status	Nominal	Employed, Not Working, Retired, Disabled/Student/ Part Time

Demographic Factors

Three demographic factors that may affect treatment-completion were collected and used to explore associations with treatment-completion within the sample (Table 3.5). Age at diagnosis; race/ethnicity, which was divided into five groups: Asian/Pacific Islander, Black, Other, Spanish/Hispanic, and white; and marital status, which was divide into four groups: Married, Single, Divorced/Legally Separated, and Other/Widowed.

Table 3-5 Demographic Factors

Demographic factors	How measured	Location/Note/Measurement instrument
Age at diagnosis	Scale	Measured in years
Race/ethnicity	Nominal	Asian/Pacific Is, Black, Native American, Other, (Spanish, Hispanic), white
Marital status	Nominal	Married, Single, Divorced/Legally Separated, and Other/Widowed

Medical Care Factors

Clinical characteristics of this study about breast cancer treatment-completion were represented by 11 different variables found in Table 3.6. The following medical care factors were examined for relationships between different cancer treatments and treatment-completion. The primary tumor size was measured by diameter and calculated in centimeters (cm). Primary tumor grade was divided into the following three categories: G1, G2, and G3 (i.e., well-differentiated-low grade, moderately differentiated-intermediate grade, and poorly differentiated-high grade), as defined by the NCI (National Cancer Institute, 2013). Because the number of sentinel nodes removed is related to lymphedema (Susan G. Komen, 2019), both the number of sentinel lymph nodes removed, and the number of nodes with cancer were measured for a count of the frequency examined, ranging from (0 to 60) (Dialani et al., 2015). The type of surgery received was explored for an association with treatment-completion and was divided into the following four categories: Lumpectomy Alone, Mastectomy Alone, Lumpectomy W/Axillary Node Dissection, and Mastectomy W/Axillary

Node Dissection. Because the interval between the diagnostic biopsy and the start of neoadjuvant chemotherapy, as well as the interval between surgery and the start of adjuvant chemotherapy, measured in days, is related to survival (Cabrera et al., 2016), days-to-start chemotherapy was examined for a relationship with chemotherapy treatment-completion within both samples and divided into: 0-20 days, 21-41 days, 42-62 days, 63≤ days. Finally, the first hormone therapy drug prescribed, which includes Arimidex, Letrozole, Tamoxifen, and Other/Aromasin hormone therapy agents were examined for having any role in treatment-completion among the hormone therapy sample. Four chemotherapy regiments prescribed were examined: Cyclophosphamide, Doxorubicin, and Paclitaxel; Cyclophosphamide and Doxorubicin; Cyclophosphamide, Doxorubicin, Fluorouracil, and Paclitaxel, and Cyclophosphamide, Doxorubicin, and Paclitaxel (Dose-Dense).

Table 3-6 Medical Care Factors

Medical care factors	How measured	Location/Note/Measurement instrument
Pathological primary-tumor size	Scale	Diameter measured in mm
Primary tumor grade (combined index)	Ordinal	G1: well-differentiated-low grade, G2: moderately differentiated-intermediate grade, and G3: poorly differentiated-high grade
Sentinel nodes removed	Scale	Measured in mm (normal size <2 mm)
Sentinel nodes positive	Scale	Measured in mm (normal size <2 mm)
Definitive surgery procedure side 1	Nominal	Lumpectomy Alone, Mastectomy Alone, Lumpectomy W/Axillary Node Dis, Mastectomy W/Axillary Node Dis
Interval between diagnostic biopsy and neoadjuvant chemotherapy start date	Ordinal	0-20 days, 21-41 days, 42-62 days, 63≤ days
Interval between definitive surgery and adjuvant chemotherapy start date	Ordinal	0-20 days, 21-41 days, 42-62 days, 63≤ days
Adjuvant hormone agents 1	Nominal	Name of first AI medication (Arimidex, Letrozole, Tamoxifen, and Other/Aromasin)
Chemotherapy agents	Nominal	Cyclophosphamide, Doxorubicin, and Paclitaxel; Cyclophosphamide and Doxorubicin; Cyclophosphamide, Doxorubicin, Fluorouracil, and Paclitaxel, and Cyclophosphamide, Doxorubicin, and Paclitaxel (Dose-Dense)

Aim 1 Hypotheses

Tables 3.7 through 3.11 depict a directional list of the hypotheses for Aim 1 grouped by factors related to treatment-completion. The first Aim of this dissertation is to identify demographic, clinical, and treatment factors associated with breast cancer treatment-completion, and Aromatase Inhibitor medication switching in women with non-metastatic breast cancer.

Table 3-7 Psychosocial Variables Hypotheses

Psychosocial variables hypotheses	**How measured**	**Hypothesized direction of relationship with treatment-completion**
Distress	Scale 1-10	Patients who complete treatment will have lower mean distress scores than those who do not complete treatment
Family problems	Nominal	Those who have family problems will have lower rates of treatment-completion, than those who do not have family problems
Emotional problems	Nominal	Those who have emotional problems will have lower rates of treatment-completion, than those who do not have emotional problems
Patient Health Questionnaire 2	Scale	Patients who complete treatment will have lower mean PHQ-2 scores than those who do not complete treatment
SF-12 MCS	Scale	Patients who complete treatment will have higher mean SF-12 MCS scores than those who do not complete treatment

Table 3-8 Biomedical Factors Hypotheses

Biomedical factors hypotheses	**How measured**	**Hypothesized direction of relationship with treatment-completion**
Physical problems	Nominal	Those who have physical problems will have lower rates of treatment-completion than those who do not have physical problems
Prior cancer	Scale	Patients who complete treatment will have fewer prior cancers than those who do not complete treatment
Pain Scale	Scale	Patients who complete treatment will have lower mean pain scores than those who do not complete treatment
BMI	Scale	Patients who complete treatment will have lower mean BMI scores than those who do not complete treatment
SF-12 PCS	Scale	Patients who complete treatment will have higher mean SF-12 PCS scores than those who do not complete treatment

Table 3-9 Socioeconomic Factors Hypotheses

Socioeconomic factors hypotheses	**How measured**	**Hypothesized direction of relationship with treatment-completion**
Practical problems	Nominal	Those who have practical problems will have lower rates of treatment-completion than those who do not have practical problems
Insurance type	Nominal	Those who use managed care insurance will have higher rates of treatment-completion than those who do not use managed care insurance
Median census tract household income	Scale	Patients who complete treatment will have higher median census tract household income than those who do not complete treatment
Employment status	Nominal	Those who are employed will have higher rates of treatment-completion than those who are not employed

Table 3-10 Demographic Factors Hypotheses

Demographic factors hypotheses	**How measured**	**Hypothesized direction of relationship with treatment-completion**
Age at dx	Scale	Patients who complete treatment will have higher mean age than the mean age of those who do not complete treatment
Race/ethnicity	Nominal	Those who identify as white race will have higher rates of treatment-completion than those who do not identify as white race
Marital status	Nominal	Those who identify as married will have higher rates of treatment-completion than those who do not identify as married

Table 3-11 Medical Care Factors Hypotheses

Medical care factors hypotheses	**How measured**	**Hypothesized direction of relationship with treatment-completion**
Pathological tumor size	Scale	Patients who complete treatment will have a smaller mean tumor size than the mean tumor size of those who do not complete treatment
Tumor grade (combined index)	Ordinal	Greater tumor grade will be associated with lower rates of treatment-completion
Sentinel nodes removed	Scale	Patients who complete treatment will have lower mean number of sentinel nodes removed than the mean number of sentinel nodes removed from those who do not complete treatment
Sentinel nodes positive	Scale	Patients who complete treatment will have lower mean number of sentinel nodes positive than the mean number of sentinel nodes positive of those who do not complete treatment
Definitive surgery procedure side 1	Nominal	No hypothesis made
Interval between diagnostic biopsy and neoadjuvant chemotherapy start date	Scale	Patients who complete treatment will have lower mean number of days interval between the diagnostic biopsy and the neoadjuvant chemotherapy start date age than those who do not complete treatment
Interval between definitive surgery and adjuvant chemotherapy start date	Scale	Patients who complete treatment will have lower mean number of days interval between the definitive surgery and the adjuvant chemotherapy start date start date age than among those who do not complete treatment
First adjuvant hormone agents	Nominal	Those who are prescribed Letrozole will have lower rates of treatment-completion, than those who are prescribed other AI medications
Chemotherapy regimen	Nominal	No hypothesis made

Aim 1 Statistical Analysis

Power Analysis: statistical significance set at $p \leq 0.001$

We have 25 questions involving 25 independent variables for which we explored the association with treatment-completion. Using a Bonferroni correction, we asked each question at a 2-sided 0.001 significance level to account for 2 groups of patients and 25

questions each (0.05/(2*25)). All sample size/power calculations were performed in PASS 2005.

A power analysis was conducted for the **categorical variables** in Aim 1. For the chemotherapy group, we estimated 2830 patient records were available. When calculating a binary chemotherapy treatment-completion outcome (yes/no), the effect of race/ethnicity (white vs. non-white) was used as an example for what we can detect assuming that 71% of patients are white, and whites have an 83% treatment-completion rate based on past analyses (Knisely et al., 2018), and unpublished work at MD Anderson. Using a logistic regression to predict chemotherapy treatment-completion rate from race/ethnicity, with a two-sided 0.001 significance level, and 80% power, we would be able to detect the difference between a treatment-completion rate for whites of 83% vs. non-whites with a treatment-completion rate of 76.2% (and a resulting odds ratio of 0.66). When adding additional variables to the model for multivariate analyses, the odds ratio we could detect changed to 0.56 if the other variables had an R^2 of 0.50 and 0.42 when the other variables had an R^2 of 0.7.

For the hormone therapy group, we estimated 2670 patient records were available. When calculating a binary hormone therapy treatment-completion outcome (yes/no), the effect of race/ethnicity (white vs. non-white) was used as an example of what we can detect assuming that 71% of the patients are white, and assuming a 75% treatment-completion rate for whites based on past analyses (Farias & Du, 2017b) and unpublished work at MD Anderson. Using a logistic regression to predict chemotherapy treatment-completion rate from race/ethnicity, with a two-sided 0.001 significance level, and 80% power, we will be able to detect the difference between a treatment-completion rate for whites of 75% vs. treatment-completion rate of 67% for non-whites (odds ratio 0.68). When adding additional

variables to the model for multivariate analyses, the odds ratio we can detect would change to 0.59 if the other variables have an R^2 of 0.50 and 0.44 if the other variables have an R^2 of 0.7.

A power analysis was conducted for the continuous variables in Aim 1. When calculating a binary chemotherapy (hormone therapy) treatment-completion outcome (yes/no), the effect of a **continuous variable** (e.g., age), is calculated as the following: When the sample size is 2830 (2670), the logistic regression test of beta = 0 and two-sided alpha = 0.001 will have 80% power to form the value of 0.830 (0.750) at the mean age to 0.799 (0.715) when age is increased to one standard deviation above the mean. This change corresponds to an odds ratio of 0.813 (0.836). This assumes that there is only one normally distributed independent variable in the model. With multiple variables in the model, we can detect an odds ratio of 0.75 (0.78) if the other variables have an R^2 of 0.50 and 0.69 (0.72) if the other variables have an R^2 of 0.7. In summary, the proposed study had enough cases to properly power the study.

Aim 1 Statistical Analysis Software

Microsoft Excel, version 2008 was used during data preparation and calculation of BMI, and chemotherapy and hormone therapy treatment-completion. IBM SPSS software version 26 was used to analyze the data for all analysis strategies.

Missing Data

The Analyze Patterns procedure in SPSS was used to look at missing values within the entire dataset. This procedure provided a summary of the missing values in a table and a visual display in a pie chart that described the patterns of missing values within the data and ruled out that values are missing not-at-random (Choi et al., 2019). Multiple imputations

(MI) was used to address missing values of the individual covariates that have missing values in the Poisson regression (Leyrat et al., 2019). The Markov chain Monte Carlo method was used to impute the data (Kaplan & Chen, 2014). Twenty imputed datasets were generated (Choi et al., 2019). Both independent and outcome variables among both the IMC and the comparison groups were included in the imputation model (Choi et al., 2019).

Aim 1 Analysis Strategy

Means and frequency descriptive statistics for all variables were summarized. A modified Poisson regression analysis, with a robust error variance procedure, was used to examine relationships between treatment-completion and both continuous and categorical variables of the multiple imputed datasets (Zou, 2004). Modified bivariate and multiple Poisson regression was also used to examine if 1) individual factors were related to the risk of treatment-completion, and 2) factors were significantly associated with the risk of treatment-completion. Exponentiated risk ratios were used to interpret the variable effects on chemotherapy/hormone therapy treatment-completion and AI medication switching. Psychosocial, biomedical, socioeconomic, demographic, and medical care factors were tested for significant associations with the risk of treatment-completion. Factors that were statistically significantly associated with treatment-completion in past research, variables deemed relevant to treatment-completion, while available in the various databases at MD Anderson, were included in a modified Poisson regression model for the analyses (Field, 2013).

Several assumptions of the study must be met to appropriately employ modified Poisson regression. The first assumption is that the dependent variable is not continuous, and can be binary (Zou, 2004). Additional assumptions include having one or more independent

variables, and independent observations where each participant has zero effect on the scores of other participants in the study. Seven women, who met inclusion criteria for both the chemotherapy and hormone therapy samples, were removed from the hormone therapy sample and included in the chemotherapy only to ensure independence across samples. The Poisson regression assumes that a Poisson distribution of the independent variables where the variance equals the means was not assumed, because we obtained 'robust' standard errors for parameter estimates (Cameron & Trivedi, 2010; Fekedulegn et al., 2010). The next assumption is multicollinearity, which was assessed using the correlation matrix to ensure that each correlation does not exceed 0.80, assessing the variance inflation factor (VIF) to ensure that it is < 10, and that the tolerance values are > 0.1 (Field, 2013). The final assumption is that there are ≥ 5 participants per cell in the model (Field, 2013).

Aim 2

Aim 2 is to explore whether women treated for non-metastatic breast cancer who receive IMC treatments have higher chemotherapy and hormone therapy treatment-completion rates, and less hormone therapy medication switching, compared with a propensity score analysis balanced sample of women treated for breast cancer who did not receive IMC clinic services.

Patients who did not receive IMC services made up a comparison group that is balanced (using select predictor variables) to the patients who received IMC services using propensity scoring (Austin, 2011; Bai & Clark, 2019; Guo & Fraser, 2015). This study tested whether there was a difference between those who visited the IMC and those who did not visit the IMC in taxane-containing chemotherapy treatment-completion, AI hormone therapy treatment-completion, and AI medication switching.

Aim 2 Samples

The matched comparison sample was created using data from patients treated in the Department of Breast Medical Oncology that met the criteria listed above but had not participated in Integrative Medicine Center services, with data coming from Breast Cancer Management System (BCMS) database, the Pharmacy database, the OneConnect database, the Integrative Medicine Center database, the Patient History database, and the Legacy database. Two different samples were created. These samples are referred to as the chemotherapy and the hormone therapy samples (the question of medication switching is asked of the hormone therapy sample).

Based on the above inclusion criteria, and existing data from the Department of Breast Medical Oncology and the IMC, the estimated sample size of the chemotherapy group that received IMC services was 250, and the estimated sample size of the chemotherapy group that did not receive IMC services was 2580. The estimated sample size of the hormone therapy group that received IMC services was 236, and the estimated sample size of the hormone therapy group that did not receive IMC services was 2434.

Aim 2 Independent Variable

The independent variable in Aim 2 is whether the patient received services in the IMC (1) or did not receive IMC services (0) after breast cancer diagnosis.

Integrative Medicine Center Intervention

The IMC offers individually tailored services that address the unique needs of patients who seek relief from the challenges brought upon them by their personal experience

with cancer. IM is a method of health care, deliberately delivered, which provides a combination of conventional medicine, complementary health treatments, and lifestyle medicine that is evidence-informed, personalized, and safe (Lopez, Mao, et al., 2017). Most patients begin with the *Physician Consultation* service, which first explores a patient's use of complementary and alternative medicine (CAM), and their current interest and expectations for IM (Lopez, McQuade, et al., 2017). A complete history and physical exam of the patient is then completed (Lopez, McQuade, et al., 2017). Guidance on treatments, as well as the risks and benefits of herbs and supplements are provided (Lopez, McQuade, et al., 2017). Acupuncture, Exercise and Physical Activity Consultation, Health Psychology Services, Meditation, Nutrition Counseling, and Oncology Massage are treatments offered using an evidence-based approach and based on the biopsychosocial model (Lopez, McQuade, et al., 2017; MD Anderson Cancer Center, 2018b). The above treatments were offered continuously throughout the study period. The intention of the IMC is to facilitate the medical treatment of the patient. One measure of effective treatment is patient completion of the treatment protocol. This study tested the following hypothesis:

Aim 2 Hypothesis

Patients who received IMC services will be significantly more likely to complete chemotherapy, hormone therapy, and less likely to switch aromatase inhibitor hormone therapy medication, than a comparison group, balanced using propensity score analysis using a covariate adjustment, who did not receive IMC services.

Aim 2 Statistical Analysis

Power analysis: statistical significance set at $p < 0.025$

Statistical significance was set at the 0.025 level because there are two questions addressed in this aim, and when added together that equals 0.05.

In Aim 2, the **chemotherapy** incompletion rate outcome examined the difference between the IMC group and the comparison group: A two group c^2 test with a 0.013 two-sided significance level will have 80% power to detect the difference between a Group 1 proportion, p_1, of 0.160 and a Group 2 proportion, p_2, of 0.285 (odds ratio of 2.093) when the sample size in each group is 250.

In Aim 2, the **hormone therapy** incompletion rate outcome examined the difference between the IMC group and the comparison group: A two group c^2 test with a 0.013 two-sided significance level will have 83% power to detect the difference between a Group 1 proportion, p_1, of 0.250 and a Group 2 proportion, p_2, of 0.400 (odds ratio of 2.000) when the sample size in each group is 236.

Aim 2 Statistical Analysis Software

Preliminary data screening was performed using IBM SPSS Statistics 26 and main analyses were performed using R 4.0.4.

Aim 2 Independent Variables Used for Balancing via Propensity Scoring

All independent variables described in Aim 1 were used for the construction of a balanced comparison group using a propensity scoring statistical procedure, as well as the variables listed below, which are exploratory independent variables or used for the propensity score analysis. The additional variables are organized by factors related to treatment-completion just as in Aim 1.

Psychosocial factors

Several psychosocial variables were used to balance the patients who received IMC services with those who did not receive IMC services using propensity scoring analysis. A list of s*piritual/religious concerns* identified by self-report during the A*mbulatory Patient Needs Screening* was an open-ended question that asked a patient to describe the spiritual/religious challenges that they were currently facing. The s*piritual/religious concerns* listed were converted to a dichotomous variable (yes/no) for s*piritual/religious concerns* from the qualitative data using the following criteria:

- *Yes*: one or more problems listed
- *No*: no answer, or statement indicating no problems

Self-injury was assessed using the last question of the PHQ 9-item assessment that asked if 'in the past two weeks' a person (has) *thoughts that you would be better off dead or hurting yourself in some way*. This ordinal question was answered with the following four discrete choices: *not at all, a few days, several days,* and *nearly every day*.

Biomedical factors

Menopausal status at time of diagnosis was divided into the following four categories: pre-menopausal, natural post-menopausal, post-menopausal unnatural (post BSO [bilateral salpingo-oophorectomy = removal of ovaries and fallopian tubes], post chemical, post hysterectomy), other/peri/pregnant.

Socioeconomic factors

Education level acts as a proxy for socioeconomic position (Galobardes et al., 2006); it was measured in the number years of education and comes from the *Patient History*, and was categorized as: < high school diploma/some GED, high school diploma/GED, technical school/some college/associate degree, college degree, and graduate/professional degree.

Demographic factors

Marital status (single, partnered (in relationship), married, separated, divorced, widowed), and demographic factors that may affect treatment-completion, were collected and used to balance the IMC and non-IMC groups using propensity score analysis.

