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Investigating age varying effect of access to cancer care on immediate choice of chemotherapy among elderly women with metastatic breast cancer

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INVESTIGATING AGE VARYING EFFECT OF ACCESS TO CANCER CARE ON IMMEDIATE CHOICE OF CHEMOTHERAPY AMONG ELDERLY WOMEN WITH METASTATIC BREAST CANCER

by

Shaowei Wan

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Pharmacy (Pharmaceutical Socioeconomics)
in the Graduate College of
The University of Iowa

July 2010

Thesis Supervisor: Professor John M Brooks

ABSTRACT

Geographic access to cancer care is an important dimension of quality of cancer care. Previous studies have shown that the more uncertain medical evidence is, the more geographic variation is observed in the medical care utilization that is attributable to local care health care system capacity and local area patient/physician preferences. Chemotherapy for metastatic breast cancer (MBC) is such a case. Although clinical trials have proven the efficacy of chemotherapy in treating MBC, whether to treat elderly MBC patients with chemotherapy is uncertain because of the underrepresentation of elderly patients in the clinical trials. As age advances, uncertainties increase due to competing causes of death, limited life expectancy, and higher risk of toxicities. As a result, geographic access may matter more in chemotherapy choice for older patients than for younger patients. Literature has shown that older patients are less likely to be treated with chemotherapy. In this study, we examined the effect of access to cancer care on age-related difference in chemotherapy use for elderly MBC patients. Access to cancer care is measured by four variables, including travel time to the nearest oncologist practice, local area per capita number of oncologists among stage IV cancer patients, local area per capita number of hospices among stage IV cancer patients, and local area chemotherapy percentage among stage IV cancer patients.

The retrospective cohort study used the 1992-2002 SEER-Medicare database. Chemotherapy use was defined as at least one chemotherapy-related claim within 6 months post diagnosis. To examine the age variant effect of access on chemotherapy choice, the analysis adopted both interaction term approach and subgroup analysis. In interaction term analysis, product term between age and access dummy variables were specified in the multivariate logistic regression model controlling for other covariates; in subgroup analysis, age subgroups were specified consistently with interaction term

approach. For each age subgroup, we used multivariate logistic regression to estimate the effect of access to cancer care on immediate chemotherapy use controlling for covariates.

Among 4533 elderly patients with MBC, 30.16% used chemotherapy. Chemotherapy rate decreased with age. Interaction term approach did not show significant interaction between age and access in each specification. Both interaction term and subgroup analysis showed that the local area treatment rate was positively associated with immediate chemotherapy use across patient age. In addition, subgroup analysis showed among patients who were 85+ years old, the local area oncologist supply was negatively associated with chemotherapy use. This effect was not observed among younger age groups. Our results suggest that estimating all patients in one equation with dummies and interactions can hide results. By estimating each group separately, subgroup analysis showed that provider access is paramount for age subgroup 85 years or older.

Our access measures suggest that access to cancer care affects chemotherapy choice among elderly patients whose clinical evidence is uncertain. This can be attributable to local practice style and physician concern of real benefits of chemotherapy for older patients. The local area chemotherapy practice styles affect chemotherapy choice for patients across age except patients aged between 80 to 84 years old; provider access plays an important role for patients 85 years or older. The more certain the evidence with age, the more access may affect chemotherapy choice.

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CERTIFICATE OF APPROVAL

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PH.D. THESIS

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To my family and the people who inspired and helped me throughout my doctoral studies and throughout my entire life

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LIST OF ABBREVIATIONS

CI	Confidence Interval
CPT	Current Procedural Terminology
HCPCS	Healthcare Common Procedure Coding System
HR	Hormone Receptor
ICD-9-CM	International Classification of Disease, Ninth Revision, Clinical Modification
IRB	Institutional Review Board
MBC	Metastatic Breast Cancer
OR	Odds Ratio
SAF	Standard Analysis File
ZIP	Zone Improvement Plan

CHAPTER I

INTRODUCTION

Introduction

Randomized clinical trials have demonstrated the efficacy of chemotherapy in moderately prolonging survival of and controlling symptoms for metastatic breast cancer (MBC). However, elderly women are underrepresented in these clinical trials. Breast cancer is a disease found primarily among elderly women with over half of the cases occurring among those 65+ years in age (Holmes and Muss 2003). Due to the lack of clinical trial data among this population, uncertainty exists as to whether or not to give elderly women chemotherapy (Bouchardy et al. 2007; Silliman et al. 1993). Researchers have reported lower chemotherapy use among this population than younger patients (Du and Goodwin 2001; Eaker et al. 2006; Freyer et al. 2006). The chemotherapy recommendation for elderly women with MBC is complicated by the heterogeneity of the population. Elderly women vary in baseline health conditions, functional and cognitive status, and social and economic resources. Not every woman diagnosed with MBC may benefit from chemotherapy. As age advances, uncertainty about the benefits of chemotherapy increases due to competing causes of death, limited life span, and higher risk of toxicities. Older patients may also face other hurdles such as diminished social and economic resources. Consequently, in balancing the pros and cons of chemotherapy use, non-clinical factors such as access to cancer care (e.g., local area oncologist availability) may increase in importance. Several studies found the increasing treatment differences associated with the age gradient and identified age as an independent

contributor to lower chemotherapy use (Enger et al. 2006; Giordano et al. 2005; Hawfield et al. 2006; Hurria et al. 2003). However, such age-related difference may reflect both clinical and non-clinical factors. No studies have looked at whether access to cancer care may contribute to such age-related treatment differences among elderly breast cancer patients. Understanding the treatment patterns and the potential access factors underlying such patterns is important as quality of cancer care is largely determined by access to cancer care and the outcomes of such care (Campbell, Roland, and Buetow 2000; Donabedian 1997).

Previous studies have shown that sizable geographic variation in health care utilization exists when clinical evidence for a certain type of care is weak or variable. In the Dartmouth Atlas of Health Care Project, researchers examined multiple chronic conditions and suggested the differences in regional utilization are largely driven by local medical opinion and local health care system capacity (Fisher et al. 2003a; Fisher et al. 2003b). In assessing the relationship among health care quality, geographic variations in health care utilization, and area supply of medical resources/providers, John Wennberg and Elliot Fisher defined three major categories of medical services, including effective care, preference-sensitive care, and supply-sensitive care (Table 1) (Fisher and Wennberg 2003). Effective care refers to services whose benefits far outweigh the risks, and which all patients with specific medical needs should receive, such as surgical repair for patients with hip fractures or beta-blockers for heart attack patients. These services are either supported by a strong medical theory, or their efficacy data has been proven by clinical trial data or valid observational studies. Fisher and Wennberg theorize that the influence of geographic access on effective-care utilization is minimal.

In contrast, they theorize that medical evidence for preference-sensitive care and supply-sensitive care is often variable or weak. Preference-sensitive care typically involves significant tradeoffs between the patient quality and length of life. Examples of preference-sensitive care include lumpectomy versus mastectomy for early stage breast cancer or aggressive treatments for end-of-life care (such as chemotherapy for elderly patients with end stage cancers). Treatment decisions depend heavily on individual patient goals and preferences, and ideally should be based on the choice of a well-informed patient with appropriate aid from physicians. In practice, however, treatment choices for such care are usually delegated to physicians, whose practical experience and clinical opinions may be formed through observance of their colleagues and may vary in different areas (Fisher and Wennberg 2003).

Supply-sensitive care is a type of care whose frequency of use is not well determined by medical theory or scientific evidence. It includes physician visits, diagnostic tests, hospitalizations, and admissions to intensive care among patients with chronic illnesses. Patient treatment decisions for such care often reflect the supply of local medical resources/providers. The researchers showed that where medical evidence is inadequate to demonstrate the effectiveness of the care, such as in the case of supply-sensitive care, health care utilization rates vary dramatically with geography, and that these variations are closely associated with area practice style and area provider supply.

Studies have shown great variations in chemotherapy use for MBC among elderly women, ranging from 38.5% in patients aged 65–69 years old to 9.7% in patients aged 80+ years old using US Medicare claims (Du and Goodwin 2001); from 43.2% in those of 50-69 years of age to 5.5% in those of 70-84 years of age in a university hospital in

Sweden (Eaker et al. 2006); and from 50% in the age group of 65–74 years of age to 28% in the age group of 75+ years old in a French specialist survey study (Freyer et al. 2006). Evidence of the tradeoff between the risks and benefits of chemotherapy use among elderly women is lacking from the available data. Besides limited life expectancy, older age may be associated with worse baseline health status, a higher number of co-existing conditions, and reduced socioeconomic resources compared with younger age. Area practice style and area provider supply are theorized to be more likely to affect older patients' treatment choices than those of younger patients. The magnitude of their effect on chemotherapy choice by older patients may increase as the uncertainties associated with chemotherapy increase. Investigating whether access to cancer care impacts chemotherapy choice and how its effect on chemotherapy use varies with age provides data on how age and access variables intertwine to affect chemotherapy choice for elderly patients.

Table I-1. Categories of Medical Services

	Factors that influence utilization			
	Medical Theory	Medical Evidence	Per Capita Supply of Resources	Importance of Patient Preferences
Effective Care *A problem of underuse*	Strong	Strong	Weak	Weak
Preference-Sensitive Care *A problem of misuse*	Strong	Variable	Variable	Strong
Supply-Sensitive Care *A problem of overuse*	Weak	Weak	Strong	Variable

Source: Health care quality, geographic variations, and the challenge of supply-sensitive care. Fisher, Elliott S. and Wennberg, John E. (Fisher and Wennberg 2003)

Background

Epidemiology of Metastatic Breast Cancer

Breast cancer is a type of cancer that forms in the tissues of the breasts. It is the most common cancer and the second most common cause of cancer-related death among women in western countries (Jemal et al. 2008). It occurs primarily among elderly women with over half of incident cases found among women aged 65+ (Harris, Morrow, and Bonadonna 1993; Miller and Sledge 1999). According to the cancer stage defined by the American Joint Committee on Cancer (AJCC), stage IV breast cancer, also called metastatic breast cancer, occurs when cancer cells have spread out of the breasts to other parts of the body (e.g., bones, lung, liver and brain). Although early breast cancer screening is widely available, metastatic breast cancer (MBC) occurs in approximately 6%-10% of breast cancer patients at initial diagnosis (Harris, Morrow, and Bonadonna 1993; Miller and Sledge 1999). Furthermore, older women have a higher rate of metastasis at diagnosis, and in this group, mortality is considerably higher than in that of their younger counterparts (Freyer et al. 2006; Yancik, Ries, and Yates 1989). Once metastasis occurs, cure is not likely for most patients (Hortobagyi 1998). Typical treatment options include chemotherapy, hormone therapy, and monoclonal antibodies (M.D. Anderson Cancer Center 2005; NCCN 2007; NIH 2001). The goals of therapy for MBC are to ameliorate tumor-related symptoms, improve or maintain quality of life, and prolong overall survival (M.D. Anderson Cancer Center 2005; NCCN 2007; NIH 2001).

The incidence of breast cancer increases with age and is highest among women aged 65+ years (Yancik, Ries, and Yates 1989). As the U.S. population continues to age, the number of women in the older age group will increase at a higher rate than the number of younger women (Fried 2000). These factors combined imply that the absolute number of elderly women with newly diagnosed breast cancer will continue to rise and

the average age of women with newly diagnosed breast cancer will also continuously increase (Silliman et al. 1993).

Elderly patients usually have a higher prevalence and a greater number of chronic conditions than younger patients. There is a greater likelihood of functional disability, dementia, and diminished social resources among them. They are demographically, socially, economically, and physically heterogeneous, varying by chronological and physiological age (Yancik and Ries 2000). Considering the remaining life span, the increasing burden of comorbidities, and the preferences of both the physician and the patient, treatment decisions are especially complex for older patients, for whom the likelihood of comorbidity-related death is greater, the benefits of treatments are less certain, and the potential risk of side effects may be higher.

Despite its high incidence rate, in its earliest stages breast cancer prognosis is relatively good compared with other types of cancers. Five-year relative survival rates are 98.1% for women with localized disease and 83.1% for women with regional disease (Ries et al. 2006). However, the five-year relative survival rate for stage IV breast cancer drops markedly to 26% (Ries et al. 2006). These numbers are improving over time due to early breast cancer screening and emerging new treatments. Therefore, breast cancer can be considered more often chronic than acute (Silliman et al. 1993). Understanding the incidence, prognosis, and the nature of the progression of breast cancer is important in considering a variety of treatment options available for women.

Clinical Trials about Chemotherapy

Chemotherapy plays an important role in the management of MBC (Hortobagyi 1998; Miller and Sledge 1999; O'Shaughnessy 2005). Recent randomized clinical trials have demonstrated the efficacy of chemotherapy to moderately prolong survival for MBC (Albain et al. 2004; Bishop et al. 1999; Feher et al. 2005; Jassem et al. 2001; Jones et al.

1999; Marty et al. 2005; Nabholtz et al. 1999; O'Shaughnessy et al. 2002; O'Shaughnessy, Nag, and Calderillo-Ruiz 2003; Slamon et al. 2001). These clinical trials include both women with MBC at diagnosis and women initially diagnosed with early stage breast cancer whose cancers later relapsed. Despite positive clinical trial data, it is not clear whether these results can be generalized beyond a small subset of patients. Patients who are older, more fragile, have higher performance status and have more comorbid conditions are often not eligible for clinical trials. An examination of the age of participants in the clinical trials mentioned above reveals that the median age ranges from 50 to 56 in 6 out of the 9 trials, and only one trial had a median age of 68 and was conducted among postmenopausal women aged 60 or older (Table 2). The age range in these clinical trials varies, with the majority of enrollees younger than 60 years old, some overlapping between 60 and 70 years of age, a few cases aged between 70 and 80 years old, and the oldest aged 85+ rarely found among clinical trial participants.

Another important factor in determining a benefit-to-toxicity ratio of chemotherapy is the performance status (PS) or activity level of the patient. Two measures used to quantify PS in oncology are the ECOG (Eastern Cooperative Oncology Group) and the Karnofsky scale (Ellison 1998; Karnofsky 1948; Oken et al. 1982). For example, a severely weakened patient with a restricted PS is quantified as ECOG 3 or 4, or Karnofsky < 50 percent (Table 3). The majority of enrollees in clinical trials have an ECOG performance status of 0-2 or a Karnofsky performance status ≥ 70 (Table 2). Therefore, the improved overall survival of about 3 months due to the regimens can be most aptly applied to patients who are younger than 70 at diagnosis and who have a relatively better performance status. Yet women newly diagnosed with MBC are often older with a higher probability of deteriorating performance status (Elston, Koch, and Weissert 1991; Goodwin, Hunt, and Samet 1991). Other measures of functional status also include ADL (the Activities of Daily Living) and IADL (the Instrumental Activities of Daily Living), which are well known in geriatrics. The ADL instrument measures six

basic functional activities, including bathing, dressing, toileting, incontinence, transferring, and feeding (Katz et al. 1963). The instrument has three descriptions for each function: independent, assisted, and dependent functioning. The IADL scale measures more elaborate functions, which consists of nine items, including telephone use, shopping, food preparation, housekeeping, handyman work, laundry, mode of transportation, responsibility for own medications, and ability to handle finances (Lawton et al. 1982). Responses to each item range from independent, to moderately independent, to dependent. Both the ADL and the IADL are commonly used in geriatrics to measure physical and psychosocial function of the aged and guide the course of chronic illness (Fleming et al. 1995). The ECOG PS has been shown to be a valid independent prognostic predictor for cancer patients (Shipp, Harrington, and Anderson 1993). Studies have shown that the ECOG PS, ADL, and IADL are moderately correlated and all should ideally be included in geriatric oncology clinical trials (Extermann et al. 1998). Independent from age and comorbidity level, functional status may reflect an interactive process between cancer stage and comorbidity level. However, with their stringent selection criteria, clinical trials, which exclude older and sicker patients, are probably unlikely to establish the treatment effectiveness of chemotherapy for older patients. The absence of data is an important omission as women over 70 years in age are a sizable body of MBC patients. This topic needs further study to provide meaningful information for clinicians, patients, and policy makers.

Based on the clinical trials for breast cancer, the NIH guidelines clearly recommend chemotherapy for all women younger than 70 years of age regardless of cancer stage (NIH 2001). For women older than 70 years, there is no clear recommendation. Literature has documented that elderly patients are less likely to be treated with chemotherapy and more likely to be treated less intensively or with a reduced dose across all stages of breast cancer (Crivellari et al. 2007; Du and Goodwin 2001; Du et al. 2005; Eaker et al. 2006; Freyer et al. 2006; Gajdos et al. 2001; Giordano et al. 2005;

Owusu, Lash, and Silliman 2007). For MBC, which may affect a higher proportion of elderly women, such treatment patterns of less use of chemotherapy may be more pronounced than in any other stages. However, current literature has not yet fully explored non-clinical factors contributing to the lower chemotherapy use among elderly women with MBC, particularly access-related factors which may lead to the increasing treatment differences associated with the age gradient. In this study, access is a measure of geographic distance to and availability of cancer care for metastatic cancer patients. In previous studies, this measure may be concealed by clinical covariates and have been studies thoroughly. For example, geographic distance to an oncologist practice may impact older patients more than their younger counterparts because elderly patients may be constrained by their mobility and have limited access to transportation.

Significance, Objectives and Aims

In the absence of the best clinical evidence for elderly women with metastatic breast cancer, the "right rate" of chemotherapy use among different age subgroups is unknown. The factors that drive the pattern of lower chemotherapy use among older patients are unclear from available literature. Previous studies have demonstrated that older age is associated with lower chemotherapy use even after controlling for comorbidities among elderly women aged 65 years or older (Enger et al. 2006). Among other variables, access to cancer care may affect patient choice more as the uncertainty in the treatment benefits of chemotherapy increases with age among elderly women.

Table I-2. Summary of Randomized Clinical Trials Showing Significant Survival Improvement in Women with MBC

Study	Regimen	No. of Patients	Median Age	Performance Status	Overall Survival
Randomized clinical trials among anthracycline-pretreated patients					
Nabholtz et al.	Docetaxel	203	51	Median KPS: 90; range:60-100	11.4 (p=.0097)
	Mitomycin/vinblatine	189	52	Median KPS: 90; range:60-100	8.7
Jones et al	Docetaxel	225	56	Median KPS:90; range:40-100	15.4 (p=.03)
	Paclitaxel	224	54	Median KPS:90; range: 60-100	12.7
O'Shaughnessy et al.	Docetaxel and capecitabine	255	52	Median KPS:90;	14.5 (p=.0126)
	Docetaxel	256	51	Median KPS:90;	11.5
Albain et al.	Paclitaxel and Gemcitabine	267	Not reported	KPS $\geq$ 70	18.5 (p=.018)
O'Shaughnessy et al.	Paclitaxel	262		KPS $\geq$ 70	15.8
Randomized clinical trials among patients with no or minimal prior anthracycline exposure					
Bishop et al.	Paclitaxel	107	Not reported	0-2 (ECOG PS)	17.3 (p=.025)
	CMFP	102		0-2 (ECOG PS)	13.9
Jassem et al.	AP	134	50	0-2 (ECOG PS)	22.3 (p=.013)
	FAC	133	50	0-2 (ECOG PS)	18.3
Feher et al.	Epirubicin	198	68	Median KPS: 80; range:60-100	19.1 (P=.0001)
	Gemcitabine	199	69	Median KPS: 80; range:60-100	11.8
Randomized clinical trials of chemotherapy and biologic combinations					
Slamon et al.	AC or paclitaxel + trastuzumab	235	53	Median KPS: 90; range:60-100	25.1 (p=.046)
	AC or paclitaxel	234	53	Median KPS: 90; range:60-100	20.3
Marty et al	Docetaxel + trastuzumab	92	53	Median ECOG: 0; range: 0-4	31.2 (p=.0325)
	Docetaxel	94	55	Median ECOG: 0; range: 0-4	22.7

KPS: Karnofsky performance status. ECOG PS: Eastern Cooperative Oncology Group Performance Status

CMFP: cyclophosphamide, methotrexate, fluorouracil, and prednisone. AP: paclitaxel and docorubicin

FAC: 5-fluorouracil, doxorubicin, and cycolophosphamide

AC: doxorubicin and cyclophosphamide

Table I-3. ECOG and Karnofsky Performance Status Scales

ECOG		Karnofsky	
0	Full active; able to carry on all predisease performance without restriction	100 percent	Normal, no complaints, no evidence of disease
		90 percent	Able to carry on normal activity; minor sings or symptoms of disease
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work)	80 percent	Normal activity with effort; some signs or symptoms of disease
		70 percent	Cares for self; unable to carry on normal activity or do active work
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50 percent of waking hours	60 percent	Requires occasional assistance, but mostly is able to care for self
		50 percent	Requires considerable assistance and frequent medical care
3	Capable of only limited self-care; confined to bed or chair more than 50 percent of waking hours	40 percent	Disabled; requires special care and assistance
		30 percent	Severely disabled; hospitalization indicated; death not imminent
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair	20 percent	Very sick; hospitalization and active supportive treatment necessary
		10 percent	Moribund; fatal processes progressing rapidly
		0 percent	Dead

Based on 1. Karnofsky DA et al. Eastern Cooperative Oncology Group (ECOG) performance status scale. Cancer. 1948; 1:634-656; 2.Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982; 5: 649-655; 3.Ellison NM. Palliative Chemotherapy. Am J Hospice and Palliative Medicine. 1998; 15:93-103.

Since the earlier study of small area variations in health care delivery 30 years ago, Wennberg and his colleagues have relentlessly studied regional treatment variations at state, county, rural/urban areas, health services areas, and hospital referral regions (Wennberg et al. 2008). They found area treatment variations to be largely attributable to local medical opinion and local health system capacity rather than to underlying illness rate. More intensive care does not necessarily translate into better outcomes for Medicare patients with hip fractures, colorectal cancer, acute myocardial infarction, or a representative sample of the Medicare Current Beneficiary Survey (Fisher et al. 2003a; Fisher et al. 2003b). Based on their conclusions, the objective of our study is to understand how access to cancer care affects chemotherapy use for MBC among elderly women and to further investigate the relationships between access factors and the age-related treatment variations among this population. The consideration of age-variant effects of access to cancer care on chemotherapy choice may reflect treatment preferences of older patients and reflect physician preferences when making treatment recommendations for elderly patients. The study uses four variables to measure access to cancer care, including patient travel time to the oncologist practice, local area per capita number of medical oncologists across cancers, local area per capita number of hospice programs across cancers, and local area chemotherapy percentage across cancers. I define the local area as the natural health care market of 50 cancer patients and measure immediate chemotherapy use within 183 days (approximately 6 months) post diagnosis (more in methods section).

To achieve the objective, the study has the following overarching hypothesis with four exploratory hypotheses.

Hypothesis: Uncertainties in the treatment benefits of chemotherapy increase with age and are the greatest for the oldest old (85+). Access to cancer care will have stronger

effects on treatment decisions among older patients than among younger patients. The analysis will explore different specifications of age groups.

Hypothesis 1: Geographic variation in chemotherapy use is associated with age differences in chemotherapy choice within 6 months of diagnosis of MBC. The effect is more pronounced among older patients.

Hypothesis 2: Patients living in areas with more hospice availability are less likely to use chemotherapy within 6 months of diagnosis. The effect is stronger among older patients.

Hypothesis 3: The per capita number of oncologists among end-stage cancer patients within an area around the patient's residence is positively associated with immediate chemotherapy choice. The effect is stronger among older patients.

Hypothesis 4: Patients living closer to an oncologist's practice are more likely to use chemotherapy within 6 months of diagnosis. The effect is stronger among older patients.

CHAPTER II

LITERATURE REVIEW

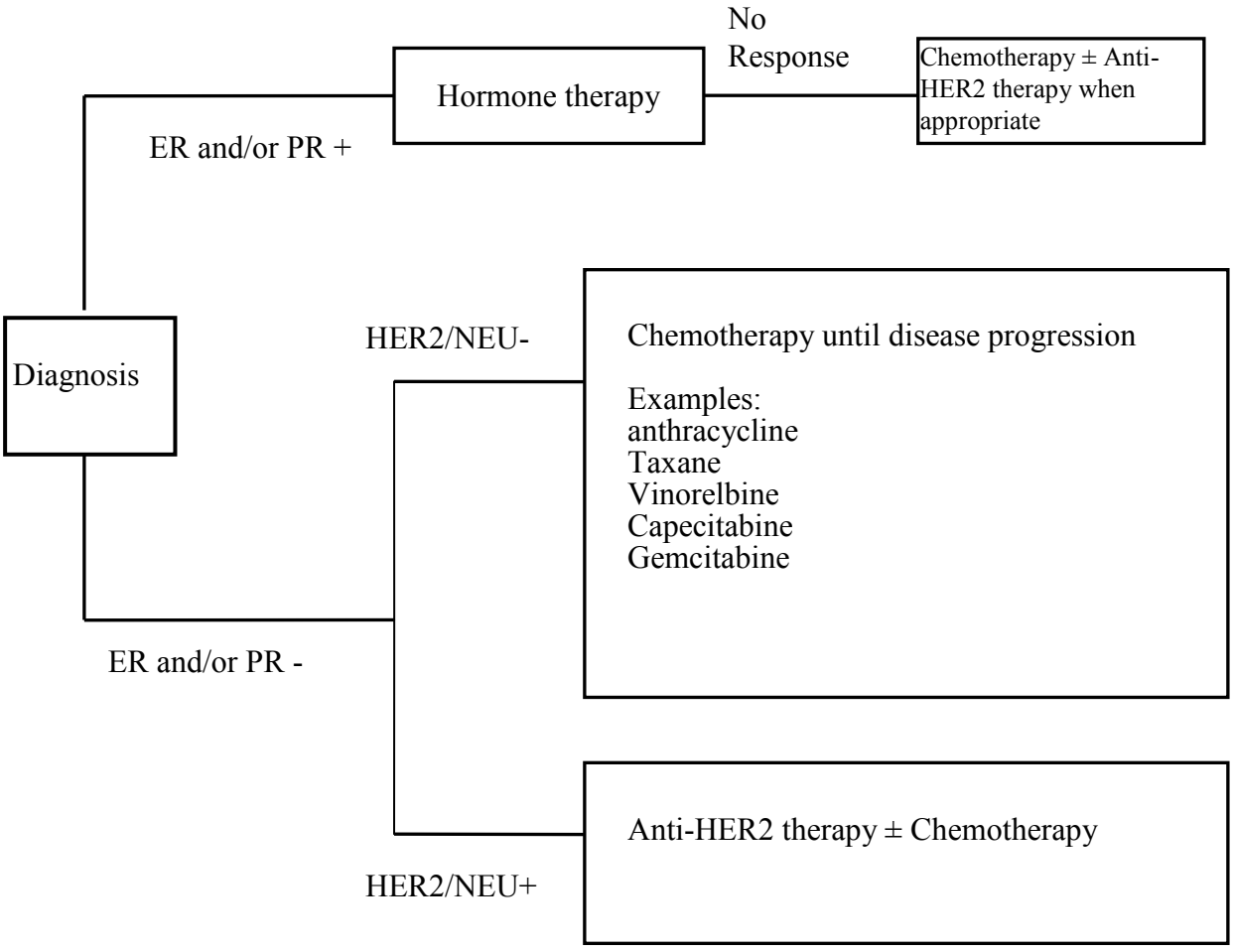
The Role of Chemotherapy in the Management of MBC

Chemotherapy is an important option in the management of MBC (Hortobagyi 1998; Miller and Sledge 1999). Approximately 6%-10% of breast cancer patients are metastatic at diagnosis (Hortobagyi 1998). Median survival for MBC ranges between 18 and 24 months (Hortobagyi 1998). Treatment options for MBC patients include chemotherapy, hormone therapy, immune therapy and watchful waiting (M.D. Anderson Cancer Center 2005; NCCN 2007; NIH 2001). Clinical guidelines for choosing appropriate treatment options are based on the assessment of hormone-receptor (HR) status, length of disease-free interval, site of metastasis, extent of disease, and age (Hortobagyi 1998). Patients with HR positive tumors are usually treated with hormone therapy (NCCN 2007). Tomoxifen is the most commonly used therapy and has the longest track record from clinical trials. Aromatase inhibitors are the new gold standard as first-line hormone therapy in postmenopausal MBC patients since the late 1990s. Eventually, in most women, MBC becomes refractory to hormonal therapy, and patients have to resort to chemotherapy or the combination of other therapies and chemotherapy.

For patients with HR- (i.e., estrogen/progesterone-receptor-negative) tumors or HR+ (i.e., estrogen/ progesterone-receptor-positive) tumors and extensive visceral disease, chemotherapy or immune therapy (e.g., Trastuzumab) can be used (NCCN 2007). Among these patients, two groups can be further classified: those with human epidermal growth factor receptor 2 (HER2/neu) negative and those with HER2/neu positive by either immuohistochemistry or FISH test. For patients with HER2/neu positive, National Comprehensive Cancer Network (NCCN) clinical practice guidelines in breast cancer suggest that Trastuzumab with or without chemotherapy should be used

until disease progression. For those with HER2/neu negative (triple negative), NCCN clinical practice guidelines in breast cancer suggest chemotherapy should be used until disease progression or maximum benefits are achieved. For women with HR- and HER-2-negative, endocrine resistant disease, chemotherapy is currently the only therapeutic option (Figure 1).

Figure 1. Treatment options for Metastatic Breast Cancer



Chemotherapy for MBC includes anthracyclines (doxorubicin, epirubicin) and taxanes (praclitaxel, docetaxel), and palliative therapy (capecitabine, vinorelbine, and gemcitabline) (Cardoso et al. 2002; Esteva et al. 2001). Meta-analysis has shown anthracycline resulted in modest improvement in overall survival compared with nonanthracycline-containing chemotherapy (A'Hern, Smith, and Ebbs 1993; Fossati et al. 1998). Clinical trials exploring the efficacy of taxanes have found that regimens containing taxanes exhibit a survival benefit among anthracycline-pretreated patients and patients with no or minimal prior anthracycline exposure (Albain et al. 2004; Jones et al. 2005; Nabholtz et al. 1999; O'Shaughnessy et al. 2002; O'Shaughnessy, Nag, and Calderillo-Ruiz 2003). Among anthracycline-pretreated patients in Phase III clinical trials, capecitabine, which is a type of antimetabolite, has been shown to improve survival when used with docetaxel compared with docetaxel alone, and with no significant increase in treatment-related side effects (O'Shaughnessy et al. 2002). The combination of gemcitabine/paclitaxel yielded statistically significant improved survival in relation to paxlitaxel alone in another Phase III clinical trial (Marty et al. 2005; O'Shaughnessy, Nag, and Calderillo-Ruiz 2003; Slamon et al. 2001). The combination of chemotherapy (e.g., docetaxel) with monoclonal antibodies (e.g., trastuzumab) exhibits positive effects on survival at the price of higher cardiotoxicity (Marty et al. 2005; Slamon et al. 2001) (Table 2). The subsequent lines of chemotherapy showed an improved palliation of symptoms without obvious prolonged survival (Blum et al. 1999; Freyer et al. 2003; Zielinski, Beslija, and Mrsic-Krmpotic 2003). Other clinical studies have examined chemotherapy with hormone therapy (Reyno et al. 2004), chemotherapy plus granulocyte colony-stimulating factor (G-CSF) (Sparano et al. 2000), and sequential single agent therapy (Sledge et al. 1997) on response rate, time to progression, length of disease-free survival, overall survival, and quality of life (Bottomley et al. 2004; Coates et al. 2000; Moinpour et al. 2004) among patients with MBC. Collectively, oncologists generally consider most chemotherapies are equivalent in treating breast cancer. The data have

shown positive results in response rates and time to progression with a growing series of clinical trials demonstrating a modest but meaningful improvement in overall survival (~3 months).

Age-related Differences in Chemotherapy Use among Elderly Women with Breast Cancer

Because of the lack of clinical trial data examining treatment effects of chemotherapy for MBC among elderly patients, great uncertainty exists as to whether to treat these patients with chemotherapy. Numerous studies have reported substandard chemotherapy use displayed in several aspects: no use, less use, or lower dose of chemotherapy among elderly patients with breast cancer in practice (Crivellari et al. 2007; Du and Goodwin 2001; Du et al. 2005; Eaker et al. 2006; Freyer et al. 2006; Gajdos et al. 2001; Giordano et al. 2005; Owusu, Lash, and Silliman 2007). The majority of these studies focused on elderly women aged 65 years or older with two exceptions that Gajdos study was across the age span from 23 to 92 years old and Eaker study covered age range between 50 to 84 years old. Several studies looked at the variation in chemotherapy use for each stage and showed that elderly women are more likely to have MBC than younger patients, and among this population, chemotherapy use decreases with age, with the lowest treatment rate among the oldest old group (Du and Goodwin 2001; Eaker et al. 2006; Freyer et al. 2006). Clinicians have been puzzled with the controversy between the potential gains versus the risks of chemotherapy as elderly women currently have longer life expectancy and many of them are fairly healthy (as quoted below). To provide evidence to answer these questions from clinical practice, researchers have investigated the reasons contributing to such treatment patterns among elderly women with breast cancer (Bouchardy et al. 2003; Silliman et al. 1993).

"We often assume that one's chronological age mimics his or her physiological age…We know now that chronological and physiological age are not always the same. The elderly are a very mixed group who should be looked at individually to decide if they could tolerate an intense cancer treatment." - Deborah Boyle, RN, MSN, AOCN, FAAN, the advanced practice nurse liaison at the University of Texas MD Anderson Cancer Center (Oliveria 2004).

With the shift of demographics of the U.S. population to an older population, elderly patients will increasingly become an important component of the society. Unlike elderly stereotypes, today many elderly people are able to live independently in the community and accomplish their everyday activities with little or no personal assistance (Suzman, Willis, and Manton 1995). Statistics have shown that a healthy elderly women 65, 75 and 85 years can expect to live another 20, 12 and 6 years on average, respectively (Holmes and Muss 2003). Many of them remain to incur low costs of medical care services. The elderly population is a very heterogeneous group: those young old just stepping into 65 years of age may remain robust and active in their personal pursuits; some older old begin to deteriorate while others continue to thrive; and the oldest old 85+ years of age have sustained to the end of their lives. When diagnosed with MBC, they may have different goals related to chemotherapy (e.g., survival and QoL), face different budget constraints and have unique preferences (e.g., intensive or less intensive treatments). Some objective reasons of less intensive chemotherapy use for elderly women include increased comorbidities, lower functional status, limited remaining life span, uncertainties in treatment benefits of chemotherapy, as well as increased risk of adverse events (Bouchardy et al. 2007; Silliman et al. 1993). Several review studies synthesizing clinical trial data have reported that healthy and fit elderly patients will be able to derive the same treatment benefits from chemotherapy as younger patients (Muss et al. 2005). However, older patients only represent a handful of participants and sicker patients are excluded. Other studies showed that there are increased hematology toxicities

and congestive heart failure associated with chemotherapy use among older patients (Doyle et al. 2005; Hassett et al. 2006; Muss et al. 2007; Pinder et al. 2007). The data from these studies are based on adjuvant chemotherapy setting. In the metastasis setting, uncertainties are further perpetuated by the incurable nature of the disease and the limited natural life expectancy; consequently, other non-clinical factors are likely to have greater impact on chemotherapy choice. This echoes Wennberg et al's studies showing when medical evidence is variable or weak, the importance of the per capita supply of physicians and patient preferences increases. Other more subjective reasons also include less social support and physician attitudes and beliefs. For example, elderly women may be bound by their mobility: transportation may prevent them from receiving chemotherapy.

