RURAL-URBAN DISPARITIES IN STAGE AT DIAGNOSIS AND TREATMENT OF BREAST CANCER AND THE INFLUENCE OF GEOGRAPHICAL LEVEL CHARACTERISTICS

A Dissertation

by

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ABSTRACT

This dissertation used multilevel regression methods to explore rural-urban disparities in stage at diagnosis of, and treatment of early-stage breast cancer among women diagnosed between 1995 and 2012, and whether other geographical characteristics explained these disparities. Trends in probability of late-stage diagnosis and treatment were explored.

The Surveillance, Epidemiology and Ends Results data was used to explore rural-urban disparities in stage at diagnosis of breast cancer and whether county poverty estimates explain these disparities. Compared to urban metropolitan residents, rural residents had higher odds of late-stage diagnosis (OR=1.09; CI= 1.03-1.15). County poverty explained the association between late stage diagnosis and urban non-metropolitan (UNM) but not rural residence. Across all years, the probability of late-stage diagnosis was highest for residents of rural high poverty areas.

The Texas Cancer Registry (TCR) was utilized to explore rural-urban disparities in stage at diagnosis, and whether racial residential segregation, census tract (CT) poverty and travel distance to the nearest primary care provider (PCP) explained these disparities. Compared to urban metropolitan residents, residents of UNM residents had higher odds of late-stage diagnosis (OR=1.08; 95% CI=1.03 -1.13). Racial residential segregation, CT poverty and distance to the nearest PCP did not explain residential disparities. Residents of UNM high CT poverty areas had the highest probability of late-stage diagnosis across all years.

The TCR was also used to explore rural-urban disparities in surgical treatment, type of surgery and adjuvant radiotherapy, and whether CT poverty and residential segregation explained these disparities. Compared to urban metropolitan residents, UNM residents had higher odds of having surgery (OR=1.39; 95%=1.27-1.53) and mastectomy (OR=1.18; 95%=1.12-1.25); UNM (OR=1.16; 95%=1.01-1.34) and rural (OR=1.66; 95% CI=1.12-2.44) residents had higher odds of adjuvant radiotherapy. CT poverty and racial residential segregation explained the association between rural residence and surgical treatment. Across all years, residents of urban metropolitan high poverty CT had the lowest probability of being treated surgically and with adjuvant radiotherapy, and the highest probability of being treated using mastectomy.

In conclusion, interventions aimed at reducing disparities in breast cancer diagnosis and treatment should be guided by both residence and area poverty levels.

DEDICATION

Dad and Mum-I can never say thank you enough for your steadfast and unwavering love, prayers, support and godly counsel. You are the best.

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NOMENCLATURE

CT	Census Tract
UNM	Urban non-metropolitan
PCP	Primary care physician
TCR	Texas Cancer Registry
SEER	Surveillance, Epidemiology and Ends Result

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1. INTRODUCTION: OVERVIEW

Breast cancer is the most common type of cancer and the second leading cause of cancer deaths among women in the United States.[1] In the year 2015, about 231,840 new cases of invasive breast cancer and 40,290 breast cancer deaths were projected to occur, accounting for 29% and 15% of cancer incidence and mortality respectively.[1] In the state of Texas about 16,510 new breast cancer cases and 2,710 breast-cancer related deaths were expected to occur.[1] Over 2.9 million women in the U.S were living with breast cancer in 2012.[2]

Breast cancer also has an enormous impact on the economy. In 2010, compared to other cancer types, direct cost of breast cancer care was highest, accounting for $16.5 billion (13%) of total cancer direct cost in the U.S, and it is projected that by 2020 the direct cost of breast cancer will be at least $21.37 billion.[3] Increasing the prevalence of early-stage diagnosis therefore has potential for reducing the economic burden of breast cancer at the individual and the societal level.

Although individual level characteristics such as race[4-7] and insurance status[7,8] have been consistently reported to influence stage at diagnosis of breast cancer, individual factors do not completely explain variations in stage at diagnosis of breast cancer.[9] Researchers have therefore sought to evaluate possible geographical characteristics that may be associated with late-stage breast cancer.