Medical care factors

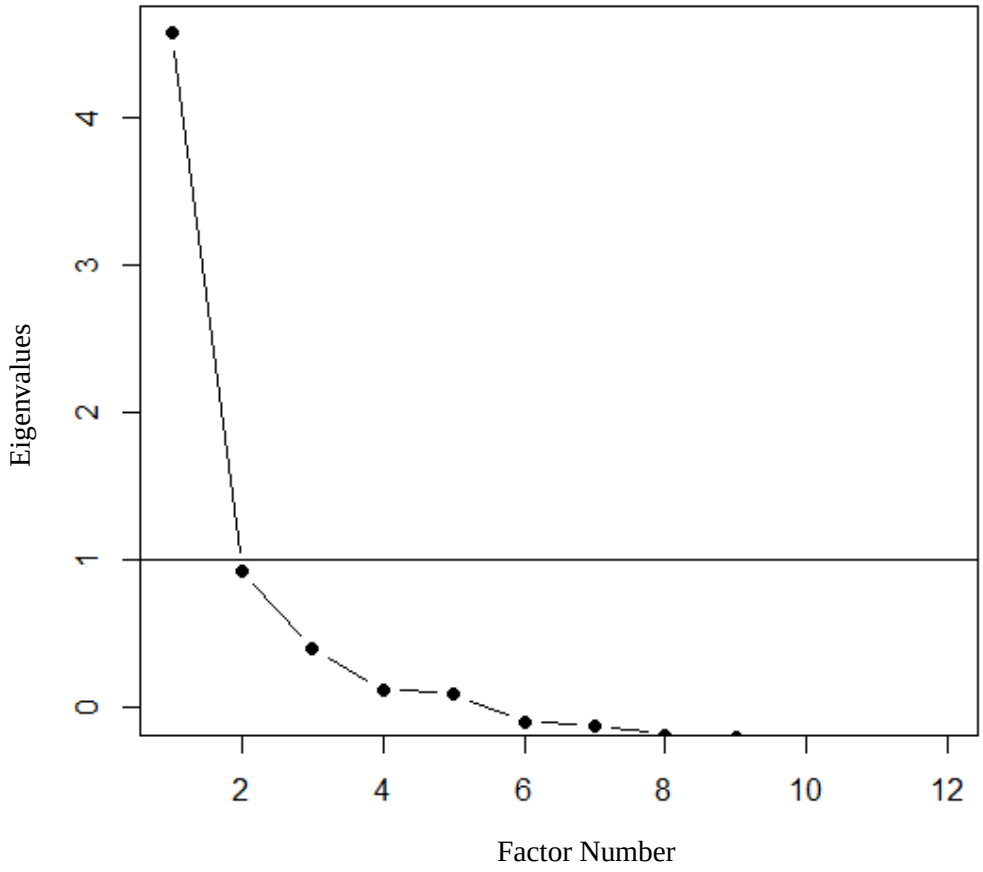
Clinical characteristics of several different variables were used to balance the IMC group with the non-IMC group through propensity score analysis. The year treatment started was used to control for changes in Breast Center and IMC treatment changes/improvements made over time and is defined as the year in which treatment started. Pathological/clinical breast cancer staging from 0-IIIC was used to describe how far the disease progressed before diagnosis. Two descriptors of hormone receptor status of the cancer were used to describe the tumor, namely estrogen receptor status (Y/N), and progesterone receptor status (Y/N). Additionally, all cancer treatments (neoadjuvant/adjuvant chemotherapy, hormone therapy, and radiation therapy), will act as additional dichotomous (Y/N) independent variables, describing the cancer treatments a person received. Furthermore, chemotherapy or hormone therapy medication type was used in each respective sample to aid the balancing of the two groups.

Psychometric Evaluation of the SF-12 for propensity score analysis

Only two variables in the present study were composed of multiple indicators: the two subscales of the SF-12 (Ware et al., 1996), described in Aim 1. This measure was used during the hormone therapy and AI medication switching analyses. A basic psychometric analysis was conducted to ensure the instrument performed as designed in the study sample. Given the reported factor structure of the SF-12, a two-factor (physical and mental health)

confirmatory factor analysis (CFA) model fit was not met according to commonly-cited guidelines (Hu & Bentler, 1999). The CFA approach was abandoned in favor of exploratory factor analysis (EFA) (Brown, 2015). EFA was performed and a scree plot was generated (Figure 3.1), which strongly favors a single-factor solution since the plot levels off at the second factor. In addition, although the Kaiser criterion (i.e., retaining factors with eigenvalues greater than one) tends to cause retention of minor factors (Finch, 2020), there is only one factor with an eigenvalue greater than one in Figure 3.1. Given these results, a one-factor solution was retained, and factor scores (using the regression method) were estimated. To determine the degree of indeterminacy, Grice (2001) recommended the correlation between the estimated scores and the latent factor should exceed 0.9 if the score will be used as a replacement for the latent variable. In the present study, factor score determinacy was excellent at 0.94.

Figure 3.1 Scree Plot of Eigenvalues for SF-12



Note. Leveling off of the plot at the second factor indicates a one-factor solution is favored.

Propensity Score Analysis

Propensity Score Analysis Overview

Aim two examined the influence of IMC group membership on chemotherapy treatment-completion, hormone therapy treatment-completion, and AI medication switching. However, assignment to the treatment or control group was not random. Propensity score methods are used to estimate a treatment effect when random assignment to treated and untreated groups is not possible (Bai & Clark, 2019). Therefore, three separate propensity score analyses were carried out for each of the three dependent variables. Despite separate outcomes being modeled, the general analytic approach taken in each case was similar.

The propensity score is a calculation for every participant in a study of the chance to be assigned to the treated group (in this case receive services in the Integrative Medicine Center), given the values of the independent variables (Austin, 2011; Guo & Fraser, 2015). The purpose of a propensity score is to balance the baseline covariates between two groups in order to compare outcome variable scores (Austin, 2011; Guo & Fraser, 2015). Several different methods of propensity scoring exist including matching on the propensity score, stratification on the propensity score, inverse probability treatment weighting, propensity score weighting, and covariate adjustment on the propensity score (Austin, 2011; Bai & Clark, 2019; Li & Greene, 2013). Propensity score analysis, using the covariate adjustment approach, was employed for this analysis.

Propensity Score Estimation and Evaluation

Among the most common propensity score methods, the covariate adjustment approach is the most straightforward to implement (Bai & Clark, 2019). In this method, a multi-step approach is taken where propensity scores are first estimated and then used as a covariate in an ANCOVA framework, with the grouping variable serving as the independent variable (IV) as usual. Using propensity scores in this way generally provides a more effective statistical control than traditional ANCOVA when groups are unbalanced on covariates (Bai & Clark, 2019).

Propensity scores were estimated and evaluated using the approach outlined in Bai and Clark (2019). The process began with identifying variables to be included in the computation of the propensity scores. In essence, variables should be included if they are related to the outcome variable. Variables related only to the grouping variable (but not the outcome variable) should be included if they could influence the treatment. Since all

variables in the dataset were selected specifically because they were related to chemotherapy/hormone therapy treatment-completion or AI medication switching in some way, variables that were related to the grouping variable were used for the calculation of propensity scores even if they did not relate to the outcome variable. The criteria used to determine relevant associations were $r \geq .1$ for the dependent variable and $d \geq .05$ ($r \geq .025$) for the grouping variable.

Propensity scores were computed using the *lavaan* structural equation modeling package for R to perform a regression utilizing the probit link (Rosseel, 2012), which is described in detail in the following section titled Model Assumptions. Once the regression coefficients were obtained, a propensity score was computed for each respondent. The propensity score is the probability of being in the IMC treatment group and was obtained by using a standard equation developed by Aldrich and Nelson (1984, p. 49). Table 3.12 lists the variables that were considered and included in the computation of the propensity scores.

Table 3-12 Variables Considered and Included in Computation of Propensity Scores

Variables Considered and Included in Computation of Propensity Scores		
Chemotherapy Sample	Hormone Therapy Sample	AI Medication Switching Sample
Psychosocial factors	**Psychosocial factors**	**Psychosocial factors**
Distress	SF 12 Mental Component Summary	SF 12 Mental Component Summary
Family problems		
Emotional problems		
Health Questionnaire 2		
Biomedical factors	**Biomedical factors**	**Biomedical factors**
Physical problems	Episode number	Episode number
BMI	Pain Scale*	Pain Scale*
Practical problems	BMI*	BMI*
	SF 12 Physical Component Summary*	SF 12 Physical Component Summary*
Socioeconomic factors	**Socioeconomic factors**	**Socioeconomic factors**
Insurance type	Insurance type*	Insurance type*
Median Census Tract Household Income	Median Census Tract Household Income*	Median Census Tract Household Income*
Employment	Employment status*	Employment status*
	Education*	Education
Demographic factors	**Demographic factors**	**Demographic factors**
Age at dx	Age at dx*	Age at dx*
Race/ethnicity	Race/ethnicity*	Race/ethnicity*
Marital status	Marital status	Marital status*
Medical care factors	**Medical care factors**	**Medical care factors**
Tumor size (cm)	Tumor size (cm)*	Tumor size (cm)*
Tumor grade	Tumor grade	Tumor grade
Sentinel Nodes removed	No Sentinel Nodes removed*	No Sentinel Nodes removed*
Sentinel Nodes positive	No Sentinel Nodes positive*	No Sentinel Nodes positive*
Primary surgery	Definitive surgery procedure side 1*	Definitive surgery procedure side 1*

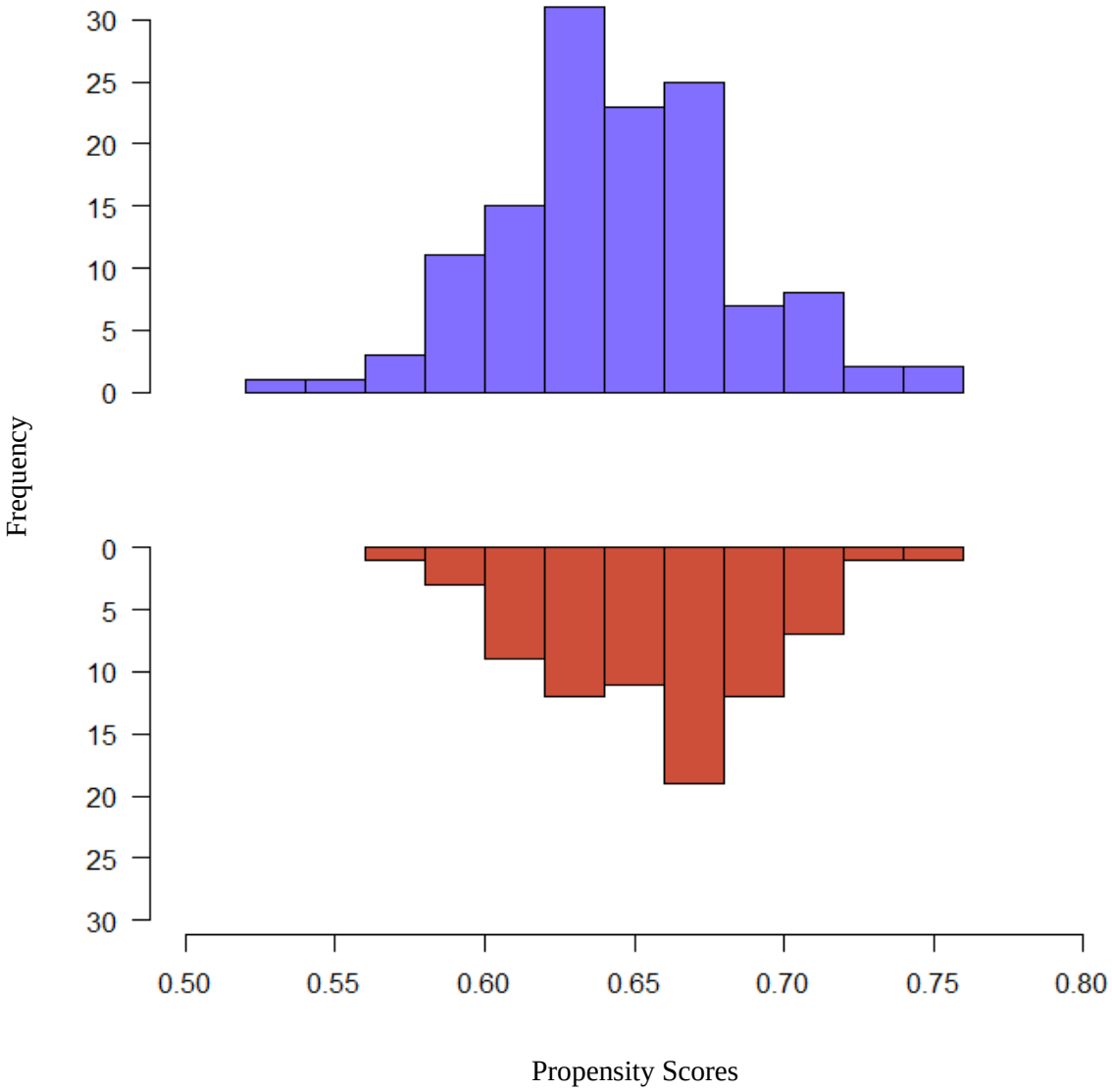
Once the propensity scores were obtained, they were evaluated as described in Bai and Clark (2019). The overall objective is to determine if the distributions of propensity scores are sufficiently overlapping in each group to ensure the groups are comparable; this concept is called common support. Several methods exist to check whether common support is present, including plotting histograms to ensure they "appear similar in terms of the shape, mean, and minimum and maximum values" (Bai & Clark, 2019, p. 65). Basic descriptive statistics presented in Table 3.13 and Figures 3.2 through 3.4 reveal these criteria are generally supported. In all analyses, all propensity scores of the IMC group fell within the range of scores in the comparison group except for one case in the hormone analysis. The flatter distribution of the IMC groups within the hormone therapy sample and the AI subset is likely due to a difference in size of the groups. This exceeds the recommendation that 75% of scores in the treatment group are within the range of scores in the comparison group. Results of *t*-tests for mean differences in propensity scores across the groups are given in Table 3.13. For the chemotherapy analysis, the effect size is below the recommended cutoff of $d = 0.5$, but the effect sizes for the hormone and switching analyses are slightly higher (0.68 and 0.74, respectively), and both latter tests achieved significance at the 0.001 level. However, considering all the evidence, the propensity scores have sufficient common support across all three analyses.

Table 3-13 Results of t-Tests Comparing Propensity Score Means Across Groups

	Comparison Group		IMC Group					
Sample	M (SD)	Range	M (SD)	Range	*t*	df	sig.	Cohen's *d* [95% CI]
Chemotherapy	0.64 (.04)	0.54 - 0.75	0.66 (0.04)	0.56 - 0.74	2.61	169.33	0.01	-0.36 [-0.66, -0.08]
Hormone	0.54 (0.02)	0.47 - 0.60	0.55 (0.02)	0.51 - 0.62	6.54	130.74	<0.001	0.68 [0.47, 0.88]
Switching	0.54 (0.02)	0.48 - 0.61	0.55 (0.02)	0.52 - 0.60	4.60	59.74	<0.001	0.74 [0.46, 1.03]

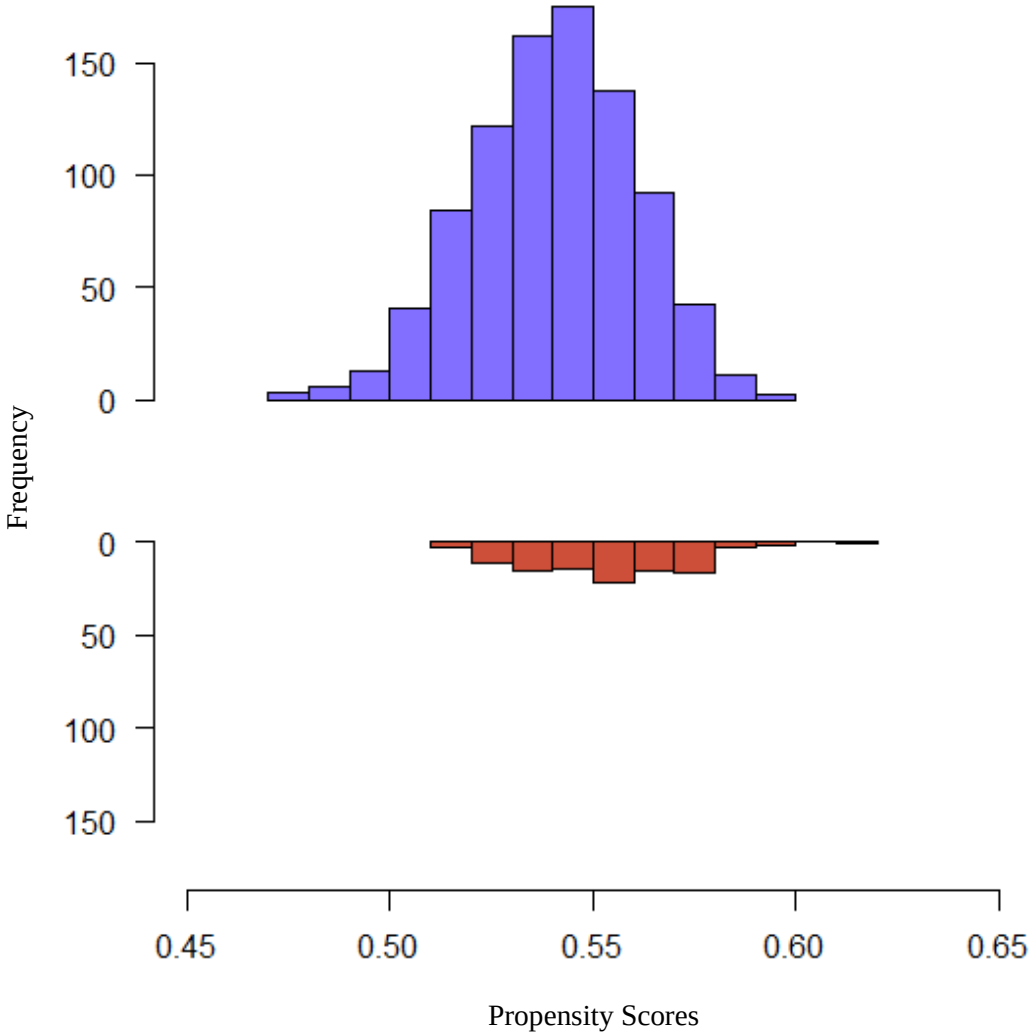
Note. *t* statistics computed using Welch's formula, which is robust to heterogeneity of variance.

Figure 3.2 Mirrored Histograms Depicting Distribution of Propensity Scores in Each Group for the Chemotherapy Sample



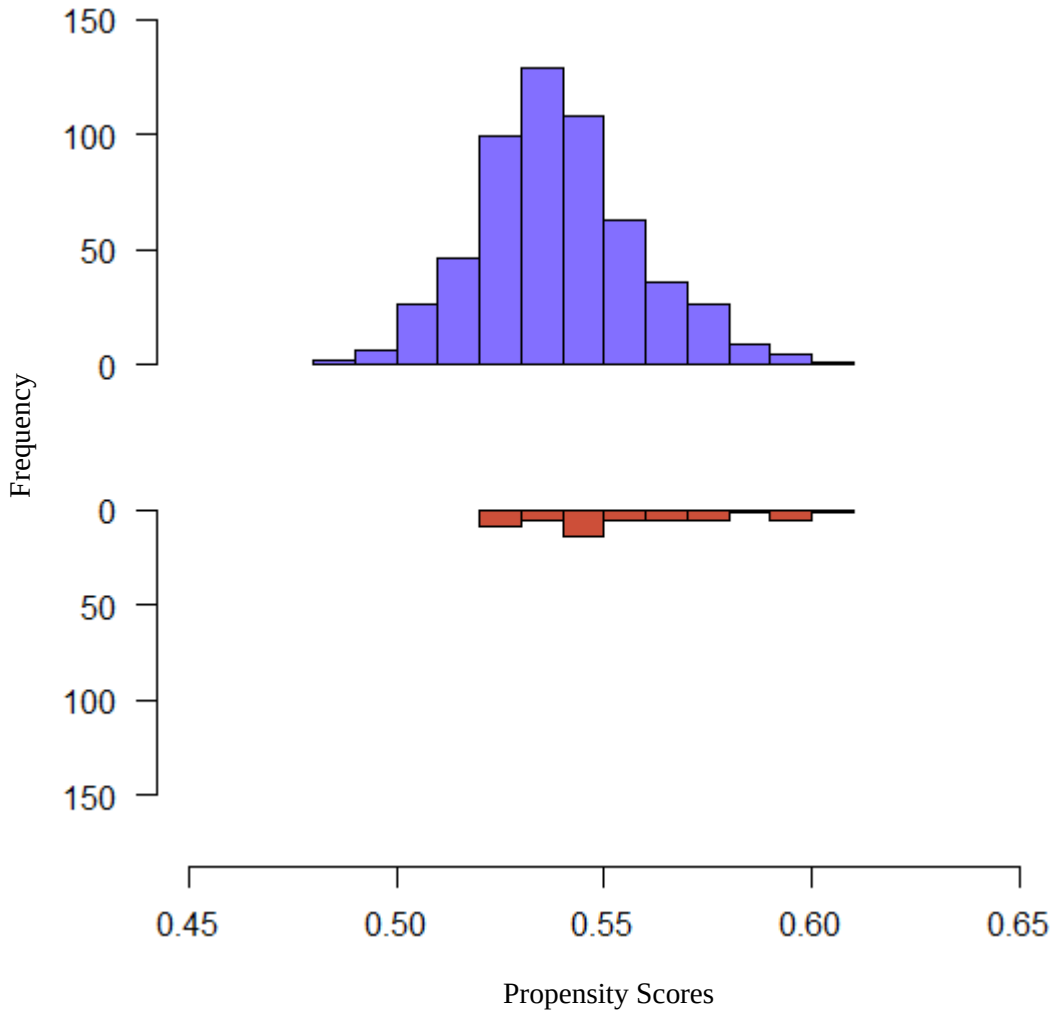
Note: Top panel shows distribution of propensity scores in comparison group; bottom panel shows IMC group.