Several observational studies examine whether there is a disparity in mortality/prognosis of breast cancer due to age-related treatment differences among older women with breast cancer, including surgery, radiation therapy, chemotherapy, and hormone therapy. Owusu et al. showed that the age-related disparity in breast cancer survival is associated with sub-optimal treatment by older women 75+ years of age (Owusu, Lash, and Silliman 2007). Using cancer registry data, Bouchardy et al. looked at the treatment pattern among women ≥ 80 years and demonstrated that undertreatment was associated with a reduced breast cancer-specific survival (Bouchardy et al. 2007). In another population-based study, Eaker showed that women ≥70 years with stage III and unstaged breast cancer had poorer survival associated with sub-optimal therapy (Eaker et al. 2006). In contrast, in a retrospective analysis, Gajdos et al. found no association between undertreatments and the rates of distant metastasis among older women ≥71 years (Gajdos et al. 2001). The suboptimal therapy or under-treatment in these studies was defined as being less likely to receive treatments or lower doses of therapies in these studies. Three of these studies suggest that increasing age was associated with receipt of less standard breast cancer care even after controlling for comorbidities, tumor factors

and other covariates, and such treatment differences among older women with breast cancer lead to a lower survival rate compared to those who received treatment. However, the observed association between age and less standard treatments may reflect patient/physician concerns and may not suggest underuse among elderly women with metastatic breast cancer. No study has yet separately looked at the effects of access to cancer care on age-related differences in chemotherapy use among older women with metastatic breast cancer. More importantly, investigating the heterogeneity of chemotherapy choices among different age groups would help answer questions like "which factors predict chemotherapy use?", "why do some patients choose chemotherapy while others don't?", "are those factors modifiable by policy intervention?" etc.

Access-related Factors and Treatment Choice of Chemotherapy among Elderly Women with MBC

Despite all the available treatments, metastatic breast cancer remains an incurable disease. All treatment options are palliative and associated with differential effects on the patient quantity and quality of life. In addition to hormone therapy, chemotherapy, monoclonal antibody, supportive care, and watchful waiting may also be used. The objective is to control the cancer, improve the symptoms, maintain or improve quality of life and prolong survival (Hortobagyi 1998).

Treatment goals of disease treatment versus symptom control for chemotherapy are not always non-conflicting. For example, using chemotherapy for disease treatment (e.g., tumor shrinkage and progression prevention) may be at the price of symptom control (e.g., cancer-related pain, chemotherapy-induced symptoms). The choice of chemotherapy for MBC is particularly complicated for elderly patients because of the trade-offs between the potential survival gains from the treatment and its effect on quality of life. These trade-offs also involve important factors for the elderly population, such as

natural life expectancy and tolerance to the toxicity related to the treatment. The possible survival benefit and the improvement of quality of life from chemotherapy on symptom control come with nontrivial acute toxicity, including hair loss, nausea and vomiting, fatigue and weakness, poor appetite, stomach irritation and occasional diarrhea. In addition, chemotherapy may significantly lower blood counts, increasing the patient's chances of infection, fever, and possibly hospitalization (Elit et al. 2003; Moumjid et al. 2003). These acute side-effects exert an immediate and obvious impact on quality of life, especially among elderly patients who generally have less tolerance for drugs. The results are likely more catastrophic among the elderly once side-effects occur. The choice between the improved survival and a higher quality of life depends on patients' preferences and values.

Patients with MBC may prefer chemotherapy for the purpose of life prolongation or symptom control. A survey on patient preferences for treatment of MBC among patients with stage I-IIIA breast cancer elucidated that although patients were less likely to choose chemotherapy with more toxicity, 15% of them were still willing to assume substantial toxicity and a compromised quality of life for even a very small increase in life expectancy (McQuellon et al. 1995). In addition, younger patients were more likely to risk the toxicity of treatment for minimal gain of survival. An important factor in patients choosing chemotherapy is pain reduction. This same study showed that 75% of patients would choose chemotherapy for reducing pain even without increasing overall survival. A prospective study explaining metastatic cancer patients' treatment preference and choice shows a preference for chemotherapy and the choice of palliative chemotherapy were negatively associated with striving for quality of life, demonstrating patients' strong preference for life prolongation in a metastatic setting (Koedoot et al. 2003). Such treatment preferences are a result of the effects of many intertwining factors, including patients' age (Penson, Daniels, and Lynch 2004; Yellen, Cella, and Leslie

1994), oncologists' recommendations (Siminoff and Fetting 1991; Yellen and Cella 1995), as well as social (Yellen and Cella 1995) and clinically relevant factors.

Studies suggest patient age is an important factor in shaping patient or oncologist preferences, and consequently, influences their clinical decision making. In a survey study of oncologist preferences for palliative chemotherapy versus watchful waiting based on 8 case descriptions with hypothetical patient age at 40, 60 and 80 years old and other patient characteristics and parameters (e.g., physical condition, psychologic distress, patient's wish to be treated, expected toxicity of chemotherapy, disease-related complaints expected in the future, chance of tumor response, and possible chemotherapy-related survival gain), patient age is the strongest predictor of the oncologist's preference, that is, chemotherapy was more preferred for younger patients (Koedoot et al. 2002). This is followed by patient desire for treatment and expected survival benefit. Yet patient desire may differ from their oncologist's. In a study about the effect of age on clinical decision making among cancer patients, the results show that older cancer patients may agree to aggressive therapy for curative or palliative purposes as frequently as younger patients in both early and advanced disease stage. But they were less willing to tolerate severe side effects in exchange for their current quality of life compared with younger patients (Yellen, Cella, and Leslie 1994). In practice, elderly cancer patients often receive less treatment, or are treated differently (Turner et al. 1999). Even after controlling for comorbidities, age is still independently associated with less intensive treatment (Enger et al. 2006). It is not well understood how age determines oncologist/patient preferences and beliefs about treatment, which leads to different treatment choices. Age may be a surrogate for higher number of chronic conditions and frail functional status. Age may influence patient treatment choices through the perceived risk of toxicities or perceived difficulty of getting treatment. For example, access to an oncologist practice is likely to impact elderly patients to a greater extent than their younger counterparts due to their deteriorated mobility and less social support to organize transportation for them.

Studies have shown that oncologist recommendations are the most influential factor in patient decision making with respect to advanced disease treatment and in situations with uncertain clinical benefits (Kutner et al. 2000; Siminoff and Fetting 1991). In fact, older patients listed oncologist recommendation as the primary reason for their chemotherapy treatment decision. MBC is a disease for which great uncertainty and heterogeneity in clinical benefit exist (Cardoso et al. 2002; Chung and Carlson 2003; Hortobagyi 1998; Lippman et al. 1978; Powles et al. 1980). As mentioned before, local practice style may influence provider recommendations through a "recognized" practice pattern (Eddy 1984; Wennberg and Gittelsohn 1973; Wennberg 1985). Practice style is defined as physicians' set of beliefs about the efficacy and appropriateness of various forms of care (Wennberg and Gittelsohn 1973; Wennberg 1985). It therefore has deep roots in one's professional training, be it defining a disease, making a diagnosis, selecting a procedure, evaluating outcomes, assessing patients' preferences or synthesizing all the data (Eddy 1984). In his series of small geographic area variation analysis, John Wennberg showed that the variation in medical care stems from physicians' beliefs about how a treatment option likely benefits the patient as opposed to pure economic incentives (Wennberg, Barnes, and Zubkoff 1982). For example, Wennberg showed that in neighboring communities with similar population demographics and consumer demand and resource availability, such as New Haven, CT and Boston, MA, hospitalization rates were dramatically different (Wennberg and Gittelsohn 1982). Such variation is positively associated with the uncertainty between the risks and benefits of the treatment. The bigger the uncertainty, the more physicians vary in their clinical practice across different regions. That area clinical practice utilization is influenced by local practice style has been demonstrated in the case of primary care, surgery and hospital service (Grytten and Sørensen 2003; Wennberg and Gittelsohn 1982; Wennberg, Barnes, and Zubkoff 1982).

Provider treatment recommendations are often based on their expectations on how patients are likely to benefit from the treatment. Such beliefs may be shaped by the

availability of area treatment resources, possibly through the word of mouth and informal communication channels among colleagues. The greater the availability of certain treatment resources are, the higher the use rate is (Fisher et al. 2000; Fisher and Wennberg 2003; Wennberg, Fisher, and Stukel 2004). In areas where there is more hospice availability, hospice providers may be able to provide specialized supportive care and spread the word that hospice care is a good option for end-stage cancer patients. A previous study showed that areas with greater local availability of hospices had less aggressive care (e.g., intensity of chemotherapy) among lung, breast, colorectal or other gastrointestinal cancer patients near the end of life (Earle et al. 2004). It has also been shown that the distance to the nearest hospice is inversely associated with hospice use among elderly women with MBC (Wan, Brooks, and Chrischilles 2010). If the distance to the nearest hospice can be perceived as a proxy for general access to hospice, then MBC patients with better access to hospice care had higher hospice use rates. Since Medicare requires patients who choose hospice to forgo curative treatments for terminal illness, hospice availability may be relevant to chemotherapy use. Palliative chemotherapy use may also be incorporated in hospice setting and other palliative care programs. Yet palliative chemotherapy is different from curative chemotherapy in their treatment goals: palliative chemotherapy aims at symptom control and pain relief while curative chemotherapy aims at disease control, such as tumor shrinkage, progression prevention, and survival prolongation. Also under Medicare Hospice Benefit, hospice providers are reimbursed on a per diem basis. Thus palliative chemotherapy use may not be easily identifiable in hospice claims.

It has been suggested that physicians are able to alter patient preferences for medical care, i.e, provider-induced demand (PID), in the context of information asymmetry and clinical uncertainty (Culyer and Newhouse 2000). The concept of PID is discussed in major health economics textbooks and previous literature. PID exists when the physician influences patient demand for care against the physicians' interpretation of

the best interest of the patient. In the health economics literature, research on PID has mainly tested three effects. First, the availability may increase the demand for physician services; second, areas with high levels of demand for certain services may attract more providers to relocate; and third, greater supply increases quantity demanded through an improved price (Culyer and Newhouse 2000). Fuchs used a multivariate analysis to demonstrate that a ten percent increase in the number of surgeons increased the rate of surgery by three percent and an increase in price (Fuchs 1978). Based on the results of this study, Fuchs suggested that an increase in the supply of surgeons results in an increase in demand. Following Fuchs's study, subsequent studies further illustrated the inducement effect of supply by comparing their own models with basic economic model of supply and demand, and also found evidence supporting this effect of supply in areas of high surgeon workload (Cromwell and Mitchell 1986) and the effect of the number of dentists per capita on the volume of dental visits (Birch 1988), respectively. McGuire and Pauly further improved this type of study by incorporating physician disutility from inducement in a physician utility model. In their model, physician utility was assumed to depend on income, leisure and reputation to maximize their utility (McGuire and Pauly 1991). The disutility from inducement or physician concern about reputation is essentially a constraint on inducement. Their findings showed when income effects are strong, physicians induce demand to maintain an appropriate level of income. If we put the concept of PID into this analysis, an increasing local area oncologist supply will increase oncologist recommendations of chemotherapy for patients in response to the increased competition in the area. More recent studies used disaggregated data from individual physician practice and examined the availability effect of physician supply. The results of these studies show patients living in areas with more physicians were more likely to seek distinctive types of medical care, but were not treated more intensively by each physician (Carlsen and Grytten 1998; Stano 1985). In other words, areas with more physicians are associated with more utilization through improved availability rather than

inducement of additional unnecessary services. This study will use a similar utility maximization model as in previous studies (Birch 1988; Brown 3rd 1996; Carlsen and Grytten 2000; Gruber, Kim, and Mayzlin 1999; McGuire and Pauly 1991; Nattinger et al. 2001; Punglia et al. 2006; Rossiter and Wilensky 1983). Oncologists practicing in an area with higher oncologist-to-patient ratio are able to specialize and are more likely to address patients' different concerns through the referral process. Therefore, patients living in areas with more oncologists are more likely to get chemotherapy. On the other hand, patients living in areas with lower oncologist-to-patient ratios may have fewer choices and are less likely to get chemotherapy because of the higher cost associated with the lower availability of oncologist services.

Furthermore, local area per capita oncologist supply would affect a patient's decision about receiving chemotherapy through access to the oncologist practice once patients are recommended chemotherapy. Previous studies have shown that geographical distance affected patients' treatment because of the added cost in reaching their respective care facilities (Nattinger et al. 2001; Punglia et al. 2006). Considering the frailty of elderly women with MBC, who often have compromised mobility due to bone metastasis and osteoporosis, the preference for a convenient and close facility over a distant one can be well understood. Patients who live closer to the oncologists' office may prefer to use chemotherapy more than those living further because of access-related costs, including waiting and travel time. In addition, patients' out-of-pocket cost associated with chemotherapy use, such as food, lodging and wage loss, can be substantial (Houts et al. 1984). Therefore, patients living in areas with more oncologists or living closer to the oncologist office will have better access to cancer treatments.

Current literature perceives access as individuals' access to the health structures and processes of care which they need (Campbell, Roland, and Buetow 2000; Penchansky and Thomas 1981). It incorporates five dimensions: availability, accessibility, accommodation, affordability and acceptability. The most basic dimension

of access to health structure is geographic/physical access. For example, how convenient it is for the patient to get to the physician's office? Rurality or travel distance may be related to geographic barriers to getting to health care facilities. Availability is the extent to which the health care system provides facilities and services which meet the needs of individuals. For example, the availability of specialists or hospice programs for patients in a local area. The third dimension, affordability, is a measure of the relationship of provider insurance and service price to the patient income, ability to pay, and existing health insurance. It is a key component of access in countries where patients have to pay out-of-pocket for health care they need. Accommodation is a measure of the appropriateness of how the resources are provided and organized in the way that patients are easy to accommodate and follow up. For example, appointment system, hours of operation, and telephone services. Acceptability is a measure how clients' attitudes about provider characteristics are matched with the providers in real practice as well as with provider attitudes about acceptable patient characteristics. Such provider attributes may include age, sex, ethnicity, type of facility, and neighborhood of facility; providers may also have preferred patient attributes. These five dimensions of access are related to each other closely yet still distinct enough to be measured separately. Penchansky used the survey to measure five dimensions of access related to customer satisfaction. Their study showed that five measures were valid and independent from each other, which distinguish with each other from patient perspectives.

As described above, the extent to which access influence treatment choices may vary among different age groups. With advancing age, the hypothesis is access would have bigger effects among older age groups as uncertainties of treatment benefits from chemotherapy increase. For example, it could be that local hospice availability affects older patients more when they are approaching to the end of their lives. For another example, it could also be that local practice style tends to influence older patient choice more as younger patients are usually assumed to be able to benefit from chemotherapy.

Other clinical factors, such as comorbidities, performance status, site of metastasis and extent of disease, as well as socio-demographic factors, such as race and socioeconomic status, may also influence the patient's treatment choice through patients' expected benefits on survival and quality of life (QoL) from chemotherapy (Largillier et al. 2008; Mandelblatt et al. 2002). Younger patients, and those with fewer comorbid conditions or better performance status or higher socioeconomic status are more likely to receive chemotherapy.

CHAPTER III
THEORETICAL MODEL

Overview

A patient's choice of chemotherapy for MBC is a complex decision, involving both the patient and the provider. This study theorizes that the final treatment decision is based on (1) the patient's health beliefs as to the effects of chemotherapy on survival and QoL; (2) the patient's preferences over change in survival and QoL expected to result from chemotherapy; (3) resources that are available to the patient, including money, time, and social capital; (4) costs associated with chemotherapy, including out-of-pocket expenditure and access-related costs. Furthermore, providers' recommendations play a significant role in patients' decision through their influence on patients' expectations toward the relationship between chemotherapy, survival, and QoL. In the theoretical model, local practice style impacts physicians' recommendations through its effect on the formation of physician beliefs toward the treatment as well as physician reputation. This study theorizes that physicians practicing inconsistently with "area treatment norms" put their reputations at risk. Hospice availability affects physician beliefs about patient health without chemotherapy. Area provider supply surrounding the patients' residence is theorized to affect patient treatment choice through the availability effect in this study. The following sections develop a theoretical framework of oncologists' recommendations of chemotherapy use and patients' choice of chemotherapy.

Oncologist Recommendation on Chemotherapy Use

This section includes the theoretical model linking the area treatment percentage, area hospice availability, and area-level provider supply to the chemotherapy recommendation of a particular provider. Using utility theory, previous studies that have

modeled provider behavior suggested that providers gain utility through increased income, patient health, leisure, and reputation (McGuire and Pauly 1991). In the model developed below, we adopt the same theoretical utility framework. The oncologist recommends chemotherapy to a patient if the recommendation improves his/her utility (U) through its effects on different goals - expected patient health (E), income (I), leisure (L) and reputation (R).

(1) $U = U(E, I, L, R; \beta(Y))$

Where β is the parameter vector summarizing the preferences that relate the changes in obtaining these objective to changes in provider utility. Y is patient age. β is theorized to be a function of patient age Y, which is the focus of our interests among other factors. The preference parameter vector (β) is constrained such that marginal utilities associated with each goal are all positive, denoted as the positive first derivative of the utility function holding all other variables constant. Marginal utility is defined as the increase in utility as a result of increasing one more unit of the i^{th} objective (i = E, I, L, R), or $\boldsymbol{U_i} = dU/di$. The assumption that an increase in each objective increases utility is written as $\boldsymbol{U_E} > 0$, $\boldsymbol{U}_I > 0$, $\boldsymbol{U_L} > 0$, and $\boldsymbol{U_R} > 0$ for health, income, leisure, and reputation, respectively. It is further theorized that the preference parameters **(**β**)** are constrained such that the utility gained from increasing each objective diminishes at higher initial levels of each objective. The notion of diminishing marginal utility describes the idea that the marginal utility associated with each goal decreases as the total quantity of the "objective" increases, holding all other objectives constant. In other words, utility increases more slowly with a consistent increase in each objective at higher levels of each objective. It can be represented by a negative second derivative of the utility function with respect to each objective, or $\boldsymbol{U_{ii}} = d^2U/di^2$. The diminishing marginal utility for each objective increases can be written as $\boldsymbol{U_{EE}} < 0$, $\boldsymbol{U}_{II} < 0$, $\boldsymbol{U_{LL}} < 0$, and $\boldsymbol{U_{RR}} < 0$ for health, income, leisure, and reputation, respectively. The assumption of diminishing marginal utility describes the idea that incremental utility gain at a higher baseline level is

smaller for each objective than at a lower baseline level. Further, it suggests that provider treatment recommendations depend on the initial level of each objective achievement. For example, a given increase in income will provide more added utility to a provider that has a lower initial income than a provider starting at a higher income level. Treatment recommendation is theorized to enter into provider utility functions through the following relationships:

(2) $E=E_0(Y, D, Cl, Co, M, H) + \alpha(Y, D, Cl, Co, M, B) \bullet T;$

(3) $I = \mu \bullet (F(Cl)) + \pi \bullet N(O);$

(4) $L=V - \delta \bullet (F(Cl)) - \zeta \bullet N(O);$

(5) $R=R(\rho(F(Cl)),B),$ where;

E, expected patient health, is modeled as the expected baseline health of the patient without chemotherapy plus treatment benefits gained from the treatment (Phelps 1998; Rossiter and Wilensky 1983). E_0 is provider expectation of patient health without chemotherapy that is a function of the patient's Age (Y), other socio-demographic characteristics (D), clinical characteristics (Cl), comorbidities (Co), other health services used (M), and area non-intensive treatment availability (H), such as hospice; T is an indicator variable equaling 1 if the patient receives the treatment, 0 otherwise; α is the providers' beliefs as to the health benefit available to the patient from treatment that is a function of the average beliefs of all providers in the area (B) and other patient-related factors. I, oncologist income, is theorized to generate from specialized cancer care and chemotherapy-related services (Birch 1988; Gruber, Kim, and Mayzlin 1999). N is the number of total patients the oncologist sees as a function of area-level oncologist supply characteristics (O); F is the number out of total patients (N) the oncologist sees who have received chemotherapy; π is the income received by the oncologist from an untreated patient; μ is the additional income received by the oncologist from chemotherapy. L, leisure time available to the oncologist, is theorized to be the time left after subtracting the hours devoted to patients from the total hours (V) (Brown 3rd 1996). ζ is the amount

of physician time required by each patient without chemotherapy; δ is the additional amount of physician time required for each patient who receives chemotherapy. R, provider reputation, is modeled as a function of ρ, the share of the patients treated with chemotherapy by the provider (F (Cl))/N, patients' clinical characteristics (Cl), and the average beliefs of the providers in the area (B) (McGuire and Pauly 1991).

According to this theory, an oncologists will recommend chemotherapy if his/her utility from a chemotherapy recommendation is greater than his/her utility without a recommendation. The net utility gained from recommending additional chemotherapy can be obtained by substituting equation (3)-(6) into equation (2) and subtracting the utility associated with not recommending chemotherapy from the utility associated with such recommendation. Or if NU >0 then W=1; otherwise W=0 if NU<0, where R represents oncologists' recommendation of chemotherapy.

(6) $NU = U(E_0(Y, D, Cl, Co, M, H) + \alpha(D, Cl, Co, M, B), \mu \bullet ((F+1)(Cl)) + \pi \bullet N(O), V - \delta \bullet ((F+1)(Cl)) - \zeta \bullet N(O); \beta) - U(E_0(Y, D, Cl, Co, M), \mu \bullet (F(Cl)) + \pi \bullet N(O), V - \delta \bullet (F(Cl)) - \zeta \bullet N(O); \beta)$

A chemotherapy recommendation (W) increases provider utility through expected increases in patient health (via α), provider income (via μ), and provider reputation (R), if the provider's treatment share is below area treatment norms. A recommendation reduces provider utility through a decrease in leisure time (via δ), and reputation (R), if the provider's treatment share is above area norms. The net effect on provider utility of these intervening objectives can vary with provider preferences (β) and the level of each objective that the provider had achieved prior to each treatment recommendation decision. For example, a provider with plenty of leisure time and low income may be more inclined to recommend chemotherapy at a low α than a provider with high income and little leisure time.

Further write (6) in a succinct way to get:

(7) $NU = U(Y, D, Cl, Co, M, H, B, O, \mu, \pi, V, \delta, \zeta, \alpha, \beta)$

(8) P(W=1) = P (NU>0), i.e., the probability of making a chemotherapy recommendation equals the probability that net utility for an oncologist is greater than 0.

where W represents the oncologist's recommendation. In areas where providers share positive beliefs about the effectiveness of chemotherapy, we expect providers will tend to make more treatment recommendations and vice versa.

Oncologist treatment recommendations also depend on the initial level of expected health of patients without chemotherapy. Hospice availability can be viewed as non-intensive treatment in the area available to the patients in addition to chemotherapy. Providers in areas with higher hospice availability may have higher expectations for the patient's health without chemotherapy. Therefore, when they recommend chemotherapy, they might consider whether the added benefit of chemotherapy is worthy of the effort or not. In areas with higher hospice availability, the provider may believe that the added benefit of chemotherapy is not great, and as a result, the utility associated with treatment recommendations in areas with higher availability of hospice may be smaller than that in areas with lower availability of hospice.

Area-level-oncologist-availability characteristics affect chemotherapy recommendations through their effects on physician utility including income and leisure. Oncologists in areas with fewer patients per provider will have fewer patients leading to lower income and more leisure time than providers in areas with more patients per provider. Therefore, the net utility associated with a recommendation decision will be higher for providers in areas with fewer patients and as a result, they are more likely to recommend chemotherapy. Provider utility increases resulting from extra treatment will be constrained by the effect of such treatment decisions on provider reputation. That is, if an individual provider's treatment percentage is beyond the area-level treatment percentage (B), provider reputation will be at risk. Conversely, oncologists in areas with fewer patients may be able to devote more time to each patient and discuss other alternative choices other than chemotherapy. If this hypothesis is true, then higher

oncologist availability is inversely associated with a lower likelihood of chemotherapy recommendations.

The model theorizes that physician preference is a function of patient age. With increasing age, uncertainties increase. When seeing older patients, oncologists may be less willing to recommend chemotherapy because the marginal benefit gained from chemotherapy may not be justified considering the natural life expectancy and a higher risk of toxicity for the patient as summarized in the background section. Physicians may tend to follow clinical consensus among local clinicians; the older the patient is, the more likely such local practice norms would exert a bigger influence over the chemotherapy recommendations. Because our model theorizes that oncologists practicing in areas with more oncologists have less income and more time, all else equal, they may tend to recommend chemotherapy more to older patients than those living in areas with fewer oncologists to secure more revenue. Conversely, oncologists may be able to have more time for each patient visit and figure out other treatment options for older patients. In areas with greater hospice availability, oncologists may tend to recommend hospice care instead of chemotherapy for older patients probably due to more experience with hospice care that benefits older patients.

Similarly, providers may be less likely to recommend treatment to frail patients with higher performance status and patients with more comorbidities. Other health services, such as hormone and radiation therapy, will influence provider chemotherapy recommendations but the direction of such effects cannot be assigned apriori. For example, radiation therapy may make the patient more vulnerable to the toxicity of chemotherapy, therefore decreasing this treatment recommendation by the provider. Or, patients who have previously used radiation therapy may have greater trust in medication in general and this would predict the future use of chemotherapy.

Patients' Choice of Chemotherapy

Based on utility theory, this section develops a theoretical model of patient chemotherapy choice. Patient utility is assumed to be a function of goal achievement. Following Becker's household production function, this study models the patient treatment choice as a function of expected survival, expected QoL, and the patient budget (Becker 1978). Patients choose chemotherapy to maximize their utility (V) derived from patients' survival (S), QoL (Q), and resources available for the consumption of all other goods and services (X).

(8) $V=V(S, Q, X; \gamma (Y))$

Where "γ" is a vector of preference parameters that relate the changes in each goal to changes in patient utility. Y is patient age. Among a set of factors which influence the relative weight of change in S, Q, X associated with utility change, age (Y) is the main factor this model focuses on. Consistent with the utility theory, the model assumes increases in survival, QoL, and the consumption of other goods and services increase patient utility ($V_S > 0$, $V_Q > 0$, $V_X > 0$), but the marginal utility of each goal diminishes as higher levels of the objectives are reached ($V_{SS} < 0$, $V_{QQ} < 0$, $V_{XX} < 0$). The choice of chemotherapy affects patient utility through patient expected survival, QoL, and its effect on the consumption of other goods and service via the budget constraint:

(9) $S=S_0 (Y, D, Cl, Co, M, H) + \sigma (W, \theta (Y, D, Cl, Co, M)) \bullet T$

(10) $Q=Q_0 (Y, D, Cl, Co, M, H) + \lambda (W, \xi (Y, D, Cl, Co, M)) \bullet T$

(11) $I= (P_T + P (A, RA)) \bullet T + P_x \bullet X$

S, expected survival, is modeled as the expected survival without chemotherapy, plus the estimated effect of chemotherapy on survival if treated. Where S_0 is the patient's expectation of survival without chemotherapy that is a function of the patient age (Y), other social-demographic characteristics (D) and clinical (Cl) characteristics, comorbidities (Co), other health services used (M), and the availability of non-intensive

treatment in the area (H); H is the availability of non-intensive treatments, using hospice availability as a measure; T is an indicator variable equaling 1 if the patient chose chemotherapy, 0 otherwise; σ (W, θ) is the patient's beliefs as to the survival benefit from chemotherapy and this is a function of the provider's recommendation W (Y, D, Cl, Co, M, H, B, O, μ, π, V, δ, ζ, α, β) from (7), and the patient's initial expectation of survival benefit associated with treatment prior to consultation (θ) that is a function of patient-related factors and other health services used (M). Q, expected QoL, is modeled as the expected baseline QoL without chemotherapy, plus the estimated effect of chemotherapy on QoL if treated. Q_0 is the patient's expectation of quality of life with non-intensive treatment that is a function of patient-related factors, other health services used (M), and the availability of non-intensive treatment in the area (H); λ (R, ξ) is the patient's beliefs as to the effect of chemotherapy on QoL that is a function of the providers' recommendation W (Y, D, Cl, Co, M, H, B, O, μ, π, V, δ, ζ, α, β) from (7), and the patient's initial expectation of the effect of chemotherapy on QoL (ξ) prior to consultation. I, the level of resources available to the patient, is theorized to include income, social capital, and wealth, which the patient can use to spend either on T or X. P_T is the patient's out-of-pocket costs associated with chemotherapy; P is the patient's access-related costs associated with receiving chemotherapy that are a function of distance to the nearest oncologist practice (A) and rural/urban degree of residence area (RA); P_x is a measure reflecting the dollar value per unit of the composite good.

Patients will choose chemotherapy if their utility with chemotherapy is greater than their utility without treatment, that is, T=1 when NV>0 while T=0 when NV<0, where T represents patients' chemotherapy choice. We can describe this relationship in terms of net patient utility (NV) by substituting equations (9) - (11) into equation (8) and subtracting the utility associated with no chemotherapy from the utility associated with treatment:

(12) $NV= V(S_0 (Y, D, Cl, Co, M, H) + \sigma(W, \theta (Y, D, Cl, Co, M)), Q_0(Y, D, Cl, Co, M, H)+\lambda(W, \xi(Y, D, Cl, Co, M)), (I- P_T - P (A, RA))/ P_x ; \gamma) -V(S_0 (Y, D, Cl, Co, M, H), Q_0(Y, D, Cl, Co, M, H), I/P_x ; \gamma)$

Further, substituting (7) oncologists' recommendation in equation (12) and writing it in a succinct way, produces:

(13) $NV= V (Y, D, Cl, Co, M, H, W, O, A, RA, I, P_T, P_x, \sigma, \lambda, \gamma)$ where $W (Y, D, Cl, Co, M, H, B, O, \mu, \pi, V, \delta, \zeta, \alpha, \beta)$ is from (7)

(14) $P(T=1) = P(NV>0)$, i.e., the probability of getting chemo equals the probability that a patient's net utility is larger than 0

Choosing chemotherapy increases patient utility through expected prolongation in survival (via σ), increase in QoL (via λ), and reduces utility through a decrease in the resources available to spend on X for the patient ($I/P_x - (I- P_T – P (A, RA))/ P_x$) and a decrease in QoL due to acute toxicity. The greater the benefit on survival and QoL the more a patient expects to receive from chemotherapy, and the more likely the patient will choose chemotherapy. Patients in areas with greater hospice availability may be more likely to be referred to hospice because the model theorizes the expected benefit from chemotherapy is lower for patients with greater hospice availability than those living in areas with lower hospice availability; consequently, the availability of hospice may be negatively associated with chemotherapy use. Constrained by the budget available to each patient, the more the patient is willing to spend on chemotherapy, the more likely the patient will choose treatment, all else being equal. Area oncologist availability (O) affects chemotherapy use through the access effect. It could be that the higher the oncologist availability in the area around a patient, the more likely the oncologist will recommend chemotherapy for the patient because oncologists with few patients have lower revenue and may recommend chemotherapy to generate more income. It could be that the higher oncologist availability in the area is associated with more time for individual patient visits; as a result, physicians are able to spend more time with each

patient and help them to examine alternatives other than chemotherapy. Moreover, the further the patient lives from a chemotherapy provider and the more patients per provider in the area around each patient, the greater the access cost to the patient and the less likely the patient will receive chemotherapy. In addition, rural residence may represent a geographic barrier in access to the oncologist practice or other cancer care, such as lab services. Patients living in rural areas may be less likely to choose chemotherapy with incurred transportation cost and extra burdens on family members.

The model theorizes that patient preference is a function of patient age. Older patients may face a limited life span and concern about worsening of comorbidities and a heightened risk of toxicity. When putting the benefit of chemotherapy into perspective, the absolute benefit will be weighed against the life expectancy, QoL, and costs, such as transportation arrangements and extra burdens on family members. As illustrated in the introduction section, greater uncertainty may cause access-related factors to matter more in chemotherapy choices for older patients, therefore, changing their perceptions of each treatment goal. For example, older patients tend to have higher numbers of comorbidities and be bound by chronic conditions, such as osteoarthritis, rheumatologic disease, and vision loss. Long travel distances to oncologists may be more challenging for older patients and thus may be a barrier for them to get chemotherapy. These patient preferences may be compounded with physician concerns that older patients may not be able to benefit from chemotherapy to the same degree as younger patients after weighing between patient limited life expectancy and the higher risk of chemotherapy toxicities. As a result, older patients are less likely to be treated with chemotherapy.

Modeling Effect Modification by Age

In equation (14) $P(T=1) = P(NV>0)$**,** NV is the latent preferences which we cannot observe. Alternatively, we can measure the treatment choice as a dichotomous variable and a function of NV, which is

(15) $T= b_0+ b_1 \bullet Y_i + b_2 \bullet D_i + b_3 \bullet Cl_i + b_4 \bullet Co_i + b_5 \bullet M_i + b_6 \bullet B_i + b_7 \bullet H_i + b_8 \bullet O_i + b_9 \bullet A_i + e_i$

Where Y, D, Cl, Co and M are defined as in the last section; B, H, O, and A are local area treatment rate, local hospice availability, local area per capita oncologist supply, and the patient distance to the nearest oncologist practice; e is the error term; i is an observation index. T, chemotherapy choice, is related to the variables on the right hand side of the equation by the probability P, a transformation of net utility (NV). The logistic regression model assumes the logistic distribution of the error term e_i. To test whether the effects of access on treatment choice vary with age, interaction terms between age and access can be added into the model. The hypothesis for interaction effects is that age modifies the impact of access-related factors on the utilization of chemotherapy (as illustrated in the introduction). Access to cancer care, including *B, H, O, A,* are the focal independent variables. Y_i representing age is the moderating variable. The model is specified as below:

(16) $T= b_0+ b_1 \bullet Y_i + b_2 \bullet D_i + b_3 \bullet Cl_i + b_4 \bullet Co_i + b_5 \bullet M_i + b_6 \bullet B_i + b_7 \bullet H_i + b_8 \bullet O_i + b_9 \bullet A_i + b_{10} \bullet (Y_i A_i) + b_{11} (Y_i H_i) + b_{12} (Y_i O_i) + b_{13} (Y_i B_i) + u_i$

A parallel method to test whether the effect of access on chemotherapy choice is modified by age is stratified age subgroup analysis. As illustrated before, different cutting-off points of age are explored in this analysis. Results from stratified analysis can be compared with the model using the interaction term approach.

Recent discussion about subgroup analyses suggested such analyses are important when there are biological, physiological, and practical reasons related to how treatment effects may differ with characteristics at baseline and related to uncertainties treating certain subgroups, such as the elderly population 85 years of age or older (Rothwell 2005). However, published data reveal that a number of important statistical and conceptual limitations arise with separate subgroup regression approaches to examine group differences. For example, the inability to adequately control for variables

confounded with group membership, loss of power resulting from artificial dichotomization, and less stable regression estimates, and comparison of coefficients from different regression models (Assmann et al. 2000; Newsom et al. 2003).