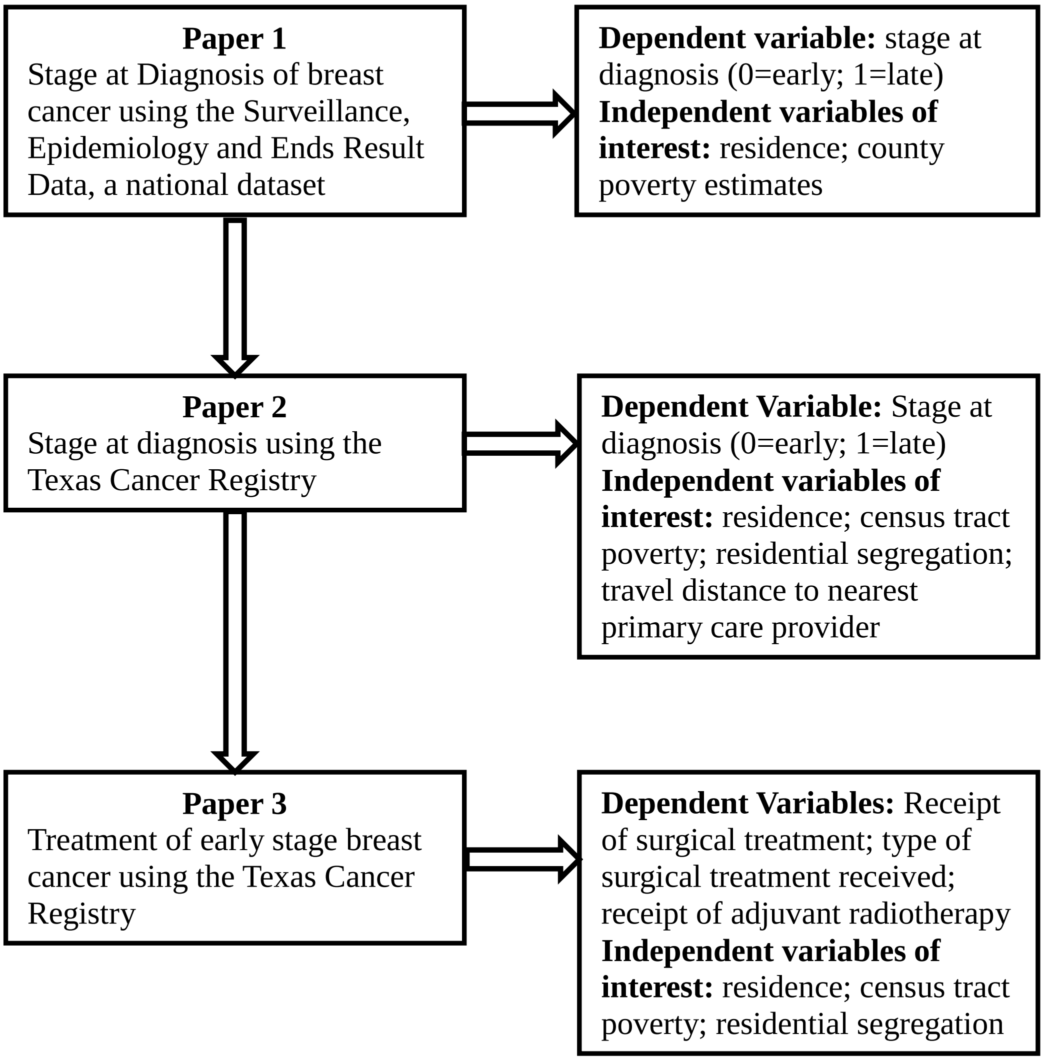
Rural residence is one of the geographical factors that has been associated with late stage diagnosis;[10,11] however, results have been inconsistent. A study reported a reversal, with urban residents having higher risk compared to rural residents[12] while some studies report no difference between urban and rural residents.[13-15] These inconsistencies make it necessary to continue to try to identify the associations between residence and late-stage breast cancer diagnosis, and how these associations may vary across various subpopulations. It is also important to identify possible geographical factors that could mediate residential disparities in stage at diagnosis of breast cancer.

Residential segregation is defined as the physical separation of groups living in an area away from other groups and has been found to be associated with stage at diagnosis of breast cancer,[16,17] it is however not clear whether residential segregation explains rural-urban disparities in stage at diagnosis of breast cancer. It is also not clear whether area poverty levels which have been found to be associated with late-stage breast cancer diagnosis[4,13,18,19] explains rural-urban disparities in stage at diagnosis of breast cancer. Various studies have examined the association between proximity to diagnosing facilities and stage at diagnosis of breast cancer,[9,20] but there is a gap in the literature about whether travel distance to the nearest primary care provider (PCP) is associated with stage at diagnosis of breast cancer. There is also a gap in literature about whether travel distance to nearest PCP explains rural-urban disparities. Since PCPs play a pivotal role in recommending breast cancer screening and explaining results to patients, it is important to identify whether access to PCPs is associated with or explains stage at diagnosis of breast cancer.

In order to maintain the survival advantage of early-stage diagnosis, initiation of appropriate therapy following diagnosis is crucial. Early-stage breast cancer can be treated surgically with mastectomy or breast conserving surgery.[21] Whole breast irradiation is recommended following breast conserving surgery.[21] Studies have found that rural residents have a higher likelihood of inadequate treatment following breast cancer diagnosis.[4,22-24] Residents of areas that are racially segregated have also been found to have an increased likelihood of inadequate therapy.[25] Haas and colleague also found that racial residential segregation mediated the association between race and adequate treatment.[25] The findings by Haas et al indicate that there is a need to understand the influence of residential segregation on other reported breast cancer treatment disparities such as rural-urban residence. It is also important to identify whether area poverty level, which has been associated with inadequate breast cancer treatment [4, 26, 27] explains rural-urban disparities in treatment of breast cancer.

This dissertation aims to bridge the gap in breast cancer research literature by identifying rural-urban disparities in stage-at diagnosis of breast cancer, and treatment of early-stage diagnosis using the three paper approach. Paper 1 utilized the Surveillance, Epidemiology, and Ends Results (SEER) data to provide national estimates of rural-urban disparities in late-stage diagnosis among individuals diagnosed with breast cancer between 1995 and 2012, and explore whether county poverty level explained these disparities. Paper 2 utilized the Texas Cancer Registry (TCR) data to analyze rural-urban disparities in late-stage diagnosis among female residents of Texas diagnosed with breast cancer between 1995 and 2012, and whether census tract (CT) poverty, racial residential segregation and travel distance to the nearest primary health care provider explained these disparities. Finally, paper 3 utilized the Texas Cancer Registry data to analyze disparities in treatment of breast cancer among residents of Texas diagnosed with early-stage breast cancer between 1995 and 2012, and whether CT poverty and residential segregation explains residential disparities. Figure 1-1 gives an overview of the connection and progression of the three papers.