Figure 3.3 Mirrored Histograms Depicting Distribution of Propensity Scores in Each Group for the Hormone Therapy Sample



Note. Top panel shows distribution of propensity scores in comparison group; bottom panel shows IMC group.

Figure 3.4 Mirrored Histograms Depicting Distribution of Propensity Scores in Each Group for the AI Medication Switching Sample



Note. Top panel shows distribution of propensity scores in comparison group; bottom panel shows IMC group.

Missing Data Handling

In general, PS methods are optimal when "there is very little missing data within each covariate" (Bai & Clark, 2019, p. 26). This was a challenge for the present study given the prevalence of missing data (Appendix Tables 1 through 3 present a summary of missingness for each variable included in the analyses). This was a major factor in selecting the covariate adjustment propensity score approach since it more readily facilitates current methods of handling missing data. Naïve methods such as pairwise or listwise deletion are acceptable if they do not result in the loss of many cases (leading to a loss of statistical power) and if data are missing completely at random (MCAR). Under the MCAR assumption, missingness on any given variable is not related to any other study variable (Enders, 2010).

In addition to causing the deletion of an excessive number of cases, pairwise or listwise deletion were not appropriate in the present study because the MCAR assumption was not met. Visual inspection of missing data boxplots using the *VIM* package for R (Templ & Filzmoser, 2008) revealed some missing data patterns depended upon levels of other variables. This situation (so-called missing at random, or MAR, not missing systematically) is required to utilize contemporary methods of handling missing data such as multiple imputation or missing at random maximum likelihood, also known as full-information maximum likelihood, or FIML (Enders, 2010). In the present study, FIML was implemented using *lavaan*. FIML makes use of all cases in the dataset whether missingness is on predictor or outcome variables. A robust maximum likelihood estimator (White, 1980) was used to relax the multivariate normal assumption required when using FIML (Enders, 2010).

Model Assumptions

Since all three outcome variables were dichotomous, probit regression was used. Probit regression is the default analysis in *lavaan* when modeling binary outcomes. Probit regression uses the cumulative distribution function of the normal distribution and produces nearly identical results to logistic regression, although the parameter estimates are interpreted differently (Aldrich & Nelson, 1984). Several assumptions are necessary for probit regression (Aldrich & Nelson, 1984). The specification of the model assumes the outcome varies according to the predictor variables, and the link function is the cumulative distribution function of the normal distribution. A lack of serial correlation among errors is also necessary, as is homoscedasticity or constant variance of the error term. A lack of perfect correlation between two or more predictor variables is also assumed. Bivariate correlations were screened, and no problem was detected with collinearity among covariates selected for inclusion, but a check of multicollinearity is not implemented in *lavaan*. Additionally, technical problems with model convergence and large standard errors that are tell-tale signs of collinearity problems were not observed. Therefore, although structural equation modeling software such as *lavaan* frequently lacks the usual plots and diagnostics for checking assumptions (Allison, 2002), a deviation is unlikely to affect results in the present study due to the use of robust standard errors and an extremely large sample size (Pek et al., 2018).

Since the propensity scores were used as a covariate in an ANCOVA context, it is important to consider the assumptions of the ANCOVA model (Bai & Clark, 2019). The relevant consideration in the present analysis is the assumption of homogeneity of regression slopes (Wildt & Ahtola, 1978). This was checked by ensuring an interaction term comprised of the IMC grouping variable and the propensity scores was not significant. In all cases, the homogeneity of

regression slopes was reasonable, indicating the influence of the propensity scores was consistent across groups.

Human Subjects' Protections

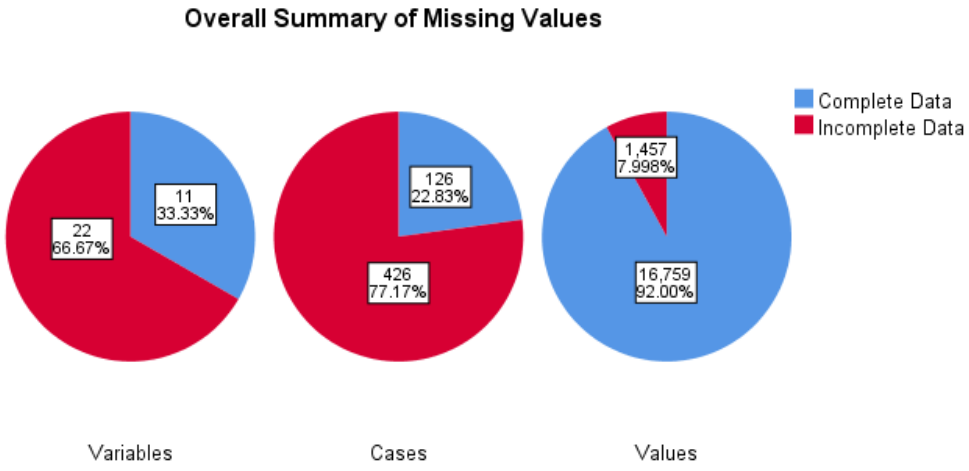
Data were not received, nor did data cleaning commence, until after receiving approval from the MD Anderson IRB, and the University of Houston CPHS. All data were kept on MD Anderson protected servers. Access to the files was solely through VPN protected, remotely accessed, MD Anderson on-site computers that are password protected. The data were stripped of identifiers (e.g., MRN, and name), de-identified, and stored separately for analyses. Addresses were used to identify census tracts where residents resided, and then discarded from the dataset as soon as possible. Original data files with identifying information were stored in the MDACC departmental shared folder in a password protected file known only to the primary investigator and stored in perpetuity on a REDCap database. REDCap (https://redcap.mdanderson.org) is hosted on a secure server by MD Anderson Cancer Center's Department of Research Information Systems & Technology Services (Harris et al., 2009).

Missing Data

As is common with medical record data, there was a large amount of missing data among some of the predictor variables. As stated above, Appendix Tables 1 through 3 depict a summary of missing values by variable for all three samples, with variables that have zero missing values not shown. The chemotherapy sample (Figure 3.5) had 426 participants with at least one cell of missing data out of 508 participants, and a total of 8.00% of all the cells were missing data; Appendix Figure 9 displays the pattern of missingness. The hormone therapy sample (Figure 3.6) had 2790 participants with at least one cell missing data out of 3764 participants, and a total of 17.96% of all the cells were missing data; Figure 4.4 displays the pattern of missingness. The AI

Medication Switching sample (Figure 3.7) had 1677 participants with at least one cell missing data out of 2253 participants, and a total of 17.67% of all the cells were missing data; Appendix Figure 9 displays the pattern of missingness.

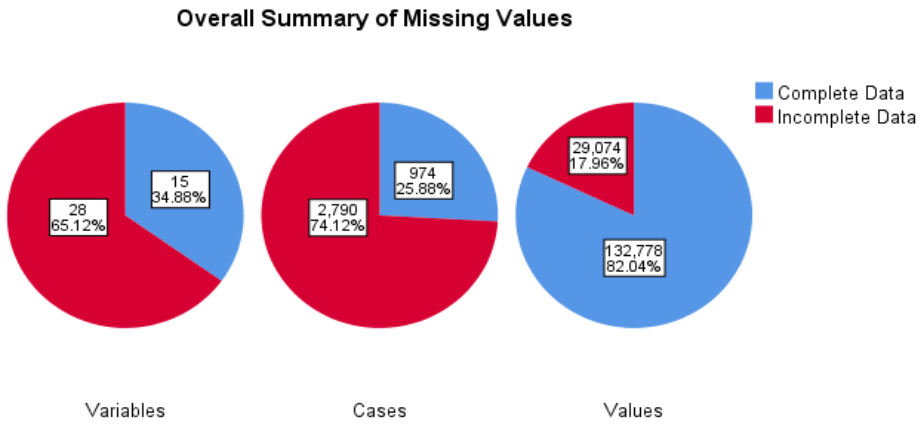
Figure 3.5 Pie Charts Depicting Missing Values for the Chemotherapy Sample



Chemotherapy Missing Values

Note. Left chart shows variables containing missing values; center chart shows cases containing missing values; right chart shows the cumulative percent of missing values of the entire chemotherapy dataset.

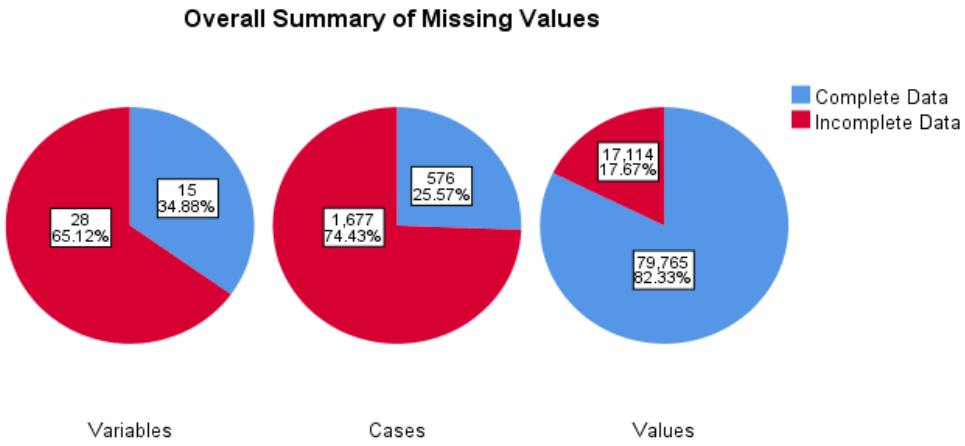
Figure *3.6 Pie Charts Depicting Missing Values for the Hormone Therapy Sample*



Hormone Therapy Missing Values

Note. Left chart shows variables containing missing values; center chart shows cases containing missing values; right chart shows the cumulative percent of missing values of the entire hormone therapy dataset.

Figure 3.7 Pie Charts Depicting Missing Values for the AI Medication Switching Sample



AI Medication Switching Missing Values

Note. Left chart shows variables containing missing values; center chart shows cases containing missing values; right chart shows the cumulative percent of missing values of the entire AI Medication Switching dataset.

CHAPTER 4 RESULTS

This chapter discusses the findings of this dissertation. The first section reports the results from the analysis of the first Aim that identified which factors were associated with treatment-completion and hormone therapy medication switching among women treated for breast cancer. The second section reports the results from the analysis of the second Aim, which examined the hypothesis that patients who receive Integrative Medicine Center (IMC) services complete treatment more often than a propensity score balanced comparison group. As with prior chapters, the datasets are in the following order: chemotherapy sample, hormone therapy sample, and Aromatase Inhibitor medication switching subset. Within each dataset, the factors are reported in the same order described in previous chapters: psychosocial factors, biomedical factors, socioeconomic position factors, demographic factors, and medical care factors.

Aim 1 Results

Chemotherapy

The chemotherapy sample included 508 participants. Complete descriptive characteristics can be viewed in Table (4.1), and are organized by psychosocial, biomedical, socioeconomic, demographic, and treatment factors. Bivariate (Table 4.2), and multivariate (Table 4.3) regression tests of statistical significance are reported. Overall, 53.1% completed treatment and 46.9% did not complete treatment, with completion defined as receiving a relative dose-intensity of at least 85% of their prescribed chemotherapy medication delivered over the prescribed time (Ferreira Filho et al., 2002). The mean distress score was 1.57 out of 10 and the mean BMI was 30.35. Of the socioeconomic factors, 65.4% of participants paid for their treatment using managed care, 50.1% were employed, and the average of the median household income of study participants was $79,320. The average age was 52. Participants were mostly white (70.1%) and

married (70.7%). The mean pathological tumor size was 2.42 cm, 33.9% received a Mastectomy W/Axillary Node Dissection surgical procedure, and 85.6% were treated with Cyclophosphamide Doxorubicin Paclitaxel chemotherapy regiment. Sixty-one-point-two percent received neoadjuvant chemotherapy, 50.4% received adjuvant chemotherapy, and 80.1% received radiation therapy.

Table 4-1 Chemotherapy Sample and Bivariate Descriptives

Chemotherapy Sample Descriptives	All patients n (%)		Missing	< 85% RDI		≥ 85% RDI	
All Participants n (%)	508	(100.0)		238	(46.9)	270	(53.1)
Psychosocial factors							
Distress, Mean (Std. Error of Mean)	1.57 (0.24)		40	1.14 (0.23)		1.78 (0.28)	
Family problems			83				
No	440	86.6%		214	89.9%	226	83.7%
Yes	68	13.4%		24	10.1%	44	16.3%
Emotional problems			86				
No	425	83.7%		207	87.0%	218	80.7%
Yes	83	16.3%		31	13.0%	52	19.3%
Health questionnaire 2 (Std. Error of Mean)	0.49 (0.14)		52	0.3 (0.11)		0.65 (0.19)	
Biomedical factors							
Physical problems			96				
No	424	83.5%		203	85.3%	221	81.9%
Yes	84	16.5%		35	14.7%	49	18.1%
BMI, Mean (Std. Error of Mean)	30.35 (1.18)		35	30.39 (0.93)		30.33 (1.51)	
Practical problems			81				
No	417	82.1%		203	85.3%	215	79.6%
Yes	91	17.9%		35	14.7%	55	20.4%
Socioeconomic factors							
Insurance type			0				
Managed care	332	65.4%		135	56.7%	197	73.0%
Medicaid	59	11.6%		32	13.4%	27	10.0%
Medicare	94	18.5%		59	24.8%	35	13.0%
Government/embassy/self-pay	23	4.5%		12	5.0%	11	4.1%
Median census tract household income	$79,320 (4160)		26	$78,040 (5210)		$80,440 (4120)	
Employment			30				
Employed	259	50.1%		107	45.0%	152	56.3%
Not working	136	26.8%		60	25.2%	77	28.5%
Retired	73	14.4%		49	20.6%	25	9.3%
Disabled/part time/student	39	7.7%		23	9.7%	16	5.9%
Demographic factors							
Age at Dx, Mean (Std. Error of Mean), Years	51.65 (0.49)		0	54.17 (0.73)		49.00 (0.63)	
Race/ethnicity			0				
White	356	70.1%		167	70.2%	189	70.0%
Other	11	2.2%		32	13.4%	40	14.8%
Asian/Pacific Is	27	5.3%		6	2.5%	5	1.9%
Spanish, Hispanic	42	8.3%		11	4.6%	16	5.9%
Black	72	14.2%		22	9.2%	20	7.4%

Chemotherapy Sample Descriptives	All patients		Missing	< 85% RDI		≥ 85% RDI	
Marital status			1				
Married	359	70.7%		158	66.4%	200	74.2%
Single	70	13.8%		32	13.4%	38	14.2%
Divorced/Legally Separated	58	11.4%		32	13.4%	26	9.7%
Other/Widowed	21	4.1%		16	6.7%	5	2.0%
Medical care factors							
Pathological Primary-Tumor Size, Mean (Std. Error of Mean)	2.42 (0.11)		0	2.59 (0.16)		2.28 (0.15)	
Primary tumor grade (combined index)			68				
1	63	12.4%		31	13.0%	32	11.8%
2	242	47.6%		126	52.8%	116	43.1%
3	203	40.0%		81	34.2%	122	45.1%
Sentinel Nodes Removed, Mean (Std. Error of Mean)	19.79 (4.26)		192	19.65 (4.68)		19.91 (3.96)	
Sentinel Nodes Positive, Mean (Std. Error of Mean)	11.43 (4.78)		192	11.17 (5.17)		11.30 (4.51)	
Primary surgery			9				
Lumpectomy alone	179	35.2%		98	41.3%	81	29.9%
Mastectomy alone	100	19.7%		39	16.5%	61	22.5%
Lumpectomy w/axillary node dis	57	11.2%		29	12.1%	29	10.7%
Mastectomy w/axillary node dis	172	33.9%		72	30.2%	100	37.0%
Days Between Biopsy and Neoadjuvant Chemo			0				
N/a	197	38.8%		98	41.2%	99	36.7%
0-20 days	39	7.7%		12	5.0%	27	10.0%
21-41 days	149	29.3%		69	29.0%	80	29.6%
42-62 days	98	19.3%		44	18.5%	54	20.0%
>62 days	25	4.9%		15	6.3%	10	3.7%
Days Between Biopsy and Adjuvant			0				
N/a	253	49.8%		115	48.3%	138	51.1%
0-20 days	7	1.4%		4	1.7%	3	1.1%
21-41 days	88	17.3%		44	18.5%	44	16.3%
42-62 days	84	16.5%		36	15.1%	48	17.8%
>62 days	76	15.0%		39	16.4%	37	13.7%
Chemotherapy medication			0				
Cyclophosphamide Doxorubicin Cpdr%	7	1.4%		0	0.0%	7	2.6%
Cpdr Paclitaxel	436	85.6%		223	93.7%	213	78.9%
Cpdr Fluorouracil Paclitaxel	43	8.5%		11	4.6%	32	11.9%
Cpdr Paclitaxel Dose-Dense%	22	4.3%		4	1.7%	18	6.7%

Participant Factors and Treatment-Completion

A generalized linear model (GLM) employing a modified Poisson regression with robust variance estimators was used to examine the relationship between individual variables and chemotherapy treatment-completion (see Table 4.2). As a reminder, statistical significance was set at $p \leq 0.001$. No psychosocial or biomedical factors were significantly associated with treatment-completion. Among the socioeconomic position factors, having Medicare health insurance was related to a 37% significantly lower relative risk ratio of treatment-completion (RR 0.63; 95% CI: 0.48 to 0.83; p=0.001). For demographic factors, greater mean age at diagnosis was correlated with significantly lower risk of treatment-completion (RR, 0.98; 95% CI, 0.97 to 0.99; p<0.001) where a 2% decrease in the number of chemotherapy treatment-completers was observed for each year older at the age of diagnosis.

Of the medical care factors, only chemotherapy regimen was significantly correlated with treatment-completion. Receiving Cyclophosphamide Doxorubicin significantly increased the probability of treatment-completion by 105% (RR 2.05; 95% CI: 1.86 to 2.25; p<0.001), Cyclophosphamide Doxorubicin Fluorouracil Paclitaxel by 58% (RR, 1.58; 95% CI, 1.28 to 1.94; p<0.001), and Cyclophosphamide Doxorubicin with dose dense Paclitaxel by 68% (RR 1.68; 95% CI: 1.35 to 2.09; p<0.001), when compared to receiving Cyclophosphamide Doxorubicin Paclitaxel.