The moderated regression approach, which is based on a general approach to testing statistical interactions, is recommended to address these limitations (Brookes et al. 2004; Lagakos 2006; Pocock et al. 2002; Wang et al. 2007). In this analysis, age and access variables are specified as both continuous and dummy variables based on their means and quartiles, and interaction term analyses were conducted. Yet concerns exist that dichotomization can hide nonlinear relationships between dependent and independent variables and results based on analysis after dichotomization can hide differences between groups (MacCallum et al. 2002). The purpose of using both interaction approach and subgroup analyses is to compare results from different approaches and make appropriate inferences based on such comparisons. Such practices are recommended in the guidelines for reporting subgroup analysis (Wang et al. 2007). Recent clinical trials and observational studies increasingly adopt this practice (Jackson et al. 2006; Sacks et al. 1996).

The heterogeneity of the association between access and chemotherapy choice across age is the central hypothesis in this study. To assess such heterogeneity, I begin with a statistical test for interaction to test whether the effect of access to cancer care on immediate choice of chemotherapy is modified by age, which is followed by stratified subgroup analysis. The empirical evidence in subgroup analysis may pinpoint an important access variable or identify subgroups for which an access variable is especially prominent.

CHAPTER IV

METHODS

Data Sources

This project used the Surveillance, Epidemiology and End Results (SEER)-Medicare linked database. The SEER program is a population-based cancer registry funded by the National Cancer Institute to track cancer incidence and mortality across the nation (National Cancer Institute 2009). SEER sites include 16 geographically-defined areas. SEER data, also known as Patient Entitlement and Diagnosis Summary File (PEDSF), record patient demographic and clinical variables. Demographic variables include race/ethnicity, sex, marital status, date of birth, place of birth, vital status, and cause of death; clinical variables include month and year of diagnosis, type of cancer, histology, behavior, grade, AJCC (American Joint Committee on Cancer) cancer stage, and treatments (data include surgery, radiation therapy, and chemotherapy, although the information may be incomplete) given during the first course of treatment. In addition, the U.S. Census Bureau's zip code summary file is linked to SEER to provide census-tract level socioeconomic information, including median household income and percentage of population with high school education.

Medicare claims from the Centers for Medicare and Medicaid Services (CMS) include inpatient, outpatient, physician services, home health care, hospice, and durable medical devices files. The linkage between SEER and Medicare data for patients aged 65 years and older is based on an algorithm involving a match of social security number, name, sex, and date of birth, which combines clinical information from population-based cancer registries with claims information from the Medicare program. 93% of the patients who were 65 years or older in the SEER data were found in the Medicare claims at the time of linkage (Warren et al. 2002). Treatment information such as chemotherapy and

radiation therapy can be captured from physician, outpatient and inpatient claims. The hospice file can be used to identify patients that used hospice.

The analysis used the Medicare Provider of Service (POS) File to obtain the zip codes and the number of Medicare-certified hospices in a local area. The POS file is collected through CMS Regional Offices and contains an individual record for each Medicare-approved provider, including name, location, ownership, organizational type, and other characteristics of the participating institutional provider.

Zip code information was obtained from zip-codes.com. The longitude and latitude coordinates of zip codes were used to calculate the travel time from the centroid of the patient residence to the centroid of the nearest oncologist practice and the nearest hospice office.

Research Design

This study was a retrospective cohort study. Due to the data availability, the study cohort was elderly women first diagnosed with metastatic breast cancer between 1992 and 2002. The cohort was followed up to 183 days post diagnosis to retrieve the information on chemotherapy use from Medicare claims. Aggregate model and subgroup analysis were analyzed and compared. Specification of age subgroups were based on the convention in the literature to classify patients into two groups of above or below 75 years of age, three groups of 66 – 69, 70-79, or 80+ years of age, as well as five groups of 66-69, 70-74, 75-79, 80-84, or 85+ years of age.

Study Population

The study subjects are women aged 66+ and initially diagnosed with stage IV metastatic breast cancer between 1992 and 2002. Patients were restricted to those aged 66+ at the time of diagnosis to ensure at least one year of Medicare eligibility prior to diagnosis to measure comorbid conditions. Patients were included if they have continuous Medicare Part A and Part B coverage at least 12 months before diagnosis and the minimum of 12 months or date of death after diagnosis. Medicare Part A covers hospital insurance, including inpatient care at hospitals, skilled nursing facilities, and other institutions such as home health care services; Part B covers medically-necessary services like doctors' services, outpatient care, home health services, and other medical services, as well as some preventive services (Centers for Medicare and Medicaid Services 2010). The analysis excluded patients with Medicare managed care coverage in our study because of the unavailability of their claims in the Medicare datasets. Measurement of the extent or severity of cancer (stage IV in this analysis) was based on the cancer stage defined by the American Joint Committee on Cancer (AJCC) that is recorded in PEDSF file.

Unit of Analysis

Individual incident patient diagnosed with MBC aged 66 years or older was the unit of analysis for this study.

Table IV-1. The Inclusion and Exclusion Criteria for Selecting Study Subjects

	Inclusion and Exclusion Criteria	No. of Patients (%)	No. of Patients remaining
1.	Total number of breast cancer patients in 2002 PEDSF file	242121 (100%)	242121
2.	Patients who were first diagnosed with MBC	9087 (3.75%)	9087
	All percentages below out of 9087		
3.	Patients with unknown diagnosis date	36 (0.40%)	9051
4.	Patients with an invalid death date Diagnosis of MBC after the date of death or an invalid date of death from SEER data but blank date of death from Medicare claims	31(0.34%)	9020
5.	Patients diagnosed between 1992 and 2002	8521(94.39%)	8521
6.	Patients who are 66 years or older at diagnosis	6269(68.99%)	6269
7.	Patients with complete Medicare coverage and no HMO coverage from 12 months before diagnosis to the earlier of 1 years after diagnosis or death	4612(50.75%)	4612
8.	Patients with a zip code that has no latitude and longitude data available	1(0.01%)	4611
9.	Patients with a residence zip code not within their SEER areas	78 (0.86%)	4533

Dependent and Key Independent Variables

The dependent variable was chemotherapy use within 183 days of the diagnosis of MBC. Chemotherapy use can be identified using NCH, Outpatient, and Medpar claims (APPENDIX A Table A-1).

Key independent variables include age and access variables. Age was specified in both continuous and categorical forms and tested in the models. The four variables used to measure access to cancer care were: patient travel time to the nearest oncologist practice, local area per capita number of medical oncologists among stage IV cancer patients, local area per capita number of hospices among stage IV cancer patients, and local area chemotherapy percentage among stage IV cancer patients, all measured within

a specified radius from the patient residence. These variables were computed using patient Medicare claims (NCH, Outpatient & Medpar claims), patient residence zip codes at diagnosis from the PEDSF file, oncologist zip codes from the NCH file, and hospice zip codes from the Medicare provider file to develop these measures.

Control Variables

Control variables in the model include patient demographic characteristics (age, race, marital status), socioeconomic characteristics (income and education at census level), diagnosis year, residing SEER regions, rural/urban area characteristics, clinical characteristics (comorbidities, hormone receptor status), and radiation therapy (APPENDIX B Table B-1). Over three fourths of the elderly patients diagnosed with breast cancer have positive hormone receptor status and are treated first with hormone therapy. We do not have data available to control for hormone therapy and Medicare claims of hormone therapy are incomplete (Du et al. 2006). However, the influence of HR status on hormone therapy choice for MBC among elderly women can be assumed homogeneous after controlling for HR status. This study also controlled for radiation therapy in the regression analysis. Comorbidities were abstracted from NCH, outpatient, and inpatient claims. Diagnosis year was controlled for in the model in an effort to control temporal trends such as stage migration and better treatments available due to technological advances. Rural/urban area codes were added to account for the effect of rural/urban residency on chemotherapy use. SEER sites were controlled in the model in an effort to capture residual factors specific to given regions, such as regional policy differences.

Measurements

Measurement of Immediate Chemotherapy Use

This is the dependent variable in the model. Chemotherapy use can be identified from NCH, Outpatient, and Medpar claims (Appendix A Table A-1). Immediate chemotherapy use was identified using chemotherapy claims within 183 days of diagnosis in the analysis. The time window of 183 days was selected based on clinical practice: MBC patients who opt for chemotherapy are typically treated within 3 months post diagnosis. In practice there will be a small subset of patients who have a delayed start for a variety of issues such as wound healing or patient/physician choice (personal correspondence). The analysis used a 183-day (approximately 6 months) time frame to capture immediate choice of chemotherapy for both groups. Chemotherapy administration, as part of a complex and individualized cancer treatment, needs oncologists' close monitoring. Patients also get counseling services regarding chemotherapy use when visiting oncologists. The analysis included various modes of chemotherapy administration (subcutaneous, intravenous infusion, and oral form) at the physician's office, at outpatient clinics, and in inpatient settings. Follow-up examination or care after chemotherapy at an oncologist practice or in an outpatient setting was also included. Only the first chemotherapy claim was kept for each patient based on the date of service. The delivery of chemotherapy occurs largely at oncologist practices or in outpatient settings because hospitals and medical centers have sought to decrease the number of patient hospitalizations and average length of stay.

Medicare codes used for identifying chemotherapy include: the International Classification of Disease (ICD)-9-CM procedure code 9925 for an inpatient claims of chemotherapy and the ICD-9-CM V codes of V58.1, V66.2, or V67.2 for follow-up examination or care after chemotherapy in inpatient setting; the Common Procedure

Terminology codes 96400-96549, J9000-J9999, and Q0083-Q0085 for a physician or outpatient claim of chemotherapy administration; the revenue center codes of 0331 (chemotherapy injected), 0332 (oral chemotherapy), and 0335 (chemotherapy intravenous) for an outpatient claim of chemotherapy;. Among them, J9000 to J9999 are used to reimburse different chemotherapies.

Measurement of Age

Age was specified as both a continuous variable and a set of indicator variables to classify patients into different age groups. Both continuous and categorical forms of age were tested in the models. For example, two age subgroups above and below the median age of 75 years old, three age groups of 66 – 69, 70-79 and 80+ years of age, or five age groups of 66-69, 70-74, 75-79, 80-84 and 85+ years of age. Age is calculated based on birth date information from the PEDSF file.

Measurements of Access Variables

Patient travel time to the nearest oncologist practice

This variable is conceptualized as general access of each patient to cancer care provided by oncologists. It was measured as the minimum time to travel to a medical oncologist practice for each MBC patient. In the models, patient travel time was specified as both a continuous variable and a set of categorical variables (median and quartiles).

Medical oncologists who were treating breast, prostate, colorectal, and lung cancer patients were identified by specialist codes in Medicare physician services file (Appendix D Table D-1) to obtain their zip codes and practice years. Specialists in hematology/ oncology, medical oncology, surgical oncology, and gynecology/oncology were included, and radiation oncologists were excluded. Data from Medicare claims showed the frequency of these specialist codes were among the highest for cancer

patients. Patient residence zip codes and diagnosis years are identified in PEDSF file. Using Microsoft Geographic Information System Mappoint® 2009, the longitude and latitude data of these zip codes were used to calculate the shortest distance by road or the shortest travel time between centroids of zip codes.

Geographical distance can also be measured as straight line distance between the centroids of zip codes. Although straight line distance has been shown to correlate well with travel time and has the advantage of relatively easy calculation, travel time and travel distance are more comprehensive measures than straight line distance considering actual road experience, such as mountains, lakes, bridges, and traffic flow (Jordan et al. 2004; Phibbs and Luft 1995). This study used travel time/distance for the analysis and compared the results based on travel distance and travel time.

Local area per capita number of medical oncologists across metastatic cancers

This variable is conceptualized as the oncologist availability within a local market. It was measured as the number of medical oncologists per 1000 stage IV cancer patients within a certain radius from an MBC patient residence zip code for each diagnosis year. In the models, the local area per capita number of medical oncologists across metastatic cancers was specified as both a continuous variable and a set of categorical variables (median and quartiles).

The numerator of this variable is the number of medical oncologists who were treating breast, prostate, colorectal, and lung cancer patients and practicing within an area in a diagnosis year. Medical oncologists were identified from the Medicare claims using the same specialist codes in the Appendix D Table D-1. The denominator is the number of stage IV lung, colorectal, breast, and prostate cancer patients, as a proxy for all metastatic cancer patients, within the area in that year. The same selection criteria for the study population of MBC patients were used to select four types of metastatic cancer

patients. These patients were first diagnosed with metastatic cancers between 1992 and 2002, were aged 66 years or older at diagnosis, and had continuous Medicare coverage up to one year after diagnosis. These four types of cancer cases were identified from PDESF file.

The area surrounding the MBC patient residence is defined as the driving time radius from each patient dwelling zip code to the oncologist practice. ZIP code to ZIP code driving time data were created using Microsoft Geographic Information System Mappoint® 2009 based on the centroid of each ZIP code. Centered around the patient residence zip code, an area is drawn which is composed of a list of ZIP codes within a driving time starting from 5 minutes and expanding incrementally by 10 minutes until at least 50 patients are identified. The sum of the four types of metastatic cancer patients living at these zip codes was used as the denominator. The analysis adopted an area of 50 patients as the measure of the local health care market.

Alternatively, the local area per capita number of medical oncologists could be measured among breast cancer patients only. However, treatment patterns for early stage breast cancer patients are very different from stage IV breast cancer. Treatment patterns for stage IV cancer patients was considered to be more closely associated than early-stage breast cancer treatment patterns with treatment patterns among metastatic breast cancer patients. Another way to measure the local area is to choose a fixed radius surrounding the patient residence. Studies of small areas have suggested that each state and region has many hospital-service areas, and local area health care market structure and practice patterns vary substantially. Thus, the geographic unit used in the analysis should not mask variability by combining dissimilar geographic areas. Previous studies used a 50-mile radius as the measure of a local health care market (Brooks et al. 2003; Brooks and Chrischilles 2007). A more recent study has defined a local market as an area of 50 patients on the grounds that there is an imbalance of patient characteristics between high

and low utilization areas when the number of patients is less than 50 (Lu-Yao et al. 2008).

Local area per capita number of hospices across cancers

This variable is conceptualized as the availability of non-intensive treatment resources within the local area where patients live. It was measured as the number of hospices per 1000 stage IV cancer patients within a certain area around the patient residence for each diagnosis year. In the models, the local area per capita number of hospices across cancers was specified as both a continuous variable and a set of categorical variables (median and quartiles).

The numerator is the number of hospices within the area in that diagnosis year. The denominator is the number of stage IV breast, lung, colorectal, and prostate cancer patients, as a proxy for all metastatic cancer patients, within the area in that year. Similarly, the analysis adopted an area of 50 patients as the measure of the local health care market. The same algorithm described in the measurement of local area per capita number of oncologists across cancers is used to compute the driving time radius from the patient residence zip code.

Previous studies used other measures of local area hospice availability. In a recent study examining the effect of hospice access on hospice use, the authors used distance to the nearest hospice, per capita number of hospices, and per capita number of hospice staff among elderly patients of 65 years or older to measure hospice access among elderly patients (Wan, Brooks, and Chrischilles 2010). Two measures of hospice availability, per capita number of hospices and hospice staff among elderly patients in a local area, were highly correlated with each other. Therefore, the local area per capita number of hospice staff across cancers could potentially be used as another measure of the local area hospice availability. This study used the local area per capita number of hospices across cancers

in the main models because it is more intuitive than the other measure. Sensitivity analysis was applied to test the robustness of the results.

Local area chemotherapy percentage across cancers

This variable is conceptualized as the local practice style of oncologists in an area where patients live. It was measured as the number of patients receiving chemotherapy within 183 days after diagnosis per 100 stage IV cancer patients in an area surrounding the MBC patient residence. Immediate chemotherapy choice was defined as as at least one chemotherapy-related claim within 183 days of diagnosis. In the models, the local area chemotherapy percentage across cancers was specified as both a continuous variable and a set of categorical variables (median and quartiles).

The denominator of this variable is the number of stage IV lung, colorectal, breast, and prostate cancer patients, as a proxy for all metastatic cancer patients, within an area across diagnosis years. It is the same with denominators of per capita number of oncologists and hospices across four types of metastatic cancers. The numerator is the number of patients identified in the denominator who were treated by chemotherapy. The radius is calculated using the same algorithm identifying the size of a local market for local area per capita number of oncologists and hospice availability across metastatic cancers.

Alternatively, area chemotherapy percentage could be calculated among metastatic breast cancer patients. Area chemotherapy percentage measured among four types of stage IV cancer patients may be a practically better measure. There were fewer MBC patients in the data and the local health care market of 50 MBC patients can be highly misleading. Table IV-2 lists the dependent and key independent variables in the analysis.

Table IV-2. Measurement of Dependent and Key Independent Variables

Variables	Coding	Data Source
Dependent Variable		
Chemotherapy	1 = Chemo within 183 days of diagnosis 0 = No Chemo	NCH &OUTPATIENT &INPATIENT
Key Independent Variables (continuous form not shown)		
Age	Age5_1 = 1 if 66-69, 0 otherwise (referent) Age5_2 = 1 if 70-74, 0 otherwise Age5_3 = 1 if 75-79, 0 otherwise Age5_4 = 1 if 80-84, 0 otherwise Age5_5 = 1if 85+, 0 otherwise	PEDSF
	Age2_1 = 1 if 66-75, 0 otherwise (referent) Age2_2 = 1 if 75+, 0 otherwise	PEDSF
	Age3_1 = 1 if 66-69, 0 otherwise (referent) Aag3_2 = 1 if 70-79, 0 otherwise Age3_3 = 1 if 80+, 0 otherwise	PEDSF
Per Capita Number of Hospices	Hospices4_1 = 1 if 1st quartile, 0 otherwise (referent) Hospices4_2 = 1 if 2nd quartile, 0 otherwise Hospices4_3 = 1 if 3rd quartile, 0 otherwise Hospices4_4 = 1 if 4th quartile, 0 otherwise	POS
	Hospices2_1 = 1 if 1st half, 0 otherwise (referent) Hospices2_2 = 1 if 2nd half, 0 otherwise	POS
Travel time to the Nearest Oncologist Practice	Time4_1 = 1 if 1st quartile, 0 otherwise (referent) Time4_2 = 1 if 2nd quartile, 0 otherwise Time4_3 = 1 if 3rd quartile, 0 otherwise Time4_4 = 1 if 4th quartile, 0 otherwise	NCH PEDSF
	Time2_1 = 1 if 1st half, 0 otherwise (referent) Time2_2 = 1 if 2nd half, 0 otherwise	NCH PEDSF
Per Capita Number of Medical Oncologists	Oncologist4_1 = 1 if 1st quartile, 0 otherwise (referent) Oncologist4_2 = 1 if 2nd quartile, 0 otherwise Oncologist4_3 = 1 if 3rd quartile, 0 otherwise Oncologist4_4 = 1 if 4th quartile, 0 otherwise	NCH PEDSF
	Oncologist2_1 = 1 if 1st half, 0 otherwise (referent) Oncologist2_2 = 1 if 2nd half, 0 otherwise	NCH PEDSF
Area Treatment Percentage	Chemo4_1 = 1 if 1st quartile, 0 otherwise (referent) Chemo4_2 = 1 if 2nd quartile, 0 otherwise Chemo4_3 = 1 if 3rd quartile, 0 otherwise Chemo4_4 = 1 if 4th quartile, 0 otherwise	NCH PEDSF
	Chemo2_1 = 1 if 1st half, 0 otherwise (referent) Chemo2_2 = 1 if 2nd half, 0 otherwise	NCH PEDSF

Note:

- The continuous forms of the variables are not shown in the table.
- PEDSF: Patient entitlement and Diagnosis Summary File, also known as SEER data.
- NCH: Physician/supplier file from Medicare Part B claims.
- POS: Medicare Provider of service file.
- Outpatient: Outpatient claims from Medicare Part B claims.
- Inpatient: Inpatient claims from Medicare Part A claims.

Measurement of Control Variables

Race

Race is specified as a set of indicator variables, including non-Hispanic white, black, and other (American Indian/Alaska Native, Chinese, Japanese, Filipino, Hawaiian, Pacific Islander, Spanish, and other unspecified). This variable is from the PEDSF file.

Hormone receptor status

Hormone receptor status is specified as a set of indicator variables. It will be coded as "positive", "negative," OR "unknown". This variable is from the PEDSF file.

Radiation therapy

This variable is specified as an indicator variable, coded as "yes" or "no". Radiation therapy can be identified using NCH, Outpatient and Medpar claims.

Marital status

Marital status is specified as a set of indicator variables, coded as "single", "married," or "divorced/widowed" in our analysis. This variable is from the PEDSF file.

Education

Education is specified as a set of indicator variables based on the census tract percentage of non-high school graduates. This variable describes the average educational level of the area where the patient resides, as indicated in US census 2000 data, available in the PEDSF file. This variable is classified based on the quartiles of its distribution in specific geographic regions.

Income

Income level is specified as a set of indicator variables based on the census tract median income of the patient residence area in US census 2000 data, available in the PEDSF file. This variable is specified by the quartile of its distribution in specific geographic regions.

Comorbidities

This analysis adopts the approach described by Klabunde et al. (2002) to measure the comorbidities in Medpar, NCH, and Outpatient files. Based on the Charlson comorbidity index, this approach uses ICD-9-CM diagnosis codes, ICD-9-CM procedure codes, and HCPCS codes to determine major medical conditions for cancer patients (Appendix E Table E-1 and Appendix F Table F-1). To measure comorbid conditions, this algorithm identifies patient claims one year prior to the diagnosis and measures chronic diseases during the one-year time window. All ICD-9-CM codes on inpatient claims are used to pick up relevant diagnosis of chronic diseases to indicate comorbidities. For Outpatient/NCH claims, strict selection criteria are needed to avoid over-estimation of comorbidities because diagnosis codes in Outpatient and NCH claims have not been validated. The SEER-Medicare website provides specific SAS programs to rule out conditions that do not appear on two different claims more than 30 days apart in the Outpatient/NCH claims. This variable is specified as an indicator variable. Each indicator variable represents a specific medical condition and equals one if the patient presented it and zero otherwise.

Rural/urban area code

Rural/urban area code is classified into nine categories that distinguish metropolitan counties by population size and nonmetropolitan counties by degree of urbanization and adjacency to a metro or non-metro area. This variable is based on rural/urban continuum codes from the Economic Research Service (ERS) Department of Agriculture, available in the PEDSF file.

SEER areas

This variable is specified as a set of indicator variables. SEER sites of San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose, and Los Angeles are included.

Diagnosis year

This variable is specified as a set of indicator variables for diagnosis years 1992 - 2002 in the models.

Unmeasured Variables

Concepts unmeasured in the model include patient and provider preference regarding chemotherapy, family member perspectives, unmeasured clinical characteristics (disease severity, disease symptom, and functional status), reimbursement of the providers, physician time to provide oncology care, and local cost of living index.

Although comorbid conditions and concomitant use of radiation therapy were controlled in the model as an attempt to control disease severity, notably absent variables are patient functional status. These unmeasured variables could potentially be good markers of disease severity yet are unavailable in our data. Sicker and weaker patients probably have a higher risk of toxicities (such as fatigue or neutropenia), and therefore may be less likely to choose chemotherapy. Other symptoms, especially pain, are major predictors of chemotherapy choice. Patients suffering severe pain are more likely to choose chemotherapy for pain relief. Others with larger-sized tumors might use chemotherapy to shrink tumor size. These unmeasured clinical characteristics associated with both age and chemotherapy choice could potentially introduce bias into the interpretation of our results. For example, if all patients with more severe disease are older and are more likely to live in remote areas, then the estimate of the interaction term between age and access could be biased high, that is, the estimate of the effect change of access on chemotherapy choice when age increases is bigger than the true estimate.

Family member perspective also influences patient choice, especially for older patients. The older the patient, the more assistance she will need from family members

Table IV-3. Measurement of Control Variables

Variables	Coding	Data Source
Demographic Characteristics		
Race	White = 1 if Non Hispanic white, 0 otherwise (referent) Black = 1 if black, 0 otherwise Other = 1 if other, 0 otherwise	PEDSF
Marital Status	Single = 1 if single, 0 otherwise (referent) Married = 1 if married, 0 otherwise Ever married = 1 if Divorced/Seperated/widowed, 0 otherwise Unknown = 1 if unknown, 0 otherwise	PEDSF
Household income	Income_1 = 1 if 1st quartile of census tract income, 0 otherwise (referent) Income_2 = 1 if 2nd quartile of census tract income, 0 otherwise Income_3 = 1 if 3rd quartile of census tract income, 0 otherwise Income_4 = 1 if 4th quartile of census tract income, 0 otherwise Income_5 = 1 if Unknown, 0 otherwise	PEDSF
Education	Edu_1 = 1 if 1st quartile of census tract non-high school edu., 0 otherwise(referent) Edu_2 = 1 if 2nd quartile of census tract non-high school edu., 0 otherwise Edu_3 = 1 if 3rd quartile of census tract non-high school edu., 0 otherwise Edu_4 = 1 if 4th quartile of census tract non-high school edu., 0 otherwise Edu_5 = 1 if Unknown , 0 otherwise	PEDSF
Clinical Characteristics		
Comorbidity	0 = No comorbidities (referent) 1 = At least one comorbid condition	NCH &OUTPATIENT &INPATIENT
Hormone receptor status	HR_1 = 1 if Positive, 0 otherwise (referent) HR_2 = 1 if Negative, 0 otherwise HR_3 = 1 if Unknown, 0 otherwise	PEDSF
Radiation therapy	0 = No XRT (referent) 1 = XRT	NCH &OUTPATIENT &INPATIENT
Rural/urban area codes	Urban_1 = 1 if Metro areas of ≥1 M pop., 0 otherwise (referent) Urban_2 = 1 if Metro areas of 250K-1M pop., 0 otherwise Urban_3 = 1 if Metro areas of ≤250K pop., 0 otherwise Urban_4 = 1 if Urban areas adjacent to a metro area of >20K pop., Urban_5 = 1 if Urban areas not adjacent to a metro area of >20K pop. Urban_6 = 1 if Urban areas adjacent to a metro area of <20K pop. Urban_7 = 1 if Urban areas not adjacent to a metro area of <20K pop. Urban_8 = 1 if Rural areas adjacent to a metro area of <2500 pop Urban_9 = 1 if Rural areas not adjacent to a metro area of <2500 pop	PEDSF
Diagnosis year (1992 - 2002)	0 = Not diagnosed in a particular year 1 = Diagnosed in a particular year	PEDSF

Note:

- PEDSF: Patient entitlement and Diagnosis Summary File, also known as SEER data.
- NCH: Physician/supplier file from Medicare Part B claims.
- POS: Medicare Provider of service file.
- Outpatient: Outpatient claims from Medicare Part B claims.
- Inpatient: Inpatient claims from Medicare Part A claims.

should her activities be bounded by poor eyesight, declining mobility, or decreasing cognitive ability. The prospects of chemotherapy use would concern family members because risks of adverse events are high.

Moreover, patients and physicians who prefer chemotherapy for other, unaccounted-for reasons are more likely to choose treatment. Physicians who recommend chemotherapy more often may have a higher regard or be more optimistic toward the benefits of chemotherapy. Patients who prefer chemotherapy may have a higher trust in medical technology. For example, if all providers with high chemotherapy preference live in areas with high provider access, then the estimate of the effect change of access on chemotherapy choice when age increases could be biased high.

Other variables that are unmeasured yet may impact chemotherapy choice include reimbursement to the provider, time to provide oncology care (Radecki et al. 1988), and local cost of living. Previous studies have shown that Medicare reimbursement has little effect on a physician's decision to administer chemotherapy to metastatic cancer patients but does influence the type of chemotherapy received. More generous reimbursement is associated with more costly chemotherapy regimens (Jacobson et al. 2006). Similarly, the busier the physician is, the less likely he/she is to give more time to each cancer patient, which may have a greater impact on patients with more complicated conditions. Local cost of living may influence patient chemotherapy choice through its effect on the budget because out-of-pocket and access-related costs are likely to be a measurable proportion of a patient's budget.

Empirical Model and Interpretation

Two empirical models are used to evaluate the effect of access to cancer care on the choice to pursue chemotherapy by elderly women with MBC and the relationship between patient age and access in this choice.

The first model is based on equation (16) with interaction terms between age and each access variable. We can write down all the interaction terms in the model as the following:

(17) $P(T_i = 1) = \upsilon_0 + \upsilon_1 Y_i + \upsilon_2 D_i + \upsilon_3 Cl_i + \upsilon_4 Co_i + \upsilon_5 M_i + \upsilon_6 B_i + \upsilon_7 H_i + \upsilon_8 O_i + \upsilon_9 A_i + \upsilon_{10}(B_i Y_i) + \upsilon_{11}(H_i Y_i) + \upsilon_{12}(O_i Y_i) + \upsilon_{13}(A_i Y_i) + \epsilon_i$

where T_i is a binary variable indicating whether the patient received chemotherapy or not. The logit function of the probability of chemotherapy use is developed as a linear function of the patient age (Y), demographic characteristics (D), hormone receptor status (Cl), comorbidities (Co), other health service utilization (M), the distance to the nearest oncologist practice (A), and the local area chemotherapy percentage (B), the local area per capita number of hospices (H), and the local area per capita number of oncologists across cancers (O). ϵ_i, is the error term. The analysis uses Chow F-statistics, a test of restrictions on parameter estimates, to test hypothesis a, b, c whether all the relevant terms for one interaction effect simultaneously equal to zero.

In the logistic regression model, the exponential form of each parameter is the odds of having chemotherapy versus no chemotherapy use, per unit change in an independent variable, holding other variables constant. The same interpretation applies to both dummy and continuous variables. For example, a unit change in race indicates switching from “non-white” to “white” in dummy variable called “white”, or from “non-black” to “black” in the dummy variable called “black”. Similarly, a unit change in comorbidities means switching from “no comorbidities” to “at least one comorbid condition”. When the parameter is positive and statistically significant, it means the odds of having chemotherapy are greater when the indicator variable equals 1 than when it equals 0 for the reference group. When the parameter is negative and statistically significant, it means the odds of having chemotherapy are lower when the indicator variable equals 1 than for the reference group.

The interpretation of the parameters for interaction terms between age and access are also expressed in terms of odds. The exponent of the logistic coefficient for the product term is a multiplicative factor by which the odds of one unit change in the access measure compared with the referent given one additional year of age. If the coefficient is positive and statistically significant (e.g, the local area treatment percentage), then the interpretation is that the effect of one unit change in the access measure (e.g., one more patient receives chemotherapy) on the probability of getting chemotherapy is stronger with increasing age. If the coefficient is negative and statistically significant (e.g., one more mile to travel to the nearest oncologist practice), then the interpretation is that the effect of one unit change in the access measure on the probability of not getting chemotherapy is stronger with increasing age.

The second empirical model aims to obtain the estimate of chemotherapy choice for each age category. The analysis uses logistic regression models to obtain this estimator. The model is based on equation (15), shown as the following:

(18) $$T_i = \varphi_0 + \varphi_1 D_i + \varphi_2 Cl_i + \varphi_3 Co_i + \varphi_4 M_i + \varphi_5 B_i + \varphi_6 H_i + \varphi_5 O_i + \varphi_5 A_i + \acute{r}_i$$

In this logistic regression model, chemotherapy choice is a binary variable. To achieve the objective, our analysis uses this empirical model for each age category respectively. The effect of access to cancer care may be different for each age category based on the theory laid out in the choice model. For example, it could be that distance does not significantly affect the chemotherapy choice for a younger patient but becomes a significant factor for an older patient. Interpretation of how the effect of access on chemotherapy choice varies by age for stratified models should not be overstated (Wang et al. 2007). Statistical inferences can be generalized only to the population from which the sample stratum was drawn and not to the entire original sample.

Analytical Methods

The first aggregate model uses multivariate logistic regression with interaction terms between age and access variables. Both age and access variables were specified as continuous variables and categorical variables as below/above median and quartiles in the model. The squared term of age can be added into the equation to explore the nonlinear effects of age. Notice that when age and access variables are specified as indicator variables, the interaction terms between each access variable and age has one category omitted as the referent like other indicator variables.

The subgroup analysis uses a logistic regression model in each age subgroup. Two age groups of above/below 75 years old, three age groups of 66-69, 70-79 and 80+ years old, and five age groups of 66-69, 70-74, 75-79, 80-84, and 85+ years old are specified and tested in the models. Access variables are specified as both continuous variable and indicator variables based on their quartiles. Using a continuous variable in the logistic regression model allows more information of each variable for the analysis and can avoid misclassification. The results from subgroup analysis are compared with the results from the aggregate model with interaction terms. In addition, the results based on the model with both continuous and indicator variables of access variables are present to compare whether results are consistent.

All data analysis will be performed by using SAS 9.00 at the significance level .05 (SAS Institute Inc, Cary, NC).

Data Permission and Confidentiality

I submitted a research proposal to the University of Iowa Institutional Review Board (IRB) on May 23, 2009 and obtained permission to conduct the study on June 10,

2009 (IRB ID number: 200905781). The use of data for this project was approved on June 4, 2009 by the SEER-Medicare contact at Information Management Services Inc. Restricted variables, including patient and provider zip codes, were stored in a separate folder that can only be accessed by the principle investigator (PI) and co-PI who conducted this study, the data manager, and the IT staff at the School of Public Health at the University of Iowa. In addition, since this study involves human subjects, I have completed an education program about human subject protection to abide by the policies and procedures in the Investigator's Guide to Human Subjects Research at the University of Iowa.

CHAPTER V

RESULTS

Overview

This chapter summarizes the empirical results from data analysis. First, it described patient characteristics for the whole study population and compared them for each age subgroup. Chemotherapy use for each age group was then summarized. The distribution of each access variable by diagnosis year was calculated. Univariate analysis of each access variable was performed for patients who chose chemotherapy versus those who did not for the whole group as well as in the subgroups. In the aggregate multivariate logistic regression models, age and access variables were specified in categorical and continuous variables with interaction effects between age and each access variable while controlling for other covariates. In the subgroup analysis, disaggregate multivariate logistic regression models were specified equivalent to age dummies and interactions in the aggregate models while controlling for other covariates.

Description of Patient Characteristics

Table V-1 shows patient characteristics for the whole study population and across age subgroups. The average age of the study population is 77.62, ranging from 66.04 to 103.15. Among the total 4533 MBC patients, there were 747, 1111, 1068, 856, and 751 in age subgroups aged 66-69, 70-74, 75-79, 80-84, and 85+ years old, respectively. White patients made up 82.51% of the whole study population, followed by black (10.77%) and other (6.73%). Older age groups tended to have a lower proportion of African Americans and patients with other ethnical background. Chi-square test showed a statistically significant difference in race distribution across age groups.

Overall 30.69% of patients were married at diagnosis while single never-married patients made up 10.46% of the population. Divorced, widowed, or separated patients accounted for 55.08% of the population. Elderly women in the older age group were more likely to be widowed, which was shown by a steadily increased proportion of patients in this category. There was a statistically significant variation in marital status across age groups.

31.94% of the patients had positive HR status while 25.39% of them had negative HR status. Patients with unknown HR status constituted 42.66% of the study population. Older patients tended to have a higher percentage of positive HR status. Chi-square tests showed a statistically significant variation in HR status across age groups.