Figure 1-1.Overview and Progression of the Three Papers



2. DOES COUNTY POVERTY LEVEL EXPLAIN RURAL-URBAN DISPARITIES IN LATE-STAGE DIAGNOSIS?

2.1 Introduction

Early-stage diagnosis of breast cancer increases the chances of surviving breast cancer;[2] survival rates for localized breast cancer are 98.6% compared to 24.3% if distant metastasis has occurred.[2] Increasing the incidence of early-stage breast cancer diagnosis is crucial because breast cancer is the most common type of cancer and the second leading cause of cancer deaths among women in United States.[1] In the year 2015, it was projected that about 231,840 new cases of invasive breast cancer and 40,290 breast cancer deaths would occur, accounting for 29% and 15% of all cancer incidence and mortality respectively.[1] Increasing the number of women diagnosed at an early-stage has potential for reducing mortality rates.

Early-stage breast cancer diagnosis also reduces cost of treatment. Using 2000 U.S dollar value, it was reported that the cost effectiveness ratio of treating stage I breast cancer was $1,960 compared to $70,380 for stage IV disease.[28] Decreasing the prevalence of late-stage breast cancer diagnosis could therefore reduce the economic burden of breast cancer, improve compliance with treatment regimen due to cheaper treatment, and potentially, decrease mortality rates. Identifying factors that are associated with late-stage diagnosis and how trends in late-stage diagnosis have varied across socio-demographic groups could aid development of targeted interventions to increase rates of early-stage diagnosis among subpopulations.

In addition to individual level characteristics such as race[29, 22] and ethnicity,[18] geographical-level characteristics such as residence and area poverty level have been found to influence stage-at diagnosis of breast cancer. Rural residence has been associated with significantly increased likelihood of late-stage diagnosis of breast cancer.[10] However some studies have found no associations between rural residence and late-stage breast cancer diagnosis[13,14,22] while another study found that urban residents had a higher likelihood of being diagnosed at a late-stage compared to rural residents.[12] Residents of high poverty areas have also been reported to have a higher likelihood of late-stage diagnosis compared to their counterparts.[13, 19]

Since there are inconsistent research findings regarding the association between residence and stage at diagnosis of breast cancer, it is necessary to continue to explore rural-urban disparities in late-stage breast cancer diagnosis and how these disparities have varied over the years. It is also important to explore whether poverty levels explain the association between residence and late-stage diagnosis.

This study aims to analyze:

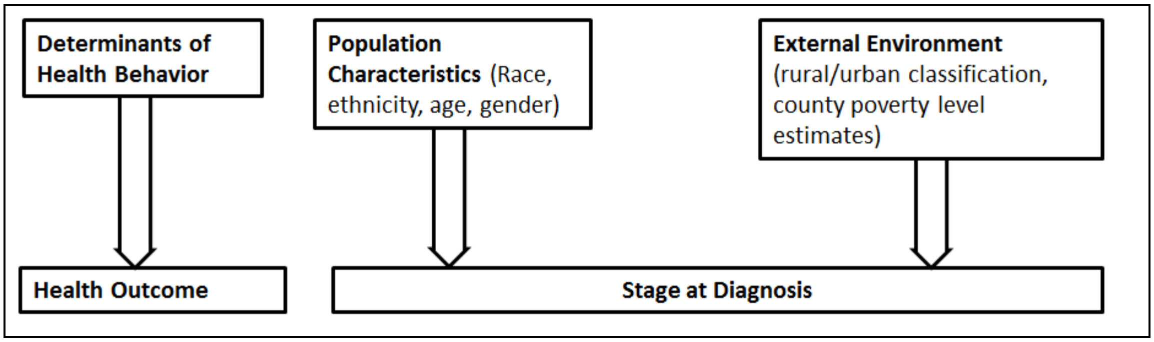
1. The independent association between rural/urban residence and county poverty level, and stage at diagnosis of breast cancer.
2. Whether county poverty level explains rural-urban disparities in stage at diagnosis of breast cancer.
3. The trends in probabilities of receiving a late-stage breast cancer diagnosis by residence and county poverty level for women diagnosed with breast cancer between 1995 and 2012.

This study will add to literature by identifying sub-populations that may be at higher risk for late-stage diagnosis. Any such findings will potentially guide more efficient and effective implementation of interventions. Identifying trends in late-stage diagnosis could also help in crafting and assessing policies and efforts to reduce these disparities.

2.2 Conceptual Framework

The conceptual frame work (Fig. 2-1) for this paper is based upon a modified version of the Andersen behavioral model.[30] Three constructs are identified in the Anderson behavioral model namely: 1) primary determinants of health behavior, 2) health behavior and 3) health outcomes. This paper explores two of the three constructs: 1) primary determinants of health behavior and 2) health outcomes. Primary determinants of health considered include: i) population characteristics such as age, race and ethnicity; and ii) external environmental factors such as rural versus urban residence, and county poverty level estimates. It is expected that these determinants of health will influence health outcome (stage at diagnosis).

Figure 2-1: Conceptual Model of Factors Influencing Stage at Diagnosis of Breast Cancer



2.3 Methods

The SEER data was the primary dataset that was used for this study. Using SEER*Stat software, individual data including residence and county poverty estimates were extracted. The county poverty estimates used were from the 2000 census estimates of percent of individuals living below poverty in a given county. Inclusion criteria for our study were females 18 years and older diagnosed with breast cancer between 1995 and 2012 who had only one primary tumor. Final sample size was 576,022 individuals nested in 612 counties. This study was approved by the Texas A&M Institutional Review Board.