Table 4-2 Chemotherapy Bivariate Regression Analysis

Chemotherapy Bivariate Regression Analysis	B	Relative Risk Exp (B)	95% C.I. for Risk Ratio Lower	Upper	p-value
Psychosocial variables					
Distress	0.04	1.04	1.01	1.07	0.003
Family problems: No compared to Yes	0.24	1.28	1	1.63	0.049
Emotional problems: No compared to Yes	0.19	1.21	0.96	1.53	0.101
Patient Health Questionnaire 2	0.11	1.11	1.04	1.19	0.004
Biomedical factors					
Physical problems: No compared to Yes	0.05	1.05	0.71	1.55	0.796
BMI	0	1	0.98	1.01	0.788
Practical problems: No compared to Yes	0.16	1.17	0.93	1.49	0.181
Socioeconomic factors					
Insurance: compared to Managed Care					
Medicaid	-0.3	0.77	0.58	1.03	0.081
Medicare	-0.5	0.63	0.48	0.83	0.001*
Government/Embassy/Self-Pay	-0.2	0.81	0.52	1.25	0.332
Income	0	1	1	1	0.541
Employment - Compared to Employed					
Not working	-0	0.96	0.79	1.17	0.675
Retired	-0.6	0.57	0.4	0.82	0.002
Disabled/Part Time/Student	-0.3	0.71	0.47	1.08	0.112
Demographic factors					
Age at dx	-0	0.98	0.97	0.99	<0.001*
Race/ethnicity - Compared to White					
Other	-0.2	0.86	0.44	1.65	0.642
Asian/Pacific Is	0.11	1.12	0.8	1.55	0.511
Spanish, Hispanic	-0.1	0.9	0.64	1.25	0.521
Black	0.05	1.05	0.83	1.32	0.697
Marital status - Compared to Married					
Single	-0	0.97	0.77	1.23	0.829
Divorced/Legally Separated	-0.2	0.8	0.6	1.08	0.153
Other/Widowed	-0.8	0.45	0.21	0.95	0.036
Medical care factors					
Tumor size	-0	0.97	0.94	1.01	0.175
Tumor - Compared to Nuclear Grade 1					
Nuclear grade 2	-0.1	0.94	0.68	1.31	0.716
Nuclear grade 3	0.16	1.18	0.86	1.61	0.312
Sentinel Nodes removed	0	1	0.99	1.01	0.778
Sentinel Nodes positive	0	1	0.99	1.02	0.857

Chemotherapy Bivariate Regression Analysis	B	Relative Risk Exp (B)	95% C.I. for Risk Ratio Lower	Upper	p-value
Primary surgery - Compared to Lumpectomy					
Mastectomy Alone	0.3	1.35	1.08	1.7	0.009
Lumpectomy W/Axillary Node Dis	0.12	1.13	0.83	1.53	0.446
Mastectomy W/Axillary Node Dis	0.26	1.3	1.05	1.59	0.014
Days between biopsy and neoadjuvant chemo - Compared to 0-20 days					
No neoadjuvant chemotherapy	-0.3	0.73	0.56	0.93	0.012
21-41 days to start neoadj chemo	-0.3	0.78	0.6	1	0.052
42-62 days to start neoadj chemo	-0.2	0.8	0.6	1.05	0.104
>62 days to start neoadj chemo	-0.6	0.58	0.34	0.98	0.04
Days between biopsy and adjuvant chemo - Compared to 0-20 days					
No adjuvant chemotherapy	0.24	1.27	0.54	3.02	0.584
21-41 days to start adj chemo	0.15	1.17	0.48	2.81	0.732
42-62 days to start adj chemo	0.29	1.33	0.56	3.2	0.519
>62 days to start adj chemo	0.13	1.14	0.47	2.76	0.778
Compared to CpDr Paclitaxel					
Cyclophosphamide Doxorubicin (CpDr)	0.72	2.05	1.86	2.25	<0.001*
CpDr Fluorouracil Paclitaxel	0.42	1.52	1.25	1.86	<0.001*
CpDr Paclitaxel(Dose-Dense)	0.52	1.68	1.35	2.09	<0.001*
Propensity score variables					
Spiritual Religious Concerns	0.08	1.08	0.69	1.69	0.735
Progesterone receptor status: Pos compared to Neg	0.02	1.02	0.83	1.24	0.881
Neoadjuvant Chemotherapy: Yes compared to No	0.09	1.09	0.92	1.3	0.304
Adjuvant Chemotherapy: Yes compared to No	-0.1	0.96	0.81	1.13	0.586
Adjuvant Radiation Therapy: Yes compared to No	0.06	1.07	0.86	1.32	0.559
Diagnosis in 2016 compared to 2015	0.26	1.3	0.69	2.44	0.421
Diagnosis in 2017 compared to 2015	0.27	1.32	0.7	2.48	0.396
Diagnosis in 2018 compared to 2015	0.39	1.48	0.78	2.81	0.233

*Statistically significant at p≤0.001

To assess the assumptions necessary for the Poisson regression to be appropriately employed, multiple regression analysis was used to assess multicollinearity. None of the variables included in the model were correlated at 0.8 or higher, no tolerance value was below 0.2, and no Variance Inflation Factor (VIF) value was above 10. Additionally, less than 20% of cells have fewer than five occurrences. Therefore, no variables were excluded from the model.

When all variables were included in the Poisson regression, no psychosocial, biomedical, socioeconomic position, or demographic factors were statistically significant in the model (see Table 4.3). However, participants receiving Cyclophosphamide Doxorubicin (RR 2.7; 95% CI: 1.81 to 4.04; $p<0.001$), and Cyclophosphamide Doxorubicin Fluorouracil Paclitaxel (RR 1.58; 95% CI: 1.27 to 1.96; $p<0.001$), had a 170% and 58% significantly higher relative risk ratio for completing chemotherapy treatment, respectively.

Table 4-3 Chemotherapy Multivariate Regression Analysis

Chemotherapy Multivariate Regression Analysis	B	Relative Risk Exp (B)	95% C.I. for Risk Ratio		p-value
			Lower	Upper	
Distress	0.02	1.02	0.98	1.06	0.274
Family problems	0.19	1.21	0.87	1.68	0.26
Emotional problems	0.07	1.07	0.76	1.5	0.704
PHQ2	0.05	1.05	0.97	1.14	0.259
Physical problems	-0.19	0.83	0.58	1.19	0.304
BMI	0	1	0.99	1.02	0.661
Practical problems	-0.02	0.98	0.72	1.32	0.871
Insurance - Compared to Managed Care					
Medicaid	-0.2	0.82	0.6	1.13	0.229
Medicare	0.03	1.03	0.72	1.49	0.865
Government/Embassy/Self-Pay	-0.12	0.89	0.53	1.5	0.665
Census tract median income	0.00	1.00	1.00	1.00	0.738
Employment - Compared to Employed					
Not Working	-0.07	0.94	0.76	1.15	0.537
Retired	-0.31	0.74	0.48	1.12	0.156
Disabled/Part Time/Student	-0.46	0.63	0.41	0.98	0.042
Age at Diagnosis	-0.01	0.99	0.98	1.00	0.033
Race/ethnicity - Compared to White					
Other	-0.36	0.7	0.39	1.27	0.241
Asian/Pacific Is	0.08	1.08	0.78	1.51	0.641
Spanish, Hispanic	-0.18	0.84	0.62	1.14	0.257
Black	-0.01	0.99	0.77	1.28	0.94
Marital status - Compared to Married					
Single	-0.04	0.96	0.74	1.24	0.751
Divorced/Legally Separated	-0.21	0.81	0.61	1.09	0.168
Other/Widowed	-0.7	0.5	0.25	0.99	0.047
Tumor Size	-0.02	0.98	0.94	1.01	0.198
Tumor - Compared to Nuclear Grade 1					
Nuclear grade 2	0.02	1.02	0.73	1.43	0.896
Nuclear grade 3	0.24	1.27	0.91	1.76	0.158
Sentinel nodes removed	0	1	0.98	1.01	0.609
Sentinel nodes positive	0.01	1.01	0.99	1.03	0.46

Chemotherapy Multivariate Regression Analysis	B	Relative Risk Exp (B)	95% C.I. of Risk Ratio		p-value
			Lower	Upper	
Primary surgery - Compared to Lumpectomy					
Mastectomy Alone	0.31	1.36	1.09	1.7	0.007
Lumpectomy W/Axillary Node Dis	0.2	1.23	0.86	1.74	0.255
Mastectomy W/Axillary Node Dis	0.35	1.41	1.07	1.86	0.015
Days between biopsy and neoadjuvant chemo - Compared to 0-20 days					
No neoadjuvant chemotherapy	-0.23	0.79	0.56	1.13	0.200
21-41 days to start neoadj chemo	-0.15	0.86	0.64	1.16	0.317
42-62 days to start neoadj chemo	-0.1	0.9	0.66	1.24	0.53
>62 days to start neoadj chemo	-0.33	0.72	0.43	1.19	0.201
Days between biopsy and adjuvant chemo - Compared to 0-20 days					
No adjuvant chemotherapy	0.07	1.07	0.41	2.78	0.891
21-41 days to start adj chemo	0.04	1.04	0.4	2.7	0.937
42-62 days to start adj chemo	0.17	1.19	0.46	3.07	0.722
>62 days to start adj chemo	0.01	1.01	0.39	2.63	0.986
Compared to CpDr Paclitaxel					
Cyclophosphamide Doxorubicin (CpDr)	0.99	2.7	1.81	4.04	<0.001*
CpDr Fluorouracil Paclitaxel	0.46	1.58	1.27	1.96	<0.001*
CpDr Paclitaxel(Dose-Dense)	0.33	1.39	1.06	1.82	0.018

*Statistically significant at $p \leq 0.001$

Hormone Therapy

The hormone therapy sample included 3764 participants. Complete descriptive characteristics can be viewed in Table 4.4, and are organized by psychosocial, biomedical, socioeconomic, demographic, and treatment factors. Bivariate (Table 4.5), and multivariate (Table 4.6) regression tests of statistical significance are reported. Of the psychosocial factors, the hormone therapy sample had a mean SF-12 MCS raw score 16.50, and a mean SF-12 total raw score of 30.84. Of the biomedical factors, the mean pain score was 3.39 out of 10, while the mean SF-12 PCS raw score was 14.34. The mean BMI was 28.48. Of the socioeconomic position factors, 48.6% of participants paid for their treatment using managed care, the average of the median household income of study participants was $80,820, and 59.8% were employed. In demographic factors, the average age was 54.75, while 72.4% of participants identified as white, and 70.7% were married. The mean pathological tumor size was 2.29 cm, 38.5% received a Lumpectomy Alone surgical procedure, and 46.9% were treated with Arimidex hormone therapy. For treatment, 75.6% received neoadjuvant chemotherapy, 64.2% received adjuvant chemotherapy, and 67.9% received radiation therapy. Overall, 64.3% completed treatment and 35.7% did not complete treatment, defined as possessing a prescription of hormone therapy medication for at least 54 months (Chirgwin et al., 2016).

Table 4-4 Hormone Therapy Sample and Bivariate Descriptives

Hormone Therapy Variables	All patients		Missing	Incompletion		Completion	
All participants n (%)	3764	(100.0%)	0	1342	(35.7%)	2422	(64.3%)
Psychosocial factors							
SF 12 Mental component raw score, mean (Std. Error of Mean)	16.50 (0.80)		1980	15.77 (0.88)		16.90 (0.78)	
SF 12 Total raw score, mean (Std. Error of Mean)	30.84 (0.76)		N/A	29.48 (0.85)		31.60 (0.74)	
Biomedical factors							
Episode number			0				
One	3597	95.6%		1278	95.2%	2319	95.7%
More than one	167	4.5%		64	4.8%	103	4.2%
Pain Scale, mean (Std. Error of Mean)	3.39 (0.62)		1876	3.41 (0.66)		2.83 (0.59)	
BMI, mean (Std. Error of Mean)	28.48 (0.15)		166	28.37 (0.21)		28.55 (0.17)	
SF 12 Physical component raw score, mean (Std. Error of Mean)	14.34 (0.33)		1905	13.70 (0.39)		14.70 (0.30)	
Socioeconomic factors							
Insurance type			0				
Managed Care	1830	48.6%		612	45.6%	1218	50.3%
Medicaid	176	4.7%		79	5.9%	98	4.0%
Medicare	1477	39.2%		474	35.3%	1004	41.4%
Government/Embassy or Self-Pay	280	7.4%		178	13.2%	103	4.2%
Median Census Tract Household Income	$80,820 (880)		93	$79,670 (1,210)		$81,090 (960)	
Employment status			638				
Employed	2250	59.8%		754	56.2%	1495	61.7%
Not working	621	16.5%		233	17.3%	389	16.0%
Retired	584	15.5%		207	15.4%	377	15.6%
Disabled/student/part time	309	8.2%		148	11.0%	161	6.6%
Demographic factors							
Age at dx, mean (Std. Error of Mean), in years	54.75 (0.19)		0	53.88 (0.34)		55.23 (0.23)	
Race/ethnicity			0				
White	2725	72.4%		999	74.4%	1726	71.3%
Other	43	1.1%		19	1.4%	24	1.0%
Asian/Pacific Is	202	5.4%		64	4.8%	138	5.7%
Spanish, Hispanic	477	12.7%		152	11.3%	325	13.4%
Black	317	8.4%		107	8.0%	209	8.6%
Marital status			7				
Single	366	9.7%		143	10.7%	223	9.2%
Married	2661	70.7%		912	24.2%	1749	72.2%
Divorced/Legally Separated	404	10.7%		157	11.7%	246	10.2%
Other/Widowed	333	8.8%		130	9.6%	204	8.4%

Hormone Therapy Sample and Bivariate Descriptives	All patients		Missing	Incompletion		Completion	
Medical care factors							
Pathological primary-tumor size, mean (Std. Error of Mean)	2.29 (0.04)		343	2.38 (0.06)		2.24 (0.04)	
Primary tumor grade (combined index)			200				
1	508	13.5%		179	13.3%	333	13.7%
2	2079	55.2%		729	54.3%	1369	56.5%
3	1178	31.3%		435	87.7%	720	29.7%
No sentinel nodes removed, mean (Std. Error of Mean)	9.45 (0.28)		283	9.52 (0.53)		9.25 (0.33)	
No sentinel nodes positive, mean (Std. Error of Mean)	1.72 (0.10)		257	2.14 (0.16)		1.48 (0.09)	
Definitive surgery procedure side 1			4				
Lumpectomy Alone	1450	38.5%		459	34.2%	991	40.9%
Mastectomy Alone	972	25.8%		373	27.8%	598	24.7%
Lumpectomy W/Axillary Node Dis	338	9.0%		110	8.2%	228	9.4%
Mastectomy W/Axillary Node Dis	1004	26.7%		400	29.8%	604	25.0%
Days between diagnostic biopsy and neoadjuvant chemotherapy			0				
N/A	2844	75.6%		993	74.0%	1851	76.4%
Applicable	920	--		349	--	571	--
0-20 days	210	22.8%		109	31.2%	101	17.7%
21-41 days	414	45.0%		133	38.1%	281	49.2%
42-62 days	217	23.6%		78	22.3%	139	24.3%
>62 days	79	8.6%		29	8.3%	50	8.8%
Days between definitive surgery and adjuvant chemotherapy			0				
N/A	2425	64.4%		828	61.7%	1597	65.9%
Applicable	1339	--		514	--	825	--
0-20 days	168	12.5%		74	14.4%	94	11.4%
21-41 days	552	41.2%		224	43.6%	328	39.8%
42-62 days	357	26.7%		120	23.3%	237	28.7%
>62 days	262	19.6%		96	18.7%	166	20.1%
Hormone therapy medication			0				
Arimidex	1765	46.9%		583	43.4%	1182	48.8%
Letrozole	407	10.8%		156	11.6%	251	10.4%
Tamoxifen	1511	40.1%		567	42.3%	944	39.0%
Other/Aromasin	126	3.4%		51	3.8%	75	3.0%

Participant Factors and Treatment-completion

A GLM employing a modified Poisson regression with robust variance estimators was used to examine the relationship between individual variables and the relative risk of hormone therapy treatment-completion (Table 4.5). No psychosocial factors were significantly correlated with the risk of hormone therapy treatment-completion. Of the biomedical factors, increased pain score was correlated with a significantly lower risk of treatment-completion (RR, 0.97; 95% CI, 0.95 to 0.98; $p<0.001$), where a 3% decrease in the number of hormone therapy treatment-completers was observed for each pain score point increase. Greater SF-12 Physical health component summary score (PCS) was significantly correlated with increased risk of treatment-completion (RR, 1.03; 95% CI, 1.02 to 1.05; $p<0.001$), where the number of hormone therapy treatment-completers increased 2% for each SF-12 PCS score point increase. Greater SF-12 Total raw score was also significantly correlated with relative risk of treatment-completion (RR, 1.01; 95% CI, 1.01 to 1.02; $p=0.001$), where the number of hormone therapy treatment-completers increased 1% for each SF-12 PCS score point increase. No socioeconomic position factors were significantly related to treatment-completion. For demographic factors, older age at diagnosis was significantly correlated with the risk of treatment-completion (RR, 1.00; 95% CI, 1.00 to 1.01; $p=0.001$), where a non-zero percent increase in the number of hormone therapy treatment-completers was observed for each one-year increase in age.

Table 4-5 Hormone Therapy Bivariate Regression Analysis

Hormone Therapy Bivariate Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
Psychosocial factors					
SF-12 MCS	0.01	1.01	1.01	1.02	0.004
Biomedical factors					
Episode 1 compared to Episode >=2	-0.04	0.96	0.85	1.08	0.477
Pain	-0.03	0.97	0.95	0.98	0.000
BMI	0.00	1.00	1.00	1.01	0.387
SF-12 PCS	0.03	1.03	1.02	1.05	<0.001*
SF-12 Total	0.01	1.01	1.01	1.02	0.001*
Socioeconomic factors					
Insurance: compared to Managed Care					
Medicaid	-0.16	0.85	0.58	1.24	0.391
Medicare	0.02	1.02	0.83	1.26	0.848
Government/Embassy or Self-Pay	-0.54	0.58	0.37	0.92	0.022
Median Census Tract Household	0.00	1.00	1.00	1.00	0.360
Employment - Compared to Employed	0.00	0.00	0.00	0.00	
Not Working	-0.06	0.94	0.87	1.02	0.131
Retired	-0.03	0.97	0.89	1.06	0.528
Disabled/Student/Part Time	-0.27	0.76	0.64	0.91	0.003
Demographic factors					
Age at dx	0.00	1.00	1.00	1.01	0.001*
Race/ethnicity - Compared to White					
Other	-0.13	0.88	0.67	1.15	0.354
Asian/Pacific Is	0.08	1.08	0.98	1.19	0.131
Spanish, Hispanic	0.07	1.08	1.01	1.15	0.035
Black	0.04	1.04	0.96	1.13	0.350
Marital status - Compared to Married					
Single	0.08	1.08	0.99	1.18	0.083
Divorced/Legally Separated	0.00	1.00	0.89	1.12	0.975
Other/Widowed	0.00	1.00	0.89	1.13	0.948
Medical care factors					
Tumor size	-0.01	0.99	0.98	1.01	0.237
Tumor - Compared to Nuclear Grade 1	0.00	0.00	0.00	0.00	
Nuclear Grade II	-0.01	0.99	0.92	1.07	0.759
Nuclear Grade III	-0.06	0.94	0.87	1.03	0.169

*Statistically significant at $p \leq 0.001$

Hormone Therapy Bivariate Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
Sentinel Nodes removed	0.00	1.00	1.00	1.00	0.426
Sentinel Nodes positive	-0.02	0.98	0.97	0.99	<0.001*
Primary surgery - Compared to Lumpectomy					
Mastectomy Alone	-0.11	0.90	0.85	0.96	0.001*
Lumpectomy W/Axillary Node Dis	-0.01	0.99	0.91	1.07	0.733
Mastectomy W/Axillary Node Dis	-0.13	0.88	0.83	0.94	<0.001*
No neoadjuvant chemotherapy	0.34	1.41	1.21	1.65	<0.001
21-41 days to start neoadj chemo	0.29	1.33	1.12	1.58	0.001
42-62 days to start neoadj chemo	0.28	1.32	1.06	1.64	0.014
>62 days to start neoadj chemo	0.30	1.35	1.17	1.56	<0.001*
No adjuvant chemotherapy	0.16	1.18	1.03	1.35	0.020
21-41 days to start adj chemo	0.06	1.06	0.91	1.23	0.435
42-62 days to start adj chemo	0.12	1.13	0.96	1.33	0.134
>62 days to start adj chemo	0.17	1.19	1.02	1.38	0.029
Hormone medication: compared to Arimidex					
Letrozole	-0.08	0.92	0.85	1.00	0.052
Tamoxifen	-0.19	0.83	0.68	1.01	0.064
Other/Aromasin	-0.07	0.93	0.89	0.98	0.008
Menopausal status: Compared to Pre-					
Other Peri/Pregnant	-0.14	0.87	0.67	1.14	0.302
Post Natural	-0.04	0.96	0.89	1.04	0.328
Post Unnatural	0.06	1.06	0.98	1.14	0.142
Education level: < HS graduate					
HS graduate	0.09	1.09	0.91	1.31	0.321
Voc./Tech. school/2 yr. Degree/College	0.08	1.09	0.76	1.57	0.644
Bachelor's degree	0.13	1.14	0.93	1.38	0.203
Advanced degree	0.18	1.19	0.99	1.45	0.068
Other	0.04	1.04	0.87	1.24	0.687
Estrogen Receptor Status Pos compared to Neg	1.24	3.44	1.24	9.54	0.018
Progesterone Receptor Status: Pos vs. Neg	0.02	1.02	0.95	1.10	0.537
Neoadjuvant Chemotherapy: Yes vs. no	-0.05	0.95	0.90	1.01	0.104
Adjuvant Chemotherapy: Yes vs. no	-0.07	0.93	0.88	0.98	0.006
Radiation Therapy: Yes vs. no	0.10	1.10	1.04	1.16	<0.001*

*Statistically significant at $p \leq 0.001$

Of the medical care factors, having more Sentinel Nodes diagnosed as positive was correlated with significantly lower risk of treatment-completion (RR, 0.98; 95% CI, 0.97 to 0.99; $p<0.001$), where a 2% decrease in the number of hormone therapy treatment-completers was observed for each Sentinel Node with cancer found during surgery. When compared to the lumpectomy alone surgical procedure, receiving a mastectomy alone surgery type (RR, 0.9; 95% CI, 0.85 to 0.96; $p=0.001$), or a mastectomy w/axillary node dissection surgery type (RR, 0.88; 95% CI, 0.83 to 0.94; $p<0.001$), both were associated with a 10%, and 12% significantly lower probability of hormone therapy treatment-completion, respectively. Compared to starting neoadjuvant chemotherapy within 0-20 days after the diagnostic biopsy, beginning neoadjuvant chemotherapy 21-41 days after diagnostic biopsy (RR, 1.41; 95% CI, 1.21 to 1.65; $p<0.001$), or 42-62 days after diagnostic biopsy (RR, 1.33; 95% CI, 1.12 to 1.58; $p=0.001$), significantly increased the probability of treatment-completion (41% and 33%, respectively), while not receiving neoadjuvant chemotherapy was also related to a 41% increased probability of treatment-completion (RR 1.41; 95% CI: 1.21 to 1.65; $p<0.001$). Among the exploratory variables, receiving radiation therapy was related to a 10% significantly higher probability of treatment-completion (RR, 1.1; 95% CI, 1.04 to 1.16; $p<0.001$).