With increasing age, patients with co-morbidities increased. Chi-square tests showed a statistically significant difference in the presence of comorbidities across age groups. Within the range of comorbidities captured in this study, the existence of chronic conditions varied significantly across age groups. These conditions included dementia, congestive heart failure (CHF), diabetes with complications, peripheral vascular disease (PVD), and cerebrovascular disease (CVD). The prevalence of dementia, CHF, PVD, and CVD appeared to increase with age.

About 91.85 % of the patients lived in metropolitan or urban areas with populations of at least 20,000. Chi-square tests showed no statistically significant variations in patient distribution across SEER areas or diagnosis years by age groups.

Table V-1. Description of Patient Characteristics

	Age Subgroups												
	66 – 69		70 – 74		75 -79		80 - 84		85+		Total		
	N = 747		N = 1111		N = 1068		N = 856		N = 751		N = 4533		
Characteristics	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	*p*
Average age	68.10		72.56		77.41		82.41		89.44		77.62		
Race													0.0059
Non-Hispanic white	600	80.32	898	80.83	873	81.74	738	86.21	631	84.02	3740	82.51	
Black	94	12.58	120	10.80	122	11.42	68	7.94	84	11.19	488	10.77	
Other	53	7.10	93	8.37	73	6.84	50	5.84	36	4.79	305	6.73	
Marital status													<0.0001*
Single	97	12.99	129	11.61	94	8.80	73	8.53	81	10.79	474	10.46	
Married	327	43.78	429	38.61	341	31.93	205	23.95	89	11.85	1391	30.69	
Divorced/Widowed	294	39.36	513	46.17	591	55.34	543	63.43	556	74.03	2497	55.08	
Unknown	29	3.88	40	3.60	42	3.93	35	4.09	25	3.33	171	3.77	
HR status													<0.0001*
Positive	286	38.29	369	33.21	355	33.24	262	30.61	176	23.44	1448	31.94	
Negative	211	28.25	312	28.08	284	26.59	206	24.07	138	18.38	1151	25.39	
Unknown	250	33.47	430	38.70	429	40.17	388	45.33	437	58.19	1934	42.66	
Comorbidites													
Rheumatologic disease	9	1.20	13	1.17	21	1.97	15	1.75	7	0.93	65	1.43	0.2958
COPD	40	5.35	81	7.29	76	7.12	56	6.54	44	5.86	297	6.55	0.4220
Old MI	4	0.54	9	0.81	13	1.22	8	0.93	8	1.07	42	0.93	0.6357
Dementia	1	0.13	6	0.54	11	1.03	16	1.86	19	2.53	53	1.17	<0.0001*
MI	6	0.80	3	0.27	7	0.66	7	0.82	8	1.07	31	0.68	0.3079
PVD	11	1.47	21	1.89	19	1.78	25	2.92	26	3.46	102	2.25	0.0321*
CVD	14	1.87	45	4.05	33	3.09	38	4.44	30	3.99	160	3.53	0.0394*
Diabetes with complications	18	2.41	19	1.71	19	1.78	8	0.93	5	0.67	69	1.52	0.0356*
Diabetes	72	9.64	110	9.90	132	12.36	96	11.21	70	9.32	480	10.59	0.1690
CHF	36	4.82	41	3.69	63	5.90	71	8.29	91	12.12	302	6.66	<0.0001*

Table V-1 Continued

	Age Subgroups											
	66 – 69		70 – 74		75 -79		80 - 84		85+		Total	
	N = 747		N = 1111		N = 1068		N = 856		N = 751		N = 4533	
Characteristics	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	*p*
Paralysis	2	0.27	8	0.72	9	0.84	6	0.70	3	0.40	28	0.62	0.5185
Peptic ulcer disease	6	0.80	4	0.36	7	0.66	8	0.93	7	0.93	32	0.71	0.5213
Renal disease	8	1.07	14	1.26	11	1.03	10	1.17	11	1.46	54	1.19	0.9311
No comorbidities	611	81.79	867	78.04	78	73.78	619	71.31	533	70.97	3418	75.40	<0.0001*
Rural/urban area code													0.9591
Metro areas of ≥1 M pop.	441	59.04	673	60.58	650	60.86	536	62.62	454	60.45	2754	60.75	
Metro areas of 250K-1M pop.	141	18.88	213	19.17	190	17.79	161	18.81	140	18.64	845	18.64	
Metro areas of ≤250K pop.	48	6.43	71	6.39	74	6.93	51	5.96	49	6.52	293	6.46	
Urban areas adjacent to a metro area of >20K pop.	28	3.75	32	2.88	35	3.28	18	2.10	23	3.06	136	3.00	
Urban areas not adjacent to a metro area of >20K pop.	24	3.21	36	3.24	23	2.15	26	3.04	18	2.40	127	2.80	
Urban areas adjacent to a metro area of <20K pop.	25	3.35	36	3.24	39	3.65	33	3.86	27	3.60	160	3.53	
Urban areas not adjacent to a metro area of <20K pop.	30	4.02	30	2.70	39	3.65	21	2.45	22	2.93	142	3.13	
Rural areas adjacent to a metro area of <2500 pop	6	0.80	12	1.08	10	0.94	6	0.70	10	1.33	44	0.97	
Rural areas not adjacent to a metro area of <2500 pop	4	0.54	8	0.72	8	0.75	4	0.47	8	1.07	32	0.71	
SEER area													0.2563
San Francisco	40	5.35	58	5.22	60	5.62	50	5.84	45	5.99	253	5.58	
Connecticut	82	10.98	139	12.51	133	12.45	94	10.98	83	11.05	531	11.71	

Table V-1 Continued

	Age Subgroups											
	66 – 69		70 – 74		75 -79		80 - 84		85+		Total	
	N = 747		N = 1111		N = 1068		N = 856		N = 751		N = 4533	
Characteristics	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	*p*
Detroit	99	13.25	152	13.68	170	15.92	132	15.42	104	13.85	657	14.49	
Hawaii	13	1.74	24	2.16	20	1.87	10	1.17	5	0.67	72	1.59	
Iowa	93	12.45	114	10.26	113	10.58	88	10.28	99	13.18	507	11.18	
New Mexico	17	2.28	42	3.78	27	2.53	18	2.10	24	3.20	128	2.82	
Seattle	55	7.36	89	8.01	77	7.21	69	8.06	56	7.46	346	7.63	
Utah	31	4.15	29	2.61	34	3.18	20	2.34	22	2.93	136	3.00	
Atlanta	47	6.29	58	5.22	54	5.06	41	4.79	31	4.13	231	5.10	
San Jose	27	3.61	42	3.78	36	3.37	34	3.97	29	3.86	168	3.71	
Los Angeles	87	11.65	112	10.08	109	10.21	91	10.63	80	10.65	479	10.57	
Rural Georgia	3	0.40	2	0.18	1	0.09	2	0.23	4	0.53	12	0.26	
Great California	44	5.89	63	5.67	53	4.96	55	6.43	50	6.66	265	5.85	
Kentucky	29	3.88	30	2.70	43	4.03	33	3.86	13	1.73	148	3.26	
Louisiana	24	3.21	42	3.78	36	3.37	19	2.22	25	3.33	146	3.22	
New Jersey	56	7.50	115	10.35	102	9.55	100	11.68	81	10.79	454	10.02	
Year of diagnosis													0.6125
1992	78	10.44	95	8.55	87	8.15	64	7.48	50	6.66	374	8.25	
1993	61	8.17	89	8.01	76	7.12	57	6.66	53	7.06	336	7.41	
1994	48	6.43	82	7.38	62	5.81	54	6.31	60	7.99	306	6.75	
1995	54	7.23	86	7.74	77	7.21	62	7.24	60	7.99	339	7.48	
1996	61	8.17	85	7.65	78	7.30	58	6.78	54	7.19	336	7.41	
1997	43	5.76	81	7.29	69	6.46	71	8.29	54	7.19	318	7.02	
1998	43	5.76	76	6.84	74	6.93	54	6.31	42	5.59	289	6.38	
1999	55	7.36	76	6.84	84	7.87	55	6.43	42	5.59	312	6.88	
2000	105	14.06	139	12.51	153	14.33	126	14.72	127	16.91	650	14.34	
2001	102	13.65	151	13.59	163	15.26	118	13.79	110	14.65	644	14.21	
2002	97	12.99	151	13.59	145	13.58	137	16.00	99	13.18	629	13.88	

Note: * P<0.05

Chemotherapy Use within 6 Months of Diagnosis of MBC

by Age Subgroups

Table V-3 shows the percentage of patients who used chemotherapy by age subgroups and chi-square statistics to test the association between chemotherapy choice and age.

30.16% of 4533 MBC patients used chemotherapy. Chemotherapy percentage decreased steadily with age, with percentages of 49.26%, 40.50%, 31.84%, 17.64% and 7.72% shown in the subgroups aged 66-69, 70-74, 75-79, 80-84 and 85+, respectively (Figure 2). Patients who used chemotherapy averaged 74.18 years of age while those who did not use chemotherapy averaged 79.12 years of age. Chemotherapy use percentage decreased with increasing age, with the highest rate shown among those aged 66-69 years old and the lowest rate shown among those aged 85 years and older.

According to the National Comprehensive Cancer Network (NCCN) and M.D. Anderson clinical guidelines for breast cancer, patients diagnosed with MBC should use hormone therapy first if they have positive HR status (M.D. Anderson Cancer Center 2008; National Comprehensive Cancer Network 2010). To fully understand the age-ralated treatment patters of chemotherapy, it must also be noted that chemotherapy use post-diagnosis was further stratified by HR status. There were 1448, 1151, and 1934 patients who had positive, negative, and unknown hormone receptor status, respectively. Results showed that 41.53% of patients who had negative HR status used chemotherapy while only 29.70% of those who had positive HR status used it. Among patients with positive HR status, the highest chemotherapy percentage was 45.45% found in the age group of 66-69, which steadily decreased to 36.59%, 29.30%, 17.18%, and 9.09% in the age groups of 70-74, 75-79, 80-84, and 85+ years old. Among patients with negative HR status, the highest chemotherapy percentage was 56.40% observed in the age group of 66-69, which steadily decreased to 50.96%, 44.72%, 25.24%, and 15.22% in the age

groups of 70-74, 75-79, 80-84, and 85+ years old. Chi-square tests showed that after stratification by HR status, chemotherapy use decreased with advancing age and significantly varied across age groups.

Table V-2 shows different chemotherapies chosen by the MBC patients. It seemed that more toxic anthracycline were used less frequent than other types of chemotherapies (such as Methotrexate and Cyclophosphamide) although some major inpatient and outpatient claims related to chemotherapy administration were unknown. Chemotherapies chosen the MBC patients by age groups and time periods are shown in the APPENDIX C Table C-1 and Table C-2.

Figure 2. Percentage Chemotherapy Use by Age Subgroups

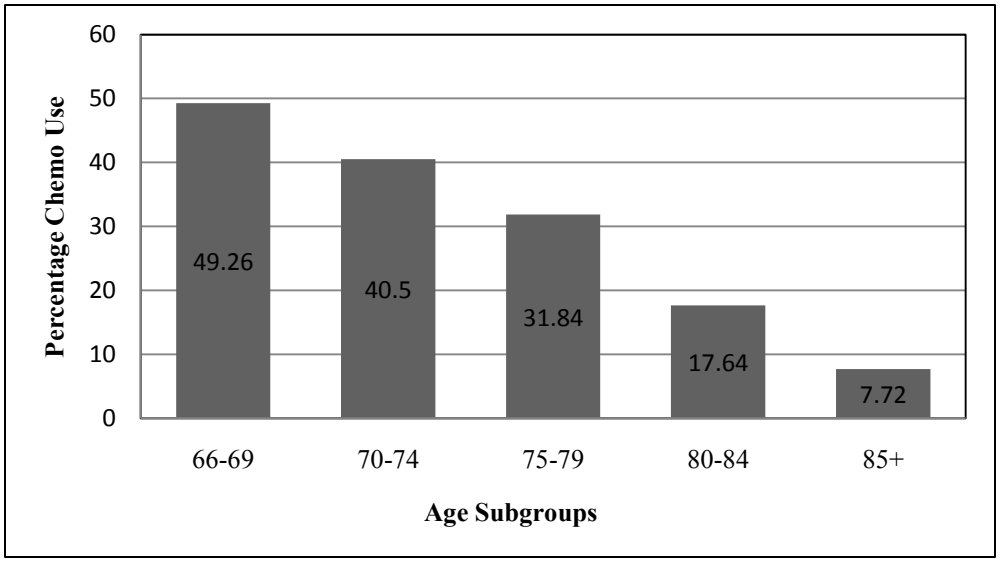


Table V-2. Chemotherapies chosen by Medicare metastatic breast cancer patients between 1992 and 2002

Chemotherapy types	Frequency
BCG	1
Etoposide	1
Goserelin	1
Mesna	1
Carboplatin	2
Leuprolide	2
Mitoxantrone	2
Vincristine	2
Vinorelbine/tartrate	2
Alemtuzumab	4
Trastuzumab	4
Paclitaxel	8
Docetaxel	13
NOS	13
Doxorubicin	17
Methotrexate	33
Fluorouracil	36
Cyclophosphamide	65
Inpatient chemo administration	274
Unknown	886
Total	1367

Table V-3. Chemotherapy Use within 6 Months of Diagnosis of MBC by Age Subgroups

	Age Subgroups												
	66 – 69		70 – 74		75 -79		80 - 84		85+		Total		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	*p*
Overall chemo percentage	747	49.26	1111	40.50	1068	31.84	856	17.64	751	7.72	4533	30.16	
HR status†													
HR +	286		369		355		262		176		1448		<0.0001*
Chemo percentage	130	45.45	135	36.59	104	29.30	45	17.18	16	9.09	430	29.70	
HR -	211		312		284		206		138		1151		<0.0001*
Chemo percentage	119	56.40	159	50.96	127	44.72	52	25.24	21	15.22	478	41.53	
HR Unknown	250		430		429		388		437		1934		<0.0001*
Chemo percentage	119	47.60	156	36.28	109	23.75	54	11.76	21	4.81	459	23.73	

Note: * P< 0.05

† Hormone receptor status

Distribution and Univariate Analysis of Access Variables

Table V-4 shows the distribution of access variables. The mean travel time from patient to nearest oncologist practice was 0.28 hr or 16.8 minutes, with half of patients living within 0.17 hr or 10.3 minutes to the nearest oncologist practice. On average, patients lived in a local area with 118.85 medical oncologists and 28.46 hospice programs per 1000 metastatic breast, prostate, lung, and colorectal cancer patients. The average local area chemotherapy percentage was 37.67% across these four types of metastatic cancer patients. Correlation analysis between the four access variables showed that the correlation between each two variables was small (see Appendix H Table H-8).

Table V-4. Distribution of Access Variables

Access Variables	Mean	Minimum	The 1st Quartile	Median	The 3rd Quartile	Maximum
Travel Time	0.2788	0	0.0657	0.1711	0.3181	3.7187
# oncologist	118.8510	12.8205	62.3335	98.5915	157.4070	712.7660
# hospices	28.4603	0	8.4507	19.2308	38.4615	400
Area treatment percentage	37.6702	9.3333	31.4006	37.9310	44	70

Note:

- N=4284
- Travel time is calculated as proportion of an hour.
- # oncologists is calculated as local area number of oncologists per 1000 metastatic breast, prostate, lung and colorectal cancer patients.
- # hospices is calculated as local area number of hospices per 1000 metastatic breast, prostate, lung and colorectal cancer patients.
- Area treatment percentage is calculated as local area number of patients who received chemotherapy per 100 end-stage breast, prostate, lung and colorectal cancer patients.

Table V-5 shows the univariate analysis between each access variable and chemotherapy use by age subgroups. In the whole group analysis, percentage of chemotherapy use increased with the local area chemotherapy percentage across metastatic cancers ($p<0.0001$). Although it appeared MBC patients living farther away from the nearest oncologist practice or living in an area with a higher local area per capita number of oncologists across metastatic cancers used less chemo, univariate analysis did not achieve statistical significance ($p=0.8552$, 0.1016 respectively). There was no obvious trend in chemotherapy use associated with the local area per capita number of hospices across metastatic cancers ($p=0.7722$). When the percentages break down into five age categories (66-69, 70-74, 75-79, 80-84, and 85+ years old), the increasing trend in chemotherapy use associated with the local area chemotherapy percentage maintained in each age category. The association was statistically significant in all age groups except in the age group of 80-84 years old (Figure 3). Univariate analysis of the association between chemotherapy use and patient travel time to the nearest oncologist in the age subgroup analysis did not achieve statistical significance (Figure 4). Neither did the association between chemotherapy use and the local area per capita number of oncologists across metastatic cancers in the subgroup univariate analysis (Figure 5).

Table V-5. Univariate Analysis between Each Access Variable and Chemotherapy Use by Age Subgroups

Access variables	66 – 69 N = 747 %Chemo use	P	70 – 74 N = 1111 %Chemo use	P	75 -79 N = 1068 %Chemo use	P	80 - 84 N = 856 %Chemo use	P	85+ N = 751 %Chemo use	P	Total N = 4533 %Chemo use	P
Area chemo percentage		0.0007*		0.0235*		0.0031*		0.2073		0.0833		<0.0001*
1st quartile	39.26	↓	34.07	↓	24.90	↓	13.85		4.64	↓	23.72	↓
2nd quartile	46.19		40.08		27.86		21.16		7.51		29.54	
3rd quartile	52.30		44.76		35.80		15.71		8.60		31.91	
4th quartile	60.95		45.74		38.30		19.37		11.98		35.81	
Travel time		0.6762		0.5071		0.5754		0.1369		0.1405		0.8552
1st quartile 2nd quartile	50.41		39.52		31.98		19.76		9.57		30.59	
3rd quartile	46.63		43.82		33.33		17.22		4.62		30.19	↑
4th quartile	50.85		41.61		29.13		13.20		8.19		29.64	
# Oncologists		0.2956		0.2331		0.5770		0.3781		0.1414		0.1016
1st quartile	55.49		44.09		34.43		14.89		9.20		32.77	↑
2nd quartile	47.80		44.44		31.33		20.18		11.06		30.93	
3rd quartile	49.12		39.16		28.69		19.11		6.55		29.04	
4th quartile	46.07		37.12		31.62		15.14		5.03		28.26	
# Hospices		0.6254		0.6304		0.6698		0.5048		0.0317*		0.7722
1st quartile	52.27		39.37		33.09		19.59		4.62		30.68	
2nd quartile	52.07		40.98		32.37		14.69		13.02		31.06	
3rd quartile	47.54		44.53		32.48		16.67		6.74		30.20	
4th quartile	46.86		39.85		28.52		19.40		8.11		29.09	

Note:

- Area chemo percentage: 100*percentage chemotherapy use among metastatic breast, prostate, lung, and colorectal cancer patients in the local area of 50 patients (four types of metastatic cancer patients) surrounding the residency of a metastatic breast cancer patient.
- Travel time: driving time from the patient residency to the nearest oncologist practice. Travel time only has 3 quartiles because the first quartile and the second quartile are merged into one category due to the first quartile value = 0.
- #Oncologists: 1000*per capita number of oncologists among metastatic breast, prostate, lung, and colorectal cancer patients in the local area of 50 patients (four types of metastatic cancer patients) surrounding the residency of a metastatic breast cancer patient.
- #Hospices: 1000* per capita number of hospices among metastatic breast, prostate, lung, and colorectal cancer patients in the local area of 50 patients (four types of metastatic cancer patients) surrounding the residency of a metastatic breast cancer patients.
- The direction of the arrow represents the general trend of percentage chemotherapy use associated with the increasing quartiles.

Figure 3. Age Subgroup Percentage of Chemo Use by Quartiles of the Local Area Chemo Percentage

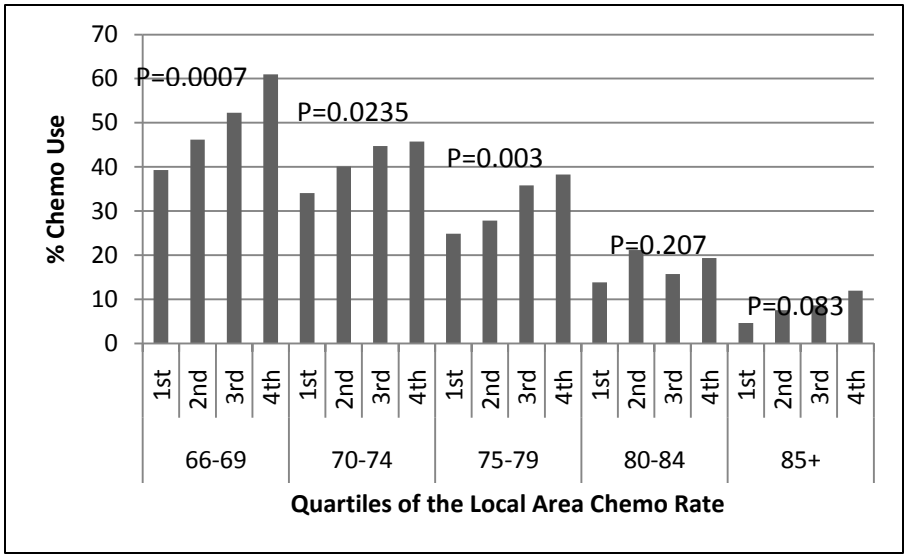


Figure 4. Age Subgroup Percentage of Chemo use by quartiles of patient travel time

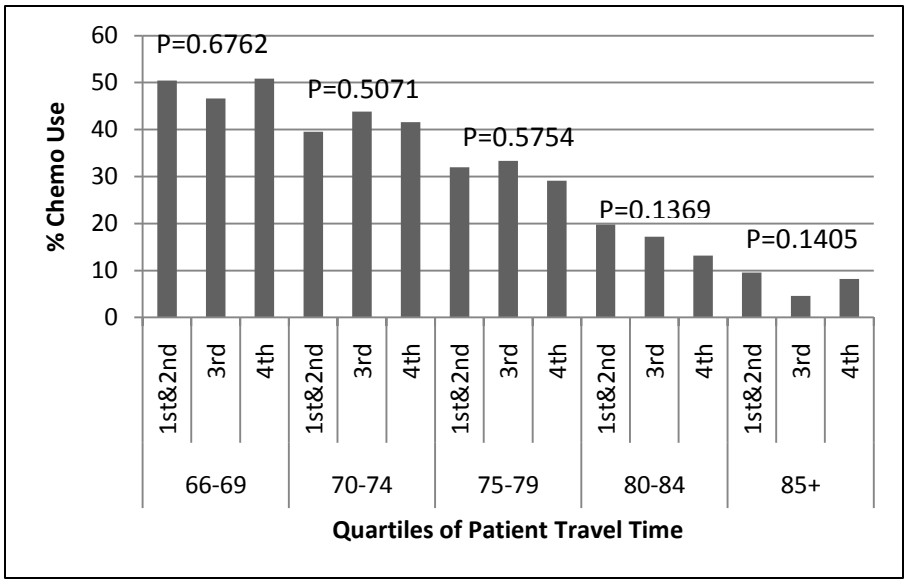
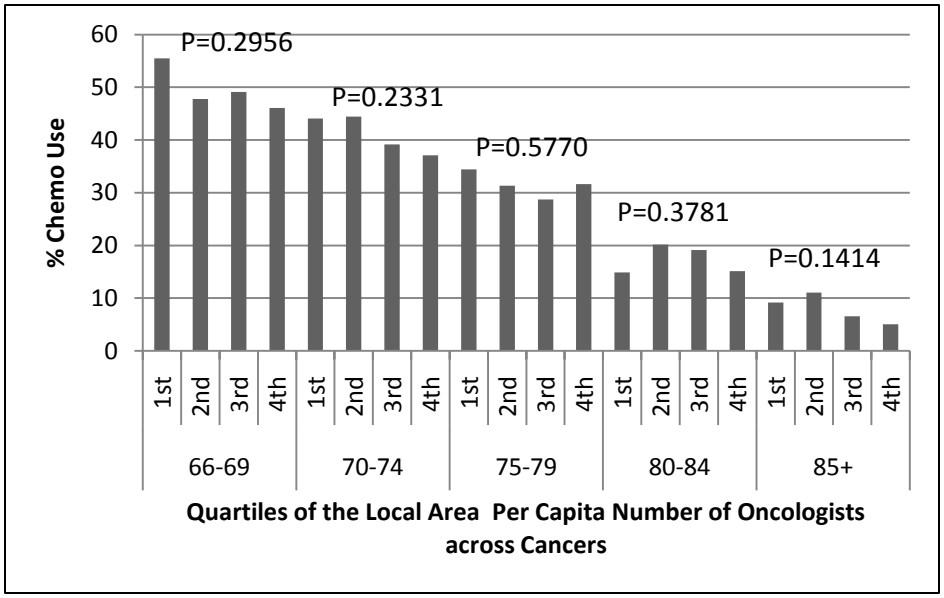


Figure 5. Age Subgroup Percentage of Chemo Use by Quartiles of the Local Area Per Capita Number of Oncologists



Interaction Term Approach to Estimate the Effect of Access to Cancer Care on Chemotherapy Choice in the Whole Study Population

To test the hypotheses, multiple logistic regression with dependent variable chemotherapy use was estimated on patient age, access variables, and control variables with interaction terms between patient age and each access variable. Each multiple regression included one access variable at a time, including patient travel time to the nearest oncologist practice, the local area per capita number of hospices across metastatic cancers, the local area per capita number of oncologists across metastatic cancers, and the local area chemotherapy percentage across metastatic cancers. In the first model, both age

and access variable were specified as continuous variables with interaction terms between them. The second model added the squared terms of age and access variable in addition to continuous form of age and access variable with the interaction terms between age and access variable and interaction terms between squared terms of age and access variable. In the third model, age and access variable were specified as above and below the median with interaction terms between them. In the fourth model, age and access variable were specified as quartiles with interaction terms between them (Tables V-6-V-9). In addition, consistent with the convention to specify age groups in the literature, models were run with age dummy variables (classified above/below median, three age groups of 66-69, 70-79, and 80+ years old, and five age groups of 66-69, 70-74, 75-79, 80-84, and 85+ years old) and access quartiles as well as interaction terms between them (Tables V-10-V-12). F-statistics were used to assess whether the association between chemotherapy choice and individual access variables was statistically significant, as well as the significance of interaction terms.

In Tables V-6-V-9, which includes individual access variables with age, results showed that age was consistently significantly associated with chemotherapy use in all models regardless of whether it was specified as continuous form, median dummies, or quartile dummies. When both age and squared term of age were included in the model, the squared term of age was significant but not age itself (except for the model with the local area per capita number of hospices, where both age and squared term of age were significant). The significant effect of local area chemotherapy percentage across metastatic cancers on immediate choice of chemotherapy was also observed in the models. Other access variables, however, have not been consistently associated with immediate chemotherapy choice. None of the interaction terms specified in the models were significant here.

In Tables V-10-V-12, age dummies were specified consistent with the convention in the literature, i.e., below/above median age 75, every ten-year range, and every five-

year range, as well as the interaction terms of age dummies and access quartiles. Results showed age and local area chemotherapy percentage across metastatic cancers to be statistically significantly associated with immediate chemotherapy choice across all three models. However, F-statistics showed the interaction effects between age dummies and access quartiles did not achieve statistical significance. If the models had detected a modification by age of the effect of access to cancer care on immediate chemotherapy choice for elderly MBC patients, both the direction and magnitude of the coefficients of the interaction terms between age and each access variable would have shown a trend. For example, in the Table V-10, if travel time were negatively associated with chemotherapy and affected older patients more than younger patients, a consistent trend of negative signs for the coefficients of the interaction terms between age and travel time would be observed. Additionally, a bigger magnitude of the coefficient would be associated with the higher level of the age dummy variable, that is, the absolute value of the coefficient of age_3*time_3 is bigger than that of age_2*time_3. The coefficient for each interaction term is a multiplicative factor by which the log odds of chemotherapy use for that age category changes as travel time increases by one hour.

Table V-6. Estimates of Patient Age and Patient Travel Time to the Nearest Oncologist, and Interaction Term between Patient Age and Patient Travel Time on Immediate Choice of Chemotherapy in the Aggregate Model

	Continuous				Median		Quartile		
	Estimate	P value	Estimate	P value	Estimate	P value	Estimate	F-statistics	P value
Continuous									
Age	-0.1034	<0.0001†*	0.2315	0.0800†					
Time	1.5344	0.4001†	-0.4134	0.9277†					
Age * Time	-0.0248	0.3076†	0.00389	0.9489†					
Age^2			-0.00219	0.0105†*					
$Time^2$			1.0242	0.6378†					
Age^2 * $Time^2$			-0.00022	0.5679†					
Median									
Age					-1.0279	<0.001†*			
Time					-0.0101	0.9137†			
Age*Time					-0.1621	0.2689†			
Quartile									
Age								130.6185	<0.0001‡*
Age_2§							-0.4271		0.0010†*
Age_3§							-0.8571		<0.001†*
Age_4§							-1.7748		<0.0001†*
Time∓								0.0671	0.9670‡
Time_3$							0.0355		0.8218†
Time_4$							-0.00727		0.9638†
Age*Time								2.6298	0.8537‡
Age_2*Time_3							0.00510		0.9818†
Age_2*Time_4							-0.0681		0.7561†
Age_3*Time_3							-0.1902		0.4144†
Age_3*Time_4							-0.1699		0.4797†
Age_4*Time_3							-0.2801		0.3429†
Age_4*Time_4							-0.3759		0.2170†

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- § Use Age_1, Age_2, Age_3, and Age_4 to represent four quartiles of age.
- $Use Time_1, Time_2, Time_3, and Time_4 to represent four quartiles of patient travel time to the nearest oncologist.
- †P value of Wald $\chi 2$ test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- *Significance level at 0.05 level.

Table V-7. Estimates of Patient Age and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal cancer, and Interaction Term between Patient Age and the Local Area Per Capita Number of Hospices on Immediate Choice of Chemotherapy in the Aggregate Model

	Continuous				Median		Quartile		
	Estimate	P value	Estimate	P value	Estimate	P value	Estimate	F-statistics	P value
Continuous									
Age	-0.1071	<0.0001†*	0.2162	0.1001†*					
# hospices	0.00315	0.8163†	-0.0265	0.3752†					
Age * # hospices	-0.00005	0.7667†	0.000350	0.3802†					
Age^2			-0.00214	0.0121†*					
# $hospices^2$			0.000093	0.3136†					
Age^2 * $hospices^2$			-1.73E-8	0.3057†					
Median									
Age					-1.0901	<0.0001†*			
# hospices					-0.0286	0.7668†			
Age*# hospices					-0.0295	0.8400†			
Quartile									
Age								77.3459	<0.0001‡*
Age_2§							-0.5511		0.0025†*
Age_3§							-0.7960		<0.0001†*
Age_4§							-2.2441		<0.0001†*
# hospices								0.4003	0.9402‡
# hospices_2$							-0.0672		0.7101†
# hospices_3$							-0.0685		0.7091†
# hospices_4$							-0.1188		05303†
Age*# hospices								9.3270	0.4077‡
Age_2*# hospices_2							0.1535		0.5501†
Age_2*# hospices_3							0.1611		0.5321†
Age_2*# hospices_4							0.1153		0.6543†
Age_3*# hospices_2							-0.3380		0.2130†
Age_3*# hospices_3							-0.0869		0.7445†
Age_3*# hospices_4							-0.2059		0.4440†
Age_4*# hospices_2							0.5971		0.0800†
Age_4*# hospices_3							0.1641		0.6424†
Age_4*# hospices_4							0.4775		0.1698†

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- § Use Age_1, Age_2, Age_3, and Age_4 to represent four quartiles of age.
- $Use Hospices_1, Hospices_2, Hospices_3, and Hospices_4 to represent four quartiles of the local area per capita number of hospices among patients with metastatic breast, prostate, lung and colorectal cancer.
- †P value of Wald $\chi 2$ test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- *Significance level at 0.05 level.