Variables

The dependent variable of interest was stage at diagnosis of breast cancer. In line with previous studies,[22,17,31] the original stage at diagnosis variable was recoded as "0" early (in-situ and localized) and "1" late (regional or distant metastases). Independent variables of interest were residence and proportion of individuals living below poverty level. Covariates were race, ethnicity, marital status, tumor grade, receptor status (estrogen and progesterone), year of diagnosis and age at diagnosis. Rural-urban classification was obtained from the SEER database and is based on the 2003 Rural Urban Continuum Codes (RUCC).[32] The RUCC were condensed into three categories: 1) urban metropolitan (Counties in metro areas of 1 million population or more, counties in metro areas of 250,000 to 1 million population, counties in metro areas of fewer than 250,000 population) 2) urban non-metropolitan (Urban population of 20,000 or more, adjacent to a metro area, Urban population of 20,000 or more, not adjacent to a metro area, Urban population of 2,500 to 19,999, adjacent to a metro area, Urban population of 2,500 to 19,999, not adjacent to a metro area) and rural (Completely rural or less than 2,500 urban population, adjacent to a metro area, Completely rural or less than 2,500 urban population, not adjacent to a metro area). County poverty level were also classified into three categories into low poverty (<9.90% of residents living below poverty level), middle poverty (>9.90-19.90 living below poverty level) and high poverty (>19.90% of residents living below poverty level).[4]

Analytic methods

Descriptive analyses for select independent variables were conducted. Bivariate and multivariate multilevel logistic regression equations were estimated with individuals nested within counties. Three multivariate models were estimated: 1) rural/urban residence adjusting for the covariates without county poverty level 2) rural/urban residence and county poverty level adjusting for the covariates and 3) interaction between rural/urban residence and poverty levels adjusting for the covariates.

The general form of the three-level logistic regression was:

$$\mathbf{Y_{ij} = \gamma 00 + \gamma 01 X_{ij} + \gamma 02 C_j + U0_j}$$

Where Y_{ij}=log of late-stage probability divided by early stage probability for person *i* in county *j*,

γ_{00}=overall intercept for the two level model

i= indexes the individual level

j= indexes the county level

X= A vector of the individual level variables (race, ethnicity, tumor grade, estrogen receptor status, progesterone receptor status, age, and year of diagnosis),

C= A vector of the county level variables (residence, poverty estimates)

U_j = error term at the county level

Exponents of the coefficients (odds ratios) and 95% confidence interval are reported. Following multivariate model estimation, the predicted probabilities of late-stage diagnosis by residence and county poverty level were estimated across all years. All statistical tests were two-sided, and findings were considered statistically significant at $p < 0.05$. All analyses were conducted using Stata 13.1.[33]

2.4 Results

Table 2-1 shows the results of the descriptive analyses. About 82% of the study population were Whites, 10.37% were African Americans, 0.38% were American Indians/Alaskan Natives and 7.29% were Asians/Pacific Islanders. Non-Hispanics comprised 90.45% of the study population while 9.55% were Hispanics. Residents of urban metropolitan areas accounted for 90.45% of the study population, 9.53% were residents of urban non-metropolitan areas and 1.19% were residents of rural areas. About 54% of the study population were residents of middle poverty counties, residents of low poverty counties accounted for 39.50% of the study population while 7.03% of the study population were residents of high poverty counties.

Table 2-1: Descriptive Statistics of Individuals Diagnosed with Breast Cancer between 1995 and 2012: Surveillance, Epidemiology and Ends Results Data (n=576,022)

Variable		Freq.	Percent
Race			
	White	472,089	81.96
	Black	59,717	10.37
	American Indian/Alaska Native	2,197	0.38
	Asian or Pacific Islander	42,019	7.29
Ethnicity			
	non-Hispanic	520,989	90.45
	Hispanic	55,033	9.55
Residence			
	Urban metropolitan area	514,277	89.28
	Urban non-metropolitan area	54,906	9.53
	Rural area	6,839	1.19
Tumor grade			
	low grade	327,302	56.82
	high grade	198,377	34.44
	Unknown	50,343	8.74
Year of diagnosis			
	1995	14,193	2.46
	1996	14,397	2.50
	1997	15,326	2.66
	1998	15,850	2.75
	1999	16,546	2.87
	2000	33,951	5.89
	2001	36,768	6.38
	2002	36,879	6.4
	2003	35,667	6.19
	2004	36,503	6.34
	2005	36,137	6.27
	2006	37,261	6.47
	2007	39,136	6.79
	2008	40,121	6.97
	2009	41,387	7.18

Table 2-1 Continued.

Variable		Freq.	Percent
	2010	40,689	7.06
	2011	42,094	7.31
	2012	43,117	7.49
County Poverty level			
	Low (<=9.90)	227,500	39.50
	Middle (9.91-19.90)	308,040	53.48
	High (>=19.90)	40,482	7.03
		Mean	**Std. Dev.**
Age		60.11	14.11

Table 2-2 shows results from the bivariate and multivariate analyses. The bivariate model for residence did not achieve convergence and is therefore, not reported. On bivariate analysis (Model 1), compared to residents of low poverty counties, there was an increased likelihood of late-stage diagnosis among residents of middle (OR=1.08; 95% CI= 1.05-1.10) and high poverty counties (OR=1.22; 95% CI=1.18-1.27).

Controlling for the covariates (model 2), compared to urban metropolitan residents, urban non-metropolitan (OR=1.03; 95% CI=1.00-1.05) and rural residents (OR=1.15; 95% CI=1.08-1.21) had higher likelihood of receiving a late-stage diagnosis. Compared to those diagnosed in 1995, the baseline year, there was a statistically increased likelihood of late-stage diagnosis from 1998 to 2011. Compared to Whites, African Americans/Blacks (OR=1.30; 95% CI=1.27-1.32) and American Indians/Alaskan Natives (OR=1.20; 95% CI=1.10-1.31) had an increased likelihood of late stage diagnosis while Asians/pacific Islanders had a significantly decreased likelihood of late-stage diagnosis (OR=0.96; 95% CI=0.94-0.98). Hispanics had an increased likelihood (OR=1.20; 95% CI=1.18-1.23) of late-stage diagnosis compared to non-Hispanics.