To assess the assumptions necessary for the Poisson regression to be appropriately employed, multiple regression analysis was used to assess multicollinearity (Field, 2013). Three pairs of variables included in the model were correlated with one another at 0.8 or higher. A Pearson correlation of 0.93 was found between the SF-12 MCS and SF-12 total score. A Pearson correlation of 0.91 was found between categorical days to neoadjuvant chemotherapy and receiving neoadjuvant chemotherapy Y/N. A Pearson correlation of 0.90 was found between categorical days to adjuvant chemotherapy and receiving adjuvant chemotherapy Y/N.

Additionally, four tolerance values were below 0.2; the Tolerance value of categorical days to neoadjuvant chemotherapy was 0.17, the Tolerance value of categorical days to adjuvant chemotherapy was 0.18, the Tolerance value of receiving neoadjuvant chemotherapy Y/N was 0.15, and the Tolerance value of receiving adjuvant chemotherapy Y/N was 0.17. No VIF was above 10. After removing SF-12 total score, receiving neoadjuvant chemotherapy Y/N, and receiving adjuvant chemotherapy Y/N from the linear regression model, none of the remaining variables included in the model were correlated at 0.8 or higher, no tolerance value was below 0.2, and no VIF value was above 10. Additionally, fewer than 20% of cells have fewer than five occurrences, and no cell has a value less than one. Therefore, no additional variables were excluded from the model.

When all appropriate variables were included in the Poisson regression, no psychosocial, biomedical, socioeconomic position, or demographic factors significantly changed the relative risk of treatment-completion in the model (Table 4.6). Among the medical care factors, having more Sentinel Nodes positive was significantly correlated with lower risk of treatment-completion (RR, 0.96; 95% CI, 0.93 to 0.98; $p<0.001$), where a 4% decrease in the number of hormone therapy treatment-completers was observed for each additional Sentinel Node with cancer found during surgery. When compared to 0-20 days from diagnostic biopsy to the start of neoadjuvant chemotherapy, starting 21-41 days after neoadjuvant chemotherapy was correlated with 29% significantly higher risk of treatment-completion (RR, 1.29; 95% CI, 1.11 to 1.5; $p=0.001$).

Table 4-6 Hormone Therapy Multivariable Regression Analysis

Hormone Therapy Multivariable Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
SF-12 MCS	0.00	1.00	0.99	1.01	0.617
Episode 1 Compared to ≥ 2	-0.05	0.95	0.67	1.34	0.783
Pain	-0.01	0.99	0.97	1.01	0.343
BMI	0.00	1.00	1.00	1.01	0.422
SF-12 PCS	0.02	1.02	1.00	1.04	0.044
Insurance - Compared to Managed Care					
Medicaid	-0.15	0.87	0.58	1.30	0.472
Medicare	0.00	1.00	0.72	1.39	0.981
Government/Embassy or Self-Pay	-0.47	0.62	0.37	1.05	0.075
Median Census Tract Household Income	0.00	1.00	1.00	1.00	0.749
Employment - Compared to Employed					
Not Working	-0.05	0.95	0.87	1.04	0.247
Retired	-0.08	0.93	0.84	1.02	0.128
Disabled/Student/Part Time	-0.19	0.83	0.71	0.97	0.018
Age at dx	0.01	1.01	1.00	1.01	0.123
Race/ethnicity - Compared to White					
Other	0.05	1.05	0.80	1.36	0.732
Asian/Pacific Is	0.12	1.13	1.02	1.26	0.024
Spanish, Hispanic	0.11	1.12	1.04	1.20	0.004
Black	0.09	1.09	1.00	1.20	0.049
Marital status - Compared to Married					
Single	0.07	1.07	0.98	1.17	0.159
Divorced/Legally Separated	-0.02	0.98	0.87	1.09	0.667
Other/Widowed	-0.02	0.98	0.86	1.10	0.708
Tumor Size	0.00	1.00	0.99	1.01	0.917
Tumor - Compared to Nuclear Grade 1					
Grade II	0.00	1.00	0.93	1.08	0.978
Grade III	0.01	1.01	0.92	1.09	0.895
Sentinel Nodes removed	0.00	1.00	1.00	1.01	0.190
Sentinel Nodes positive	-0.05	0.96	0.93	0.98	<0.001*
Primary surgery - Compared to Lumpectomy					
Mastectomy Alone	0.00	1.00	0.92	1.09	0.983
Lumpectomy W/Axillary Node Dis	0.06	1.07	0.96	1.19	0.257
Mastectomy W/Axillary Node Dis	0.00	1.00	0.90	1.10	0.952

*Statistically significant at p ≤ 0.001

Hormone Therapy Multivariable Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
No neoadjuvant chemotherapy	0.22	1.24	1.07	1.44	0.004
21-41 days to start neoadj chemo	0.25	1.29	1.11	1.50	0.001*
42-62 days to start neoadj chemo	0.21	1.24	1.04	1.47	0.015
>62 days to start neoadj chemo	0.21	1.23	1.00	1.53	0.055
No adjuvant chemotherapy	0.02	1.02	0.89	1.18	0.748
21-41 days to start adj chemo	-0.02	0.98	0.85	1.14	0.818
42-62 days to start adj chemo	0.04	1.04	0.90	1.21	0.587
>62 days to start adj chemo	0.03	1.03	0.88	1.21	0.694
Hormone medication Compared to Arimidex					
Letrozole	-0.06	0.95	0.87	1.03	0.185
Tamoxifen	-0.03	0.97	0.89	1.06	0.470
Other/Aromasin	-0.09	0.92	0.76	1.11	0.377

Statistically significant at $p \leq 0.001$

AI Medication Switching

There were 2253 participants who were included in the AI hormone therapy switching sample. Complete descriptive characteristics can be viewed in Table 4.7, and are organized by psychosocial, biomedical, socioeconomic, demographic, and treatment factors. Bivariate (Table 4.8), and multivariate (Table 4.9) regression tests of statistical significance are reported. Of the psychosocial factors, the AI switching sample had a mean SF-12 MCS raw score 22.41, and a mean SF-12 total raw score of 37.31. Of the biomedical factors, the mean pain score was 2.91, while the mean SF-12 PCS raw score was 14.91. The mean BMI was 29.1. Of the socioeconomic position factors, 58.26% of participants paid for their treatment using Medicare, the average of the median household income of study participants was $77,390, and 53.23% were employed. In demographic factors, the average age was 60.98, while 75.72% of participants identified as white, and 67.85% were married. The mean pathological tumor size was 2.06 cm, 43.77% received a Lumpectomy Alone surgical procedure, and 78.3% were treated with Arimidex AI hormone therapy medication. 22.19% received neoadjuvant chemotherapy, 32.85% received

adjuvant chemotherapy, and 70.53% received radiation therapy. Overall, 68.8% did not switch their AI medication during treatment.

Table 4-7 Aromatase Inhibitor Switching Sample and Bivariate Descriptives

Aromatase Inhibitor Switching Sample and Bivariate Descriptives	A I therapy patients		Missing	No Switch		Switched	
All participants	2253	59.86%		1549	68.80%	704	31.20%
Psychosocial factors							
SF 12 Mental Component raw score, mean (Std. Error of Mean)	22.41 (1.38)		1187	22.48 (1.4)		22.24 (1.36)	
SF 12 Total raw score, mean (Std. Error of Mean)	37.31 (1.61)		N/A	37.47 (1.62)		36.96 (1.61)	
Biomedical factors							
Episode number			0				
One	2123	94.23%		1453	93.80%	670	95.17%
More than one	130	5.77%		96	6.20%	34	4.83%
Pain Scale, mean (Std. Error of Mean)	2.91 (0.63)		1112	2.85 (0.63)		3.05 (0.63)	
BMI, mean (Std. Error of Mean)	29.10 (0.19)		100	29.31 (0.22)		28.64 (0.26)	
SF 12 Physical component raw score, mean (Std. Error of Mean)	14.91 (0.70)		1126	14.99 (0.71)		14.72 (0.69)	
Socioeconomic factors							
Insurance type			353				
Managed care	720	31.95%		452	29.19%	268	38.03%
Medicaid	78	3.45%		48	3.08%	30	4.28%
Medicare	1313	58.26%		961	62.04%	352	49.96%
Government/Embassy or Self-Pay	143	6.35%		88	5.71%	55	7.76%
Median census tract household income	77,390 (840)		36	76,280 (1,000)		79,820 (1480)	
Employment status			434				
Employed	1199	53.23%		802	51.79%	397	56.38%
Not working	352	15.60%		236	15.24%	115	16.39%
Retired	519	23.04%		386	24.89%	134	18.98%
Disabled/student/part time	183	8.14%		125	8.08%	58	8.27%
Demographic factors							
Age at dx, mean (Std. Error of Mean), in	60.98 (0.19)		0	61.78 (0.22)		59.23 (0.36)	
Race/ethnicity			0				
White	1706	75.72%		1152	74.37%	554	78.69%
Other	19	0.84%		14	0.90%	5	0.71%
Asian/Pacific Is	100	4.44%		75	4.84%	25	3.55%
Spanish, Hispanic	249	11.05%		172	11.10%	77	10.94%
Black	179	7.94%		136	8.78%	43	6.11%
Marital status			5				
Single	175	7.78%		117	7.57%	58	8.24%
Married	1529	67.85%		1041	67.18%	488	69.32%
Divorced/Legally Separated	264	11.72%		175	11.30%	89	12.64%

Other/Widowed	285	12.66%		216	13.96%	69	9.80%

Aromatase Inhibitor Switching Sample and Bivariate Descriptives	A I therapy patients		Missing	No Switch		Switched	
Medical care factors							
Tumor size, mean (Std. Error of Mean)	2.06 (0.04)		0	2.10 (0.054)		1.97 (0.07)	
Primary tumor grade (combined index)			98				
1	311	13.80%		211	13.61%	100	14.23%
2	1287	57.10%		863	55.73%	423	60.14%
3	656	29.10%		475	30.67%	181	25.64%
Sentinel Nodes removed, mean (Std. Error of Mean)	8.99 (0.31)		149	9.12 (0.34)		8.71 (0.43)	
Sentinel Nodes positive, mean (Std. Error of Mean)	1.83 (0.11)		146	1.96 (0.13)		8.71 (0.14)	
Primary surgery			135				
Lumpectomy Alone	986	43.77%		686	44.29%	300	42.63%
Mastectomy Alone	513	22.79%		341	22.04%	172	24.43%
Lumpectomy W/Axillary Node Dis	206	9.16%		150	9.66%	57	8.07%
Mastectomy W/Axillary Node Dis	547	24.28%		372	24.01%	175	24.89%
Days between biopsy and neoadjuvant chemo			0				
N/A	1753	77.81%		1192	76.95%	561	79.69%
Applicable	500	22.19%		357	23.05%	143	20.31%
0-20 days	105	21.00%		68	4.39%	37	5.26%
21-41 days	222	44.40%		154	9.94%	68	9.66%
42-62 days	130	26.00%		100	6.46%	30	4.26%
>62 days	43	8.60%		35	2.26%	8	1.14%
Days between biopsy and adjuvant chemo			0				
N/A	1517	67.33%		1067	68.88%	450	63.92%
Applicable	736	32.67%		482	31.12%	254	36.08%
0-20 days	85	11.55%		54	69.23%	31	12.20%
21-41 days	280	38.04%		178	36.93%	102	40.16%
42-62 days	214	29.08%		147	30.50%	67	26.38%
>62 days	157	21.33%		103	21.37%	54	21.26%
Hormone therapy medication			0				
Arimidex	1765	78.30%		1241	80.12%	524	74.43%
Letrozole	407	18.10%		268	17.30%	139	19.74%
Tamoxifen							
Other/Aromasin	81	3.60%		40	2.58%	41	5.82%

Categorical variables: Pooled Frequency rounded whole

Continuous Variables: Mean (Std. Error of Mean)

Participant Factors and AI Medication Switching

A GLM employing a modified Poisson regression with robust variance estimators was used to examine the relationship between individual variables and hormone therapy medication switching (Table 4.8). No psychosocial, or biomedical factors were related to medication switching. Among the socioeconomic position factors, having Medicare health insurance was related to a 28% significantly lower risk of AI switching than having managed care insurance (RR 0.72; 95% CI: 0.61 to 0.85; $p<0.001$). For demographic factors, older age at diagnosis was significantly correlated with lower relative risk of AI medication switching (RR, 0.98; 95% CI, 0.97 to 0.99; $p<0.001$), where a 2% decrease in the number of people who switched their AI medication was observed for each year older they were at the date of diagnosis. Within the medical care factors and compared to receiving Arimidex as the first AI medication, starting with Letrozole as the first AI medication was associated with a 71% significantly increased relative risk of switching AI medication (RR, 1.71; 95% CI, 1.36 to 2.14; $p<0.001$). The exploratory variable completing Menopause Naturally (e.g., non-hysterectomy, non-oophorectomy) (RR, 0.56; 95% CI, 0.44 to 0.72; $p<0.001$), was correlated with a 44% significantly lower risk of AI medication switching. The exploratory variable progesterone receptor-positive was associated with a 42% significantly increased risk of AI medication switching (RR, 1.42; 95% CI, 1.16 to 1.73; $p=0.001$).

Table 4-8 Aromatase Inhibitor Medication Switching Bivariate Regression Analysis

Aromatase Inhibitor Medication Switching Bivariate Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
Psychosocial factors					
SF-12 MCS	-0.01	0.99	0.98	1.01	0.35
Biomedical factors					
Episode >=2 compared to Episode 1	-0.19	0.83	0.62	1.11	0.213
Pain	0.02	1.02	0.99	1.05	0.153
BMI	-0.01	0.99	0.98	1.00	0.023
SF-12 PCS	-0.02	0.98	0.96	1.01	0.149
SF-12 Total	-0.01	0.99	0.98	1.00	0.194
Socioeconomic factors					
Insurance: compared to Managed Care					
Medicaid	0.03	1.03	0.72	1.47	0.857
Medicare	-0.33	0.72	0.61	0.85	<0.001*
Government/Embassy or Self-Pay	0.00	1.00	0.71	1.41	0.997
Median Census Tract Household Income	0.00	1.00	1.00	1.00	0.035
Employment - Compared to Employed					
Not Working	-0.01	0.99	0.82	1.19	0.929
Retired	-0.25	0.78	0.65	0.93	0.007
Disabled/Student/Part Time	-0.03	0.97	0.71	1.31	0.838
Demographic factors					
Age at dx	-0.02	0.98	0.97	0.99	<0.001*
Race/ethnicity - Compared to White					
Other	-0.21	0.81	0.38	1.72	0.585
Asian/Pacific Is	-0.26	0.77	0.54	1.09	0.139
Spanish, Hispanic	-0.05	0.95	0.78	1.16	0.628
Black	-0.30	0.74	0.56	0.97	0.028
Marital status - Compared to Married					
Single	0.04	1.04	0.83	1.30	0.748
Divorced/Legally Separated	0.05	1.06	0.88	1.27	0.565
Other/Widowed	-0.28	0.76	0.61	0.94	0.013
Medical care factors					
Tumor size	-0.02	0.98	0.95	1.01	0.19
Nuclear grade: compared to I					
Nuclear Grade II	0.02	1.02	0.85	1.22	0.822
Nuclear Grade III	-0.16	0.85	0.69	1.05	0.133
No Sentinel Nodes removed	0.00	1.00	0.99	1.00	0.378
No Sentinel Nodes positive	-0.02	0.98	0.97	1.00	0.034

*Statistically significant at $p \leq 0.001$

Aromatase Inhibitor Medication Switching Bivariate Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
Primary surgery - Compared to Lumpectomy					
Mastectomy Alone	0.10	1.10	0.94	1.28	0.221
Lumpectomy W/Axillary Node Dis	-0.10	0.90	0.71	1.15	0.414
Mastectomy W/Axillary Node Dis	0.05	1.05	0.90	1.23	0.518
Days between biopsy and neoadjuvant chemo - Compared to 0-20 days					
No neoadjuvant chemotherapy	-0.10	0.91	0.69	1.19	0.481
21-41 days to start neoadj chemo	-0.14	0.87	0.63	1.20	0.4
42-62 days to start neoadj chemo	-0.42	0.66	0.44	0.98	0.042
>62 days to start neoadj chemo	-0.64	0.53	0.27	1.04	0.064
Days between biopsy and adjuvant chemo - Compared to 0-20 days					
No adjuvant chemotherapy	-0.21	0.81	0.61	1.09	0.164
21-4 days to start adj chemo	0.00	1.00	0.72	1.38	0.994
42-62 days to start adj chemo	-0.15	0.86	0.61	1.21	0.384
>62 days to start adj chemo	-0.06	0.94	0.66	1.34	0.746
Hormone medication: compared to Arimidex					
Letrozole	0.53	1.71	1.36	2.14	<0.001*
Other/Aromasin	0.14	1.15	0.99	1.34	0.072
Propensity score and exploratory analysis variables					
Menopausal status: compared to Pre					
Other Peri/Pregnant	-0.25	0.78	0.40	1.53	0.464
Post Natural	-0.57	0.56	0.44	0.72	<0.001*
Post Unnatural	-0.30	0.74	0.58	0.94	0.015
Education level: Compared to < HS graduate					
HS graduate	-0.11	0.89	0.67	1.20	0.453
Voc./Tech. school/2 yr. Degree/College	-0.03	0.97	0.73	1.28	0.81
Bachelor's degree	-0.06	0.94	0.71	1.25	0.692
Advanced degree	0.04	1.04	0.74	1.46	0.808
Other	-0.09	0.92	0.55	1.52	0.736
Estrogen Receptor Status Pos compared to Neg	-0.58	0.56	0.31	1.01	0.054
Progesterone Receptor Status: Pos compared to Neg	0.35	1.42	1.16	1.73	0.001*
Neoadjuvant Chemotherapy: No compared to yes	-0.11	0.89	0.77	1.04	0.154
Adjuvant Chemotherapy: No compared to yes	0.16	1.17	1.03	1.32	0.015
Radiation Therapy: No compared to yes	-0.09	0.91	0.80	1.04	0.174

*Statistically significant at $p \leq 0.001$

To assess the assumptions necessary for the Poisson regression to be appropriately employed, multiple regression analysis was used to assess multicollinearity (Field, 2013). Three pairs of variables included in the model were correlated with one another at 0.8 or higher. A Pearson correlation of 0.93 was found between the SF-12 MCS and SF-12 total score. A Pearson correlation of 0.91 was found between categorical days to neoadjuvant chemotherapy and receiving neoadjuvant chemotherapy Y/N. A Pearson correlation of 0.91 was found between categorical days to adjuvant chemotherapy and receiving adjuvant chemotherapy Y/N. Additionally, four tolerance values were below 0.2; the Tolerance value of categorical days to neoadjuvant chemotherapy was 0.16, the Tolerance value of categorical days to adjuvant chemotherapy was 0.16, the Tolerance value of receiving neoadjuvant chemotherapy Y/N was 0.14, and the Tolerance value of receiving adjuvant chemotherapy Y/N was 0.15. No VIF was above 10. After removing SF-12 total score, receiving neoadjuvant chemotherapy Y/N, and receiving adjuvant chemotherapy Y/N from the linear regression model, none of the remaining variables included in the model were correlated at 0.8 or higher, no tolerance value was below 0.2, and no VIF value was above 10. Additionally, fewer than 20% of cells have fewer than five occurrences, and no cell has a value less than one. Therefore, no additional variables were excluded from the model.