Table V-8. Estimates of Patient Age and the Local Area Per Capita Number of Oncologists among Patients with Metastatic Breast, Prostate, Lung, and Colorectal cancer, and Interaction Term between Patient Age and the Local Area Per Capita Number of Oncologists on Immediate Choice of Chemotherapy in the Aggregate Model

	Continuous				Median		Quartile		
	Estimate	P value	Estimate	P value	Estimate	P value	Estimate	F-statistics	P value
Continuous									
Age	-0.1081	<0.0001†*	0.2299	0.0875†					
# oncologists	-0.00101	0.8628†	-0.00342	0.8314†					
Age * # oncologists	-5.43E-6	0.9441†	6.761E-6	0.9751†					
Age^2			-0.00219	0.0104†*					
# $oncologists^2$			4.851E-6	0.8140†					
Age^2 * $oncologists^2$			-181E-12	0.9619†					
Median									
Age					-1.1085	<0.0001†*			
# oncologists					-0.1575	0.1200†			
Age*# oncologists					0.00631	0.9656†			
Quartile									
Age								87.3619	<0.001‡*
Age_2§							-0.5298		0.0031†*
Age_3§							-1.0843		<0.0001†*
Age_4§							-2.1264		<0.0001†*
# oncologists								6.5351	0.0884‡
# oncologists_2$							-0.2625		0.1560†
# oncologists_3$							-0.2706		0.1526†
# oncologists_4$							-0.5039		0.0107†*
Age*# oncologists								7.0934	0.6274‡
Age_2*# oncologists_2							0.00710		0.9779†
Age_2*# oncologists_3							-0.00258		0.9920†
Age_2*# oncologists_4							0.3511		0.1671†
Age_3*# oncologists_2							0.1495		0.5827†
Age_3*# oncologists_3							0.0522		0.8473†
Age_3*# oncologists_4							0.3555		0.1891†
Age_4*# oncologists_2							0.4365		0.1775†
Age_4*# oncologists_3							0.2216		0.5139†
Age_4*# oncologists_4							0.0764		0.8313†

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- § use Age_1, Age_2, Age_3, and Age_4 to represent four quartiles of age.
- $ use Oncologists_1, Oncologists_2, Oncologists_3, and Oncologists_4 to represent four quartiles of the local area per capita number of oncologists among metastatic cancer patients of breast, prostate, lung and colorectal cancer.
- †P value of Wald $\chi 2$ test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-9. Estimates of Patient Age and the Local Area Chemotherapy Percentage among Patients with Metastatic Breast, Prostate, Lung, and Colorectal cancer, and Interaction Term between Patient Age and the Local Area Chemotherapy Percentage on Immediate Choice of Chemotherapy in the Aggregate Model

	Continuous				Median		Quartile		
	Estimate	P value	Estimate	P value	Estimate	P value	Estimate	F-statistics	P value
Continuous									
Age	-0.0791	0.0026†*	0.3638	0.0800†					
Chemo percentage	0.0891	0.0789†	0.3194	0.3006†					
Age * Chemo percentage	-0.00078	0.2455†	-0.00357	0.3821†					
Age^2			-0.00255	0.0126†*					
Chemo $percentage^2$			-0.00164	0.4080†					
Age^2 * Chemo $percentage^2$			2.407E-7	0.4807†					
Median									
Age					-1.0650	<0.0001†*			
Chemo percentage					0.4022	<0.0001†*			
Age*# Chemo percentage					-0.0847	0.5643†			
Quartile									
Age								56.8166	<0.0001‡*
Age_2							-0.2814		0.1360†
Age_3							-0.9075		<0.0001†*
Age_4							-1.8139		<0.0001†*
Chemo percentage								18.4581	0.0004‡*
Chemo_2							0.3910		0.0329†*
Chemo_3							0.5982		0.0017†*
Chemo_4							0.7949		<0.001†*
Age*Chemo percentage								2.9285	0.9671‡
Age_2*Chemo_2							-0.2242		0.3930†
Age_2*Chemo_3							-0.1892		0.4695†
Age_2*Chemo_4							-0.2298		0.3752†
Age_3*Chemo_2							-0.0129		0.9635†
Age_3*Chemo_3							0.0112		0.9686†
Age_3*Chemo_4							-0.1648		0.5554†
Age_4*Chemo_2							0.0339		0.9230†
Age_4*Chemo_3							-0.2841		0.4177†
Age_4*Chemo_4							-0.1685		0.6256†

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- § Use Age_1, Age_2, Age_3, and Age_4 to represent four quartiles of age.
- $ Use Chemo_1, Chemo_2, Chemo_3, and Chemo_4 to represent four quartiles of the local area chemotherapy percentage among metastatic cancer patients of breast, prostate, lung and colorectal cancer.
- †P value of Wald $\chi 2$ test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-10. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer on Immediate Choice of Chemotherapy with Age Specified as Two-category Dummy Variables (below and above 75 years of age) in the Aggregate Model

	Estimate	F-statistics ‡	P-value
Age§		19.8466	<0.0001*
Age_1	Reference		
Age_2	-1.0252		<0.0001*
Chemo percentage$		23.2437	<0.0001*
Chemo_1	Reference		
Chemo_2	0.3370		
Chemo_3	0.5338		
Chemo_4	0.7128		
Travel time$		0.0861	0.9679
Time_1	Reference		
Time_2			
Time_3	0.00190		0.9879
Time_4	-0.0351		0.7868
# oncologists$		4.0064	0.2608
Oncologist_1	Reference		
Oncologist_2	-0.2245		0.1385
Oncologist_3	-0.2551		0.1028
Oncologist_4	-0.3227		0.0658
# Hospices$		0.7333	0.8653
Hospices_1	Reference		
Hospices_2	-0.0253		0.8639
Hospices_3	0.0941		0.5369
Hospices_4	0.0493		0.7631
Age*Chemo percentage		0.5322	0.9118

Age_2*chemo _2	0.0258		0.9022
Age_2*chemo_3	-0.0781		0.7094
Age_2*chemo_4	-0.0990		0.6346
Age*time		0.7640	0.6825
Age_2*time_3	-0.0856		0.6248
Age_2*time_4	-0.1551		0.3988
Age*#oncologists		0.9033	0.8246
Age_2*oncologists_2	0.1840		0.3690
Age_2*oncologists_3	0.1166		0.5781
Age_2*oncologists_4	0.1615		0.4715
Age*#hospices		1.2511	0.7408
Age_2*hospices_2	0.0190		0.9258
Age_2*hospices_3	-0.1891		0.3732
Age_2*hospices_4	-0.0336		0.8799

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- §Use Age_1 and Age_2 to represent two categories of age variable.
- $ Notation for quartiles of each access variable
  - Use Time_1, Time_2, Time_3, and Time_4 to represent four quartiles of patient travel time to the nearest oncologist.
  - Use Chemo_1, Chemo_2, Chemo_3, and Chemo_4 to represent four quartiles of the local area chemotherapy percentage among patients with metastatic breast, prostate, lung, and colorectal cancer patients..
  - Use Hospices_1, Hospices_2, Hospices_3, and Hospices_4 to represent four quartiles of the local area per capita number of hospices among patients among patients with metastatic breast, prostate, lung, and colorectal cancer patients.
  - Use Oncologists_1, Oncologists_2, Oncologists_3, and Oncologists_4 to represent four quartiles of the local area per capita number of oncologists among patients with metastatic breast, prostate, lung, and colorectal cancer patients.
- ‡A Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- *Significance level at 0.05 level.

Table V-11. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer on Immediate Choice of Chemotherapy with Age specified as Three-category Dummy variables (66-69, 70-79, and 80+ years of age) in the Aggregate Model

	Estimate	F-statistics‡	P-value
Age§		24.5187	<0.0001*
Age_1	Reference		
Age_2	-0.7037		0.0074*
Age_3	-0.7782		<0.0001*
Chemo percentage$		17.1316	0.0007*
Chemo_1	Reference		
Chemo_2	0.3074		0.1726
Chemo_3	0.5413		0.0213*
Chemo_4	0.9633		<0.0001*
Travel time$		0.6510	0.7222
Time_1	Reference		
Time_2			
Time_3	-0.1583		0.4274
Time_4	-0.0252		0.9009
# oncologists$		2.3743	0.4984
Oncologist_1	Reference		
Oncologist_2	-0.3634		0.1245
Oncologist_3	-0.1814		0.4442
Oncologist_4	-0.2140		0.4023
# Hospices$		0.7286	0.8665
Hospices_1	Reference		
Hospices_2	-0.1074		0.6407
Hospices_3	-0.1951		0.4021
Hospices_4	-0.0885		0.7291
Age*Chemo percentage		3.6442	0.7247
Age_2*chemo_2	-0.0131		0.9591

Age_2*chemo_3	-0.1130		0.6665
Age_2*chemo_4	-0.4142		0.1176
Age_3*chemo_2	0.1601		0.7537
Age_3*chemo_3	0.0175		0.9723
Age_3*chemo_4	-0.0937		0.8491
Age*time		5.6338	0.2282
Age_2*time_3	0.1902		0.3941
Age_2*time_4	-0.0909		0.6887
Age_3*time_3	-0.7203		0.1160
Age_3*time_4	-0.3945		0.3418
Age*#oncologists		5.7978	0.4462
Age_2*oncologists_2	0.2973		0.2556
Age_2*oncologists_3	-0.0151		0.9539
Age_2*oncologists_4	0.0223		0.9352
Age_3*oncologists_2	0.3976		0.3702
Age_3*oncologists_3	-0.2278		0.6482
Age_3*oncologists_4	-0.7135		0.1937
Age*#hospices		11.0111	0.0880
Age_2*hospices_2	-0.00148		0.9954
Age_2*hospices_3	0.2241		0.3943
Age_2*hospices_4	0.0721		0.7990
Age_3*hospices_2	1.3533		0.0072*
Age_3*hospices_3	0.7783		0.1539
Age_3*hospices_4	1.1275		0.0450*

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- §Use Age_1, Age_2, and Age_3 to represent three categories of age variable.
- $ Notation for quartiles of each access variable
    - Use Time_1, Time_2, Time_3, and Time_4 to represent four quartiles of patient travel time to the nearest oncologist.
    - Use Chemo_1, Chemo_2, Chemo_3, and Chemo_4 to represent four quartiles of the local area chemotherapy percentage among patients with metastatic breast, prostate, lung, and colorectal cancer patients..
    - Use Hospices_1, Hospices_2, Hospices_3, and Hospices_4 to represent four quartiles of the local area per capita number of hospices among patients among patients with metastatic breast, prostate, lung, and colorectal cancer patients.
    - Use Oncologists_1, Oncologists_2, Oncologists_3, and Oncologists_4 to represent four quartiles of the local area per capita number of oncologists among patients with metastatic breast, prostate, lung, and

Table V-12. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer on Immediate Choice of Chemotherapy with Age specified as Five-category Dummy variables (66-69, 70-74, 75-79, 80-84, and 85+ years of age) in the Aggregate Model

	Estimate	F-statistics‡	P-value
Age		34.0971	<0.0001*
Age_1	Reference		
Age_2	-0.7019		0.1423
Age_3	-0.4870		0.0276*
Age_4	-0.7458		<0.0001*
Age_5	-1.6326		<0.0001*
Chemo percentage		17.1972	0.0006*
Chemo_1	Reference		
Chemo_2	0.3089		0.1699
Chemo_3	0.5424		0.0209*
Chemo_4	0.9651		<0.0001*
Travel time		0.6032	0.7396
Time_1	Reference		
Time_2			
Time_3	-0.1525		0.4441
Time_4	-0.0259		0.8982
# oncologists		2.3235	0.5080
Oncologist_1	Reference		
Oncologist_2	-0.3583		0.1291
Oncologist_3	-0.1742		0.4620
Oncologist_4	-0.2129		0.4048
# Hospices		0.6963	0.8741
Hospices_1	Reference		
Hospices_2	-0.0945		0.6812
Hospices_3	-0.1921		0.4085
Hospices_4	-0.0925		0.7170

Age*Chemo percentage		7.8836	0.7942
Age_2*chemo_2	0.0122		0.9670
Age_2*chemo_3	-0.0252		0.9328
Age_2*chemo_4	-0.4025		0.1773
Age_3*chemo_2	-0.1151		0.7065
Age_3*chemo_3	-0.00203		0.9948
Age_3*chemo_4	-0.2987		0.3431
Age_4*chemo_2	0.2659		0.4601
Age_4*chemo_3	-0.2551		0.4935
Age_4*chemo_4	-0.4643		0.2035
Age_5*chemo_2	0.1624		0.7501
Age_5*chemo_3	0.0238		0.9621
Age_5*chemo_4	-0.0874		0.8590
Age*time		7.6911	0.4642
Age_2*time_3	0.2776		0.2759
Age_2*time_4	-0.0106		0.9672
Age_3*time_3	0.1756		0.5034
Age_3*time_4	-0.0985		0.7154
Age_4*time_3	0.0147		0.9613
Age_4*time_4	-0.3972		0.2242
Age_5*time_3	-0.7315		0.1102
Age_5*time_4	-0.3965		0.3386
Age*#oncologists		13.8692	0.3091
Age_2*oncologists_2	0.2386		0.4252
Age_2*oncologists_3	-0.1423		0.6368
Age_2*oncologists_4	-0.2043		0.5188
Age_3*oncologists_2	0.1985		0.5187
Age_3*oncologists_3	-0.1010		0.7442
Age_3*oncologists_4	0.2054		0.5242
Age_4*oncologists_2	0.7429		0.0415*
Age_4*oncologists_3	0.4828		0.1899
Age_4*oncologists_4	0.1501		0.7111

Age_5*oncologists_2	0.3925		0.3757
Age_5*oncologists_3	-0.2265		0.6494
Age_5*oncologists_4	-0.7073		0.1970
Age*#hospices		15.2124	0.2300
Age_2*hospices_2	0.1047		0.7258
Age_2*hospices_3	0.4956		0.1035
Age_2*hospices_4	0.2344		0.4678
Age_3*hospices_2	0.0216		0.9431
Age_3*hospices_3	0.1509		0.6277
Age_3*hospices_4	-0.0696		0.8339
Age_4*hospices_2	-0.2338		0.5148
Age_4*hospices_3	-0.00179		0.9961
Age_4*hospices_4	0.1215		0.7507
Age_5*hospices_2	1.3211		0.0086*
Age_5*hospices_3	0.7716		0.1568
Age_5*hospices_4	1.1257		0.0449*

Note:

- Variables in this table are defined in the same way as in the Table V-5.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- §Use Age_1, Age_2, Age_3, Age_4, and Age_5 to represent five categories of age variable.
- $ Notation for quartiles of each access variable
  - Use Time_1, Time_2, Time_3, and Time_4 to represent four quartiles of patient travel time to the nearest oncologist.
  - Use Chemo_1, Chemo_2, Chemo_3, and Chemo_4 to represent four quartiles of the local area chemotherapy percentage among patients with metastatic breast, prostate, lung, and colorectal cancer patients..
  - Use Hospices_1, Hospices_2, Hospices_3, and Hospices_4 to represent four quartiles of the local area per capita number of hospices among patients among patients with metastatic breast, prostate, lung, and colorectal cancer patients.
  - Use Oncologists_1, Oncologists_2, Oncologists_3, and Oncologists_4 to represent four quartiles of the local area per capita number of oncologists among patients with metastatic breast, prostate, lung, and colorectal cancer patients.
- ‡A Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- *Significance level at 0.05 level.

The Effect of Access to Cancer Care on Immediate Choice of Chemotherapy in Age Subgroups

As discussed in the previous section, stratified subgroup analysis is another way to investigate interaction effects. Three stratification approaches were used in the analysis, that is, two age groups above and below 75 years of age, three age groups of 66-69, 70-79 and 80+ years of age, and five age groups of 66-69, 70-74, 75-79, and 80-84, and 85+ years of age. In this section, Table V-13 –Table V-18 present results from age subgroup analyses. Each stratification approach included two sets of tables, one for the model including all access variables, the other only including one access variable at a time. Access variables were specified as quartile dummies (categorical model) or in a continuous form (continuous model) and results from both models are present.

Results from two-subgroup analyses with age specified above and below 75 years old are present in the Tables V-13 and V-14 , F-statistics and Wald chi-square statistics showed the local area chemotherapy percentage was consistently positively associated with immediate chemotherapy choice in each age subgroup across all models. In each age subgroup, the odds ratios of chemotherapy use increases with the higher quartiles of chemotherapy percentage and the biggest odds ratio is associated with the 4^{th} quartile of chemotherapy percentage. Wald chi-square statistics show that patient travel time to the nearest oncologist practice was significantly associated with immediate chemotherapy choice in the age group 75 years or older when measured as a continuous variable and controlling for other access variables in the model. In the Table V-14, however, the continuous form of local area per capita number of oncologists across metastatic cancers was the significant predictor of immediate chemotherapy choice in the age group 75 years or older when each model only included one access variable at a time.

Results from three-subgroup analysis with age specified as groups of 66-69, 70-79, and 80+ years old are present in the Tables V-15 and V-16. F-statistics and Wald chi-square statistics showed the local area chemotherapy percentage was consistently positively associated with immediate chemotherapy choice in each age subgroup across all models. Higher odds ratios of chemotherapy use were associated with higher quartiles of chemotherapy percentage. Other access variables were not statistically significantly associated with immediate chemotherapy choice among all the age subgroups whether they were included in the model simultaneously or measured one at a time as a continuous or categorical variable.

Results from five-subgroup analyses with age specified as groups of 66-69, 70-74, 75-79, 80-84, and 85+ year old are present in the Tables V-17 and V-18. F-statistics showed the local area chemotherapy percentage across metastatic cancers was consistently positively associated with immediate chemotherapy choice except in the subgroup aged 80 to 84 and 85+ years old in both tables. Wald chi-square statistics for the continuous form of chemotherapy percentage confirmed it was not associated with chemotherapy choice in the age subgroup of 80 to 84 years old but was a significant predictor for chemotherapy use in the age subgroup of 85+ years old. In addition, the local area per capita number of oncologists across metastatic cancers was significantly negatively associated with immediate chemotherapy choice in the subgroup of 85 years or older, which was confirmed with the Wald chi-square statistics in the Table V-17 and V-18. This effect was not observed among other age subgroups.

Table V-13. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer on Immediate Choice of Chemotherapy in Two Age Subgroup Analysis Above and Below 75 years of age

	<75		≥75	
Variables	Categorical Model	Continuous Model	Categorical Model	Continuous Model
Chemo percentage				
F-statistics | P-value‡ OR(95% CI)	20.2761 | 0.0001*		14.1725 | 0.0027*	
1st quartile	Reference		Reference	
2nd quartile	1.400 (1.039 – 1.887)		1.496 (1.083 – 2.066)	
3rd quartile	1.716 (1.258 – 2.342)		1.622 (1.163 – 2.263)	
4th quartile	2.042 (1.479 – 2.821)		1.919 (1.362 – 2.704)	
χ2 statistics | P-value†		27.7939 | <0.0001*		14.2693 | 0.0002*
OR(95% CI)		1.036 (1.022 – 1.049)		1.026 (1.012 – 1.040)
Travel time				
F-statistics | P-value‡ OR (95% CI)	0.2261 | 0.8951		1.9604 | 0.3752	
1st quartile	Reference		Reference	
2nd quartile	0.971 (0.757 – 1.247)		0.894 (0.695 – 1.151)	
3rd quartile	0.936 (0.709 – 1.236)		0.814 (0.597 – 1.109)	
χ2 statistics | P-value †		2.0260 | 0.1546		4.0911 | 0.0431*
OR(95% CI)		0.707 (0.439 – 1.139)		0.567 (0.327 – 0.983)
# Oncologists				
F-statistics | P-value ‡ OR (95% CI)	1.6083 | 0.6575		3.2844 | 0.3498	
1st quartile	Reference		Reference	
2nd quartile	0.849 (0.621 – 1.161)		0.879 (0.645 – 1.198)	
3rd quartile	0.823 (0.593 – 1.144)		0.760 (0.543 – 1.063)	
4th quartile	0.816 (0.555 – 1.199)		0.724 (0.486 – 1.077)	
χ2 statistics | P-value †		0.6540 | 0.4187		2.8787 | 0.0898
OR(95% CI)		0.999 (0.998 – 1.001)		0.998 (0.996 – 1.000)
#Hospices				
F-statistics | P-value ‡				
OR (95% CI)	1.3340 | 0.7211		1.6364 | 0.6512	
1st quartile	Reference		Reference	
2nd quartile	1.048 (0.778 – 1.412)		1.017 (0.755 – 1.371)	
3rd quartile	1.184 (0.867 – 1.617)		0.875 (0.635 – 1.205)	
4th quartile	1.156 (0.816 – 1.638)		1.046 (0.736 – 1.487)	
χ2 statistics | P-value †		0.8041 | 0.3699		0.0541 | 0.8160
OR(95% CI)		1.002 (0.998 – 1.006)		1.000 (0.996 – 1.005)

Note:

- Variables in this table are defined in the same way as in the Table V-5. All four access variables were included in the model.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- †P value of Wald χ2 test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-14. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer (one-at-a-time) on Immediate Choice of Chemotherapy in Two Age Subgroup Analysis Above and Below 75 years of age

	<75		≥75	
Variables	Categorical Model	Continuous Model	Categorical Model	Continuous Model
Chemo percentage				
F-statistics | P-value‡ OR(95% CI)	21.1159 | <0.0001*		15.1924 | 0.0017*	
1st quartile	Reference		Reference	
2nd quartile	1.411 (1.049 – 1.900)		1.491 (1.083 – 2.054)	
3rd quartile	1.724 (1.266 – 2.347)		1.642 (1.183 – 2.278)	
4th quartile	2.067 (1.499 – 2.850)		1.943 (1.385 – 2.724)	
χ2 statistics | P-value†		28.3452 | <0.0001*		15.4814 | <0.001*
OR(95% CI)		1.036 (1.023 – 1.050)		1.027 (1.013 – 1.041)
Travel time				
F-statistics | P-value‡ OR (95% CI)	0.1847 | 0.9118		1.4917 | 0.4743	
1st quartile				
2nd quartile	Reference		Reference	
3rd quartile	0.968 (0.756 – 1.241)		0.910 (0.709 – 1.168)	
4th quartile	0.944 (0.718 – 1.242)		0.837 (0.617 – 1.137)	
χ2 statistics | P-value †		1.6813 | 0.1948		3.1988 | 0.0737
OR(95% CI)		0.732 (0.457 – 1.173)		0.609 (0.354 – 1.049)
# Oncologists				
F-statistics | P-value ‡ OR (95% CI)	2.1669 | 0.5385		5.7792 | 0.1229	
1st quartile	Reference		Reference	
2nd quartile	0.845 (0.624 – 1.146)		0.819 (0.607 – 1.105)	
3rd quartile	0.802 (0.586 – 1.097)		0.709 (0.516 – 0.975)	
4th quartile	0.806 (0.564 – 1.152)		0.669 (0.464 – 0.963)	
χ2 statistics | P-value †		1.0381 | 0.3083		4.3958 | 0.0360*
OR(95% CI)		0.999 (0.998 – 1.001)		0.998 (0.996 – 1.000)
#Hospices				
F-statistics | P-value ‡ OR (95% CI)	0.3926 | 0.9418		2.0046 | 0.5715	
1st quartile	Reference		Reference	
2nd quartile	1.028 (0.767 – 1.377)		1.006 (0.749 – 1.351)	
3rd quartile	1.096 (0.812 – 1.480)		0.831 (0.610 – 1.132)	
4th quartile	1.040 (0.751 – 1.439)		0.905 (0.653 – 1.256)	
χ2 statistics | P-value †		0.0154 | 0.9012		0.8190 | 0.3655
OR(95% CI)		1.000 (0.997 – 1.004)		0.998 (0.995 – 1.002)

Note:

- Variables in this table are defined in the same way as in the Table V-5. All four access variables were specified one-at-a-time.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- †P value of Wald χ2 test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-15. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer on Immediate Choice of Chemotherapy in Three Age Subgroup Analysis of 66 to 69, 70 to 79, and 80 + years of age

Variables	66-69		70-79		80+	
	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model
Chemo percentage						
F-statistics| P-value ‡	17.5243|0.0006*		18.7632 | 0.0003*		7.8491 | 0.0492*	
OR (95% CI)						
1st quartile	Reference		Reference		Reference	
2nd quartile	1.396 (0.864 – 2.256)		1.278 (0.953 – 1.714)		1.808 (1.102 – 2.969)	
3rd quartile	1.810 (1.084 – 3.021)		1.683 (1.247 – 2.271)		1.467 (0.866 – 2.486)	
4th quartile	3.141 (1.802 – 5.475)		1.876 (1.373 – 2.564)		1.960 (1.162 – 3.307)	
χ2 statistics |P-value†		18.7895|<0.0001*		23.8780|<0.0001*		4.8336|0.0279*
OR (95% CI)		1.049 (1.026 – 1.071)		1.032(1.019-1.045)		1.023(1.002-1.044)
Travel time						
F-statistics| P-value ‡	1.2707|0.5298		1.7925|0.4081		4.9299|0.0850	
OR (95% CI)						
1st quartile						
2nd quartile	Reference		Reference		Reference	
3rd quartile	0.812 (0.533 – 1.236)		1.066 (0.841 – 1.352)		0.661 (0.445 – 0.982)	
4th quartile	1.060 (0.664 – 1.693)		0.869 (0.659 – 1.144)		0.709 (0.436 – 1.152)	
χ2 statistics |P-value†		1.6450 |0.1996		3.1709 |0.0750		2.1037|0.1469
OR(95% CI)		0.605(0.281-1.303)		0.651(0.406-1.044)		0.503(0.198-1.273)
# Oncologists						
F-statistics| P-value ‡	2.2989|0.5127		2.9748|0.3955		6.7682 |0.0797	
OR (95% CI)						
1st quartile	Reference		Reference		Reference	
2nd quartile	0.721 (0.429 – 1.212)		0.860 (0.641 – 1.153)		1.137 (0.703 – 1.839)	
3rd quartile	0.830 (0.483 – 1.425)		0.761 (0.557 – 1.041)		0.873 (0.515 – 1.481)	
4th quartile	1.005 (0.534 – 1.891)		0.793 (0.552 – 1.137)		0.550 (0.285 – 1.062)	
χ2 statistics |P-value†		0.1054 |0.7454		0.9652| 0.3259		3.5913 | 0.0581
OR(95% CI)		1.000(0.997-1.002)		0.999(0.997-1.001)		0.997(0.994-1.000)
#Hospices						
F-statistics| P-value ‡ OR (95% CI)	1.5633|0.6677		1.8047 |0.6139		4.5224 | 0.2103	
1st quartile	Reference		Reference		Reference	
2nd quartile	1.096 (0.673 – 1.786)		0.960 (0.721 – 1.278)		1.223 (0.768 – 1.949)	
3rd quartile	0.923 (0.560 – 1.521)		1.082 (0.798 – 1.468)		1.066 (0.647 – 1.757)	
4th quartile	1.255 (0.705 – 2.233)		0.894 (0.640 – 1.249)		1.656 (0.965 – 2.841)	
χ2 statistics |P-value†		2.1521 |0.1424		0.2297|0.6317		1.4160 | 0.2341
OR(95% CI)		1.005(0.998-1.011)		0.999(0.995-1.003)		1.004(0.998-1.010)

Note:

- Variables in this table are defined in the same way as in the Table V-5. All four access variables were included in the model.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- †P value of Wald χ2 test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-16. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer (one-at-a-time) on Immediate Choice of Chemotherapy in Three Age Subgroup Analysis of 66 to 69, 70 to 79, and 80 + years of age

Variables	66-69		70-79		80+	
	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model
Chemo percentage						
F-statistics| P-value ‡	17.7829|0.0005*		21.0387| 0.0001*		7.9361| 0.0474*	
OR (95% CI)						
1st quartile	Reference		Reference		Reference	
2nd quartile	1.421 (0.885 – 2.282)		1.300 (0.970 – 1.742)		1.743 (1.070 – 2.839)	
3rd quartile	1.871 (1.134 – 3.086)		1.738 (1.290 – 2.341)		1.415 (0.843 – 2.373)	
4th quartile	3.142 (1.812 – 5.450)		1.931 (1.417 – 2.631)		1.964 (1.172 – 3.291)	
χ2 statistics |P-value†		17.9009|<0.0001*		17.9009|<0.0001*		5.3371|0.0209*
OR (95% CI)		1.047 (1.025 – 1.069)		1.047(1.025-1.069)		1.024(1.004-1.045)
Travel time						
F-statistics| P-value ‡	1.4091|0.4943		1.9822|0.3712		3.9073|0.1418	
OR (95% CI)						
1st quartile						
2nd quartile	Reference		Reference		Reference	
3rd quartile	0.809 (0.536 – 1.221)		1.065 (0.843 – 1.346)		0.691 (0.467 – 1.022)	
4th quartile	1.071 (0.680 – 1.685)		0.861 (0.655 – 1.131)		0.754 (0.467 – 1.218)	
χ2 statistics |P-value†		1.0488|0.3058		3.1311|0.0768		1.3326|0.2483
OR(95% CI)		0.677(0.321-1.428)		0.655(0.410-1.047)		0.582(0.232-1.459)
# Oncologists						
F-statistics| P-value ‡	3.0548|0.3833		5.7989|0.1218		4.6249|0.2014	
OR (95% CI)						
1st quartile	Reference		Reference		Reference	
2nd quartile	0.715 (0.437 – 1.170)		0.827 (0.622 – 1.102)		1.106 (0.696 – 1.760)	
3rd quartile	0.789 (0.475 – 1.310)		0.713 (0.529 – 0.960)		0.905 (0.550 – 1.489)	
4th quartile	1.030 (0.576 – 1.841)		0.705 (0.504 – 0.985)		0.632 (0.348 – 1.151)	
χ2 statistics |P-value†		0.0006|0.9808		3.2802| 0.0701		3.0410 | 0.0812
OR(95% CI)		1.000(0.998-1.002)		0.999(0.997-1.000)		0.997(0.995-1.000)
#Hospices						
F-statistics| P-value ‡ OR (95% CI)	1.5490|0.6710		3.2853|0.3497		2.1277 | 0.5463	
1st quartile	Reference		Reference		Reference	
2nd quartile	1.050 (0.653 – 1.688)		0.950 (0.717 – 1.258)		1.204 (0.759 – 1.911)	
3rd quartile	0.863 (0.537 – 1.385)		1.001 (0.745 – 1.344)		1.003 (0.619 – 1.624)	
4th quartile	1.156 (0.681 – 1.962)		0.789 (0.577 – 1.079)		1.329 (0.803 – 2.201)	
χ2 statistics |P-value†		0.9405|0.3321		1.6054|0.2051		0.0005 | 0.9819
OR(95% CI)		1.003(0.997-1.008)		0.998(0.994-1.001)		1.000(0.995-1.005)

Note:

- Variables in this table are defined in the same way as in the Table V-5. All four access variables were included in the model.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- †P value of Wald χ2 test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-17. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer on Immediate Choice of Chemotherapy in Five Age Subgroup Analysis of 66 to 69, 70 to 74, 75 to 79, 80 to 84, and 85 + years of age

Variables	66-69		70-74		75-79		80-84		85+	
	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model
Chemo percentage										
F-statistics | P-value ‡	17.5243| 0.0006*		7.2028| 0.0657		13.0791|0.0045*		4.5978|0.2037		6.6024|0.0857	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	
2nd quartile	1.396 (0.864 – 2.256)		1.354 (0.901 – 2.033)		1.313 (0.829 -2.080)		1.801 (0.986-3.289)		1.635 (0.562-4.757)	
3rd quartile	1.810 (1.084 – 3.021)		1.651 (1.089 – 2.503)		1.936 (1.217–3.080)		1.221 (0.640-2.327)		2.718 (0.899-8.216)	
4th quartile	3.141 (1.802 – 5.475)		1.689 (1.104 – 2.585)		2.214 (1.355-3.619)		1.578 (0.835-2.983)		3.865 (1.296-11.525)	
χ2 statistics|P-value†		18.7859|<0.0001*		11.9329|0.0006*		11.9315|0.0006*		1.7658| 0.1839		4.9721| 0.0258*
OR (95% CI)		1.049 (1.026 -1.071)		1.032 (1.014-1.050)		1.034 (1.015-1.054)		1.017 (0.992-1.043)		1.045 (1.005-1.086)
Travel time										
F-statistics|P-value ‡	1.2707|0.5298		0.7390|0.6911		0.8027|0.6694		2.3470|0.3093		9.7722| 0.0076*	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	
2nd quartile										
3rd quartile	0.812 (0.533 – 1.236)		1.088 (0.783 – 1.513)		0.979 (0.683-1.403)		0.758 (0.472-1.217)		0.212 (0.080-0.560)	
4th quartile	1.060 (0.664 – 1.693)		0.910 (0.628-1.320)		0.820 (0.528-1.273)		0.671 (0.367-1.225)		0.668 (0.246-1.816)	
χ2 statistics| P-value †		1.6450|0.1996		0.5819|0.4456		3.7901|0.0516		2.4423|0.1181		0.0151|0.9022
OR (95% CI)		0.605 (0.281-1.303)		0.774 (0.401-1.495)		0.479 (0.228-1.005)		0.389 (0.119-1.271)		0.891 (0.141-5.613)
# Oncologists										
F-statistics | P-value ‡	2.2989|0.5127		3.2381|0.3563		2.5282|0.4702		3.6864|0.2974		7.9858|0.0463*	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	

2nd quartile	0.721		0.837		0.807		1.319		0.573	
	(0.429 – 1.212)		(0.550 – 1.273)		(0.520-1.253)		(0.722-2.407)		(0.209-1.569)	
3rd quartile	0.830		0.728		0.732		1.024		0.237	
	(0.483 – 1.425)		(0.467 – 1.137)		(0.460-1.165)		(0.535-1.958)		(0.069-0.813)	
4th quartile	1.005		0.630		0.938		0.690		0.174	
	(0.534 – 1.891)		(0.374 – 1.060)		(0.551-1.596)		(0.305-1.558)		(0.042-0.724)	
χ2 statistics | P-value †		0.1054| 0.7454		0.8358|0.3606		0.1829|0.6689		0.9302|0.3348	4.8492|0.0277*
OR (95% CI)		1.000		0.999		0.999		0.998		0.992
		(0.997-1.002)		(0.996 – 1.001)		(0.997-1.002)		(0.994-1.002)		(0.985-0.999)
#Hospices										
F-statistics | P-value ‡	1.5633|0.6677		2.1827|0.5354		1.4207|0.7007		3.6446|0.3025		10.4867|0.0149*	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	
2nd quartile	1.096		1.097		0.898		0.769		5.847	
	(0.673 -1.786)		(0.729 – 1.652)		(0.587-1.375)		(0.428-1.381)		(1.984-17.230)	
3rd quartile	0.923		1.343		0.840		0.902		3.361	
	(0.560 – 1.521)		(0.876 – 2.058)		(0.530-1.332)		(0.491-1.659)		(1.036-10.903)	
4th quartile	1.255		1.098		0.737		1.368		4.684	
	(0.705 – 2.233)		(0.688 - 1.752)		(0.444-1.225)		(0.707-2.646)		(1.326-16.548)	
χ2 statistics|P-value †		2.1521|0.1424		0.0087|0.9256		0.5301|0.4666		2.1404|0.1435	0.8230|0.3643
OR (95% CI)		0.605		1.000		0.998		0.389		1.005
		(0.281-1.303)		(0.994 – 1.005)		(0.991-1.004)		(0.119-1.271)		(0.904-1.015)

Note:

- Variables in this table are defined in the same way as in the Table V-5. All four access variables were included in the model.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- †P value of Wald χ2 test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Table V-18. Estimates of Patient Travel Time, and the Local Area Chemotherapy Percentage, the Local Area Per Capita Number of Oncologists, and the Local Area Per Capita Number of Hospices among Patients with Metastatic Breast, Prostate, Lung, and Colorectal Cancer (one-at-a-time) on Immediate Choice of Chemotherapy in Five Age Subgroup Analysis of 66 to 69, 70 to 74, 75 to 79, 80 to 84, and 85 + years of age

Variables	66-69		70-74		75-79		80-84		85+	
	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model	Categorical Model	Continuous Model
Chemo percentage										
F-statistics | P-value ‡	17.7829| 0.0005*		7.9118|0.0479*		14.1338|0.0027*		4.3012|0.2307		7.9468|0.0471*	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	
2nd quartile	1.421 (0.885 – 2.282)		1.373 (0.916 – 2.058)		1.332 (0.845 -2.099)		1.686 (0.934-3.044)		1.928 (0.708-5.252)	
3rd quartile	1.871 (1.134 – 3.086)		1.660 (1.098 – 2.508)		2.003 (1.268–3.162)		1.112 (0.592-2.088)		2.963 (1.016-8.638)	
4th quartile	3.142 (1.812 – 5.450)		1.747 (1.146 – 2.663)		2.230 (1.376-3.613)		1.496 (0.802-2.792)		4.327 (1.515-12.360)	
χ2 statistics|P-value†		17.9009|<0.0001*		13.0018|0.0003*		12.6033|0.0004*		1.7274| 0.1887		6.2795 | 0.0122*
OR (95% CI)		1.047 (1.025 -1.069)		1.033 (1.015-1.051)		1.035 (1.016-1.055)		1.017 (0.992-1.043)		1.049 (1.011-1.089)
Travel time										
F-statistics|P-value ‡	1.4091 | 0.4943		0.6084|0.7377		1.1287 |0.5687		1.8645|0.3937		6.5213| 0.0384*	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	
2nd quartile										
3rd quartile	0.809 (0.536 – 1.221)		1.081 (0.781 – 1.497)		0.990 (0.696-1.409)		0.797 (0.501-1.269)		0.301 (0.119-0.757)	
4th quartile	1.071 (0.680 – 1.685)		0.922 (0.639-1.331)		0.796 (0.516-1.227)		0.695 (0.384-1.258)		0.783 (0.303-2.024)	
χ2 statistics| P-value †		1.0488|0.3058		0.5538|0.4568		3.6498|0.0516		1.7891|0.1810		0.0038|0.9507
OR (95% CI)		0.677 (0.321-1.428)		0.780 (0.405-1.501)		0.490 (0.235-1.019)		0.449 (0.139-1.451)		1.058 (0.179-6.245)
# Oncologists										
F-statistics | P-value ‡	3.0548|0.3833		4.1942 | 0.2412		4.4188 |0.2197		1.9756|0.5775		6.8572|0.0766	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	

2nd quartile	0.715		0.855		0.726		1.220		0.868	
	(0.437 – 1.170)		(0.567 – 1.288)		(0.475-1.110)		(0.680-2.189)		(0.360-2.096)	
3rd quartile	0.789		0.725		0.634		1.079		0.356	
	(0.475 – 1.310)		(0.474 – 1.107)		(0.408-0.984)		(0.586-1.987)		(0.126-1.003)	
4th quartile	1.030		0.619		0.742		0.789		0.345	
	(0.576 – 1.841)		(0.382 – 1.003)		(0.456-1.209)		(0.372-1.675)		(0.109-1.097)	
χ2 statistics | P-value †		0.0006| 0.9808		2.0466|0.1525		1.2613|0.2614		0.2465|0.6196	5.4807|0.0192*
OR (95% CI)		1.000		0.998		0.999		0.999		0.993
		(0.998-1.002)		(0.996 – 1.001)		(0.996-1.001)		(0.996-1.003)		(0.987-0.999)
#Hospices										
F-statistics | P-value ‡	1.5490|0.6710		1.7519|0.6255		3.1228 |0.3731		2.7942|0.4245		8.4718|0.0372*	
OR (95% CI)										
1st quartile	Reference		Reference		Reference		Reference		Reference	
2nd quartile	1.050		1.091		0.895		0.742		4.038	
	(0.653 -1.688)		(0.731 – 1.627)		(0.590-1.358)		(0.416-1.324)		(1.511-10.789)	
3rd quartile	0.863		1.190		0.810		0.865		1.933	
	(0.537 – 1.385)		(0.787 – 1.797)		(0.519-1.262)		(0.480-1.560)		(0.684-5.463)	
4th quartile	1.156		0.930		0.663		1.184		2.090	
	(0.681 – 1.962)		(0.598 - 1.446)		(0.414-1.060)		(0.641-2.186)		(0.690-6.330)	
χ2 statistics|P-value †		0.9405 |0.3321		0.5301|0.4666		1.5346|0.2154		1.1250|0.2889	0.2339|0.6287
OR (95% CI)		1.003		0.998		0.996		1.004		0.998
		(0.997-1.008)		(0.993 – 1.003)		(0.990-1.002)		(0.996-1.013)		(0.998-1.007)

Note:

- Variables in this table are defined in the same way as in the Table V-5. All four access variables were included in the model.
- Other variables in the model include patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.
- †P value of Wald χ2 test testing whether the coefficient is significantly different from zero.
- ‡P value of a Chow F-statistics testing whether all of the interaction terms are simultaneously equal to zero.
- * Significance level at 0.05 level.