Controlling for poverty (Table 2-2, model 3), rural residents continued to have a significantly increased likelihood of late-stage diagnosis (OR=1.09; CI= 1.03-1.15) compared to urban residents although the effect size decreased by 6%; the association between urban non-metropolitan residence and late stage diagnosis was no longer statistically significant. Compared to residents of low-poverty counties, there was an increased likelihood of late-stage diagnosis among residents of middle poverty (OR=1.07; 95% CI=1.05-1.09) and high poverty counties (OR=1.13; 95% CI=1.09-1.17). On interacting residence and county poverty level, there was no significant association between the interaction term and stage at diagnosis of breast cancer (data not shown).

Table 2-2: Bivariate and Multivariate Analysis of Individuals Diagnosed with Breast Cancer between 1995 and 2012: Surveillance, Epidemiology and Ends Results Data (n=576,022)

	Unadjusted	**Adjusted**	
	Model 1	Model 2	Model 3
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Residence			
Urban metropolitan area	Ref.	Ref.	Ref.
Urban non-metropolitan area	----------	**1.03 (1.00-1.06)**	0.98 (0.95-1.00)
Rural area	----------	**1.15 (1.09-1.21)**	**1.09 (1.03-1.15)**
County poverty level			
Low poverty (≤9.90% below FPL)	Ref.	Ref.	Ref.
Middle poverty (9.91% - 19.90% below FPL)	**1.08 (1.05-1.10)**	----------	**1.07 (1.05-1.09)**
High poverty (≥19.90% below FPL)	**1.22 (1.18-1.27)**	----------	**1.13 (1.09-1.17)**
Race			
White		Ref.	Ref.
Black		**1.30 (1.27-1.32)**	**1.29 (1.27-1.31)**
American Indian/Alaska Native		**1.20 (1.10-1.31)**	**1.19 (1.09-1.30)**
Asian or Pacific Islander		**0.96 (0.94-0.98)**	**0.97 (0.95-0.99)**
Marital status			
Married		Ref.	Ref.
Single/Unmarried		**1.19 (1.17-1.20)**	**1.19 (1.17-1.21)**
Divorced/Separated		**1.15 (1.13-1.17)**	**1.15 (1.13-1.17)**
Widowed		**1.24 (1.22-1.26)**	**1.24 (1.21-1.26)**

*Bold font indicates statistical significance

Table 2-2 Continued

	Unadjusted	Adjusted	
Ethnicity			
Non-Hispanic		Ref.	Ref.
Hispanic		**1.20 (1.18-1.23)**	**1.21 (1.19-1.23)**
Tumor grade			
Low grade		Ref.	Ref.
High grade		**2.03 (2.00-2.05)**	**2.03 (2.00-2.05)**
Unknown		**1.82 (1.79-1.86)**	**1.82 (1.79-1.86)**
Estrogen receptor status			
Positive		Ref.	Ref.
Negative		**0.87 (0.85-0.88)**	**0.87 (0.85-0.88)**
Borderline		0.99 (0.87-1.13)	0.99 (0.87-1.12)
Unknown		1.00 (0.96-1.05)	1.00 (0.95-1.05)
Progesterone receptor status			
Positive		Ref.	Ref.
Negative		**1.09 (1.07-1.11)**	**1.09 (1.07-1.11)**
Borderline		1.01 (0.94-1.09)	1.01 (0.94-1.09)
Unknown		0.98 (0.94-1.03)	0.99 (0.94-1.03)
Age at diagnosis		0.99 (0.99-0.99)	0.99 (0.99-0.99)

*Bold font indicates statistical significance

Table 2-2 Continued

	Unadjusted	Adjusted	
Year of diagnosis			
		Ref.	Ref.
1996		1.02 (0.97-1.07)	1.02 (0.97-1.07)
1997		1.01 (0.96-1.06)	1.01 (0.96-1.06)
1998		**1.06 (1.01-1.12)**	**1.06 (1.01-1.12)**
1999		**1.08 (1.03-1.14)**	**1.08 (1.03-1.14)**
2000		**1.14 (1.10-1.19)**	**1.13 (1.09-1.18)**
2001		**1.16 (1.11-1.21)**	**1.14 (1.10-1.19)**
2002		**1.17 (1.12-1.22)**	**1.15 (1.11-1.20)**
2003		**1.16 (1.11-1.21)**	**1.15 (1.10-1.19)**
2004		**1.14 (1.09-1.19)**	**1.13 (1.08-1.17)**
2005		**1.13 (1.08-1.18)**	**1.12 (1.07-1.16)**
2006		**1.13 (1.08-1.18)**	**1.11 (1.07-1.16)**
2007		**1.11 (1.06-1.16)**	**1.10 (1.05-1.14)**
2008		**1.10 (1.06-1.15)**	**1.09 (1.05-1.14)**
2009		**1.07 (1.02-1.11)**	**1.05 (1.01-1.10)**
2010		**1.06 (1.02-1.11)**	**1.05 (1.01-1.09)**
2011		**1.06 (1.01-1.10)**	**1.04 (1.00-1.09)**
2012		1.01 (0.97-1.05)	1.00 (0.96-1.04)