When all appropriate variables were included in the Poisson regression, no factors were significantly correlated with the relative risk of AI medication switching (Table 4.9).

Table 4-9 Aromatase Inhibitor Medication Switching Multivariable Regression Analysis

Aromatase Inhibitor Medication Switching Multivariable Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
SF-12MCS	0.01	1.01	0.99	1.02	0.516
episode 1 compared to ≥ 2	-0.26	0.77	0.58	1.03	0.082
Pain	0.01	1.01	0.98	1.05	0.526
BMI	-0.01	0.99	0.98	1.00	0.141
SF-12 PCS	-0.03	0.97	0.94	1.00	0.086
Insurance - Compared to Managed Care					
Medicaid	0.25	1.29	0.88	1.88	0.188
Medicare	-0.12	0.89	0.70	1.13	0.320
Government/Embassy or Self-Pay	0.10	1.10	0.76	1.60	0.594
Median Census Tract Household Income	0.00	1.00	1.00	1.00	0.053
Employment - Compared to Employed					
Not Working	0.04	1.04	0.86	1.25	0.709
Retired	-0.13	0.88	0.72	1.08	0.214
Disabled/Student/Part Time	-0.07	0.94	0.69	1.27	0.671
Age at dx	-0.01	0.99	0.98	1.00	0.012
Race/ethnicity - Compared to White					
Other	-0.40	0.67	0.33	1.37	0.274
Asian/Pacific Is	-0.35	0.70	0.49	1.00	0.051
Spanish, Hispanic	-0.14	0.87	0.71	1.07	0.196
Black	-0.19	0.83	0.63	1.10	0.192
Marital status - Compared to Married					
Single	0.05	1.05	0.84	1.32	0.644
Divorced/Legally Separated	0.09	1.09	0.91	1.32	0.338
Other/Widowed	-0.09	0.92	0.73	1.15	0.461
Tumor Size	-0.02	0.98	0.95	1.02	0.324
Nuclear Grade I compared to					
Grade II	0.02	1.02	0.85	1.23	0.816
Grade III	-0.17	0.84	0.68	1.04	0.116
No Sentinel Nodes removed	0.00	1.00	0.99	1.01	0.975
No Sentinel Nodes positive	-0.03	0.97	0.95	0.99	0.009

*Statistically significant at $p \leq 0.001$

Aromatase Inhibitor Medication Switching Multivariable Regression Analysis	B	Relative Risk Exp (B)	95% CI		p-value
			Lower	Upper	
Primary surgery - Compared to Lumpectomy					
Mastectomy Alone	0.04	1.04	0.83	1.29	0.757
Lumpectomy W/Axillary Node Dis	-0.04	0.96	0.72	1.28	0.789
Mastectomy W/Axillary Node Dis	0.12	1.12	0.88	1.44	0.351
Days between biopsy and neoadjuvant chemo - Compared to 0-20 days					
No neoadjuvant chemotherapy	-0.11	0.90	0.67	1.21	0.480
21-41 days to start neoadj chemo	-0.03	0.98	0.70	1.35	0.881
42-62 days to start neoadj chemo	-0.36	0.70	0.46	1.06	0.088
>62 days to start neoadj chemo	-0.68	0.51	0.26	1.00	0.048
Days between biopsy and adjuvant chemo - Compared to 0-20 days					
No adjuvant chemotherapy	-0.15	0.86	0.64	1.16	0.313
21-41 days to start adj chemo	0.00	1.00	0.73	1.36	0.994
42-62 days to start adj chemo	-0.16	0.85	0.61	1.19	0.345
>62 days to start adj chemo	-0.02	0.98	0.69	1.38	0.906
Hormone medication: compared to Arimidex					
Letrozole	0.36	1.43	1.13	1.81	0.003
Other/Aromasin	0.13	1.14	0.98	1.33	0.097

*: Statistically significant at $p \leq 0.001$

Aim 2 Results

Descriptive statistics comparing both chemotherapy and hormone therapy treatment-completion, and AI medication switching, sorted by IMC use can be found in Table 4.10. Tables 4.11, 4.12, and 4.13 present results from aim two, examining the effect of receiving Integrative Medicine Center services on chemotherapy treatment-completion, hormone therapy treatment-completion, and AI medication switching, while including the propensity scores as a covariate. Table 4.11 shows probit regression results for the chemotherapy sample. After controlling for the propensity scores and select other covariates/auxiliary variables, the difference in the probability of completing treatment between the comparison and IMC groups was not larger than would be expected by chance. The same results were noted for the hormone therapy sample in Table 4.12 where the difference in treatment-completion did not vary significantly across groups after balancing on the propensity scores. One of the covariates/auxiliary variables did achieve

significance at the .003 level; SF-12 factor scores associated positively with treatment-completion. The probit coefficient may be interpreted on the *z*-score metric; thus, for a one-unit difference in SF-12 factor score, the difference in the *z*-score associated with treatment-completion is .059 (higher *z*-scores are associated with higher probabilities of treatment-completion). It should be noted, however, this finding is not of primary importance in the propensity score model since inclusion of covariates/auxiliary variables only serves to correct the estimate of the influence of the grouping variable. Finally, the results in Table 4.13 indicate that the probability of switching is not significantly different across groups after accounting for propensity scores.

Table 4-10 Treatment-Completion and Aromatase Inhibitor Switching by IMC Attendance

Chemotherapy Sample IMC Descriptives	Non-IMC Use		IMC Use	
All participants	321	63.2%	187	36.8%
≥ 85% RDI				
No	159	49.5%	79	42.2%
Yes	162	50.5%	108	57.8%
Hormone Therapy Variables	**Non-IMC Use**		**IMC Use**	
All participants	3358	89.2%	406	10.8%
≥ 85) RDI				
Incompletion	1180	35.10%	162	39.9%
Completion	2178	64.9%	244	60.1%
Aromatase Inhibitor Switching	**Non-IMC Use**		**IMC Use**	
All participants	2035	90.3%	218	89.7%
Ai medication switch				
No	1417	69.6%	132	60.6%
Yes	618	30.4%	86	39.4%

Table 4-11 Chemotherapy Sample: Propensity Score Probit Regression Model of Treatment-Completion

Chemotherapy Sample: Propensity Score Probit Regression Model of Treatment-Completion				
Variable	Coeff. [95% CI]	SE	*z*	Sig.
IMC Group	0.066 [-0.028, 0.148]	0.048	1.385	0.166
PS	0.513 [-1.947, 2.243]	0.946	0.542	0.588
Constant	0.403 [-0.975, 1.781]	0.703	0.574	0.566

Note. R^2 not reported because none of the terms achieved significance. Robust standard errors reported. Analysis included 508 cases.

Table 4-12 Hormone Therapy Sample: Propensity Score Probit Regression Model of Treatment-Completion

Hormone Therapy Sample: Propensity Score Probit Regression Model of Treatment-Completion				
Variable	Coeff. [95% CI]	SE	*z*	Sig.
IMC Group	-0.031 [-0.084, 0.022]	0.027	-1.175	0.240
PS	-0.313 [-2.681, 2.055]	1.208	-0.26	0.795
Pain*	-0.010 [-0.022, 0.002]	0.006	-1.604	0.109
BMI*	0.002 [-0.002, 0.006]	0.002	1.275	0.202
Median income*	0.009 [-0.044, 0.062]	0.027	0.322	0.747
Age at diagnosis*	0.019 [-0.003, 0.041]	0.011	1.700	0.089
Tumor size*	-0.002 [-0.102, 0.098]	0.051	-0.039	0.969
Node removed*	0.000 [-0.020, 0.020]	0.010	-0.016	0.988
Path t stage*	-0.005 [-0.017, 0.007]	0.006	-0.833	0.405
SF-12 factor score*	0.059 [0.022, 0.096]	0.019	3.006	0.003
Constant*	0.689 [-0.695, 2.073]	0.706	0.977	0.329

Note. R^2 = .026. Robust standard errors reported. Analysis included 3764 cases.

*Auxiliary variables employed to correct the estimate of the influence of IMC grouping assignment

Table 4-13 Aromatase Inhibitor Switching Sample: Propensity Score Probit Regression Model of AI Switching

AI switching sample: Propensity score probit regression model of AI switching				
Variable	Coeff. [95% CI]	SE	*z*	Sig.
IMC Group	0.058 [-0.011, 0.127]	0.035	1.637	0.102
PS	1.979 [-0.577, 4.535]	1.304	1.517	0.129
Pain*	0.007 [-0.007, 0.021]	0.007	1.073	0.283
Median income*	0.029 [-0.038, 0.096]	0.034	0.866	0.386
Age at diagnosis*	-0.045 [-0.082, -0.008]	0.019	-2.399	0.016
Tumor size*	0.019 [-0.108, 0.146]	0.065	0.287	0.774
Node removed*	-0.028 [-0.052, -0.004]	0.012	-2.39	0.017
Path t stage*	-0.016 [-0.032, 0.000]	0.008	-2.013	0.044
SF-12 factor score*	-0.029 [-0.070, 0.012]	0.021	-1.38	0.168
Constant*	-0.410 [-1.907, 1.087]	0.764	-0.536	0.592

Note. R^2 not reported because none of the terms achieved significance. Robust standard errors reported. Analysis included 2253 cases. *Auxiliary variables employed to correct the estimate of the influence of IMC grouping assignment.

CHAPTER 5 DISCUSSION

This dissertation investigated hormone receptor-positive breast cancer chemotherapy and hormone therapy treatment-completion. This was done by determining the rates of completion and then exploring the factors correlated with treatment-completion. While other studies have explored factors related to treatment-completion, this study is, to our knowledge, the first to use propensity score analysis to compare treatment-completion rates between those who did and those who did not receive Integrative Medicine Center services.

Aim 1

Chemotherapy

This study revealed several findings that were unexpected, with only a few results that were in line with our hypotheses and/or prior research. An unexpectedly high number, 46.9%, of participants did not complete treatment (defined as receiving a relative dose intensity (RDI) of their chemotherapy treatment of at least 85%, the cutoff for treatment-completion in this study). Recent studies using similar treatment-completion criteria found about 30% could not reach an RDI of 85% or more (Cespedes Feliciano et al., 2020). However, Zhang et al. (2018) found 39.2% of their sample receiving Cyclophosphamide Doxorubicin Paclitaxel treatments did not reach 85% RDI, which is closer to our findings. This number of people not reaching 85% RDI is substantial and warrants further investigation. Given the somewhat advantaged attributes of the sample compared to Houston TX demographics in terms of race/ethnicity, income, and marital status,, it is difficult to speculate on the reasons for this different outcome. One reason for the high rate of <85% RDI could be due to treatment related side effects, such as neurological or cardiac problems caused by the chemotherapies, which were not measured here. Oncologists do order dose

delays and dose reductions because of these serious side effects, which invariably reduces the RDI of the treatment. In addition, bivariate regression analysis found that receiving any chemotherapy regimen other than cyclophosphamide, doxorubicin, and paclitaxel was linked to a significantly higher relative risk ratio of chemotherapy treatment-completion. This finding suggests that the dose-dense treatment of cyclophosphamide and doxorubicin, preceded or followed by paclitaxel is hard to stick with for the entire course of cycles in the allotted time. The other regimens in this study, such as the one that included fluorouracil, were prescribed three weeks between cycles of cyclophosphamide and doxorubicin; that is less than the dose dense regimen of cyclophosphamide and doxorubicin every two-weeks. These differences remained significant in the multiple regression model.

Collecting data on patient reported outcomes like distress, as well as mental and physical problems, is a growing field in cancer care (Lopez et al., 2019). We measured these outcomes in this dissertation with the expectation that greater difficulties would be correlated with lower treatment-completion. However, we found no differences between those who did and did not meet the 85% RDI threshold. One reason could be that when data was collected, study participants had not yet experienced symptoms that would affect their distress scores or their mental health, which resulted in very few cases of distress and few high PHQ2 scores.

Like Qi et al. (2020), we found that older age was correlated with significantly increased risk of treatment-incompletion. Similarly, paying for treatment was linked with a lower treatment-completion, which matches our sample given the increased risk of having a lower treatment-completion as one gets older. Surprisingly, we found no significant relationship between BMI and treatment-completion, which differs from Cespedes Feliciano et al. (2020) (no significant relationship between BMI and treatment-completion was found

in the three samples we analyzed). One difference between our study is that Cespedes Feliciano et al. (2020) compared differences in RDI using the variable body surface area (BSA), a formula parallel to BMI, but perhaps superior because it is also used to calculate the chemotherapy dose. Using BSA seems like a promising strategy to take in future RDI related studies.

Hormone Therapy

The hormone therapy sample experienced a 54-month treatment-completion rate of 64.3%, which is more than the 45-56% 3-year treatment-completion rate found by Hadji et al. (2013), and closer to the finding of 69% treatment-completion rate found in a pair of other studies (Hershman et al., 2011; Murphy et al., 2012). As hypothesized, both pain and physical health (measured by the SF-12 PCS) were significantly correlated with hormone therapy treatment-completion in the expected directions. Those with more pain were less likely to complete treatment. Those in better physical health were more likely to complete treatment. These findings align with (Mao et al., 2020) who found chronic pain linked to treatment interruptions and severe symptoms linked to discontinuation. Higher SF-12 PCS score (better health) was related to significantly higher risk of treatment-completion in the final Poisson regression model. This adds to the growing body of evidence suggesting that prior self-reported good health is linked to breast cancer treatment-completion.

A relatively small but significant relationship between older age at the time of diagnosis and treatment-completion was unexpected. However, this difference may be due to the large sample size and could fall into the not-clinically-relevant category of statistical significance. This may be due to older people with cancer having fewer responsibilities that would get in the way of treatment like caring for children, work, or community

responsibilities. Hadji et al. (2013) found both older (>65) and younger (<40) patients at greater risk of discontinuation. The mean age of our sample was about 54, so it is not likely that age can explain the low rate of completion.

Several medical factors were linked with treatment-incompletion at the bivariate level of analysis, including finding more sentinel nodes with cancer cells during the diagnostic biopsy or surgery was associated with lower risk of treatment-completion. This finding is odd in that women with more serious disease in this sample were more likely to stop their hormone therapy medication. This warrants replication. Of the surgeries examined, both mastectomy and mastectomy with axillary node dissection were correlated with increased risk of treatment-incompletion when compared to receiving a lumpectomy. These findings differ from findings by Kemp et al. (2014) who found a relationship between not having a mastectomy and treatment discontinuation. Given side effects like lymphedema affecting women receiving axillary surgery, it is surprising that there was no difference between a lumpectomy procedure and a lumpectomy with axillary node dissection procedure. However, the type of surgical procedure was not correlated with risk of treatment-completion in the final model, so these bivariate results should be interpreted with caution.

Another surprising finding was that people who were prescribed neoadjuvant chemotherapy and started chemotherapy cycles between three and nine weeks after the diagnostic biopsy were more likely to complete hormone therapy than people who started chemotherapy within three weeks of the diagnostic biopsy. We had hypothesized that people starting chemotherapy right away would be more likely to complete treatment, but that was not the case here. These findings remained statically significant in all multiple Poisson regression models. These findings suggest even a seemingly injurious patient behavior of

starting treatment after a substantial delay is related to treatment-completion and illustrates how sometimes unexpected factors influence treatment-completion. One explanation may be that people who wait for treatment use the time to gather resources, make plans, and otherwise prepare psychologically for the arduous journey entailed with completing treatment.

The exploratory dichotomous variable, "having received radiation therapy," was correlated with increased treatment-completion at the bivariate level, and in the final two multiple Poisson regression models. These findings align with Nichol et al. (2017) who found that 65% of those who received both hormone and radiation therapy completed four years of hormone therapy compared to 55% who completed four years of hormone therapy and did not receive radiation therapy. This illustrates that it is difficult to predict factors leading to treatment-completion, which can be counter intuitive. It is important to consider that the combination treatment may provide added attention and apparent commitment to the patient's ultimate success, which could provide additional motivation for continuing.

AI Medication Switching

Like the hormone therapy sample, more than two-thirds of the AI medication switching group stuck to one hormone therapy for their entire treatment and increased their chances of a better outcome. Being prescribed Letrozole as the first hormone therapy medication significantly increased the risk of switching to a different hormone therapy medication in bivariate analysis, when compared to Arimidex. However, in the multiple regression model, differences were no longer statistically significant for letrozole. Again, these findings should be interpreted with caution given the modest risk ratios and large sample size of this study.

Interestingly, age related factors such as being on Medicare health insurance, being older in age, and having entered menopause naturally were all significantly correlated with remaining on the same hormone therapy medication when compared to women who began their treatment while pre-menopausal. Menopause is physiologically and psychologically complex, so not having this added challenge may be a benefit to some women, while the benefits may depreciate over time. Menopausal status was an exploratory factor in this study, and findings suggest this variable may be an important factor affecting hormone therapy treatment-completion.

Finally, the exploratory and immutable factor, progesterone receptor positive status of the breast cancer was related to significantly increased risk of switching AI therapies during treatment in both the bivariate and final two multiple Poisson regression models. While this factor is part of the patient's diagnosis and, therefore, unchangeable, oncologists and their entire treatment team should remain aware of increased risk of switching, and work to mitigate the risks that switching hormone therapy poses for women with breast cancer.

Aim 2

No significant differences were found between women who received services at the IMC, and those who did not receive IMC services, in relation to treatment-completion or AI medication switching. These findings are surprising because individual IMC services provide treatments and lifestyle counseling that has consistently been correlated with treatment-completion. Our findings are similar to Shalom-Sharabi et al. (2017), who found that IM significantly increased chemotherapy RDI for gynecological cancer treatment at six weeks, but was not significantly different to control participants at 12 weeks for selective

chemotherapies. Our findings differ from prior work that found complementary or alternative medicine use was related to early AI hormone therapy discontinuation (Huiart et al., 2013).

We speculate that one reason this study did not find a treatment-completion benefit for IMC users compared to nonusers, through the covariate adjustment propensity score analysis, is that both groups were remarkably similar. We expected that people completing treatment would have much less pain and distress, and much better mental and physical health. That was not what we found here. IMC users and non-users were very similar on these predictor variables. In our model checking process during the propensity score analysis (Table 3.13), we found the two groups to have very similar propensity scores. If we used a different inclusion criterion for a subset of these samples, such as having a pain or distress score ≥ 1, perhaps a difference in treatment-completion rates might be revealed.

Another reason the outcome variables were not different between groups could be that the criterion for being selected into the IMC group did not have a sufficiently impactful cutoff for the minimum service, meaning that attending even one group yoga, or cooking class, or one integrative oncology physician consultation enabled inclusion into the IMC sample. No peer reviewed study found one-hour group class or one meeting with a doctor produced lasting changes across multiple domains of human behavior, and a stricter criterion of the number of treatments a person received to be eligible for IMC grouping assignment may have led to different results.

Limitations

Not all factors that have been found to significantly affect treatment-completion in prior research could be assessed in this study because not all relevant variables were available in this exploration of medical record data. Important factors related to treatment-

completion, like the quality of the oncologist/patient relationship, were not measured. As is common in using existing medical record data for research, there was a substantial amount of missing data in all three samples, which resulted in statistical procedures that complicated the analysis. Due to the specific nature of this sample, findings of this study do not generalize to other populations with different cancers that occur in different populations (e.g., prostate) and have different side effects (e.g., sexual dysfunction) than people with breast cancer.

One critical assumption in propensity scoring is that all confounding variables are measured (Eulenburg et al., 2016), and there is no way to definitively determine whether this was done. Having a minimum number of treatments (e.g., 8 acupuncture treatments, or 10 massages, or 20 yoga classes) may be a better criterion for IMC use designation among study participants in future research. IMC services are individually tailored, therefore intentionally unequal and unstandardized, which makes it hard to assume that IMC services have similar effects on different patients. A future analysis could examine specific IM services and their possible association with treatment-completion.