Summary of Results

In this section the results from both the interaction term approach in the aggregate model and the corresponding subgroup analysis were presented. The interaction term approach did not show significant results. Subgroup analysis showed that by disaggregating data into finer age categories, the age-variant effect of access to cancer care on immediate chemotherapy choice is identified for the oldest patients. The local area chemotherapy percentage was associated with patient chemotherapy choice, with a higher percentage predicting a higher probability of getting chemotherapy across patient age groups. In each age subgroup, the odds of receiving chemotherapy were more highly associated with higher quartiles of the chemotherapy percentage (Figure 2). In addition, among patients 85 years and older, the local area per capita number of oncologists across metastatic cancers was negatively associated with chemotherapy choice. The association between the local area per capita number of oncologists across cancers and chemotherapy choice was consistent whether or not controlled for other access variables in the models. This effect was not observed among younger age groups.

Consistent with current literature, this study measured access using travel distance, the availability of oncologists per capita across metastatic cancers in the local area, and the availability of hospice programs per capita across metastatic cancers in the local area. In addition, the local area chemotherapy percentage was added to measure the local culture of chemotherapy use for metastatic cancer patients. This variable may be related to acceptability of access in the previous literature. If a local culture favors chemotherapy use, patients are more likely to be treated with chemotherapy; if a local culture perceives chemotherapy efficacy pessimistically, then patients are less likely to get chemotherapy. The local area chemotherapy percentage across metastatic cancers is

an access measure of the local area practice style of chemotherapy use which determines whether patients have the means and know-how to access to chemotherapy.

The full logistic regression model with patient characteristics and other control variables for the five age subgroup analyses is shown in the Appendix I Table I-2 – Table I-6. Briefly, among 4533 elderly patients diagnosed with MBC between 1992 and 2002, only 30.16% of them received chemotherapy within 6 months post diagnosis. There were dramatic differences in chemotherapy use associated with age among elderly patients. Chemotherapy percentage decreased with advancing age. Patients aged 66 to 69 years old were nearly 7 times more likely to receive chemotherapy than patients aged 85 years and older. Chemotherapy choice was found to be consistently associated with hormone receptor status across patient age. Patients with HR- status were more likely to receive chemotherapy, which was adherent with clinical guidelines for treating MBC. Whether patients had other chronic conditions influenced their chemotherapy choice for all ages except those aged 80 to 84 years old. For patients aged 66 to 69 years old and 70-74 years old, marital status seemed to influence chemotherapy choice. Race and ethnicity appeared to affect chemotherapy choice for patients aged 66 to 69 years old and for patients aged 85 years and older. Other variables in the model, including census tract income and education level, rural/urban characteristics of the patient residency, SEER regions the patient resided, and the diagnosis year, were not associated with chemotherapy choice among our study population.

CHAPTER VI

DISCUSSION

Main Findings

By examining access variables and other covariates on chemotherapy choice, our findings added substantially to the understanding of age-related differences in treatment patterns of chemotherapy. With advancing age, the proportion of MBC patients who received chemotherapy within 6 months post diagnosis progressively decreased. The treatment patterns of decreasing chemotherapy percentages with older age were observed after controlling for patient socio-demographic and clinical characteristics, geographic location, and diagnosis year. Previous studies examining age-linked differences in chemotherapy use suggested that these differences may be attributed to age-related bias that older patients will not benefit from chemotherapy in the same way as their younger counterparts (Woodard et al. 2003). This study found to a certain degree access to cancer care can explain the increasing difference in chemotherapy use associated with the age gradient among elderly women with MBC.

Although chemotherapy was proven efficacious for MBC in clinical trials, lower chemotherapy rates have been observed among older patients. Controversy surrounding whether to give chemotherapy to older patients with MBC may be the reason for age-related decreases in chemotherapy use. On one hand, clinical trial data have shown that chemotherapy is efficacious for MBC in terms of life prolongation and symptom relief. For elderly patients, though, the evidence has not been conclusive because of the underrepresentation of older patients in clinical trials. On the other hand, elderly patients may face limited life expectancy, a higher number of co-existing chronic conditions, greater challenges in cognitive, functional, and emotional role, and higher risks from chemotherapy toxicity due to multiple medications and to the natural aging process. The

inconclusive evidence regarding the benefits versus harm of chemotherapy among elderly patients, coupled with the biological and socioeconomic changes of aging, are the major sources of uncertainties in treatment decision-making for geriatric patients. These uncertainties may cause non-clinical factors, such as access, to matter more to older patients. Evidence from the Dartmouth Atlas project illustrates this phenomenon. In that project, researchers suggested that when medical evidence is weak, as in the case of chemotherapy use for elderly women with MBC, variations in health care utilization are largely driven by local medical opinion and local health system capacity. This study measured local area practice style or local medical opinion on how to treat geriatric end-stage cancer patients by using local area chemotherapy percentage across metastatic cancers; and measured local health system capacity to provide cancer care and counseling for geriatric end-stage cancer patients using local per capita oncologist supply across metastatic cancers. In addition, local area per capita number of hospices across metastatic cancers intends to measure local health system capacity to provide end-of-life palliative care and patient travel time to the nearest oncologist practice intends to measure general geographic access to an oncologist for an elderly MBC patient. Data showed the choice to receive or not to receive immediate chemotherapy within 6 months of diagnosis was affected by local area chemotherapy percentages across patient age. Also the effect of the local per capita number of oncologists across metastatic cancers on immediate chemotherapy choice achieved significance in patients aged 85 years and older, for whom it is most difficult to weigh the relative benefits and risks of chemotherapy.

The analysis of investigating the heterogeneity of the association between chemotherapy and access at different ages began with the statistical test for interaction. The results showed interaction terms between age and access variables were not significant. This may be attributable to unmeasured confounders associated with both age and chemotherapy choice. As discussed in the previous section, several variables, including disease severity, disease symptoms, and family member perspective, are highly

correlated with age. Without controlling for these variables, our model cannot disentangle the effect of age modifying the association between access to cancer care and chemotherapy choice. Examining the dynamic relationships between age and disease severity/disease symptoms may be a potential topic for future study.

Recent discussion on subgroup analysis suggested researchers base analyses of the heterogeneity on tests for interaction and present them along with effect estimates within each level of the baseline characteristics analyzed (Wang et al. 2007). The subgroup analysis in this study was based on the pre-specified age stratification criteria. Age subgroups were defined consistent with the literature, which has clinical and practical implications. The results showed that estimating all patients in one equation with dummies and interactions can hide results. By estimating the groups separately, this study found results from the subgroup of 85+ years old that would have been ignored.

Aging and Chemotherapy Choice

There is substantial variation in chemotherapy choice for MBC. Because aging is a highly heterogeneous process, which involves changes in functional, emotional, cognitive, social, and emotional domains, and is associated with a higher prevalence of comorbidities, a different outlook on remaining life, and diminished social and financial resources, a decision to use chemotherapy on elderly patients must take into account the trade-offs between benefits and harm to address individual patient needs and preferences. Previous studies have documented hormone receptor (HR) status, comorbidities, race, education, marital status, access to transportation, and place of residence are all significant predictors of type of breast cancer treatment received (Earle et al. 2008; Giordano et al. 2005; Matsuyama, Reddy, and Smith 2006). Our analysis has identified similar patterns of association between these factors and chemotherapy choice. Moreover, the results in this analysis showed each age subgroup to be slightly different from the

others, uncertainties regarding whether to choose chemotherapy increasing with advancing age.

Consistent with clinical guidelines for breast cancer, HR- status was the single covariate associated with receiving chemotherapy receipt among all age subgroups. It appeared that there was a higher proportion of HR+ patients than that of HR- patients in the whole group as well as across all age subgroups. HR+ patients are typically first treated by hormone therapy and HR- patients would be treated by chemotherapy or trastuzumab with or without chemotherapy. The gradually decreasing chemotherapy rate with each older age group was observed in both HR+ and HR- subpopulations.

Older patients suffer from higher rates of comorbid conditions, which may increase the risks and potentially decrease the benefits of chemotherapy. However, age should not be considered as a surrogate for comorbidities even though there is an association between age and the degree and nature of comorbidities to a certain degree. For example, among the younger age groups, diabetes was the most prevalent condition, followed by congestive heart failure and chronic obstruction pulmonary disease, while among the oldest group, congestive heart failure became the most prevalent condition, and the prevalence of dementia increased. Controlling for comorbidities, age was independently associated with lower chemotherapy use in our analysis consistent with previous studies. As physiological age may differ from chronological age for an elderly person, ideally whether physiological age is associated with chemotherapy choice is the topic of interest. Adding access in addition to age and comorbidities, our theory suggested that access may represent an extrinsic cost to the patient and is higher among older patients. Our results echoed our theory and suggested that the lower chemotherapy use among older patients can be partially attributable to access. Local practice style affected chemotherapy choice for MBC patients except for patients aged between 80-84 years old and physician access is paramount for patients 85 years of age or older.

The percentage of patients without comorbidities progressively decreased with each older age group, with 51.55% among patients aged 66 to 69 years old, followed by 42.56% among those aged 70 to 74 years old, 33.63% among those aged 75 to 79 years old, 17.45% among those aged 80 to 84 years old, and the lowest 9.01% among those aged 85 years and older. Presence of comorbidities appeared strongly associated with receiving chemotherapy except for patients aged 80 to 84 years old. In this group, chemotherapy choice was shown to be unrelated to the presence of comorbidities. This group was probably in the process of rapidly declining in the functional reserve of multiple organ systems and may have developed more complex clinical symptoms; therefore, a more specific measure related to disease severity and disease symptoms may better predict treatment choice. The oldest group reported a higher prevalence of conditions associated with advanced age. Thus, the comorbidity profiles of these subpopulations seemed consistent with their age levels and largely associated with chemotherapy choice.

Race was associated with chemotherapy receipt among the youngest (66-69) and the oldest group (85+) but not in other age groups. The results showed among patients aged 66 to 69 years old, African American women seemed less likely to receive chemotherapy. However, when adding access variables, the odds of receiving chemotherapy between African American and white women was no longer significantly different, demonstrating this difference can be attributed to access to cancer care. However, among patients aged 85 years and older, the opposite trend was observed. African American women were more likely to receive chemotherapy than white patients. This effect remained after adding access variables in the model. African American women may prefer more aggressive treatment as their end-of-life treatment option, as shown in previous studies (Crawley et al. 2000), while among younger African American women, geographic access to cancer care may lead to lower chemotherapy use.

The proportion of married elderly patients decreased with advancing age, with 43.78% among patients aged 66 to 69 years old, followed by 38.61% among those aged 70 to 74 years old, 31.93% among those aged 75 to 79 years old, 23.95% among those aged 80 to 84 years old, and the lowest 11.85% among those aged 85 years and older. This may be because older women outlived their partners and were widowed. This phenomenon was demonstrated by our data showing the proportion of patients who were widowed, separated, or divorced was increasing with advancing age. Single women were less likely to receive chemotherapy than married patients. Marital status may be a proxy for external resources, such as time, money, standard of living, and social support. Such support may include the provision of material support, such as financial assistance and assets, and emotional support, such as the caring or concern individuals receive from friends and family members, and the provision of information to help individuals understand and manage cancer more effectively (Suzman, Willis, and Manton 1995). Therefore, the older the patient becomes, the less social support she may have, which would affect patient and physician treatment decision-making.

Other variables that may also be associated with aging but unmeasured in this study include functional status, disease severity, disease symptoms, patient preferences, and family member perspectives. An important variable predicting chemotherapy use and its effectiveness is functional status. Functional dependence is associated with frailty, therefore patients are less likely to choose chemotherapy and are more likely to experience poor survival associated with the treatment. Aging is presumably associated with higher disease severity and more complicated disease symptoms but individual patients can be highly heterogeneous in terms of how sick they are and what symptoms they experience. Aging may also influence a patient's outlook toward her remaining life; therefore, she may be more likely to reject intensive treatment. Family member perspective may also play an important role in treatment decision-making. Considerable age-related heterogeneity in functional ability, patient ability to tolerate chemotherapy,

and patient and family member preferences exists among elderly patients 65 years and older. Future research should take into account these factors to examine the dynamic relationship between each variable and treatment choices among different age groups.

Effect of Access to Cancer Care on Chemotherapy Choice among Elderly Women with MBC

The evidence from this study showed that local area chemotherapy percentages were positively associated with receiving chemotherapy among elderly women diagnosed with MBC between 1992 and 2002. In addition, among patients 85 years of age and older, the local area per capita number of oncologists across metastatic cancers was negatively associated with chemotherapy choice (While the direction of this effect on chemotherapy choice has been consistently negative, its magnitude has not reached this significance level in other age groups). The results confirmed the theoretical model that access to cancer care influenced chemotherapy choice more for older patients than for younger patients. The result showed that provider access only affected the oldest group and it negatively affected chemotherapy choice for elderly MBC patients, which is different from what the study originally hypothesized; among the other three access variables, only the effect of local area chemotherapy percentage across metastatic cancer patients was significant on chemotherapy choice and it was positively associated with chemotherapy choice across age groups (except age group of 80 to 84 years old).

The direction of the cumulative odds ratios across age groups suggests that local area chemotherapy percentages affected chemotherapy choice in a consistent way, with higher chemotherapy percentages predicting higher odds of receiving chemotherapy. Because uncertainties regarding the trade-off between the patient's quality and length of life due to chemotherapy increase with age, oncologists seemed to seek out peer opinion

when making chemotherapy recommendations to elderly patients with MBC. The local area medical opinion represents a consensus of the best approach to certain clinical conditions among a group of physicians practicing in that area (Fisher et al. 2003b; Wennberg and Gittelsohn 1982), which typically are not related to the underlying baseline health status of the populations across regions (Fisher et al. 2003b). In the Dartmouth Atlas Project, Elliott Fisher and John Wennberg suggested that in preference-sensitive care, such as chemotherapy for elderly women with MBC, treatment choices often depend more on local medical opinion than on patient needs or choices. We used the local area chemotherapy percentage to measure local medical opinion. The local area chemotherapy percentage across cancers is an access measure related to whether the patient has the means and know-how to receive chemotherapy. We found that among the elderly patients diagnosed with MBC between 1992 and 2002, there was a positive association between local area chemotherapy percentage and receiving chemotherapy. This association was observed in both the whole group and stratified age subgroup analysis. The only exception was the age subgroup aged 80 to 84 years old. Patients surviving to age 80 have come to an important turning point and are highly heterogeneous in their clinical conditions. Sicker patients may have developed chronic illnesses by that time, but more robust patients would also survive to 85 years and older. Therefore, treatment choices may be highly individualized and no systematic association between the chemotherapy percentage and patients' receiving chemotherapy receipt could be identified. The results are consistent with our theory. They have highlighted the importance of local medical opinion and offered insight into the ways in which that opinion influences treatment patterns of oncologists in the absence of sufficient clinical evidence regarding chemotherapy choice for MBC in elderly patients.

Another access variable, local area per capita number of oncologist across metastatic cancers, also affected chemotherapy choice among patients aged 85 years and older. Contrary to our initial hypothesis, oncologist supply had a consistently negative

effect on receiving chemotherapy, although this effect did not reach significance in other, younger age groups. Our results showed an interaction effect between local area per capita oncologist supply and chemotherapy choice in the oldest group. The interaction effect may be additive as indicated in the subgroup analysis instead of multiplicative as demonstrated in the interaction terms of the aggregate model. Such an additive interaction effect may be still meaningful because biologically it identifies an impact factor for a specific group of patients. In the Dartmouth Atlas Project, physician visits, diagnostic tests, hospitalizations, and admissions to intensive care among patients with chronic illnesses, were positively related to local area supply of physician specialists and hospital beds. Our results are in contrast with theirs and with our original hypothesis. Initially, our hypothesis was that oncologists living in areas with higher per capita oncologist supply tended to recommend chemotherapy more to engage patients and generate more revenue because of lower income and more leisure time than oncologists practicing in areas with more patients. Our results showed that a higher per capita number of oncologists among metastatic cancer patients in the local area may be associated with more time for each patient. Therefore, oncologists were able to spend more time with each elderly patient and find alternatives for them, such as hormone therapy and hospice care. Especially for elderly patients who were 85 years and older, oncologists may dissuade elderly patients from choosing chemotherapy and recommend other less toxic treatment options, such as hormone therapy. This may be due to physician concern that the patient has limited life expectancy and higher risk of chemotherapy-related toxicity. When putting treatment benefits into perspective, the same survival benefit that is meaningful for a 65-year-old may not represent a significant survival gain in an 85-year-old whose life expectancy is 6 years and is further limited by the nature of MBC (Ganz 2007). Furthermore, age-related comorbidities and deteriorated functional status are also an integral part of the treatment consideration. Receiving chemotherapy is a stressful process. Such stress is likely to be a great challenge for older patients, especially for the

oldest, whose ability to copy with such stress may be impaired by age-related comorbidities and deteriorated functional status. Treatment gains and side effects have to be carefully weighed against the life expectancy and quality of life for an older patient (Ganz 2007). With a range of treatment choices for MBC, a physician may spend more time discussing the negative aspects of chemotherapy, assessing the socio-economic environment, familial context, patient preferences, and expectations; and recommending other treatment options for the oldest patients. Also, higher area per capita oncologist supply may be equivalent to more teaching hospitals in the area. Such teaching-oriented hospital environment may be more able to focus on patients themselves and spend more time to understand patient preferences. It is possible that although chemotherapy choice was inversely associated with local area per capita provider supply, other types of care, including diagnosis, surgery, hormone therapy and palliative care, may increase. Future study could revise the theoretical model in this study by adding concepts related to different services to understand the complete picture of the effect of increased area per capita provider supply.

The other local area health care system capacity measure, the local area per capita number of hospices across metastatic cancers, was not shown to be associated with receiving chemotherapy among the study population. A recent study of the effect of hospice access on hospice use found that hospice access, including two additional measures of distance to the nearest hospice and local area per capita number of hospice staff, affected hospice use among elderly women diagnosed with MBC between 1992 and 2002. In contrast, the results in this study did not identify a direct association between local area hospice availability and chemotherapy use. This may be attributed to a variety of treatment options available to the patients with MBC and change in palliative care philosophy that tries to find a balance between life-prolonging care such as chemotherapy, and palliative care. The direction of the effect of local area hospice availability on chemotherapy choice has not been consistently negative, suggesting a

possible non-linear relationship between this variable and the log odds of chemotherapy use for different age subgroups. The magnitude of this effect also varied among different age subgroups.

Distance to the nearest oncologist practice was not associated with chemotherapy choice among the study population. For patients with MBC, distance may be a less important concern because treatments at this stage are typically taken out of necessity. The direction of the effect of distance to the nearest oncologist practice on chemotherapy choice has been consistently negative as suggested by the theory, although the magnitude of this effect was not significant.

Policy Implications

Our results showed that the age-related decreasing rate in chemotherapy use among older patients with MBC can be partially attributed to the degree to which access influences chemotherapy use in older patients, including both local area chemotherapy percentage and the local area per capita oncologist supply.

Among elderly women diagnosed with MBC between 1992 and 2002, chemotherapy-use rates ranged from 7.72% in patients aged 85 years and older to 49.26% in the age group between 66 years to 69 years old. The lower chemotherapy rate in oldest population may reflect a lack of patient-specific data on efficacy in older patients, physician belief, or patient preference. Our results showed that local area chemotherapy percentages may contribute to the treatment patterns of progressively increasing differences in chemotherapy use in each older age group. Local area chemotherapy percentages vary from one area to another area and differ dramatically between age subgroups. When considering whether to get chemotherapy, patients usually delegate decision-making to physicians. The local medical opinion on how to treat elderly patients

with MBC becomes dominant when uncertainties arise in chemotherapy choice. Physicians appeared to recommend chemotherapy less frequently to older patients with MBC than to younger patients. To what degree the final decision incorporated patient value and preference is largely unknown. Older patients may have difference preferences; for example, they may prefer less intensive treatment to chemotherapy. Some patients are frightened of becoming a burden and many will resist chemotherapy because it could remove some of their independence. They may face physical barriers – not being able to drive, and not having a supportive network to ferry them to hospital. They may also have different goals in terms of life prolongation and quality of life. Under the current clinical evidence, the ideal treatment rate should reflect patient preference and value but not solely based on age. The best clinical practice may be preference-based discussion between doctors and patients about the most appropriate treatment. Lower chemotherapy use may not be inferior and more chemotherapy use may be unwanted or not necessarily lead to better outcomes.

Our results also showed that local area per capita oncologist supply across metastatic cancers was negatively associated with chemotherapy receipt for the oldest group. For patients whose ages ranged from 66 years to 84 years, the direction of the effect of this variable on chemotherapy receipt was consistently negative. This effect reached the significance level in the oldest group of 85 years and older. It may be that oncologists believe chemotherapy is generally more risky among older patients. For elderly patients with MBC, other treatment options, such as hormone therapy and hospice care, are available and specific recommendations are made based on HR status and HER2 status in the clinical guidelines. With a range of treatment choices, oncologists practicing in areas with a higher per capita supply of oncologists may be able to spend more time discussing the negative and positive aspects of each cancer treatment. Many doctors may recommend hormone therapy and hospice care because they are less toxic than chemotherapy. This result, together with the evidence that the mean number of

oncologists among four types of metastatic cancer patients across regions decreased between 1992 and 2002, suggests that oncologists may have actually been undersupplied during that period of time. Our results add data to the debate surrounding heath care professional workforce policy and encourage more thoughtful discussion surrounding physician workforce supply. More evidence on treatment patterns of oncology specialties and the outcomes of oncologist visits are needed.

Limitations

There are several limitations in our study. The analysis is based on the SEER-Medicare linked database. Without careful comparison of baseline characteristics with different populations, results can only be applied to the Medicare beneficiaries residing in one of the SEER areas. Another limitation related to generalization is that our study only included women first diagnosed with MBC. It might be more meaningful if patients who have recurrent cancer or who relapse to MBC are included. But for those patients, chemotherapy choice is further complicated by other clinical factors, which may be different from immediate chemotherapy choice in this study.

There are unmeasured confounders in our study. Complete data for hormone therapy is not available in the data. Although we controlled for HR status, it will be an unmeasured confounder in our study. An important confounder for the chemotherapy rate is geographical racial disparity. African-American women have a disproportionate share of triple negative disease where chemotherapy is the only treatment. Therefore, an area with more African-American women could appropriately have a higher chemotherapy percentage, or an area with fewer African-American women could have an appropriately lower chemotherapy percentage.

This work looks at a time period of 1992-2002 when we had different treatments for MBC. However, our results examining age-related difference in chemotherapy choice among elderly MBC patients and the dynamic association between age and access to cancer care are still relevant to clinical practice.

Future Research

Future studies should evaluate the outcomes of the treatment patterns of chemotherapy use among different age groups. To further understand such variation, research on risks and benefits of chemotherapy is the next step. The variation across different regions provide a natural experiment. The heterogeneous clinical conditions across patients likely lead to different patient choices and a heterogeneous benefit profile across patients. Outcomes associated with such variations need to be evaluated. For example, does chemotherapy provide a survival benefit? In which age subgroups? Is there a subgroup more susceptible to the side effects of chemotherapy? Up-to-date and comprehensive information regarding the benefits and risks of chemotherapy is likely to better inform patient and physician treatment choice and facilitate rational decision-making

To better integrate patient preference and value into decision-making, research is needed to study practical tools for decision support. For example, the communication module between physicians and patients need to be evaluated (Siminoff and Fetting 1991). Specific components and detailed procedures to increase patient knowledge, exchange views about different treatments, and elicit patient preferences should be included in the module to improve the agreement between patient values or preferences and the treatment option actually chosen.

Research is needed to trace out the real demand of patients for intensive treatment such as chemotherapy at the end of their lives under informed patient choice (Wennberg et al. 2008). The information can then be used to guide physicians to make chemotherapy recommendations based on more than their subjective judgment as to what patients would prefer or patient age.

To fully understand the effect of oncologist supply, future study should explore other oncology specialties and expand to other cancer types to obtain a complete understanding of the effect of oncologist supply on patient choice.

Conclusions

The more uncertain the evidence with age, the more access influenced chemotherapy choice. Our results showed that age-related treatment differences in chemotherapy use may be attributable to local practice style and to physician assessment of real benefits of chemotherapy, taking into account older patients' limited life expectancies and higher risk of toxicities. Local area chemotherapy practice styles affect chemotherapy choice for patients except for those aged between 80-84 years of age; provider access is paramount for patients 85 years of age or older. To understand whether such treatment patterns of decreasing chemotherapy use associated with age represents appropriate practice for elderly women with MBC, more research is needed. Future study should examine the outcomes of current treatment patterns, identify practical tools for patient and physician communication, and ensure that treatment choice reflects patient preferences and is tailored to individual patient needs.

APPENDIX A

CODES FOR IDENTIFYING CHEMOTHERAPY FROM MEDICARE CLAIMS

Table A-1. Codes for Identifying Chemotherapy from Medicare Claims

NCH claims	
HCPCS code	Q0083-Q0085, J7150, J9000-J9999, 96400, 96408, 96410, 96412, 96414, 96545
Outpatient claims	
HCPCS code	Q0083-Q0085, J7150, J9000-J9999, 96400, 96408, 96410, 96412, 96414, 96545
Revenue center code	0331, 0332, 0335
Medpar claims	
ICD-9 diagnosis code	V581, V662, V672
ICD-9 procedure code	9925
DRG code	410

Note: Two frequent prescription used for MBC: Herceptin is reimbursed under the code J9355 (effective Jan. 1, 2000, administered at Physicians' office or an outpatient clinic); Zometa is reimbursed under the code J3487 (administered at Physicians' office or an outpatient clinic)

APPENDIX B

CODES FOR IDENTIFYING RADIATION THEARPY FROM MEDICARE CLAIMS

Table B-1. Codes for Identifying Radiation Therapy from Medicare Claims

NCH claims	
ICD-9 diagnosis code	V58.0, V66.1, V67.1
HCPCS code	77401–77499, 77750–77799
Outpatient claims	
ICD-9 diagnosis code	V58.0, V66.1, V67.1
ICD-9 procedure code	92.21–92.29
HCPCS code	77401–77499, 77750–77799
Revenue center code	0330, 0333
Medpar claims	
ICD-9 diagnosis code	V58.0, V66.1, V67.1
ICD-9 procedure code	92.21–92.29

APPENDIX C

CHEMOTHERAPIES CHOSEN BY MEDICARE METASTATIC BREAST CANCER PATIENTS BETWEEN 1992 AND 2002 BY AGE GROUPS AND TIME PERIODS

Table C-1. Chemotherapies Chosen by Medicare Metastatic Breast Cancer Patient between 1992 and 2002 by Age Groups

Chemo types	66-69	70-74	75-79	80-84	85+	Total
BCG	1	0	0	0	0	1
Etoposide	0	0	1	0	0	1
Goserelin	0	0	1	0	0	1
Mesna	0	1	0	0	0	1
Carboplatin	0	0	1	1	0	2
Leuprolide	1	0	1	0	0	2
Vincristine	0	1	1	0	0	2
Vinorelbine/tartrate	0	0	2	0	0	2
Alemtuzumab	1	1	2	0	0	4
Trastuzumab	2	2	0	0	0	4
Paclitaxel	2	2	2	2	0	8
Docetaxel	3	6	2	0	2	13
NOS	3	2	5	1	2	13
Doxorubicin	8	2	6	1	0	17
Methotrexate	8	12	5	6	2	33
Mitomantrone	1	0	0	0	1	33
Fluorouracil	12	7	9	4	4	36
Cyclophosphamide	22	21	16	5	1	65
Inpatient	71	89	58	38	18	274
Unknown	233	304	228	93	28	886

Table C-2. Chemotherapies Chosen by Medicare Metastatic Breast Cancer Patients between 1992 and 2002 by Time Periods

Chemo types	1992 – 1997	1998 and later	Total
BCG	0	1	1
Etoposide	1	0	1
Goserelin	0	1	1
Mesna	1	0	1
Carboplatin	0	2	2
Leuprolide	0	2	2
Mitomantrone	2	0	2
Vincristine	1	1	2
Vinorelbine/tartrate	0	2	2
Alemtuzumab	4	0	4
Trastuzumab	0	4	4
Paclitaxel	1	7	8
Docetaxel	0	13	13
NOS	4	9	13
Doxorubicin	9	8	17
Methotrexate	12	21	33
Fluorouracil	15	21	36
Cyclophosphamide	9	56	65
Inpatient	143	131	274
Unknown	379	507	886

APPENDIX D

SPECIALTY CODES FOR IDENTIFYING MEDICAL ONCOLOGISTS FROM NCH FILES

Table D-1. Speciality Codes for Identifying Medical Oncologists from NCH Files

Specialist code	**Provider specialty**
83	Hematology / Oncology
90	Medical oncology
91	Surgical oncology
98	Gynecologist / Oncologist

Note: “32”, “92” radiation oncologists are excluded

APPENDIX E

DIAGNOSTIC CODES FOR IDENTIFYING COMORBIDITIES FROM MEDICARE CLAIMS

Table E-1. Diagnostic Codes for Identifying Comorbidities from Medicare Claims

Comorbid condition	ICD-9-CM Codes	References
Acute myocardial infarction	410.00-410.90	National Cancer Institute
Old myocardial infarction	412	National Cancer Institute
Peripheral vascular disease	441.00-441.90, 443.90, 785.40, V43.4	National Cancer Institute
Congestive heart failure	428.00-428.90	National Cancer Institute
Cerebrovascular disease	430.00-437.90, 438.00	National Cancer Institute
Chronic pulmonary disease	490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 506.40	National Cancer Institute
Dementia	290.00-290.90	National Cancer Institute
Paralysis	342.00 -342.90	National Cancer Institute
Diabetes	250, 250.00-250.30, 250.70	National Cancer Institute
Diabetes with complications	250.40-250.60, 250.80-250.90	National Cancer Institute
Moderate/severe renal disease	582.00-582.90, 583.00-583.90, 585, 586, 588.00-588.90	National Cancer Institute
Milder liver disease	571.20, 571.40, 571.50, 571.60	National Cancer Institute
Moderate/severe liver disease	572.20-572.80, 456.00-456.10, 456.20, 456.21	National Cancer Institute
Peptic ulcer disease	531.00-534.00	National Cancer Institute
Rheumatologic disease	714.81, 725.00, 710.00, 710,10, 710.40, 714.00-714.20	National Cancer Institute

APPENDIX F

PROCEDURE CODES FOR IDENTIFYING COMORBIDITIES FROM MEDICARE CLAIMS

Table F-1. Procedure Codes for Identifying Comorbidities from Medicare Claims

Comorbid condition	Codes	.
Cerebrovascualr Disease	Surgery codes: 3812, 3842	National Cancer Institute
	HCPCS codes: 35301, 35001, 35002, 35005, 35501, 35508, 35509, 35515, 35642, 35645, 35691, 35693	
Peripheral Vascular Disease	Surgery codes: 3813, 3814, 3816, 3818, 3843, 3844, 3846, 3848, 3833, 3834, 3836, 3838, 3922-3926, 3928-3929	National Cancer Institute
	HCPCS codes: 35011,35013, 35045, 35081, 35082, 35091, 35092, 35102, 35103, 35111, 35112, 35121, 35122, 35131, 35132, 35141, 35142, 35151, 35152, 35153, 35311, 35321, 35331, 35341, 35351, 35506, 35507, 35511, 35516, 35518, 35521, 35526, 35531, 35533, 35536, 35541, 35546, 35548, 35549, 35551, 35556, 35571, 35582, 35583, 35585, 35587, 35601, 35606, 35612, 35616, 35621, 35623, 35626, 35631, 35636, 35641, 35646, 35650, 35651, 35654, 35656, 35661, 35663, 35665, 35666, 35671, 35694, 35695, 35355-35381	

APPENDIX G

CORRELATION BETWEEN FOUR ACCESS VARIABLES

Table G-1. Correlation Between Access Variables

	Travel time	Area chemo percentage	# Oncologists	# Hospices
Travel time	1	-0.01278	-0.14417	0.21744
Area chemo percentage	-0.01278	1	-0.13732	-0.08251
# Oncologists	-0.14417	-0.13732	1	0.39536
# Hospices	0.21744	-0.08251	0.39536	1

Note:

- Travel time is calculated as proportion of an hour.
- # oncologists is calculated as local area number of oncologists per 1000 metastatic breast, prostate, lung and colorectal cancer patients.
- # hospices is calculated as local area number of hospices per 1000 metastatic breast, prostate, lung and colorectal cancer patients.
- Area treatment percentage is calculated as local area number of patients who received chemotherapy per 100 end-stage breast, prostate, lung and colorectal cancer patients.