*Bold font indicates statistical significance

Using estimates from the fully adjusted model, the predicted probabilities of late-stage diagnosis showed that although there was a steady decline in probability of late stage diagnosis between years 2002 and 2012 across all levels of residence and county poverty levels, disparities still exist (Fig. 2-2 -2-4). Rural residents and residents of high poverty counties (Fig. 2-2 and 2-3) consistently had the highest probabilities of late-stage diagnosis across all years. Combining residence and county poverty levels (Fig. 2-3), across all years, the probability of late-stage diagnosis was highest for residents of rural high poverty areas while residents of urban non-metropolitan low poverty counties had the lowest probability of late-stage diagnosis. Compared to residents of rural low poverty counties, residents of urban metropolitan high poverty and urban non-metropolitan high poverty counties had a persistently higher probability of late-stage diagnosis (Fig. 2-4). Residents of rural low poverty counties had a higher probability of late-stage diagnosis compared to residents of urban metropolitan middle poverty, urban non-metropolitan middle poverty, urban metropolitan low poverty and urban non-metropolitan low poverty counties respectively.

Figure 2-2: Trends in Predicted Probabilities of Late-Stage Breast Cancer Diagnosis by Residence: 1995-2012

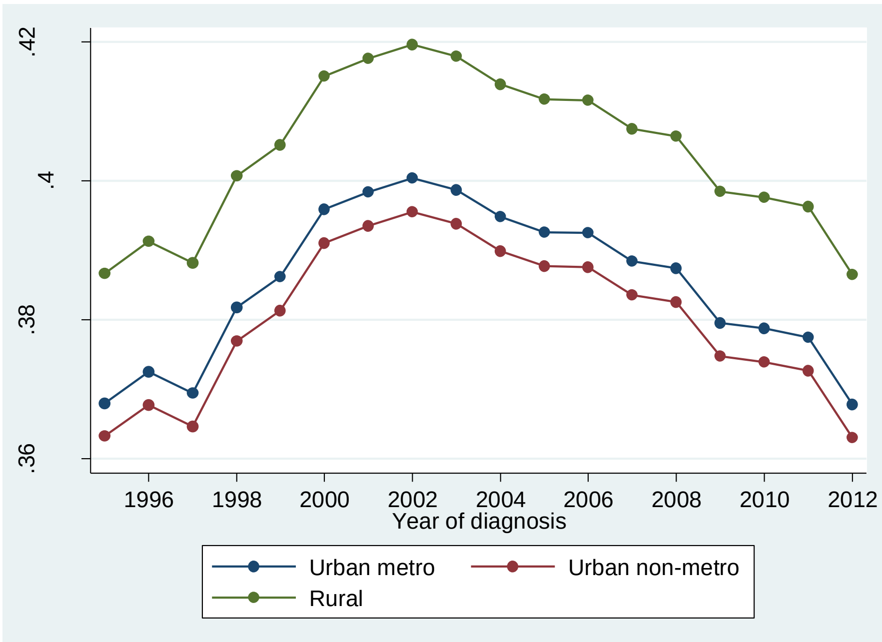


Figure 2-3: Trends in Predicted Probabilities of Late-Stage Breast Cancer Diagnosis by County Poverty Level: 1995-2012

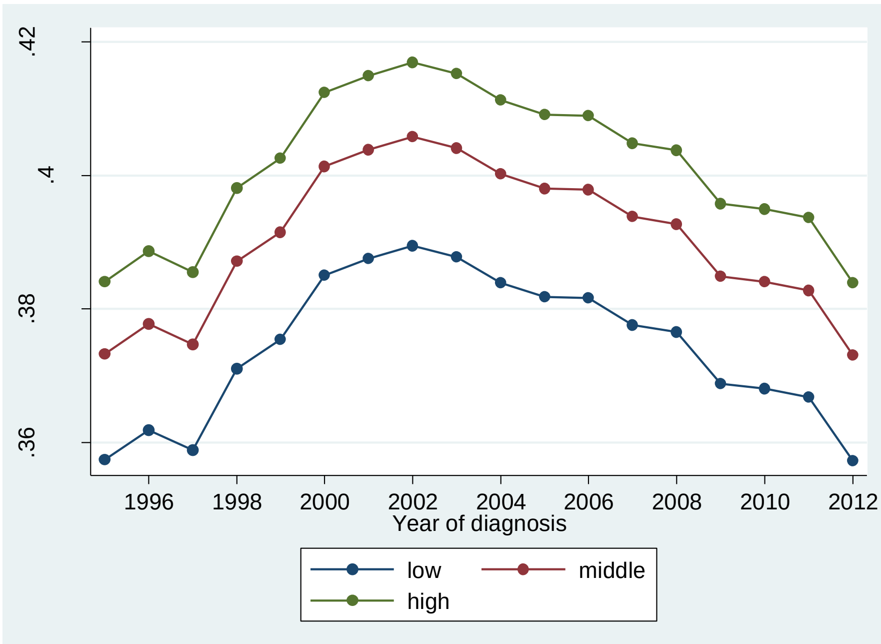
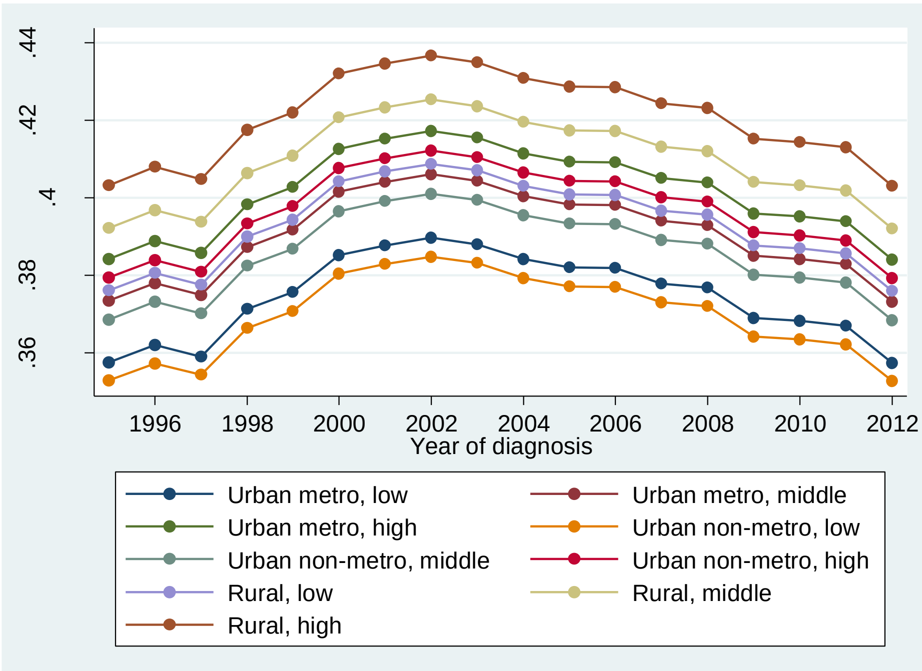