Implications and Future Directions for Practice, Policy, and Research

These findings suggest a pressing need to improve treatment-completion rates for women with breast cancer. Because this sample appears representative of a plurality of Americans with some privilege, possessing white race, health insurance, an approximate annual household income of $80,000, and the support of being married, our findings suggest that all people receiving breast cancer treatment would benefit from social workers, oncologists, nurses, and IMC clinicians initiating a dialogue about the importance of treatment-completion, how difficult it is to accomplish, and normalize obstacles that are brought up by patients.

One policy change could include designating resources towards interrupting factors that influence chemotherapy cycle treatment delays/dose reductions, such as early referral to an integrative medicine center to reduce toxicities, which has some empirical support (Greenlee et al., 2017; Shen et al., 2000). Exercise programs could also help improve dose intensity in this sample (Mizrahi et al., 2015; van Waart et al., 2015). The IMC did not correlate with greater treatment-completion, so policy changes that result in IM treatments of the appropriate dose that meaningful effects factors that impede treatment-completion could help. In addition, our findings connect reported good health with increased hormone therapy treatment-completion, which could mean that an optimal entry point to begin integrative therapies might be at the time of diagnosis and include whole families who often are united in support of a newly diagnosed loved one.

Understanding how to support women to successfully follow challenging and months/years-long medical treatments remains critical, and myriad biobehavioral interventions targeting treatment-completion are urgently needed. While we found both immutable predictors and tough-to-change factors related to treatment-completion, our results suggest targeting pain and physical health, states that can change, as very promising avenues of future research. This has implications for practice. Social workers are often the first to respond to self-reported physical, psychosocial, and behavioral problems. Ensuring that they know IM treatments can help women with breast cancer complete their treatment, offers another avenue to assistance.

Future research, employing a strong enough dose of IM treatments known to have a clinically relevant impact, that compares conventional cancer treatment outcomes between IMC users and non-users is promising. Examining individual IM treatments, while varying

the dose could help in the development of guidelines for patients and providers to understand what is needed for a clinically relevant change to occur. Furthermore, narrowing some of the eligibility criteria, such as examining a single chemotherapy type could offer greater clarity on what is happening to study participants. Lastly, how to determine the best point of entry to refer someone for IMC services so that they receive the optimal treatment is not clear and exploring when to initiate a referral to the IMC is a promising area for exploration. While daunting in appearance, adding contemporary statistical analysis procedures to a medical setting where randomization is difficult, to create an apples-to-apples comparison that evaluates real-world behaviors and outcomes allows these critical questions to be answered.

Abbreviations List

Abbreviation	Term List
(AI)	aromatase inhibitor
(BCS)	breast conserving surgery
(CBT)	cognitive behavioral therapy
(CM)	complementary medicine
(CI)	confidence interval
(CFA)	confirmatory factor analysis
(ER+)	Estrogen receptor-positive
(EFA)	exploratory factor analysis
(FIML)	full information maximum likelihood
(HR)	hazard ratio
(HR+)	hormone receptor positive
(GLM)	generalized linear model
(GMH)	Global Mental Health
(GPH)	Global Physical Health
(HER2-)	Human Epidermal Growth Factor Receptor 2-negative
(IM)	integrative medicine
(IMC)	Integrative Medicine Center
(MAR)	missing at random
(MCAR)	missing completely at random
(MCS)	Medical Outcomes Study Short Form-12: Mental Component Summary
(PCS)	Medical Outcomes Study Short Form-12: Physical Component Summary
(mm)	millimeters
(MI)	multiple imputation
(NCI)	National Cancer Institute
(nd)	No date
(OR)	odds ratio
p	p-value
(PHQ-2)	Patient Health Questionnaire
(PR+)	Progesterone-receptor positive
(RCT)	randomly controlled trial
(RDI)	relative dose intensity
(RR)	relative risk
SE	standard error
(SEP)	socioeconomic position
SF-12	Medical Outcomes Study Short Form-12
(WHO)	World Health Organization

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APPENDIX

ABBREVIATIONS LIST

Abbreviation	Term List
adj	adjuvant
AI	aromatase inhibitor
AMD	adjusted mean difference
BCS	breast conserving surgery
BMI	body mass index
CBT	cognitive behavioral therapy
CM	complementary medicine
CI	confidence interval
CFA	confirmatory factor analysis
CpDr	cyclophosphamide doxorubicin
DIS	dissection
dx	diagnosis
ER+	Estrogen receptor-positive
EFA	exploratory factor analysis
FIML	full information maximum likelihood
HR	hazard ratio
HR+	hormone receptor positive
GLM	generalized linear model
GMH	Global Mental Health
GPH	Global Physical Health
HER2-	Human Epidermal Growth Factor Receptor 2-negative
IM	integrative medicine
IMC	Integrative Medicine Center
IV	independent variable
MAR	missing at random
MCAR	missing completely at random
MCS	Medical Outcomes Study Short Form-12: Mental Component Summary
MRN	medical record number
neoadj	neoadjuvant
PCS	Medical Outcomes Study Short Form-12: Physical Component Summary
mm	millimeters
MI	multiple imputation
NCI	National Cancer Institute
nd	No date
OR	odds ratio
p	p-value
PHQ-2	Patient Health Questionnaire
PR+	Progesterone-receptor positive
RCT	randomly controlled trial
RDI	relative dose intensity

RR	relative risk
SE	standard error
SEP	socioeconomic position
SF-12	Medical Outcomes Study Short Form-12
SMD	standard mean difference
VIF	variance inflation factor
Voc	vocational
WHO	World Health Organization

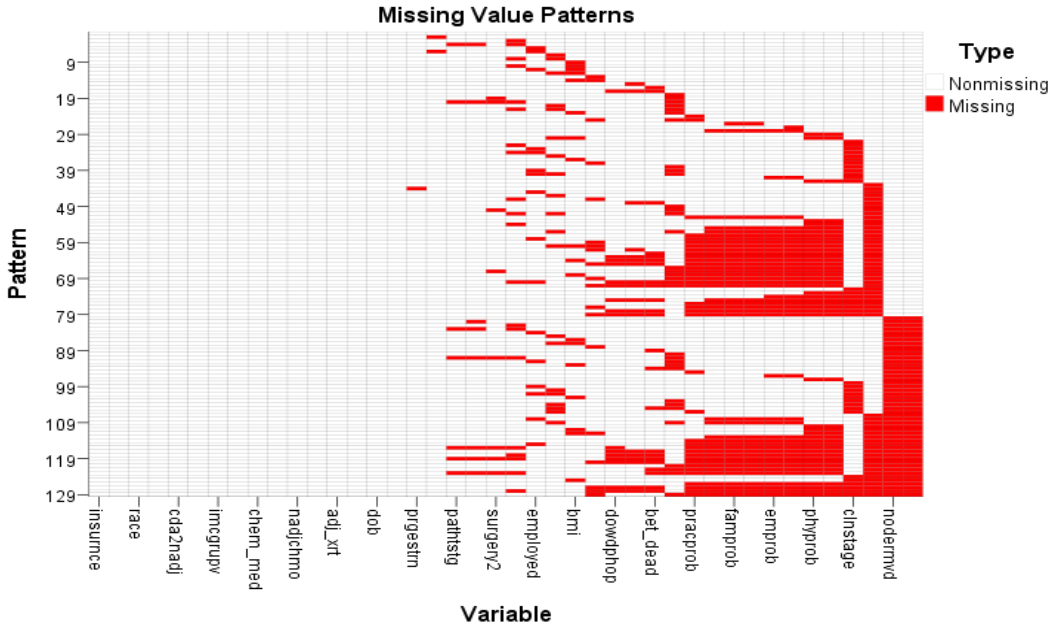
Appendix Table 1 Chemotherapy Sample Missing Information by Variable

Table 4.1 Chemotherapy Sample Missing Information by Variable.

Variable name	Missing (N)	Percent	Valid (N)
Sentinel Nodes removed	192	37.8%	316
Sentinel Nodes positive	192	37.8%	316
Spiritual Religious Concerns	118	23.2%	390
Clinical Stage	102	20.1%	406
Physical problems	96	18.9%	412
Emotional problems	86	16.9%	422
Family problems	83	16.3%	425
Practical problems	81	15.9%	427
Tumor nuclear grade	68	13.4%	440
Feeling you would be better off dead	62	12.2%	446
Little interest or pleasure in activities	50	9.8%	458
Feeling down depressed or hopeless	48	9.4%	460
Distress	40	7.9%	468
BMI	35	6.9%	473
Income	30	5.9%	478
Employment	26	5.1%	482
Pathological stage	25	4.9%	483
Primary surgery	9	1.8%	499
Pathological n stage	8	1.6%	500
Pathological t stage	7	1.4%	501
Marital status	1	0.2%	507
Progesterone receptor status	1	0.2%	507

Note: Variables ordered by missing values

Figure 8 Appendix *Chart Depicting Missing Values for the Chemotherapy Sample*



Chemotherapy Sample

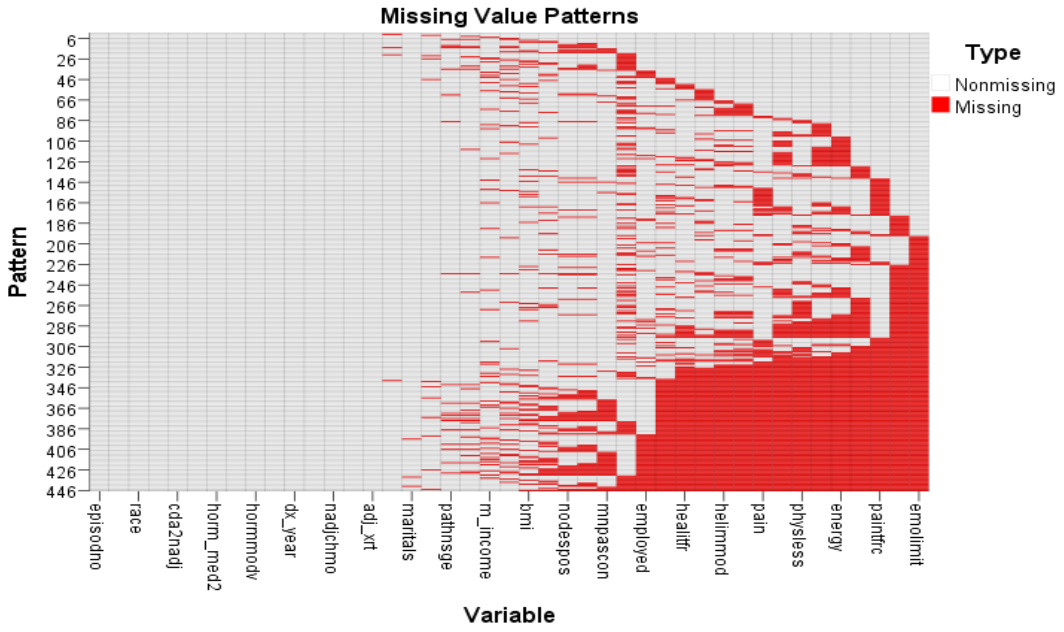
Note. chart shows missing values patterns by variable for the entire chemotherapy dataset.

Appendix Table 2 Hormone Therapy Sample Missing Information by Variable.

Table 4.2 Hormone Therapy Sample Missing Information by Variable.			
Variable name	Missing (N)	Percent	Valid (N)
SF-12 q7 MCS Did work or activities less carefully than usual.	1980	52.6%	1784
SF-12 q6 MCS Accomplished less than you would like	1957	52.0%	1807
SF-12 q8 PCS During the past 4 weeks, how much did pain interfere with your normal work	1905	50.6%	1859
SF-12 q5 PCS Were limited in the kind of work or other activities	1905	50.6%	1859
SF-12 q10 MCS Did you have a lot of energy	1900	50.5%	1864
SF-12 q11 MCS Have you felt down-hearted and blue	1894	50.3%	1870
SF-12 q4 PCS Accomplished less than you would like	1884	50.1%	1880
SF-12 q9 MCS Have you felt calm & peaceful	1883	50.0%	1881
Pain Scale	1876	49.8%	1888
SF-12 q3 PCS Climbing several flights of stairs	1863	49.5%	1901
SF-12 q2 PCS Moderate activities	1857	49.3%	1907
SF-12 q1 PCS In general, would you say your health is	1849	49.1%	1915
SF-12 q12 MCS During the past 4 weeks, how much of the time have your physical health or emotional problems interfered with your social activities	1830	48.6%	1934
Education	1762	46.8%	2002
Employment status	638	17.0%	3126
Insurance type	572	15.2%	3192
Menopausal status	317	8.4%	3447
Sentinel Nodes removed	283	7.5%	3481
Sentinel Nodes positive	257	6.8%	3507
Tumor nuclear grade	200	5.3%	3564
BMI	166	4.4%	3598
Pathological stage	118	3.1%	3646
Income	93	2.5%	3671
Pathological n stage	34	0.9%	3730
Pathological t stage	26	0.7%	3738
Progesterone receptor status	14	0.4%	3750
Marital status	7	0.2%	3757
Definitive surgery procedure side 1	4	0.1%	3760

Note: Variables ordered by missing values

Figure 9 Appendix Chart Depicting Missing Values for the Hormone Therapy Sample



Hormone Therapy Sample

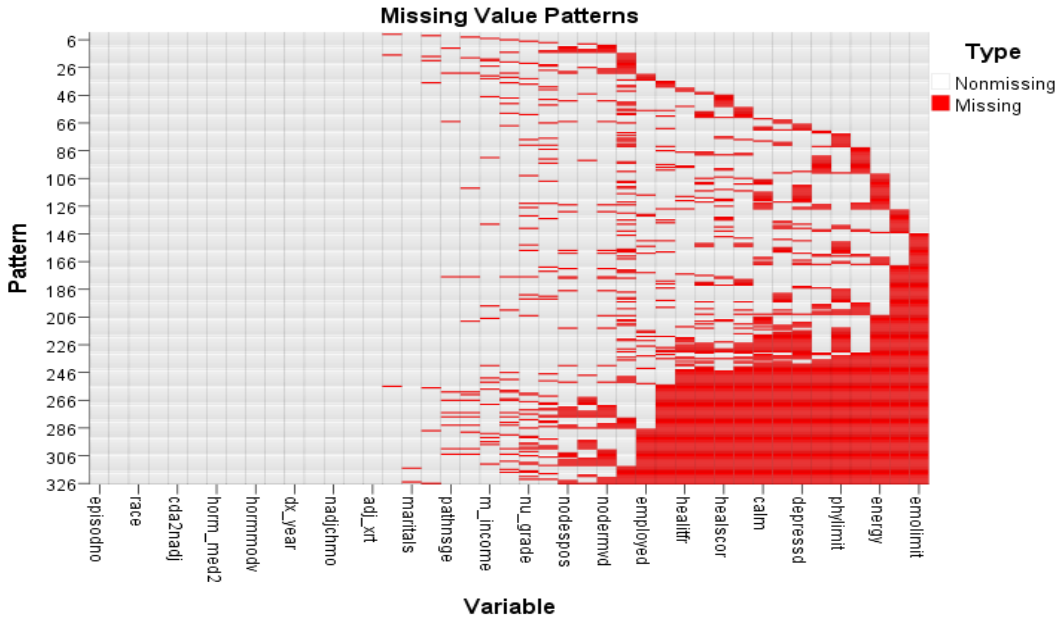
Note. chart shows missing values patterns by variable for the entire hormone therapy dataset.

Appendix Table 3 Aromatase Inhibitor Medication Switching Sample Missing Information by Variable.

AI Medication Switching Sample Missing Information by Variable.			
Variable name	Missing (N)	Percent	Valid (N)
SF-12 q7 MCS Did work or activities less carefully than usual.	1187	52.7%	1066
SF-12 q6 MCS Accomplished less than you would like	1168	51.8%	1085
SF-12 q10 MCS Did you have a lot of energy	1126	50.0%	1127
SF-12 q8 PCS During the past 4 weeks, how much did pain interfere with your normal work	1126	50.0%	1127
SF-12 q5 PCS Were limited in the kind of work or other activities	1126	50.0%	1127
Pain Scale	1112	49.4%	1141
SF-12 q11 MCS Have you felt down-hearted and blue	1111	49.3%	1142
SF-12 q4 PCS Accomplished less than you would like	1111	49.3%	1142
SF-12 q9 MCS Have you felt calm & peaceful	1109	49.2%	1144
SF-12 q3 PCS Climbing several flights of stairs	1093	48.5%	1160
SF-12 q1 PCS In general, would you say your health is	1091	48.4%	1162
SF-12 q2 PCS Moderate activities	1090	48.4%	1163
SF-12 q12 MCS During the past 4 weeks, how much of the time have your physical health or emotional problems interfered with your social activities	1076	47.8%	1177
Education	1025	45.5%	1228
Employment status	434	19.3%	1819
Insurance type	353	15.7%	1900
Sentinel Nodes removed	149	6.6%	2104
Menopausal status	146	6.5%	2107
Sentinel Nodes positive	135	6.0%	2118
BMI	100	4.4%	2153
Tumor nuclear grade	98	4.3%	2155
Pathological stage	65	2.9%	2188
Income	36	1.6%	2217
Pathological t stage	18	0.8%	2235
Pathological n stage	13	0.6%	2240
Progesterone receptor status	8	0.4%	2245
Marital status	5	0.2%	2248
Definitive surgery procedure side 1	3	0.1%	2250

Note: Variables ordered by missing values

Figure 10 Appendix *Chart Depicting Missing Values for the AI Medication Switching Sample*



AI Medication Switching Sample

Note. chart shows missing values patterns by variable for the entire AI Medication Switching dataset.

Appendix Table 4 Chemotherapy Sample Variables for Propensity Score Calculation

Chemotherapy Sample Variables for Propensity Score Calculation	All patients		Missing	< 85% RDI		≥ 85% RDI	
Propensity score variables							
Spiritual religious concerns			118				
No	458	90.2%		217	91.3%	240	89.0%
Yes	50	9.8%		21	8.7%	30	11.0%
"Better off dead"			62				
Not at All	458	90.2%		222	93.4%	236	87.3%
Several days	24	4.7%		7	3.0%	17	6.2%
Nearly every day	26	5.1%		9	3.7%	18	6.5%
Pathological stage			25				
0	36	7.0%		15	6.3%	21	7.7%
IA	106	20.9%		53	22.3%	53	19.6%
IIA	132	26.0%		63	26.4%	69	25.6%
IIB	79	15.6%		42	17.6%	37	13.7%
IIIA	110	21.7%		45	18.7%	66	24.3%
IIIB	3	0.6%		3	1.1%	1	0.2%
IIIC	42	8.3%		18	7.6%	24	8.9%
Estrogen receptor status			0				
Neg	7	1.4%		0	0.0%	7	2.6%
Pos	501	98.6%		238	100.0%	263	97.4%
Progesterone receptor status			1				0.0%
Neg	109	21.5%		52	21.8%	57	21.1%
Pos	399	78.5%		186	78.2%	213	78.9%
Neoadjuvant chemotherapy			0				
No	197	38.8%		98	41.2%	99	36.7%
Yes	311	61.2%		140	58.8%	171	63.3%
Adjuvant chemotherapy			0				
No	252	49.6%		115	48.3%	137	50.7%
Yes	256	50.4%		123	51.7%	133	49.3%
Adjuvant radiation therapy			0				
No	101	19.9%		50	21.0%	51	18.9%
Yes	407	80.1%		188	79.0%	219	81.1%
Diagnosis year			0				
2015	15	3.0%		9	3.8%	6	2.2%
2016	212	41.7%		102	42.9%	110	40.7%
2017	188	37.0%		89	37.4%	99	36.7%
2018	93	18.3%		38	16.0%	55	20.4%

Appendix Table 5 Hormone Therapy Sample Variables for Propensity Score Calculation