APPENDIX H

CHARACTERISTICS OF PATIENTS RECEIVING AND NOT RECEIVING CHEMOTHERAPY

Table H-1 shows the percentage of patients who used chemotherapy by patient characteristics and chi-square statistics to test the association between chemotherapy choice and each characteristic for the whole study population.

There were 30.16% out of 4533 MBC patients used chemotherapy. Chemotherapy rate decreased steadily with age, with 49.26%, 40.50%, 31.84%, 17.64% and 7.72% among 747 patients aged 66-69, 1111 patients aged 70-74, 1068 patients aged 75-79, 856 patients aged 80-84, and 751 patients aged 85+, respectively. Patients who used chemotherapy averaged 74.18 years while those who did not use chemotherapy averaged 79.12 years of age. Married patients were more likely to use chemotherapy than those who were single or those who were widowed, divorced or separated at diagnosis. Patients who had negative hormone receptor status had higher chemotherapy rate than those with positive or unknown hormone receptor status. There appeared to be a trend that higher income patients were more likely to use chemotherapy. No association between chemotherapy use and patient race or census tract education level was found by chi-square tests. The rural/urban characteristics of patient residence area and their dwelling SEER sites were not associated with chemotherapy use. There appeared to be an increasing trend in chemotherapy use over years although chi-square tests were not significant.

Chi-square statistics in the whole group analysis showed chemotherapy use post-diagnosis was associated with patient comorbidities prior to diagnosis. Elderly women who had no comorbidities were more likely to use chemotherapy than those who had at least one co-existing condition. In addition, patients who had diabetes, congestive heart

failure, cerebrovascular disease, paralysis, and dementia were less likely to be treated with chemotherapy than patients without these conditions.

Table H-1. Percent Chemotherapy Use by Age, Race, Marital Status, Area-level Income and Education, Comorbidities, Rural/Urban Area Code, and Year of Diagnosis of Patients Diagnosed with Metastatic Breast Cancer and Living in SEER Areas from 1992-2002: the Whole Study Population

	Percent Chemo Use	No. of Cases	*P* Value
Overall	30.16	4533	
Age at diagnosis			<0.0001*
66-69	49.26	747	
70-74	40.50	1111	
75-79	31.84	1068	
80-84	17.64	856	
85 or older	7.72	751	
Race and ethnicity			0.7810
White	30.11	3740	
Black	29.51	488	
Other	31.80	305	
Marital status			<0.0001*
Single	25.74	474	
Married	39.90	1391	
Divorced/Widowed	25.59	2497	
Unknown	29.82	171	
Hormone receptor status			<0.0001*
Positive	29.70	1448	
Negative	41.53	1151	
Unknown	23.73	1934	
Census tract income			0.0469*
1st Quartile	26.82	1115	
2nd Quartile	30.20	1126	
3rd Quartile	32.53	1125	
4th Quartile	30.89	1133	
Unknown	35.29	34	
Census tract % non-high education			0.3490
1st Quartile	31.69	1114	
2nd Quartile	29.75	1126	
3rd Quartile	30.99	1123	
4th Quartile	28.08	1136	
Unknown	35.29	34	
Comorbidities §+			
No comorbidities	32.33	3418	<0.0001*
COPD	27.27	297	0.2626
PVD	26.47	102	0.4120
Diabetes	25.83	480	0.0291*
Renal disease	24.07	54	0.3272
Old MI	23.81	42	0.3679
Diabetes with complications	23.19	69	0.2038

Rheumatologic disease	20.00	65	0.0723
Peptic ulcer disease	18.75	32	0.1583
CHF	17.88	302	<0.0001*
MI	16.13	31	0.0877
CVD	13.75	160	<0.0001*
Paralysis	7.14	28	0.0078*
Dementia	1.89	53	<0.0001*
Rural/urban area code #			0.7466
Metro areas of ≥1 M pop.	30.07	2754	
Metro areas of 250K-1M pop.	31.48	845	
Metro areas of ≤250K pop.	28.33	293	
Urban areas adjacent to a metro area of >20K pop.	34.56	136	
Urban areas not adjacent to a metro area of >20K pop.	28.35	127	
Urban areas adjacent to a metro area of <20K pop.	25.63	160	
Urban areas not adjacent to a metro area of <20K pop.	32.39	142	
Rural areas adjacent to a metro area of <2500 pop	27.27	44	
Rural areas not adjacent to a metro area of <2500 pop	25.00	32	
SEER area			0.9412
Louisiana	34.93	146	
Kentucky	32.43	148	
Connecticut	31.64	531	
Great California	31.32	265	
Los Angeles	30.90	479	
New Jersey	30.84	454	
San Jose	30.36	168	
Detroit	30.14	657	
Atlanta	29.87	231	
Seattle	29.48	346	
Iowa	28.99	507	
San Francisco	28.46	253	
Utah	27.94	136	
New Mexico	25.00	128	
Hawaii	25.00	72	
Rural Georgia	16.67	12	
Year of diagnosis			0.6677
1992	26.20	374	
1993	29.76	336	
1994	26.47	306	
1995	30.68	339	
1996	30.06	336	
1997	30.50	318	
1998	30.10	289	
1999	33.97	312	
2000	31.23	650	
2001	31.06	644	
2002	30.21	629	

Note: * $P < 0.05$.
§ Comorbidities exclude codes for AIDS and all metastatic tumors.
ǂ Total cases do not add to 100% because some patients have multiple chronic conditions.
Abbreviations: COPD, chronic obstruction pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease; CVD, cerebrovascular disease; CHF, congestive heart failure.
Rural/urban area code is based on rural/urban continuum codes from Economic Research Service (ERS), Department of Agriculture. This rural/urban variable is classified into nine categories.

Table H-2 to Table H-6 show the percentage of patients who used chemotherapy by patient characteristics and chi-square statistics to test the association between chemotherapy choice and each characteristic for individual age groups of 66-69, 70-74, 75-79, 80-84, and 85+ .

As shown in Table H-2, in the age group of 66-69 years old, 49.26% out of 747 patients used chemotherapy. Chi-square statistics showed no association between chemotherapy use and patient race, marital status, census tract income and education level, rural/urban characteristics of dwelling areas, residing SEER sites, or diagnosis year. Consistent with the clinical guidelines of breast cancer treatments, HR status was significantly associated with chemotherapy use, with 56.40% chemotherapy rate in HR+ population versus 45.45% use rate in HR- population.

Whether the patient had comorbidities prior to diagnosis was associated with chemotherapy choice among this age group. Patients who had no comorbidities were more likely to choose chemotherapy than patients who had at least one co-existing condition. Patient with diabetes, diabetes with complications, or rheumatologic disease were less likely to choose chemotherapy than those without these conditions.

Table H-2. Percent Chemotherapy Use by Age, Race, Marital Status, Area-level Income and Education, Comorbidities, Rural/Urban Area Code, and Year of Diagnosis of Patients Diagnosed with Metastatic Breast Cancer and Living in SEER Areas from 1992-2002: Age Subgroup of 66-69

	Percent Chemo Use	No. of Cases	*P* Value
Overall	49.26	747	
Race and ethnicity			0.0719
White	50.67	600	
Black	38.30	94	
Other	52.83	53	
Marital status			0.0769
Single	40.21	97	
Married	51.68	327	
Divorced/Widowed	51.02	294	
Unknown	34.48	29	
Hormone receptor status			0.0443*
Positive	45.45	286	
Negative	56.40	211	
Unknown	47.60	250	
Census tract income			0.9042
1st Quartile	47.64	191	
2nd Quartile	50.56	178	
3rd Quartile	47.16	176	
4th Quartile	51.53	196	
Unknown	50.00	6	
Census tract % non-high education			0.8439
1st Quartile	49.44	178	
2nd Quartile	48.91	184	
3rd Quartile	52.41	187	
4th Quartile	46.35	192	
Unknown	50.00	6	
Comorbidities §∓			
No comorbidities	51.55	611	0.0079*
Diabetes	36.11	72	0.0189*
COPD	40.00	40	0.2284
CHF	36.11	36	0.1057
Diabetes with complications	22.22	18	0.0202*
CVD	50.00	14	0.9556
PVD	63.64	11	0.3368
Rheumatologic disease	11.11	9	0.0213*
Renal disease	25.00	8	0.1675
Peptic ulcer disease	33.33	6	
MI	16.67	6	0.1088
Old MI	50.00	4	0.9764
Paralysis	0.00	2	
Dementia	0.00	1	
Rural/urban area code #			0.9924
Metro areas of ≥1 M pop.	49.66	441	

	Percent Chemo Use	No. of Cases	*P* Value
Metro areas of 250K-1M pop.	48.23	141	
Metro areas of ≤250K pop.	50.00	48	
Urban areas adjacent to a metro area of >20K pop.	46.43	28	
Urban areas not adjacent to a metro area of >20K pop.	45.83	24	
Urban areas adjacent to a metro area of <20K pop.	52.00	25	
Urban areas not adjacent to a metro area of <20K pop.	53.33	30	
Rural areas adjacent to a metro area of <2500 pop	50.00	6	
Rural areas not adjacent to a metro area of <2500 pop	25.00	4	
SEER area			0.0500
Louisiana	54.17	24	
Kentucky	51.72	29	
Connecticut	50.00	82	
Great California	31.82	44	
Los Angeles	57.47	87	
New Jersey	51.79	56	
San Jose	29.63	27	
Detroit	51.52	99	
Atlanta	36.17	47	
Seattle	60.00	55	
Iowa	55.91	93	
San Francisco	50.00	40	
Utah	45.16	31	
New Mexico	35.29	17	
Hawaii	38.46	13	
Rural Georgia	0.00	3	
Year of diagnosis			0.8387
1992	43.59	78	
1993	47.54	61	
1994	52.08	48	
1995	51.85	54	
1996	49.18	61	
1997	55.81	43	
1998	60.47	43	
1999	54.55	55	
2000	46.67	105	
2001	46.08	102	
2002	47.42	97	

Note: All notations are the same with Table H-1

As shown in Table H-3, in the age group of 70-74 years old, 40.50% out of 1111 patients used chemotherapy. Chi-square statistics showed no association between chemotherapy use and patient race, census tract education level, rural/urban characteristics of dwelling areas, residing SEER sites, or diagnosis year. Married patients seemed to have higher chemotherapy use than single patients or divorced, widowed, or separated patients at diagnosis. It appeared that higher income patients are more likely to choose chemotherapy than lower income patients. Same as the age group of 66-69 years old, HR status was significantly associated with chemotherapy use, with 50.96% chemotherapy rate in HR+ population versus 36.59% use rate in HR- population.

Whether the patient had comorbidities prior to diagnosis was associated with chemotherapy choice among this age group. Patients who had no comorbidities were more likely to choose chemotherapy than patients who had at least one co-existing condition. Patient with diabetes, diabetes with complications, and rheumatologic disease were less likely to choose chemotherapy than those without these conditions.

Table H-3. Percent Chemotherapy Use by Age, Race, Marital Status, Area-level Income and Education, Comorbidities, Rural/Urban Area Code, and Year of Diagnosis of Patients Diagnosed with Metastatic Breast Cancer and Living in SEER Areas from 1992-2002: Age Subgroup of 70-74

	Percent Chemo Use	No. of Cases	*P* Value
Overall	40.50	1111	
Race and ethnicity			0.1916
White	41.76	898	
Black	36.67	120	
Other	33.33	93	
Marital status			0.0016*
Single	30.23	129	
Married	46.39	429	
Divorced/Widowed	37.43	513	
Unknown	50.00	40	
Hormone receptor status			<0.0001*
Positive	36.59	369	
Negative	50.96	312	
Unknown	36.28	430	
Census tract income			0.0366*
1st Quartile	35.83	254	
2nd Quartile	40.14	294	
3rd Quartile	47.43	272	
4th Quartile	37.89	285	
Unknown	66.67	6	
Census tract % non-high education			0.3117
1st Quartile	44.73	275	
2nd Quartile	38.89	270	
3rd Quartile	39.78	274	
4th Quartile	38.11	286	
Unknown	66.67	6	
Comorbidities §∓			
No comorbidities	42.56	867	0.0085*
Diabetes	34.55	110	0.1799
COPD	43.21	81	0.6064
CVD	11.11	45	<0.0001*
CHF	26.83	41	0.0691
PVD	33.33	21	0.4992
Diabetes with complications	26.32	19	0.2038
Renal disease	21.43	14	0.1434
Rheumatologic disease	23.08	13	0.1979
Old MI	22.22	9	0.2619
Paralysis	12.50	8	0.1054
Dementia	0.00	6	
Peptic ulcer disease	0.00	4	
MI	0.00	3	
Rural/urban area code #			0.4551
Metro areas of ≥1 M pop.	39.67	673	
Metro areas of 250K-1M pop.	44.60	213	

	Percent Chemo Use	No. of Cases	*P* Value
Metro areas of ≤250K pop.	38.03	71	
Urban areas adjacent to a metro area of >20K pop.	56.25	32	
Urban areas not adjacent to a metro area of >20K pop.	33.33	36	
Urban areas adjacent to a metro area of <20K pop.	30.56	36	
Urban areas not adjacent to a metro area of <20K pop.	43.33	30	
Rural areas adjacent to a metro area of <2500 pop	33.33	12	
Rural areas not adjacent to a metro area of <2500 pop	37.50	8	
SEER area			0.1478
Louisiana	47.62	42	
Kentucky	50.00	30	
Connecticut	43.17	139	
Great California	58.73	63	
Los Angeles	33.93	112	
New Jersey	45.22	115	
San Jose	42.86	42	
Detroit	40.13	152	
Atlanta	41.38	58	
Seattle	35.96	89	
Iowa	37.72	114	
San Francisco	32.76	58	
Utah	34.48	29	
New Mexico	33.33	42	
Hawaii	25.00	24	
Rural Georgia	50.00	2	
Year of diagnosis			0.5870
1992	35.79	95	
1993	33.71	89	
1994	32.93	82	
1995	43.02	86	
1996	36.47	85	
1997	40.74	81	
1998	40.79	76	
1999	42.11	76	
2000	42.45	139	
2001	43.71	151	
2002	46.36	151	

Note: All notations are the same with Table H-1.

As shown in Table H-4, in the age group of 75-79 years old, 31.84% out of 1068 patients chose chemotherapy. Chi-square statistics showed no association between chemotherapy use and patient race, census tract income and education level, rural/urban characteristics of dwelling areas, residing SEER sites, or diagnosis year. Married patients seemed to have higher chemotherapy use than single patients or those who were divorced, widowed, or separated at diagnosis. Similarly, HR status was significantly associated with chemotherapy use, with 44.72% chemotherapy rate in HR+ population versus 29.30% use rate in HR- population.

Whether the patient had comorbidities prior to diagnosis was associated with chemotherapy choice among this age group. Patients who had no comorbidities were more likely to choose chemotherapy than patients who had at least one co-existing condition. For patients with renal disease, myocardial infarction, peptic ulcer disease, paralysis, and dementia, chi-square tests were not able to give a valid estimation because few patients with these conditions were in this age group.

Table H-4. Percent Chemotherapy Use by Age, Race, Marital Status, Area-level Income and Education, Comorbidities, Rural/Urban Area Code, and Year of Diagnosis of Patients Diagnosed with Metastatic Breast Cancer and Living in SEER Areas from 1992-2002: Age Subgroup of 75-79

	Percent Chemo Use	No. of Cases	*P* Value
Overall	31.84	1068	
Race and ethnicity			0.4363
White	31.27	873	
Black	36.89	122	
Other	30.14	73	
Marital status			0.0078*
Single	27.66	94	
Married	39.00	341	
Divorced/Widowed	28.60	591	
Unknown	28.57	42	
Hormone receptor status			<0.0001*
Positive	29.30	355	
Negative	44.72	284	
Unknown	25.41	429	
Census tract income			0.4506
1st Quartile	27.10	262	
2nd Quartile	32.97	279	
3rd Quartile	34.10	261	
4th Quartile	33.07	257	
Unknown	33.33	9	
Census tract % non-high education			0.7816
1st Quartile	31.85	248	
2nd Quartile	31.80	261	
3rd Quartile	34.23	298	
4th Quartile	28.97	252	
Unknown	33.33	9	
Comorbidities §∓			
No comorbidities	33.63	788	0.0347*
Diabetes	25.00	132	0.0717
COPD	28.95	76	0.5750
CHF	23.81	63	0.1586
CVD	18.18	33	0.0872
Rheumatologic disease	33.33	21	0.8817
PVD	42.11	19	0.3322
Diabetes with complications	21.05	19	0.3087
Old MI	46.15	13	
Renal disease	18.18	11	
Dementia	0.00	11	
Paralysis	11.11	9	
Peptic ulcer disease	0.00	7	
MI	28.57	7	
Rural/urban area code #			0.9554
Metro areas of ≥1 M pop.	31.54	650	
Metro areas of 250K-1M pop.	32.63	190	

	Percent Chemo Use	No. of Cases	*P* Value
Metro areas of ≤250K pop.	31.08	74	
Urban areas adjacent to a metro area of >20K pop.	31.43	35	
Urban areas not adjacent to a metro area of >20K pop.	39.13	23	
Urban areas adjacent to a metro area of <20K pop.	25.64	39	
Urban areas not adjacent to a metro area of <20K pop.	33.33	39	
Rural areas adjacent to a metro area of <2500 pop	30.00	10	
Rural areas not adjacent to a metro area of <2500 pop	50.00	8	
SEER area			0.7166
Louisiana	36.11	36	
Kentucky	27.91	43	
Connecticut	30.83	133	
Great California	32.08	53	
Los Angeles	32.11	109	
New Jersey	37.25	102	
San Jose	44.44	36	
Detroit	30.00	170	
Atlanta	37.04	54	
Seattle	23.38	77	
Iowa	31.86	113	
San Francisco	31.67	60	
Utah	32.35	34	
New Mexico	22.22	27	
Hawaii	30.00	20	
Rural Georgia	100.00	1	
Year of diagnosis			0.5271
1992	25.29	87	
1993	36.84	76	
1994	24.19	62	
1995	28.57	77	
1996	30.77	78	
1997	31.88	69	
1998	24.32	74	
1999	35.71	84	
2000	33.99	153	
2001	36.20	163	
2002	33.10	145	

Note: All notations are the same with Table H-1.

As shown in Table H-5, in the age group of 80-84 years old, 17.64% out of 856 patients chose chemotherapy. Chi-square statistics showed no association between chemotherapy use and patient race, marital status, comorbidities, census tract income and education level, rural/urban characteristics of dwelling areas, residing SEER sites, or diagnosis year.

In this age group, HR status was the only variable significantly associated with chemotherapy use in the model, with 25.24% chemotherapy rate in HR+ population versus 17.18% use rate in HR- population.

Table H-5. Percent Chemotherapy Use by Age, Race, Marital Status, Area-level Income and Education, Comorbidities, Rural/Urban Area Code, and Year of Diagnosis of Patients Diagnosed with Metastatic Breast Cancer and Living in SEER Areas from 1992-2002: Age Subgroup of 80-84

	Percent Chemo Use	No. of Cases	*P* Value
Overall	17.64	856	
Race and ethnicity			0.8444
White	17.34	738	
Black	19.12	68	
Other	20.00	50	
Marital status			0.1250
Single	15.07	73	
Married	21.95	205	
Divorced/Widowed	15.84	543	
Unknown	25.71	35	
Hormone receptor status			0.0026*
Positive	17.18	262	
Negative	25.24	206	
Unknown	13.92	388	
Census tract income			0.5813
1st Quartile	16.67	216	
2nd Quartile	15.12	205	
3rd Quartile	21.03	214	
4th Quartile	17.45	212	
Unknown	22.22	9	
Census tract % non-high education			0.8115
1st Quartile	18.55	221	
2nd Quartile	19.53	215	
3rd Quartile	15.46	194	
4th Quartile	16.59	217	
Unknown	22.22	9	
Comorbidities §∓			
No comorbidities	17.45	619	0.8111
Diabetes	21.88	96	0.2480
CHF	18.31	71	0.8771
COPD	12.50	56	0.2965
CVD	5.26	38	0.0406*
PVD	20.00	25	
Dementia	6.25	16	
Rheumatologic disease	13.33	15	
Renal disease	50.00	10	
Old MI	0.00	8	
Diabetes with complications	25.00	8	
Peptic ulcer disease	25.00	8	
MI	14.29	7	
Paralysis	0.00	6	
Rural/urban area code #			0.5135
Metro areas of ≥1 M pop.	18.28	536	
Metro areas of 250K-1M pop.	20.50	161	

	Percent Chemo Use	No. of Cases	*P* Value
Metro areas of ≤250K pop.	9.80	51	
Urban areas adjacent to a metro area of >20K pop.	11.11	18	
Urban areas not adjacent to a metro area of >20K pop.	15.38	26	
Urban areas adjacent to a metro area of <20K pop.	21.21	33	
Urban areas not adjacent to a metro area of <20K pop.	9.52	21	
Rural areas adjacent to a metro area of <2500 pop	0.00	6	
Rural areas not adjacent to a metro area of <2500 pop	0.00	4	
SEER area			0.8844
Louisiana	15.79	19	
Kentucky	15.15	33	
Connecticut	21.28	94	
Great California	18.18	55	
Los Angeles	18.68	91	
New Jersey	16.00	100	
San Jose	20.59	34	
Detroit	21.21	132	
Atlanta	17.07	41	
Seattle	14.49	69	
Iowa	10.23	88	
San Francisco	20.00	50	
Utah	15.00	20	
New Mexico	27.78	18	
Hawaii	10.00	10	
Rural Georgia	0.00	2	
Year of diagnosis			0.3620
1992	9.38	64	
1993	17.54	57	
1994	12.96	54	
1995	20.97	62	
1996	24.14	58	
1997	19.72	71	
1998	12.96	54	
1999	14.55	55	
2000	23.81	126	
2001	16.95	118	
2002	16.06	137	

Note: All notations are the same with Table H-1.

As shown in Table H-6, in the age group of 85+, 7.72% out of 751 patients chose chemotherapy. Chi-square tests showed that there were no association between chemotherapy choice and patient race, marital status, census tract income and education level, rural/urban characteristics of dwelling areas, residing SEER sites, and diagnosis year. Consistently as observed in other age groups, HR status was associated with chemotherapy choice, with 15.22% in HR+ population versus 9.09% in HR- population.

Chi-square tests showed that whether patients had comorbidities was associated with chemotherapy choice. Patients without comorbidities were more likely to choose chemotherapy than those who had at least one co-existing condition. Due to the limited number of patients with certain comorbidities in this age group, chi-square tests were not able to give valid test for these conditions.

Table H-6. Percent Chemotherapy Use by Age, Race, Marital Status, Area-level Income and Education, Comorbidities, Rural/Urban Area Code, and Year of Diagnosis of Patients Diagnosed with Metastatic Breast Cancer and Living in SEER Areas from 1992-2002: Age Subgroup of 85+

	Percent Chemo Use	No. of Cases	*P* Value
Overall	7.72	751	
Race and ethnicity			0.1197
White	7.29	631	
Black	7.14	84	
Other	16.67	36	
Marital status			0.4036
Single	8.64	81	
Married	10.11	89	
Divorced/Widowed	7.55	556	
Unknown	0.00	25	
Hormone receptor status			0.0003*
Positive	9.09	176	
Negative	15.22	138	
Unknown	4.81	437	
Census tract income			0.1582
1st Quartile	5.21	192	
2nd Quartile	5.29	170	
3rd Quartile	9.90	202	
4th Quartile	10.38	183	
Unknown	0.00	4	
Census tract % non-high education			0.1989
1st Quartile	11.46	192	
2nd Quartile	7.65	196	
3rd Quartile	5.29	170	
4th Quartile	6.35	189	
Unknown	0.00	4	
Comorbidities §∓			
No comorbidities	9.01	533	0.0395*
CHF	2.20	91	.0352
Diabetes	8.57	70	0.7801
COPD	2.27	44	
CVD	6.67	30	
PVD	0.00	26	
Dementia	0.00	19	
Renal disease	9.09	11	
MI	12.50	8	
Old MI	0.00	8	
Rheumatologic disease	0.00	7	
Peptic ulcer disease	28.57	7	
Diabetes with complications	20.00	5	
Paralysis	0.00	3	
Rural/urban area code #			
Metro areas of ≥1 M pop.	8.59	454	
Metro areas of 250K-1M pop.	5.71	140	

	Percent Chemo Use	No. of Cases	*P* Value
Metro areas of ≤250K pop.	8.16	49	
Urban areas adjacent to a metro area of >20K pop.	13.04	23	
Urban areas not adjacent to a metro area of >20K pop.	0.00	18	
Urban areas adjacent to a metro area of <20K pop.	0.00	27	
Urban areas not adjacent to a metro area of <20K pop.	9.09	22	
Rural areas adjacent to a metro area of <2500 pop.	20.00	10	
Rural areas not adjacent to a metro area of <2500 pop.	0.00	8	
SEER area			
Louisiana	8.00	25	
Kentucky	7.69	13	
Connecticut	7.23	83	
Great California	10.00	50	
Los Angeles	10.00	80	
New Jersey	6.17	81	
San Jose	6.90	29	
Detroit	6.73	104	
Atlanta	3.23	31	
Seattle	16.07	56	
Iowa	7.07	99	
San Francisco	8.89	45	
Utah	0.00	22	
New Mexico	4.17	24	
Hawaii	0.00	5	
Rural Georgia	0.00	4	
Year of diagnosis			
1992	4.00	50	
1993	5.66	53	
1994	11.67	60	
1995	6.67	60	
1996	3.70	54	
1997	7.41	54	
1998	11.90	42	
1999	14.29	42	
2000	10.24	127	
2001	7.27	110	
2002	4.04	99	

Note: All notations are the same with Table H-1.

APPENDIX I

FULL LOGISTIC REGRESSION MODELS IN THE WHOLE STUDY POPULATION AND FIVE AGE SUBGROUP ANALYSIS OF 66-69, 70-74, 75-79, 80-84, AND 85+ YEARS OF AGE

Table I-1 shows the results of the logistic regression models for the whole study population, including all four access variables at the same time. Model 1 does not include access variables, which is used to examine the association between covariates and chemotherapy choice. Model 2 includes all the covariates in Model 1 and access indicator variables measured based on the quartiles of access variables. Model 3 includes all the covariates in Model 1 and access continuous variables.

Adding access variables improves the goodness-of-fit of the logistic regression models. For Model 1 without access variables, results showed that age significantly predicted chemotherapy choice. The odds of chemotherapy use decreased with increasing age, with the smallest odds among the oldest old group. Single women were less likely to choose chemotherapy than women who were married at diagnosis. Consistent with univariate analysis, HR status was significantly associated with chemotherapy choice. HR- subgroup had higher odds of chemotherapy use than HR+ and unknown HR status subgroup. Elderly patients who had at least one comorbid condition were less likely to choose chemotherapy than those without comorbidities. There were no associations between census tract income/education level and chemotherapy choice. Neither was rural/urban area code of the patient residence, SEER areas where the patient lived, or the year of diagnosis associated with chemotherapy use.

In Model 2 and 3, results were consistent with access variables measured as either indicator variables or continuous variables. In Model 2, chemotherapy percentage was

positively associated with chemotherapy choice controlling for distance to the nearest oncologist practice, local area per capita number of medical oncologists across metastatic cancers, local area per capita number of hospices across metastatic cancers, and other covariates. The odds of chemotherapy use increased with higher treatment rate, with the smallest odds in the first quartile and the largest odds in 75 percentile group. In Model 3 when chemotherapy percentage was measured as a continuous variable, Wald χ^2-statistics confirmed the statistically significant association between chemotherapy rate and chemotherapy choice. Distance to the nearest oncologist practice was shown to be significantly associated with chemotherapy use as a continuous variable but not as indicator variables based on its quartiles. This may be because classification based on the quartiles of distance masked the statistically differential points. Neither the local area per capita number of medical oncologists across metastatic cancers nor the local area per capita number of hospices across metastatic cancers was associated with chemotherapy choice in the whole group analysis. Similar patterns of association between covariates and chemotherapy choice in Model 1 were observed in Model 2 and 3 adding access variables.

Table I-1. Estimates of the Effect of Access to Cancer Care on Immediate Choice of Chemotherapy among the Whole Study Population of Patients Diagnosed with Metastatic Breast Cancer Aged 66+ and Living in SEER Areas between 1992 and 2002 (N=4284)

Variable	Model 1#	Model 2‡	Model 3+
Chemo percentage			
F-statistics| P value		33.1694 | <0.0001*	
1st quartile		Referent	
2nd quartile		1.372(1.102-1.708)	
3rd quartile		1.639(1.308-2.055)	
4th quartile		1.947(1.541-2.459)	
Estimate			0.0299
Wald χ2-statistics| P value			39.5863 | <0.0001*
Distance to the nearest oncologist			
F-statistics| P value		1.9319 | 0.3806	
1st quartile		Referent	
2nd quartile			
3rd quartile		0.939(0.786-1.122)	
4th quartile		0.867(0.705-1.065)	
Estimate			-0.4363
Wald χ2-statistics| P value			5.8172 | 0.0159*
Per capita number of medical oncologist			
F-statistics| P value		3.1972 | 0.3622	
1st quartile		Referent	
2nd quartile		0.916(0.735-1.141)	
3rd quartile		0.831(0.657-1.050)	
4th quartile		0.797(0.605-1.050)	
Estimate			-0.00124
Wald χ2-statistics| P value			3.5781 | 0.0585
Per capita number of hospice			
F-statistics| P value		0.4073 | 0.9387	
1st quartile		Referent	
2nd quartile		1.001(0.810-1.238)	
3rd quartile		1.049(0.838-1.312)	
4th quartile		1.066(0.832-1.367)	
Estimate			0.00126
Wald χ2-statistics| P value			0.7369 | 0.3907
Age at diagnosis OR | (95% CI ‖)			
F-statistics| P value	300.7378 | <0.0001*	301.0866 | <0.0001*	299.6569 | <0.0001*
66-69	Reference	Referent	Referent
70-74	0.704 (0.577-0.859)	0.709 (0.580 – 0.866)	0.708 (0.580 – 0.865)
75-79	0.481(0.392-0.592)	0.485 (0.394 – 0.597)	0.487 (0.396 – 0.600)
80-84	0.224(0.176-0.286)	0.223 (0.174 – 0.284)	0.224 (0.175 – 0.285)
85 or older	0.098(0.072-0.135)	0.097 (0.071 – 0.134)	0.097 (0.071 – 0.134)
Race and ethnicity OR (95% CI)			
F-statistics| P value	1.1152 | 0.5726	1.9411 | 0.3789	1.8365 | 0.3992

White	Referent	Referent	Referent
Black	0.997(0.770-1.291)	1.132 (0.870 – 1.473)	1.112 (0.856 – 1.444)
Other	1.186(0.861-1.636)	1.211 (0.876 – 1.675)	1.219 (0.882 – 1.684)
Marital status OR (95% CI)			
F-statistics| P value	25.7470 | <0.0001*	24.9057 | <0.0001*	25.7819 | <0.0001*
Single	Referent	Referent	Referent
Married	1.766(1.367-2.281)	1.731 (1.337 – 2.241)	1.749 (1.351 – 2.266)
Divorced/Widowed	1.283(1.001-1.643)	1.246 (0.970 – 1.600)	1.252 (0.975 - 1.609)
Unknown	1.277(0.818-1.992)	1.277 (0.816 – 1.997)	1.270 (0.813 – 1.986)
Hormone receptor status OR (95% CI)			
F-statistics| P value	75.6041 | <0.0001*	75.8170 | <0.0001*	76.7449 | <0.0001*
Positive	Referent	Referent	Referent
Negative	1.896(1.583-2.270)	1.932 (1.611-2.316)	1.948(1.624 – 2.336)
Unknown	0.921(0.775-1.094)	0.940 (0.790-1.118)	0.946(0.795 – 1.125)
Radiation therapy OR (95% CI)			
F-statistics| P value	0.2532 | 0.6149	0.3255 | 0.5683	0.3673 | 0.5445
No	Referent	Referent	Referent
Yes	0.962(0.827-1.119)	0.957(0.822-1.114)	0.954 (0.819 – 1.111)
Comorbidities OR (95% CI)			
F-statistics| P value	20.4626 | <0.0001*	22.0240 | <0.0001*	21.9557 | <0.0001*
No	Referent	Referent	Referent
Yes	0.670(0.563-0.797)	0.657 (0.552 – 0.783)	0.658(0.552 – 0.784)
Census tract income OR (95% CI)			
F-statistics| P value	8.4614 | 0.0761	7.4043 | 0.1160	8.0873 | 0.0884
1st quartile	Referent	Referent	Referent
2nd quartile	1.171(0.931-1.474)	1.110 (0.879 – 1.402)	1.059 (0.871 – 1.288)
3rd quartile	1.387(1.070-1.799)	1.301 (0.999 – 1.694)	1.089 (0.873 – 1.360)
4th quartile	1.104(0.816-1.493)	1.004 (0.738 – 1.365)	1.066 (0.824 – 1.380)
Unknown	1.392(0.490-3.954)	1.207 (0.421 – 3.461)	1.029 (0.499 – 2.119)
Census tract % non-high edu. OR (95% CI)			
F-statistics| P value	2.2539 | 0.5214	2.6723 | 0.4450	2.6208 | 0.4538
1st quartile	Referent	Referent	Referent
2nd quartile	0.865(0.693-1.080)	0.857 (0.686 – 1.072)	0.859 (0.687 -1.074)
3rd quartile	0.903(0.710-1.161)	0.912 (0.707 – 1.175)	0.913 (0.708 -1.176)
4th quartile	0.982(0.735-1.313)	1.001 (0.747 – 1.340)	1.002 (0.748 – 1.342)
Rural/urban area code			
F-statistics| P value	6.5691 | 0.5838	5.7657 | 0.6735	5.0398 | 0.7533
SEER area			
F-statistics| P value	13.4020 | 0.4951	10.0844 | 0.7560	11.4333 | 0.6517
Year of Diagnosis			
F-statistics| P value	12.0497 | 0.2817	10.1056 | 0.4313	10.1565 | 0.4269

*P<0.05

#Model 1 only includes control variables.

‡Model 2 includes quartiles of access variables and control variables.

+Model 3 includes continuous access variables and control variables.

| OR: odds ratio; ‖ CI: confidence interval.

Control variables: patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.

Table I-2 shows the results from the logistic regression models for the age subgroup of 66-69 years old. Model 1 does not include access variables, which is used to examine the association between covariates and chemotherapy choice. Model 2 includes all the covariates in Model 1 and access indicator variables measured based on the quartiles of access variables. Model 3 includes all the covariates in Model 1 and access continuous variables.

In Model 1 without access variables, results showed race was significantly associated with chemotherapy choice. African American women were slightly less likely to get chemotherapy. However, when adding access variables in Model 2 and Model 3, this difference in getting chemotherapy for African American women seemed to be eliminated. Single women were less likely to choose chemotherapy than women who were married at diagnosis. Consistent with univariate analysis, HR status was significantly associated with chemotherapy choice. HR- subgroup had higher odds of chemotherapy use than HR+ and unknown HR status subgroup. Elderly patients who had at least one comorbid condition were less likely to choose chemotherapy than those without comorbidities. There were no associations between census tract income/education level and chemotherapy choice. Neither does any association exist between chemotherapy choice and rural/urban area code of the patient residence, SEER area where the patient lived, or the year of diagnosis.