Figure 2-4: Trends in Predicted Probabilities of Late-Stage Breast Cancer Diagnosis by Residence and County Poverty Level: 1995-2012



2.5 Discussion

In this study, the independent associations between late-stage breast cancer diagnoses, rural-urban residence and county poverty controlling for individual-level and tumor characteristics, and whether county poverty levels explained these residential disparities were explored. Trends in probability of late-stage diagnosis between 1995 and 2012, by residence and county poverty levels were also explored.

This study found that rural residents were at greater risk for late-stage diagnosis compared to their non-rural counterparts, a finding consistent with a previous meta-analysis.[11] County poverty level explained the association between late-stage diagnosis and urban non-metropolitan residence; however, the association between late-stage diagnosis and rural residence persisted after we controlled for county poverty level. This is in contrast to a previous study which reported that area poverty level explained the association between rural residence and late-stage diagnosis.[13] The difference between this finding and the study by Henry and colleagues may be because county poverty levels were used in this study while census tract poverty levels were used in their study.

This study is consistent with previous studies[13, 18, 19, 34] which found that county poverty level is an independent predictor of late-stage breast cancer diagnosis. In this study, the odds of late-stage breast cancer diagnosis increased with increasing county poverty level; residents of middle poverty and high poverty counties had a 7% and 13% higher odds of late-stage diagnosis respectively, compared to residents of low poverty counties. These findings highlight the importance of implementing interventions to reduce late-stage diagnosis with a focus on county poverty level rather than just residence alone.

On analyzing trends in the probability of receiving a late-stage diagnosis, a decline was seen starting from year 2002; however, disparities by residence and county poverty level persisted across all the years of analyses. Residents of rural high poverty areas consistently had the highest probability of late-stage diagnosis across all years while residents of urban non-metropolitan low poverty areas consistently had the lowest probability of late-stage diagnosis. The persistence of these disparities across all years is indicative of the need for continued research aimed at identifying factors that are associated with disparities in breast cancer stage at diagnosis among groups at risk, as well as developing strategies to mitigate the influence of such factors. These findings also suggest that although implementation of interventions to reduce late-stage breast cancer diagnosis among rural residents has potential for reducing disparities in late-stage breast cancer diagnosis, it is important to consider both residence and county poverty estimates when implementing such interventions. For example, in this study, residents of urban metropolitan high poverty and urban non-metropolitan high poverty counties had a persistently higher probability of late-stage diagnosis compared to residents of rural low poverty counties. This therefore suggests that it might be a more efficient and effective use of resources to factor in both poverty estimates and residence when deciding areas where such interventions are most needed, especially if resources are scarce.

2.6 Limitations and Strengths

This study has some limitations. The SEER data is representative of only 28 percent of the United States population; thus study findings may not be generalizable to the entire United States population. Another limitation is that the SEER data does not have lower level geographical information such as census tracts; therefore more detailed geographical analyses could not be performed. The data did not contain information on health care access measures such as availability of health care facilities, number of health care provider visits or routine breast cancer screening rates for age-eligible individuals. Thus, these factors which might mediate or moderate stage at diagnosis of breast cancer were not accounted for in the analyses.

Despite these limitations, the important contribution of this study to understanding disparities in stage at diagnosis of breast cancer is not diminished. Some significant strengths of this study include the use of a national dataset. The large number of years included in the study also enhanced understanding of trends in late-stage diagnosis in the past decade. Another strength of this study is the use of multilevel modelling as it enabled accounting for variations across counties. The use of multiple years also provided insight into continued disparities in late-stage diagnosis between 1995 and 2012, and how these disparities varied across sub-populations.

In conclusion, one of the Healthy People 2020 objectives is to reduce the incidence of late-stage breast cancer diagnosis.[35] Achieving this goal has potential for reducing the economic burden of breast cancer, as well as breast cancer-related mortality. Targeted interventions among populations with higher risk of late-stage diagnosis can play a pivotal role in achieving this important goal. The findings from this study suggest that stakeholders and policy makers should consider both residence and county poverty levels when deciding where interventions should be implemented. Such considerations will ensure that such programs or strategies are executed in areas with the highest needs. It is also important to track trends in late-stage diagnosis as this will provide insights into the impact of interventions.