Hormone Therapy Sample Variables for Propensity Score Calculation for	All patients		Missing	Incompletion		Completion	
Propensity score variables							
Menopausal status			317				
Pre	1196	31.8%		428	31.9%	768	31.7%
Other/Peri/Pregnant	237	6.3%		109	8.1%	128	5.3%
Post Natural	1406	37.3%		451	33.6%	955	39.4%
Post Unnatural	926	24.6%		355	26.4%	571	23.6%
Education			1762				
< HS grad	589	15.6%		237	17.7%	352	14.5%
HS graduate	619	16.5%		220	16.4%	400	16.5%
Voc./Tech. school/2 yr. Degree	923	24.5%		355	26.4%	568	23.5%
Bachelor's degree	648	17.2%		191	14.2%	457	18.9%
Advanced degree	512	13.6%		170	12.7%	342	14.1%
Other	473	12.6%		169	12.6%	303	12.5%
Pathological stage			118				
0	147	3.9%		52	3.9%	95	3.9%
I	408	10.8%		152	11.3%	256	10.6%
IA	1196	31.8%		393	29.3%	803	33.2%
II	9	0.2%		3	0.2%	6	0.2%
IIA	893	23.7%		289	21.6%	603	24.9%
IIB	488	13.0%		185	13.8%	303	12.5%
III	16	0.4%		6	0.4%	10	0.4%
IIIA	392	10.4%		163	12.2%	228	9.4%
IIIB	45	1.2%		15	1.1%	30	1.2%
IIIC	172	4.6%		84	6.3%	88	3.6%
Estrogen receptor status			0				
Neg	16	0.4%		13	1.0%	3	0.1%
Pos	3748	99.6%		1329	99.0%	2419	99.9%
Progesterone receptor status			14				
Neg	535	14.2%		197	14.7%	338	13.9%
Pos	3229	85.8%		1145	85.3%	2084	86.1%
Neoadjuvant chemotherapy			0				
No	2844	75.6%		993	74.0%	1851	76.4%
Yes	920	24.4%		349	26.0%	571	23.6%
Adjuvant chemotherapy			0				
No	2417	64.2%		822	61.3%	1595	65.9%
Yes	1347	35.8%		520	38.7%	827	34.1%
Radiation therapy			0				
No	1207	32.1%		481	35.8%	726	30.0%
Yes	2557	67.9%		861	64.2%	1696	70.0%

Categorical variables: Pooled Frequency rounded whole
Continuous Variables: Mean (Std. Error of Mean)

Appendix Table 6 Aromatase Inhibitor Switching Sample Variables for Propensity Score Calculation

Aromatase Inhibitor Switching Sample Variables for Propensity Score Calculation	All patients		Missing	Incompletion		Completion	
Propensity score and exploratory analysis variables							
Menopausal status			146				
Pre	135	5.99%		71	4.61%	64	9.02%
Other/Peri/Pregnant	93	4.15%		62	3.98%	32	4.52%
Post Natural	1261	55.97%		921	59.46%	340	48.30%
Post Unnatural	764	33.90%		495	31.96%	269	38.17%
Aromatase inhibitor switching	A I therapy		Missing	No Switch		Switched	
Education			1025				
< HS grad	359.5	15.96%		244.3	15.77%	115.2	16.36%
HS graduate	411.8	18.28%		290.4	18.75%	121.4	17.24%
Voc./Tech. school/2 yr. Degree/College	571.3	25.36%		390.7	25.22%	180.6	25.65%
Bachelor's degree	347	15.40%		238.7	15.41%	108.3	15.38%
Advanced degree	292.3	12.97%		193.8	12.51%	98.5	13.99%
Other	271.2	12.04%		191.1	12.34%	80.1	11.38%
Pathological stage			65				
0	70	3.09%		40.4	2.61%	29.3	4.16%
I	229	10.16%		150.6	9.72%	78.4	11.14%
IA	780	34.64%		543.3	35.07%	237.2	33.69%
II	3	0.15%		1.8	0.12%	1.5	0.21%
IIA	528	23.44%		371	23.95%	157.2	22.33%
IIB	272	12.07%		180.1	11.63%	92	13.07%
III	9	0.41%		6.3	0.41%	3.1	0.44%
IIIA	222	9.87%		145.1	9.37%	77.3	10.98%
IIIB	31	1.39%		24.2	1.56%	7.2	1.02%
IIIC	108	4.78%		86.4	5.58%	21.2	3.01%
Estrogen receptor status			0				
Neg	9	0.40%		4	0.26%	5	0.71%
Pos	2244	99.60%		1545	99.74%	699	99.29%
Progesterone receptor status			8				
Neg	370.6	16.45%		285	18.38%	86	12.20%
Pos	1882.5	83.56%		1264	81.62%	618	87.81%
Neoadjuvant chemotherapy			0				
No	1753	77.81%		1192	76.95%	561	79.69%
Yes	500	22.19%		357	23.05%	143	20.31%
Adjuvant chemotherapy			0				
No	1513	67.15%		1065	68.75%	448	63.64%
Yes	740	32.85%		484	31.25%	256	36.36%
Radiation therapy			0				
No	664	29.47%		443	28.60%	221	31.39%
Yes	1589	70.53%		1106	71.40%	483	68.61%

Categorical variables: Pooled Frequency rounded whole

Continuous Variables: Mean (Std. Error of Mean)

Appendix Table 7 Chemotherapy Variables by IMC Attendance

Chemotherapy Variables by IMC Attendance	Non-IMC Use		IMC Use	
	n	%	n	%
All participants	321	63.2)	187	36.8)
≥ 85% RDI				
No	159	49.5%	79	42.2%
Yes	162	50.5%	108	57.8%
Psychosocial factors				
Distress, Mean (Std. Error of Mean)	1.38 (0.26)		1.65 (0.25)	
Family problems				
No	276	86%	164	87.7%
Yes	46	14.3%	23	12.3%
Emotional problems				
No	268	83.5%	156	83.4%
Yes	53	16.5%	31	16.6%
Health Questionnaire 2 (Std. Error of Mean)	0.47 (0.16)		0.51 (0.14)	
Biomedical factors				
Physical problems				
No	269	83.8%	155	83.4%
Yes	52	16.2%	32	16.6%
BMI, Mean (Std. Error of Mean)	30.31 (1.00)		30.43 (1.63)	
Practical problems				
No	268	83.4%	150	80.1%
Yes	53	16.6%	37	19.9%
Socioeconomic factors				
Insurance type				
Managed care	202	62.9%	130	69.5%
Medicaid	37	11.5%	22	11.8%
Medicare	66	20.6%	28	15.0%
Government/embassy/self-pay	16	5.0%	7	3.7%
Median census tract household income	$78,660 (4,030)		$80,450 (5,620)	
Employment				
Employed	165	51.3%	94	50.5%
Not working	81	25.2%	56	29.7%
Retired	54	16.7%	20	10.8%
Disabled/part time/student	22	6.9%	17	9.1%
Demographic factors				
Age at Dx, mean (Std. Error of Mean), Years	52.59 (0.61)		50.02 (0.80)	
Race				
White	233	72.6%	123	65.8%
Other	7	2.2%	4	2.1%
Asian/Pacific Is	16	5.0%	11	5.9%
Spanish, Hispanic	27	8.4%	15	8.0%
Black	38	11.8%	34	18.2%

Chemotherapy Variables by IMC Attendance	Non-IMC Use		IMC Use	
	n	%	n	%
Marital Status				
Married	235	73.3%	123	65.8%
Single	37	11.6%	33	17.6%
Divorced/Legally Separated	36	11.2%	22	11.8%
Other/Widowed	12	3.9%	9	4.8%
Medical care factors				
Pathological Primary-Tumor Size, Mean (Std. Error of Mean)	2.31 (0.14)		2.61 (0.18)	
Primary Tumor Grade (Combined index)				
1	39	12.1%	24	12.8%
2	158	49.3%	84	44.8%
3	124	38.7%	79	42.4%
Sentinel Nodes Removed, Mean (Std. Error of Mean)	19.36 (4.20)		20.54 (4.48)	
Sentinel Nodes Positive, Mean (Std. Error of Mean)	11.18 (4.70)		11.85 (5.01)	
Primary surgery				
Lumpectomy alone	113	35.3%	66	35.1%
Mastectomy alone	65	20.3%	35	18.6%
Lumpectomy w/axillary node dis	38	11.7%	20	10.6%
Mastectomy w/axillary node dis	105	32.7%	67	35.8%
Days Between Biopsy and Neoadjuvant				
N/a	133	41.4%	64	34.2%
0-20 Days	27	8.4%	12	6.4%
21-41 Days	88	27.4%	61	32.6%
42-62 Days	59	18.4%	39	20.9%
>62 Days	14	4.4%	11	5.9%
Days Between Biopsy and Adjuvant Chemo				
N/a	157	48.9%	96	51.3%
0-20 days	5	1.6%	2	1.1%
21-41 days	59	18.4%	29	15.5%
42-62 days	55	17.1%	29	15.5%
>62 days	45	14.%	31	16.6%
Chemotherapy medication				
Cyclophosphamide Doxorubicin (CpDr)	2	0.6%	5	2.7%
CpDr Paclitaxel	278	86.6%	158	84.5%
CpDr Fluorouracil Paclitaxel	30	9.3%	13	7.0%
CpDr Paclitaxel (Dose-Dense)	11	3.4%	11	5.9%

Chemotherapy Variables Described	Non-IMC Use		IMC Use	
	n	%	n	%
Propensity Score Variables				
Spiritual Religious Concerns				
No	290	90.3%	168	89.6%
Yes	31	9.7%	19	10.4%
"Better Off Dead"				
Not at All	289	90.1%	169	90.3%
Several Days	15	4.6%	9	4.9%
Nearly Every Day	17	5.3%	9	4.9%
Pathological Stage				
0	24	7.5%	12	6.3%
IA	75	23.4%	31	16.6%
IIA	83	26.0%	49	26.0%
IIB	51	15.9%	28	15.0%
IIIA	61	18.9%	50	26.5%
IIIB	2	0.5%	1	0.7%
IIIC	25	7.9%	17	9.1%
Estrogen Receptor Status				
NEG	5	1.6%	2	1.1%
POS	316	98.4%	185	98.9%
Progesterone Receptor Status				
NEG	70	21.8%	39	20.6%
POS	251	78.2%	149	79.4%
Neoadjuvant Chemotherapy				
NO	133	41.4%	64	34.2%
YES	188	58.6%	123	65.8%
Adjuvant Chemotherapy				
NO	157	48.9%	95	50.8%
YES	164	51.1%	92	49.2%
Adjuvant Radiation Therapy				
NO	72	22.4%	29	15.5%
YES	249	77.6%	158	84.5%
Diagnosis Year				
2015	10	3.1%	5	2.7%
2016	141	43.9%	71	38.0%
2017	119	37.1%	69	36.9%
2018	51	15.9%	42	22.5%

Appendix Table 8 Hormone Therapy Variables by IMC Attendance

Hormone Therapy Variables	< Non-IMC Use		IMC Use	
All participants	3358	89.2%	406	10.8%
≥ 85) RDI				
Incompletion	1180	35.10%	162	39.9
Completion	2178	64.9%	244	60.1
Psychosocial factors				
SF 12 Mental Component raw score, mean (Std. Error of Mean)	22.20 (1.35)		21.45 (1.55)	
Biomedical factors				
Episode number				
One	3208	95.5%	389	95.8%
More than one	150	4.5%	17	4.2%
Pain Scale, mean (Std. Error of	2.88 (0.61)		3.05 (0.73)	
BMI, mean (Std. Error of Mean)	28.56 (0.18)		27.53 (0.31)	
SF 12 Physical component raw	15.07 (0.67)		14.90 (0.79)	
Socioeconomic factors				
Insurance type				
Managed care	1610	48.0%	220	54.2%
Medicaid	158	4.7%	19	4.6%
Medicare	1332	39.7%	145	35.7%
Government/Embassy or Self-	258	7.7%	23	5.5%
Median census tract household income	79,820 (810)		87,900 (2310)	
Employment status				
Employed	1985	59.1%	264	65.1%
Not working	553	16.5%	68	16.8%
Retired	543	16.2%	42	10.2%
Disabled/student/part time	277	8.2%	32	7.9%
Demographic factors				
Age at dx, mean (Std. Error of	55.14 (0.20)		51.58 (0.56)	
Race				
White	2433	72.5%	292	71.9%
Other	40	1.2%	3	0.7%
Asian/Pacific Is	174	5.2%	28	6.9%
Spanish, Hispanic	429	12.8%	48	11.8%
Black	282	8.4%	35	8.6%
Marital status				
Single	319	9.5%	47	11.6%
Married	2373	70.7%	288	71.0%
Divorced/Legally Separated	359	10.7%	44	10.9%
Other/Widowed	307	9.1%	27	6.5%

Hormone Therapy Variables	< Non-IMC Use	IMC Use

Medical care factors				
Tumor size, mean (Std. Error of Mean)	2.06 (0.04)		2.24 (0.12)	
Primary tumor grade (combined index)				
1	433	12.9%	47	11.5%
2	1877	55.9%	229	56.4%
3	1048	31.2%	130	32.1%
No Sentinel Nodes removed, mean Std. Error of Mean)	9.28 0.30)		10.85 0.63)	
No Sentinel Nodes positive, mean Std. Error of Mean)	1.72 0.09)		2.16 0.25)	
Primary surgery				
Lumpectomy Alone	1319	39.3%	131	32.3%
Mastectomy Alone	856	25.5%	116	28.6%
Lumpectomy W/Axillary Node	306	9.1%	33	8.1%
Mastectomy W/Axillary Node	879	26.2%	126	31.%
Days between diagnostic biopsy and neoadjuvant chemotherapy				
N/A	2556	76.1%	288	70.9%
Applicable	802	--	118	--
0-20 days	175	21.8%	35	29.7%
21-41 days	360	44.9%	54	45.8%
42-62 days	193	24.1%	24	20.3%
>62 days	74	9.2%	5	4.2%
Days between definitive surgery				
N/A	2170	64.6%	255	62.8%
Applicable	1188	--	151	--
0-20 days	147	12.4%	21	13.9%
21-41 days	493	41.5%	59	39.1%
42-62 days	315	26.5%	42	27.8%
>62 days	233	19.6%	29	19.2%
Hormone therapy medication				
Arimidex	1599	47.6%	166	40.9%
Letrozole	368	11.0%	39	9.6%
Tamoxifen	1323	39.4%	188	46.3%
Other/Aromasin	68	2.0%	13	3.2%

Hormone Therapy Variables	Non-IMC Use		IMC Use	
Propensity score variables				
Menopausal status				
Pre	1041	31.0%	155	38.3%
Other/Peri/Pregnant	212	6.3%	25	6.2%
Post Natural	1273	37.9%	132	32.6%
Post Unnatural	833	24.8%	93	23.0%
Education				
< HS grad	532	15.8%	57	14.1%
HS graduate	573	17.1%	47	11.5%
Voc./Tech. school/2 yr. Degree	830	24.7%	93	22.9%
Bachelor's degree	573	17.1%	75	18.5%
Advanced degree	436	13.0%	77	18.8%
Other	415	12.4%	58	14.2%
Pathological stage				
0	130	3.9%	17	4.1%
I	380	11.3%	27	6.7%
IA	1083	32.2%	114	28.0%
II	8	0.2%	1	0.2%
IIA	784	23.3%	109	26.8%
IIB	427	12.7%	61	14.9%
III	13	0.4%	3	0.6%
IIIA	347	10.3%	45	11%
IIIB	40	1.2%	5	1.3%
IIIC	146	4.3%	26	6.5%
Estrogen receptor status				
Neg	15	0.4%	1	0.2%
Pos	3343	99.6%	405	99.8%
Progesterone receptor status				
Neg	486	14.5%	288	70.9%
Pos	2872	85.5%	118	29.1%
Neoadjuvant chemotherapy				
No	2556	76.1%	288	70.9%
Yes	802	23.9%	118	29.1%
Adjuvant chemotherapy				
No	2162	64.4%	255	62.8%
Yes	1196	35.6%	151	37.2%
Radiation therapy				
No	1084	32.3%	123	30.3%
Yes	2274	67.7%	283	69.7%

Appendix Table 9 Aromatase Inhibitor Switching Sample and Descriptives

Aromatase Inhibitor Switching	Non-IMC Use		IMC Use	
All participants	2035	90.3%	218	89.7%
Ai medication switch				
No	1417	69.6%	132	60.6%
Yes	618	30.4%	86	39.4%
Psychosocial factors				
SF 12 Mental Component raw score, mean (Std. Error of Mean)	22.47 (1.37)		21.81 (1.57)	
Biomedical factors				
Episode number				
One	1917	94.2%	206	94.5%
More than one	118	5.8%	12	5.5%
Pain Scale, mean (Std. Error of Mean)	2.89 (0.62)		3.11 (0.77)	
BMI, mean (Std. Error of Mean)	29.19 (0.20)		28.27 (0.41)	
SF 12 Physical Component raw score, mean (Std. Error of Mean)	14.92 (0.69)		14.76 (0.81)	
Socioeconomic factors				
Insurance type				
Managed Care	640	31.5%	80	36.5%
Medicaid	71	3.5%	7	3.3%
Medicare	1191	58.5%	122	56%
Government/Embassy or Self-Pay	134	6.6%	9	4.3%
Median census tract household income, mean	76,780 (890)		83,030 (2520)	
Employment status				
Employed	1063	52.2%	136	62.5%
Not working	318	15.6%	33	15.2%
Retired	484	23.8%	35	16.2%
Disabled/student/part time	170	8.3%	13	6.1%
Demographic factors				
Age at dx, mean (Std. Error of Mean), in years	61.28 (0.22)		58.26 (0.61)	
Race				
White	1545	75.9%	161	73.9%
Other	19	0.9%	0	0.0%
Asian/Pacific Is	83	4.1%	17	7.8%
Spanish, Hispanic	226	11.1%	23	10.6%
Black	162	8.0%	17	7.8%
Marital status				
Single	158	7.8%	17	7.8%
Married	1371	67.4%	157	72.2%
Divorced/Legally Separated	239	11.7%	25	11.6%
Other/Widowed	267	13.1%	19	8.5%
Aromatase inhibitor medication switching	Non-IMC Use		IMC Use	
Medical care factors				

Tumor size, mean (Std. Error of Mean)	2.04 (0.05)		2.20 (0.14)	
Primary tumor grade (combined index)				
1	284	13.9 %	27	12.6 %
2	1158	56.9 %	129	58.9 %
3	594	29.2 %	62	28.5 %
Sentinel Nodes removed, mean (Std. Error of Mean)	8.78 (0.31)		10.96 (0.81)	
Sentinel Nodes positive, mean (Std. Error of Mean)	1.73 (0.11)		2.75 (0.41)	
Primary surgery				
Lumpectomy Alone	910	44.7 %	76	34.9 %
Mastectomy Alone	463	22.8 %	50	22.9 %
Lumpectomy W/Axillary Node Dis	183	9.0 %	23	10.6 %
Mastectomy W/Axillary Node Dis	478	23.5 %	69	31.7 %
N/A	1591	78.2%	162	74.3%
Applicable	444	21.8%	56	25.7%
0-20 days	86	19.4%	19	33.9%
21-41 days	198	44.6%	24	42.9%
42-62 days	119	26.8%	11	19.6%
>62 days	41	9.2%	2	3.6%
N/A	1380	67.8%	137	62.8%
Applicable	655	32.2%	81	37.2%
0-20 days	71	10.8%	14	17.3%
21-41 days	249	38.0%	31	38.3%
42-62 days	195	29.8%	19	23.5%
>62 days	140	21.4%	17	21%
Hormone therapy medication				
Arimidex	1599	78.6%	166	76.1%
Letrozole	368	18.1%	39	17.9%
Other/Aromasin	68	3.3%	13	6.0%
Menopausal status				
Pre	117	5.7%	18	8.3%
Other/Peri/Pregnant	83	4.1%	11	5.0%
Post Natural	1145	56.3%	116	53.1%
Post Unnatural	691	(33.9)	73	(33.6)

Aromatase Inhibitor Medication Switching	Non-IMC Use		IMC Use	
Education				
< HS grad	326	(16.0)	34	(15.4)
HS graduate	386	(19.0)	26	(11.8)
Voc./Tech. school/2 yr. Degree/College	520	(25.6)	51	(23.5)
Bachelor's degree	309	(15.2)	38	(17.5)
Advanced degree	253	(12.5)	39	(17.8)
Other	241	(11.8)	30	(13.9)
Pathological stage				
0	63	(3.1)	7	(3.3)
I	218	(10.7)	11	(4.9)
IA	715	(35.1)	66	(30)
II	3	(0.1)	1	(0.2)
IIA	477	(23.4)	51	(23.5)
IIB	235	(11.5)	37	(17.1)
III	8	(0.4)	1	(0.5)
IIIA	199	(9.8)	24	(10.8)
IIIB	30	(1.5)	1	(0.6)
IIIC	88	(4.3)	20	(9.1)
Estrogen receptor status				
Neg	8	(0.4)	1	(0.5)
Pos	2027	(99.6)	217	(99.5)
Progesterone receptor status				
Neg	338	(16.6)	32	(14.9)
Pos	1697	(83.4)	186	(85.2)
Neoadjuvant chemotherapy				
No	1591	(78.2)	162	(74.3)
Yes	444	(21.8)	56	(25.7)
Adjuvant chemotherapy				
No	1376	(67.6)	137	(62.8)
Yes	659	(32.4)	81	(37.2)
Radiation therapy				
No	604	(29.7)	60	(27.5)
Yes	1431	(70.3)	158	(72.5)