In Model 2 and 3, results were consistent with access variables measured as either indicator variables or continuous variables. In Model 2, chemotherapy percentage was positively associated with chemotherapy choice controlling for distance to the nearest oncologist practice, local area per capita number of medical oncologists across metastatic cancers, local area per capita number of hospices across metastatic cancers, and other covariates. The odds of chemotherapy use increased with higher treatment rate, with the smallest odds in the first quartile and the biggest odds in the 75 percentile group. In Model 3 when chemotherapy percentage was measured as a continuous variable, Wald

χ^2-statistics confirmed the positive association between chemotherapy percentage and chemotherapy use. Distance to the nearest oncologist practice was not associated with chemotherapy use either as a continuous variable or as indicator variables based on its quartiles. Neither local area per capita number of medical oncologists nor local area per capita number of hospices across metastatic cancers was associated with chemotherapy choice in this age group. Except for the variable race, similar patterns of association between other covariates and chemotherapy choice in Model 1 were observed in Model 2 and 3 with access variables.

Table I-2. Estimates of the Effect of Access to Cancer Care on Chemotherapy Use for Patients Diagnosed with Metastatic Breast Cancer Aged 66-69 and Living in SEER Areas between 1992 and 2002 (N=703)

Variable	Model 1#	Model 2∓	Model 3+
Chemo percentage			
F-statistics| P value		17.5243 | 0.0006*	
1st quartile		Referent	
2nd quartile		1.396(0.864-2.256)	
3rd quartile		1.810(1.084-3.021)	
4th quartile		3.141(1.802-5.475)	
Estimate			0.0475
Wald χ2-statistics| P value			18.7859 | <0.0001*
Distance to the nearest oncologist			
F-statistics| P value		1.2707 | 0.5298	
1st quartile		Referent	
2nd quartile			
3rd quartile		0.812(0.533-1.236)	
4th quartile		1.060(0.664-1.693)	
Estimate			-0.5018
Wald χ2-statistics| P value			1.6450 | 0.1996
Per capita number of medical oncologist			
F-statistics| P value		2.2989 | 0.5127	
1st quartile		Referent	
2nd quartile		0.721(0.429-1.212)	
3rd quartile		0.830(0.483-1.425)	
4th quartile		1.005(0.534-1.891)	
Estimate			-0.00046
Wald χ2-statistics| P value			0.1054 | 0.7454
Per capita number of hospice			
F-statistics| P value		1.5633 | 0.6677	
1st quartile		1.096(0.673-1.786)	
2nd quartile		0.923(0.560-1.521)	
3rd quartile		1.255(0.705-2.233)	
4th quartile			
Estimate			0.00476
Wald χ2-statistics| P value			2.1521 | 0.1424
Race and ethnicity OR (95% CI)			
F-statistics| P value	9.1800 | 0.0102*	8.2692 | 0.0160*	7.0477 | 0.0295
White	Referent	Referent	Referent
Black	0.533(0.302-0.940)	0.611 (0.338 – 1.103)	0.647 (0.362 – 1.159)
Other	1.975(0.931-4.191)	2.291 (1.053 – 4.988)	2.176 (1.001 – 4.732)
Marital status OR (95% CI)			
F-statistics| P value	9.1009 | 0.0280*	9.2243 | 0.0265*	10.3306 | 0.0160*
Single	Referent	Referent	Referent
Married	1.794(1.071-3.003)	1.827 (1.073 – 3.111)	1.876 (1.100 – 3.201)
Divorced/Widowed	1.701(1.013-2.857)	1.731 (1.016 – 2.951)	1.802 (1.056 - 3.075)

Variable	Model 1#	Model 2‡	Model 3+
Unknown	0.630(0.218-1.824)	0.611 (0.205 – 1.819)	0.588 (0.199 – 1.735)
Hormone receptor status OR (95% CI)			
F-statistics| P value	9.7130 | 0.0078*	11.5290 | 0.0031*	10.7001 | 0.0047*
Positive	Referent	Referent	Referent
Negative	1.880(1.258-2.812)	2.017(1.333-3.050)	1.945(1.291 – 2.931)
Unknown	1.445(0.978-2.134)	1.549 (1.038-2.312)	1.543(1.037 – 2.295)
Radiation therapy OR (95% CI)			
F-statistics| P value	1.3134 | 0.2518	1.4393 | 0.2303	1.2303 | 0.2673
No	Referent	Referent	Referent
Yes	0.820(0.585-1.151)	0.808(0.571-1.145)	0.954 (0.819 – 1.111)
Comorbidities OR (95% CI)			
F-statistics| P value	9.5748 | 0.0020*	10.1659 | 0.0014*	10.9701 | 0.0009*
No	Referent	Referent	Referent
Yes	0.505(0.328-0.779)	0.485 (0.311 – 0.757)	0.473(0.303 – 0.736)
Census tract income OR (95% CI)			
F-statistics| P value	1.7231 | 0.7865	2.5484 | 0.6360	2.5263 | 0.6399
1st quartile	Referent	Referent	Referent
2nd quartile	0.862(0.507-1.465)	0.789 (0.456 – 1.364)	0.780 (0.454 – 1.340)
3rd quartile	0.728(0.406-1.304)	0.658 (0.362 – 1.195)	0.651 (0.359 – 1.180)
4th quartile	0.841(0.425-1.663)	0.662 (0.326 – 1.345)	0.651 (0.322 – 1.318)
Unknown	1.645(0.229-11.788)	1.471(0.192 – 1.270)	1.270 (0.172 – 9.375)
Census tract % non-high edu. OR(95% CI)			
F-statistics| P value	0.9963 | 0.8021	1.8898 | 0.5956	1.8192 | 0.6108
1st quartile	Referent	Referent	Referent
2nd quartile	1.089(0.650-1.823)	1.132(0.662-1.937)	1.123 (0.662 -1.905)
3rd quartile	1.150(0.641-2.063)	1.208(0.660-2.210)	1.220 (0.670 -2.219)
4th quartile	0.905(0.459-1.785)	0.863(0.428-1.741)	0.877 (0.439 – 1.755)
Rural/urban area code			
F-statistics| P value	5.9262 | 0.6555	7.7835 | 0.4549	6.8812 | 0.5495
SEER area			
F-statistics| P value	23.9920 | 0.0459*	23.5628 | 0.0517	24.1229 | 0.0443*
Year of Diagnosis			
F-statistics| P value	3.0976 | 0.9790	4.6893 | 0.9109	4.3219 | 0.9317

*P<0.05

#Model 1 only includes control variables.

‡ Model 2 includes quartiles of access variables and control variables.

+Model 3 includes continuous access variables and control variables.

| OR: odds ratio; ‖ CI: confidence interval.

Control variables: patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.

Table I-3 shows the results from the logistic regression models for the age subgroup of 70-74 years old. Model 1 does not include access variables, which is used to examine the association between covariates and chemotherapy choice. Model 2 includes all the covariates in Model 1 and access indicator variables measured based on the quartiles of access variables. Model 3 includes all the covariates in Model 1 and access continuous variables.

In Model 1 without access variables, results showed that race was not significantly associated with chemotherapy choice in this age subgroup. Single women were less likely to choose chemotherapy than women who were married at diagnosis. Consistent with univariate analysis, HR status was significantly associated with chemotherapy choice. HR- subgroup had higher odds of chemotherapy use than HR+ and unknown HR status subgroup. Elderly patients who had at least one comorbid condition were less likely to choose chemotherapy than those without comorbidities. There were no associations between census tract education level and chemotherapy choice. Neither does any association exist between chemotherapy choice and rural/urban area code of the patient residence, SEER area where the patient lived, or the year of diagnosis.

In Model 2 and 3, results were consistent with access variables measured as either indicator variables or continuous variables. In Model 2, chemotherapy percentage was positively associated with chemotherapy choice controlling for distance to the nearest oncologist practice, local area per capita number of medical oncologists across metastatic cancers, local area per capita number of hospices across metastatic cancers, and other covariates. The odds of chemotherapy use increased with higher treatment rate, with the smallest odds in the first quartile and the biggest odds in the 75 percentile group. In Model 3 when chemotherapy percentage was measured as a continuous variable, Wald χ^2-statistics confirmed the positive association between chemotherapy percentage and chemotherapy use. Distance to the nearest oncologist practice was not associated with chemotherapy use either as a continuous variable or as indicator variables based on its

quartiles. Neither local area per capita number of medical oncologists nor local area per capita number of hospices across cancers was associated with chemotherapy choice in this age group. Similar patterns of association between other covariates and chemotherapy choice in Model 1 were observed in Model 2 and 3 with access variables.

Table I-3. Estimates of the Effects of Access to Cancer Care on Chemotherapy Use for Patients Diagnosed with Metastatic Breast Cancer Aged 70-74 and Living in SEER Areas between 1992 and 2002 (N=1042)

Variable	Model 1#	Model 2ǂ	Model 3+
Chemo percentage			
F-statistics| P value		7.2028 | 0.0657	
1st quartile		Referent	
2nd quartile		1.354(0.901-2.033)	
3rd quartile		1.651(1.089-2.503)	
4th quartile		1.689(1.104-2.585)	
Estimate			0.0311
Wald χ2-statistics | P value			11.9329 | 0.0006*
Distance to the nearest oncologist			
F-statistics| P value		0.7390 | 0.6911	
1st quartile		Referent	
2nd quartile			
3rd quartile		1.088(0.783-1.513)	
4th quartile		0.910(0.628-1.320)	
Estimate			-0.2561
Wald χ2-statistics | P value			0.5819 | 0.4456
Per capita number of medical oncologist			
F-statistics| P value		3.2381 | 0.3563	
1st quartile		Referent	
2nd quartile		0.837(0.550-1.273)	
3rd quartile		0.728(0.467-1.137)	
4th quartile		0.630(0.374-1.060)	
Estimate			-0.00114
Wald χ2-statistics | P value			0.8358 | 0.3606
Per capita number of hospice			
F-statistics| P value		2.1827 | 0.5354	
1st quartile		1.097(0.729-1.652)	
2nd quartile		1.343(0.876-2.058)	
3rd quartile		1.098(0.688-1.752)	
4th quartile			
Estimate			-0.00026
Wald χ2-statistics | P value			0.0087 | 0.9256
Race and ethnicity OR (95% CI)			
F-statistics| P value	1.6881 | 0.4300	0.9824 | 0.6119	1.0291 | 0.5978
White	Referent	Referent	Referent
Black	0.828(0.515-1.331)	0.883 (0.546 – 1.429)	0.880 (0.546 – 1.419)
Other	0.772(0.410-1.271)	0.764 (0.429 – 1.362)	0.761 (0.428 – 1.355)
Marital status OR (95% CI)			
F-statistics| P value	12.9270 | 0.0048*	12.3212 | 0.0064*	12.6250 | 0.0055*
Single	Referent	Referent	Referent
Married	2.196(1.379-3.498)	2.134 (1.334 – 3.416)	2.158(1.350-3.452)
Divorced/Widowed	1.589(1.008-2.507)	1.517 (0.957 – 2.406)	1.543 (0.975 – 2.443)

Variable	Model 1#	Model 2‡	Model 3+
Unknown	2.341(1.055-5.196)	2.267 (1.014 – 5.069)	2.351 (1.056 – 5.234)
Hormone receptor status OR (95% CI)			
F-statistics| P value	19.5454 | <0.0001*	19.7797 | <0.0001*	20.5587 | <0.0001*
Positive	Referent	Referent	Referent
Negative	1.790(1.280-2.504)	1.853(1.316-2.608)	1.873(1.332 – 2.634)
Unknown	0.891(0.646-1.229)	0.917 (0.663-1.269)	0.917(0.663 – 1.269)
Radiation therapy OR (95% CI)			
F-statistics| P value	2.0749 | 0.1497	1.9533 | 0.1622	1.9039 | 0.1676
No	Referent	Referent	Referent
Yes	0.813(0.613-1.078)	0.816(0.614-1.085)	0.819 (0.616 – 1.088)
Comorbidities OR (95% CI)			
F-statistics| P value	9.9489 | 0.0016*	10.8455 | 0.0010*	11.0656 | 0.0009*
No	Referent	Referent	Referent
Yes	0.585(0.419-0.816)	0.565 (0.403 – 0.794)	0.563(0.402 – 0.790)
Census tract income OR (95% CI)			
F-statistics| P value	9.0260 | 0.0605	9.7660 | 0.0446*	10.5791 | 0.0317*
1st quartile	Referent	Referent	Referent
2nd quartile	1.244(0.816-1.899)	1.166(0.757-1.795)	1.162 (0.758 – 1.782)
3rd quartile	1.419(0.866-2.325)	1.293(0.781-2.139)	1.291 (0.782 – 2.130)
4th quartile	0.771(0.427-1.391)	0.662(0.361-1.215)	0.642 (0.351 – 1.175)
Unknown	0.732(0.053-10.018)	0.521(0.037-7.428)	0.519 (0.038 – 7.186)
Census tract % non-high edu. OR (95% CI)			
F-statistics| P value	4.5760 | 0.2056	5.2467 | 0.1546	5.2758 | 0.1527
1st quartile	Referent	Referent	Referent
2nd quartile	0.648(0.425-0.988)	0.628(0.409-0.964)	0.627 (0.409 -0.961)
3rd quartile	0.672(0.414-1.091)	0.640(0.391-1.047)	0.654 (0.401 -1.067)
4th quartile	0.771(0.445-1.336)	0.753(0.430-1.318)	0.771 (0.441 -1.347)
Rural/urban area code			
F-statistics| P value	6.4126 | 0.6011	5.0808 | 0.7489	5.2787 | 0.7274
SEER area			
F-statistics| P value	11.5033 | 0.6461	12.3317 | 0.5797	12.0949 | 0.5987
Year of Diagnosis			
F-statistics| P value	4.5651 | 0.9183	4.1783 | 0.9389	4.3469 | 0.9303

*P<0.05

#Model 1 only includes control variables.

‡ Model 2 includes quartiles of access variables and control variables.

+Model 3 includes continuous access variables and control variables.

| OR: odds ratio; ‖ CI: confidence interval.

Control variables: patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.

Table I-4 shows the results from the logistic regression models for the age subgroup of 75-79 years old. Model 1 does not include access variables, which is used to examine the association between covariates and chemotherapy choice. Model 2 includes all the covariates in Model 1 and access indicator variables measured based on the quartiles of access variables. Model 3 includes all the covariates in Model 1 and access continuous variables.

In Model 1 without access variables, results showed that race was not significantly associated with chemotherapy choice in this age subgroup. Single women were less likely to choose chemotherapy than women who were married at diagnosis. Consistent with univariate analysis, HR status was significantly associated with chemotherapy choice. HR- subgroup had higher odds of chemotherapy use than HR+ and unknown HR status subgroup. Elderly patients who had at least one comorbid condition were less likely to choose chemotherapy than those without comorbidities. There were no associations between census tract income/education level and chemotherapy choice. Neither does any association exist between chemotherapy choice and rural/urban area code of the patient residence, SEER area where the patient lived, or the year of diagnosis.

In Model 2 and 3, results were consistent with access variables measured as either indicator variables or continuous variables. In Model 2, chemotherapy percentage was positively associated with chemotherapy choice controlling for distance to the nearest oncologist practice, local area per capita number of medical oncologists, local area per capita number of hospices, and other covariates. The odds of chemotherapy use increased with higher treatment rate, with the smallest odds in the first quartile and the biggest odds in the 75 percentile group. In Model 3 when chemotherapy percentage was measured as a continuous variable, Wald χ^2-statistics confirmed the positive association between chemotherapy percentage and chemotherapy use. Distance to the nearest oncologist practice was not associated with chemotherapy use either as a continuous variable or as indicator variables based on its quartiles. Neither local area per capita number of medical

oncologists nor local area per capita number of hospices across metastatic cancers was associated with chemotherapy choice in this age group. Similar patterns of association between other covariates and chemotherapy choice in Model 1 were observed in Model 2 and 3 with access variables.

Table I-4. Estimates of the Effects of Access to Cancer Care on Chemotherapy Use for Patients Diagnosed with Metastatic Breast Cancer Aged 75-79 and Living in SEER Areas between 1992 and 2002 (N=1003)

Variable	Model 1#	Model 2∓	Model 3+
Chemo percentage			
F-statistics| P value		13.0791 | 0.0045*	
1st quartile		Referent	
2nd quartile		1.313(0.829-2.080)	
3rd quartile		1.936(1.217-3.080)	
4th quartile		2.214(1.355-3.619)	
Estimate			0.0338
Wald χ2-statistics | P value			11.9315 | 0.0006*
Distance to the nearest oncologist			
F-statistics| P value		0.8027 | 0.6694	
1st quartile		Referent	
2nd quartile			
3rd quartile		0.979(0.683-1.403)	
4th quartile		0.820(0.528-1.273)	
Estimate			-0.7366
Wald χ2-statistics | P value			3.7901 | 0.0516
Per capita number of medical oncologist			
F-statistics| P value		2.5282 | 0.4702	
1st quartile		Referent	
2nd quartile		0.807(0.520-1.253)	
3rd quartile		0.732(0.460-1.165)	
4th quartile		0.938(0.551-1.596)	
Estimate			-0.00054
Wald χ2-statistics | P value			0.1829 | 0.6689
Per capita number of hospice			
F-statistics| P value		1.4207 | 0.7007	
1st quartile		0.898(0.587-1.375)	
2nd quartile		0.840(0.530-1.332)	
3rd quartile		0.737(0.444-1.225)	
4th quartile			
Estimate			-0.00235
Wald χ2-statistics | P value			0.5301 | 0.4666
Race and ethnicity OR (95% CI)			
F-statistics| P value	3.2660 | 0.1953	5.9918 | 0.0500	5.3490 | 0.0689
White	Referent	Referent	Referent
Black	1.580(0.962-2.598)	1.906 (1.133 -3.207)	1.820 (1.094 -3.028)
Other	1.059(0.525-2.136)	0.997 (0.485 -2.048)	1.055 (0.518 – 2.148)
Marital status OR (95% CI)			
F-statistics| P value	10.6320 | 0.0139*	11.4605 | 0.0095*	12.3248 | 0.0063*
Single	Referent	Referent	Referent
Married	1.643(0.955-2.829)	1.563 (0.902 – 2.710)	1.533(0.887-2.652)
Divorced/Widowed	0.987(0.583-1.670)	0.904 (0.530 – 1.542)	0.869(0.510 -1.482)

Unknown	1.197(0.474-3.025)	1.204 (0.469 – 3.090)	1.187 (0.467 -3.018)
Hormone receptor status OR (95% CI)			
F-statistics| P value	31.3047 | <0.0001*	31.2587 | <0.0001*	31.5095 | <0.0001*
Positive	Referent	Referent	Referent
Negative	2.196(1.529-3.156)	2.256(1.560-3.262)	2.270(1.573 – 3.277)
Unknown	0.841(0.594-1.190)	0.858 (0.603-1.221)	0.866(0.609 – 1.231)
Radiation therapy OR (95% CI)			
F-statistics| P value	0.2621 | 0.6087	0.1686 | 0.6814	0.0694 | 0.7923
No	Referent	Referent	Referent
Yes	1.082(0.800-1.463)	1.066(0.784-1.450)	1.042 (0.768-1.414)
Comorbidities OR (95% CI)			
F-statistics| P value	5.3815 | 0.0204*	5.4595 | 0.0195*	5.2671 | 0.0217*
No	Referent	Referent	Referent
Yes	0.670(0.478-0.940)	0.663 (0.470 – 0.936)	0.670(0.476 – 0.943)
Census tract income OR (95% CI)			
F-statistics| P value	6.9057 | 0.1410	5.8263 | 0.2125	6.2875 | 0.1787
1st quartile	Referent	Referent	Referent
2nd quartile	1.657(1.030-2.665)	1.648(1.015-2.675)	1.620 (1.000 – 2.625)
3rd quartile	1.902(1.113-3.251)	1.824(1.052-3.164)	1.841 (1.065 – 3.184)
4th quartile	1.874(1.022-3.436)	1.731(0.932-3.216)	1.715 (0.926 – 3.175)
Unknown	3.673(0.605-22.288)	3.232(0.526-19.870)	4.006 (0.664 -24.187)
Census tract % non-high edu. OR (95% CI)			
F-statistics| P value	1.8564 | 0.6027	2.4214 | 0.4897	2.2981 | 0.5129
1st quartile	Referent	Referent	Referent
2nd quartile	1.125(0.719-1.761)	1.082(0.686-1.704)	1.101 (0.701 -1.731)
3rd quartile	1.259(0.762-2.078)	1.233(0.743-2.045)	1.243 (0.750 -2.058)
4th quartile	1.492(0.831-2.679)	1.565(0.865-2.833)	1.555 (0.862 -2.807)
Rural/urban area code			
F-statistics| P value	4.9434 | 0.7636	5.0291 | 0.7545	5.4378 | 0.7099
SEER area			
F-statistics| P value	6.3108 | 0.9341	9.4571 | 0.7376	8.9749 | 0.7748
Year of Diagnosis			
F-statistics| P value	12.0592 | 0.2811	12.0030 | 0.2849	11.4410 | 0.3242

*P<0.05

#Model 1 only includes control variables.

‡ Model 2 includes quartiles of access variables and control variables.

+Model 3 includes continuous access variables and control variables.

| OR: odds ratio; ‖ CI: confidence interval.

Control variables: patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.

Table I-5 shows the results from the logistic regression models for the age subgroup of 80-84 years old. Model 1 does not include access variables, which is used to examine the association between covariates and chemotherapy choice. Model 2 includes all the covariates in Model 1 and access indicator variables measured based on the quartiles of access variables. Model 3 includes all the covariates in Model 1 and access continuous variables.

In Model 1 without access variables, results showed that HR status was the only variable significantly associated with chemotherapy choice. HR- subgroup had higher odds of chemotherapy use than HR+ and unknown HR status subgroup. None of other covariates, including race, marital status, radiation therapy utilization, comorbidities, census tract income and education level, rural/urban area code of the patient residence, SEER area where the patient lived, or the year of diagnosis, was associated with chemotherapy use.

In Model 2 and 3 shows the results adding access variables measured as either indicator variables or continuous variables. In Model 2, chemotherapy percentage was positively associated with chemotherapy choice controlling for other access variables and covariates. But the association between chemotherapy percentage and chemotherapy use was not confirmed in Model 3 when chemotherapy percentage was measured as a continuous variable. None of the other three access variables were associated with chemotherapy choice. Among the covariates, similar with the results from Model 1, only HR status was consistently associated with chemotherapy choice in both Model 2 and Model 3.

Table I-5. Estimates of the Effects of Access to Cancer Care (Based on Travel Time) on Chemotherapy Use for Patients Diagnosed with Metastatic Breast Cancer Aged 80-84 and Living in SEER Areas between 1992 and 2002 (N=816)

Variable	Model 1#	Model 2∓	Model 3+
Chemo percentage			
F-statistics | P value		4.5978 | 0.2037	
1st quartile		Referent	
2nd quartile		1.801(0.986-3.289)	
3rd quartile		1.221(0.640-2.327)	
4th quartile		1.578 (0.835-2.983)	
Estimate			0.0170
Wald χ2-statistics | P value			1.7658 | 0.1839
Distance to the nearest oncologist			
F-statistics | P value		2.3470 | 0.3093	
1st quartile		Referent	
2nd quartile			
3rd quartile		0.758 (0.472-1.217)	
4th quartile		0.671 (0.367-1.225)	
Estimate			-0.9437
Wald χ2-statistics | P value			2.4423 | 0.1181
Per capita number of medical oncologist			
F-statistics | P value		3.6864 | 0.2974	
1st quartile		Referent	
2nd quartile		1.319 (0.722-2.407)	
3rd quartile		1.024 (0.535-1.958)	
4th quartile		0.690 (0.305-1.558)	
Estimate			-0.00188
Wald χ2-statistics | P value			0.9302 | 0.3348
Per capita number of hospice			
F-statistics | P value		3.6446 | 0.3025	
1st quartile		0.769 (0.428-1.381)	
2nd quartile		0.902 (0.491-1.659)	
3rd quartile		1.368 (0.707-2.646)	
4th quartile			
Estimate			0.00672
Wald χ2-statistics | P value			2.1404 | 0.1435
Race and ethnicity OR (95% CI)			
F-statistics | P value	0.3356 | 0.8455	1.1318 | 0.5679	0.6502 | 0.7224
White	Referent	Referent	Referent
Black	1.216(0.582-2.540)	1.505 (0.704 -3.214)	1.348 (0.642 -2.832)
Other	1.153(0.485-2.743)	1.125 (0.464 -2.726)	1.125 (0.469 – 2.698)
Marital status OR (95% CI)			
F-statistics | P value	4.3898 | 0.2223	3.8500 | 0.2781	4.4078 | 0.2207
Single	Referent	Referent	Referent
Married	1.613(0.754-3.449)	1.639 (0.758 – 3.544)	1.158(0.565-2.373)
Divorced/Widowed	1.118(0.548-2.279)	1.150 (0.558 – 2.369)	1.683(0.783 -3.618)

Variable	Model 1#	Model 2‡	Model 3+
Unknown	2.084(0.708-6.130)	2.010 (0.671 – 6.024)	2.086 (0.705 -6.171)
Hormone receptor status OR (95% CI)			
F-statistics | P value	8.9525 | 0.0114*	7.3220 | 0.0257*	8.2595 | 0.0161*
Positive	Referent	Referent	Referent
Negative	1.719(1.036-2.853)	1.604 (0.955-2.694)	1.664(0.996 – 2.779)
Unknown	0.850(0.528-1.369)	0.832 (0.512-1.351)	0.838(0.518 – 1.355)
Radiation therapy OR (95% CI)			
F-statistics | P value	0.3897 | 0.5325	0.5179 | 0.4717	0.3015 | 0.5829
No	Referent	Referent	Referent
Yes	1.140(0.755-1.721)	1.166(0.767-1.773)	1.123 (0.742-1.702)
Comorbidities OR (95% CI)			
F-statistics | P value	0.1807 | 0.6708	0.1298 | 0.7186	0.2137 | 0.6439
No	Referent	Referent	Referent
Yes	0.912(0.595-1.397)	0.923 (0.595 – 1.430)	0.903(0.587 –1.390)
Census tract income OR (95% CI)			
F-statistics | P value	3.2758 | 0.5128	3.0230 | 0.5540	3.1988 | 0.5251
1st quartile	Referent	Referent	Referent
2nd quartile	0.825(0.436-1.560)	0.840(0.438 -1.614)	0.793 (0.416 – 1.512)
3rd quartile	1.314(0.640-2.698)	1.357 (0.652-2.826)	1.266 (0.611 – 2.623)
4th quartile	0.887(0.387-2.031)	0.945(0.403-2.217)	0.866 (0.373 – 2.009)
Census tract % non-high edu. OR (95% CI)			
F-statistics | P value	1.6205 | 0.6547	2.2236 | 0.5273	1.7799 | 0.6193
1st quartile	Referent	Referent	Referent
2nd quartile	0.953(0.541-1.682)	0.989 (0.554-1.766)	0.980 (0.555 -1.731)
3rd quartile	0.669(0.330-1.357)	0.640 (0.310-1.321)	0.669 (0.328 -1.364)
4th quartile	0.857(0.385-1.907)	0.891(0.395-2.011)	0.891 (0.398 -1.993)
Rural/urban area code			
F-statistics | P value	5.2747 | 0.7279	6.8550 | 0.5524	7.1503 | 0.5205
SEER area			
F-statistics | P value	4.9407 | 0.9866	4.4438 | 0.9921	4.9381 | 0.9867
Year of Diagnosis			
F-statistics | P value	10.1232 | 0.4297	9.7226 | 0.4652	10.5425 | 0.3942

*P<0.05

#Model 1 only includes control variables.

‡ Model 2 includes quartiles of access variables and control variables.

+Model 3 includes continuous access variables and control variables.

| OR: odds ratio; ‖ CI: confidence interval.

Control variables: patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.

Table I-6 shows the results from the logistic regression models for the age subgroup of 85+ years old. Model 1 does not include access variables, which is used to examine the association between covariates and chemotherapy choice. Model 2 includes all the covariates in Model 1 and access indicator variables measured based on the quartiles of access variables. Model 3 includes all the covariates in Model 1 and access continuous variables.

In Model 1 without access variables, results were consistent with previous models. It seems that African American women were more likely to get chemotherapy in this age group. This difference in the odds of getting chemotherapy remained after adding access variables in Model 2 and Model 3. HR status was significantly associated with chemotherapy choice. HR- subgroup had higher odds of chemotherapy use than HR+ and unknown HR status subgroup. Elderly patients who had at least one comorbid condition had lower odds of getting chemotherapy than those without comorbidities. Other covariates, including marital status, radiation therapy utilization, census tract income and education level, rural/urban area code of the patient residence, SEER area where the patient lived, and the year of diagnosis, were not associated with chemotherapy use.

Model 2 and Model 3 show the results adding access variables measured as either indicator variables or continuous variables. Local area chemotherapy percentage across metastatic cancers was positively associated with chemotherapy choice as a continuous variable. In addition, local area per capita number of medical oncologists was significantly negatively associated with chemotherapy choice. Although the signs of the effect of the number of medical oncologists were also negative in other age subgroups, the significant effect of per capita number of medical oncologists on chemotherapy choice has not been observed in other subgroup analysis. The other two access variables, including distance to the nearest oncologist practice and local area per capita number of hospices across metastatic cancers, were not associated with chemotherapy choice. Similar patterns of the association between covariates, including race, HR status, and

comorbidities, and chemotherapy choice in Model 1 were found in both Model 2 and Model 3.

Because few patients with certain characteristics existed in this age group, coefficients for several indicator variables cannot be obtained, including rural Georgia, Utah, unknown marital status, and unknown census tract income/education level. More logistic regressions were performed after merging rural Georgia with Kentucky, Utah with Detroit, and eliminating observations with unknown marital status and unknown census tract income/education level. The results were consistent.

Table I-6. Estimates of the Effects of Access to Cancer Care on Chemotherapy Use for Patients Diagnosed with Metastatic Breast Cancer Aged 85+ and Living in SEER Areas between 1992 and 2002 (N=720)

Variable	Model 1#	Model 2∓	Model 3+
Chemo percentage			
F-statistics | P value		6.6024 | 0.0857	
1st quartile		Referent	
2nd quartile		1.635(0.562-4.757)	
3rd quartile		2.718(0.899-8.216)	
4th quartile		3.865(1.296-11.525)	
Estimate			0.0437
Wald χ2-statistics | P value			4.9721 | 0.0258*
Distance to the nearest oncologist			
F-statistics | P value		9.7722 | 0.0076*	
1st quartile		Referent	
2nd quartile			
3rd quartile		0.212(0.080-0.560)	
4th quartile		0.668(0.246-1.816)	
Estimate			-0.1153
Wald χ2-statistics | P value			0.0151 | 0.9022
Per capita number of medical oncologist			
F-statistics | P value		7.9858 | 0.0463*	
1st quartile		Referent	
2nd quartile		0.573(0.209-1.569)	
3rd quartile		0.237(0.069-0.813)	
4th quartile		0.174(0.042-0.724)	
Estimate			-0.00778
Wald χ2-statistics | P value			4.8492 | 0.0277*
Per capita number of hospice			
F-statistics | P value		10.4867 | 0.0149*	
1st quartile		5.847(1.984-17.230)	
2nd quartile		3.361(1.036-10.903)	
3rd quartile		4.684(1.326-16.548)	
4th quartile			
Estimate			0.00477
Wald χ2-statistics | P value			0.8230 | 0.3643
Race and ethnicity OR (95% CI)			
F-statistics | P value	7.4001 | 0.0247*	9.1082 | 0.0105*	8.1497 | 0.0170*
White	Referent	Referent	Referent
Black	2.805(0.846-9.305)	4.572 (1.271 -16.445)	3.512 (1.031 -11.967)
Other	4.567(1.317-15.839)	4.920 (1.316 -18.402)	4.544(1.273 –16.217)
Marital status OR (95% CI)			
F-statistics | P value	0.0394 | 0.9979	1.6954 | 0.6382	0.6529 | 0.8842
Single	Referent	Referent	Referent
Married	0.939(0.289-3.055)	0.496 (0.129 – 1.901)	0.682(0.255-1.822)
Divorced/Widowed	0.911(0.350-2.372)	0.501 (0.174 – 1.437)	0.633(0.180 -2.219)

Hormone receptor status OR (95% CI)			
F-statistics | P value	9.7664 | 0.0076*	8.7854 | 0.0124*	9.0372 | 0.0109*
Positive	Referent	Referent	Referent
Negative	1.651(0.759-3.588)	1.857(0.810-4.259)	1.509(0.682 – 3.341)
Unknown	0.536(0.258-1.113)	0.572 (0.261-1.256)	0.504(0.238 – 1.067)
Radiation therapy OR (95% CI)			
F-statistics | P value	1.6732 | 0.1958	5.3771 | 0.0204*	2.2111 | 0.1370
No	Referent	Referent	Referent
Yes	1.529(0.803-2.911)	2.349(1.141-4.836)	1.652 (0.852-3.200)
Comorbidities OR (95% CI)			
F-statistics | P value	5.1719 | 0.023*	6.7367 | 0.0094*	5.1343 | 0.0235*
No	Referent	Referent	Referent
Yes	0.413(0.192-0.885)	0.333 (0.145 – 0.764)	0.409(0.189 –0.886)
Census tract income OR (95% CI)			
F-statistics | P value	3.7503 | 0.4408	4.4653 | 0.3467	2.9802 | 0.5611
1st quartile	Referent	Referent	Referent
2nd quartile	0.825(0.436-1.560)	0.559(0.143-2.192)	0.903 (0.263 – 3.103)
3rd quartile	1.314(0.640-2.698)	1.611(0.413-6.284)	2.006 (0.564 – 7.136)
4th quartile	0.887(0.387-2.031)	1.766(0.367-8.497)	2.025 (0.472 – 8.691)
Census tract % non-high edu. OR (95% CI)			
F-statistics | P value	3.1958 | 0.3624	3.4195 | 0.3314	3.3996 | 0.3340
1st quartile	Referent	Referent	Referent
2nd quartile	1.012(0.301-3.400)	0.486(0.189-1.248)	0.542 (0.221 -1.329)
3rd quartile	2.330(0.676-8.036)	0.417(0.128-1.360)	0.429 (0.139 -1.319)
4th quartile	2.322(0.556-9.693)	0.797(0.196-3.233)	0.893 (0.243 -3.277)
Rural/urban area code			
F-statistics | P value	6.4421 | 0.5978	4.4411 | 0.8153	6.3938 | 0.6032
SEER area			
F-statistics | P value	5.7322 | 0.9554	9.3210 | 0.7483	6.0928 | 0.9427
Year of Diagnosis			
F-statistics | P value	12.3464 | 0.2625	12.7841 | 0.2360	12.5149 | 0.2521

*P<0.05

#Model 1 only includes control variables.

‡ Model 2 includes quartiles of access variables and control variables.

+Model 3 includes continuous access variables and control variables.

| OR: odds ratio; ‖ CI: confidence interval.

Control variables: patient race, marital status, HR status, radiation therapy use, census tract median household income and education level, residency urban/rural characteristics, residency SEER area, and diagnosis year.

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