3. GEOGRAPHICAL DISPARITIES IN STAGE AT DIAGNOSIS OF BREAST CANCER AMONG FEMALE RESIDENTS OF TEXAS

3.1 Introduction

One of the HealthyPeople2020 cancer objectives is to reduce the occurrence of late-stage female breast cancer.[35] Reducing the occurrence of late-stage diagnosis is crucial because early-stage diagnosis improves the chances of survival.[2] (SEER n.d). Early-stage diagnosis also reduces the economic burden of breast cancer at the national and individual level, because treatment is cheaper for early-stage tumors compared to late-stage tumors.[28] Identification of factors that are associated with late-stage diagnosis of breast cancer can guide education and screening interventions aimed at reducing the prevalence of late-stage breast cancer.

Geographical level characteristics such as rural/urban residence,[9, 14, 22,] census tract poverty levels[4,13, 18, 19] and racial or ethnic residential segregation[17,36,] have been associated with stage at diagnosis of breast cancer. The association between residence and stage at diagnosis has however been inconsistent. Studies have reported no significant association between residence and late-stage diagnosis[4, 13, 14, 20, 24] while McLafferty and colleagues reported that rural residents had a decreased likelihood of being diagnosed with late-stage breast cancer.[12] A meta-analysis of 21 studies however, found that rural residents had an increased likelihood of late-stage breast cancer diagnosis.[11] Residential segregation –the physical separation of one racial/ethnic group from another[16] is another geographical level variable that has been associated with late-stage breast cancer diagnosis,[17] although, results have also been inconsistent.[36] These reported inconsistencies warrants further exploration of these factors.

Various studies have explored the association between travel distance to the nearest mammography and breast cancer stage at diagnosis with inconsistent result.[9, 20] Studies have also explored the association between travel distance to the nearest health care provider and treatment choice following a breast cancer diagnosis.[37, 38] There is however, a gap in the research literature about the association between travel distance to nearest PCP and stage at diagnosis of breast cancer. Since PCP recommendation is a predictor of breast cancer screening[39] which in turn increases the chances of early-stage diagnosis, it is important to identify the influence of travel distance to nearest PCP on stage at diagnosis of breast cancer.

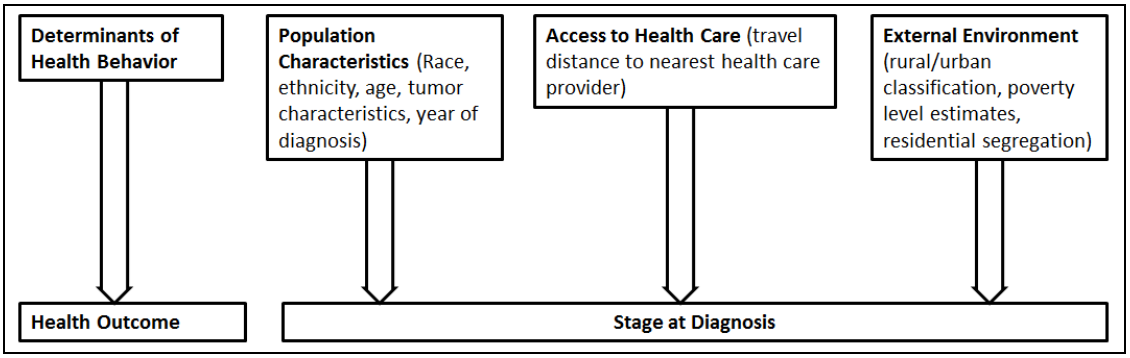
This study aims to contribute towards bridging the gap in literature by analyzing:

1. The independent association between rural/urban residence, census tract poverty levels, census tract residential segregation, travel distance to nearest PCP and stage at diagnosis of breast cancer.
2. Whether census tract poverty level, residential segregation and travel distance to the nearest PCP explains rural-urban disparities in stage at diagnosis of breast cancer.
3. The rural-urban trends in late-stage breast cancer diagnosis by census tract poverty

3.2 Conceptual Framework

The conceptual frame work (Fig. 3-1) for this paper is based upon the Andersen behavioral model.[30] The original model identifies three constructs namely: 1) primary determinants of health behavior, 2) health behavior and 3) health outcomes. For the purpose of this study, a modified version of the model which identifies two of the three constructs (primary determinants of health and health outcomes) was used. In accordance with the Andersen behavioral model, three categories of determinants of health were explored, namely: i) population characteristics (age, marital status, race and ethnicity); ii) access to health care (travel distance to the nearest PCP); and iii) external environmental factors (rural versus urban residence, census tract poverty level estimates and residential segregation). It was expected that these determinants of health would influence the health outcome of interest which was stage at diagnosis.

Figure 3-1: Conceptual Model of Factors that Could Influence Stage at Diagnosis of Breast Cancer



3.3 Methods

The primary data set that was used for the analyses was the Texas Cancer Registry. Inclusion criteria were females ages 18 and older who were diagnosed with breast cancer between 1995 and 2012, and who had only one primary tumor. Due to model non-convergence, the analyses were limited to individuals who identified their race as White or African American. Final sample size was 190,525 individuals nested in 4358 census tracts which were nested in 254 counties.

Variables

The dependent variable of interest was stage at diagnosis. In line with previous studies, [13, 17, 22] the original stage at diagnosis variable was recoded as "0" early (in-situ and localized) and "1" late (regional or distant). The independent variables of interest were residence (urban metropolitan, urban non-metropolitan and rural), census tract poverty level (low "<=9.90% of the population living below FPL", middle "9.91-19.90% of the population living below FPL", high ">19.90% of the population living below

FPL), racial residential segregation and travel distance to nearest PCP (<=5 miles, >5-10 miles, >10miles-15miles, >15 miles). Covariates included race (White, Black), ethnicity (Hispanic, Non-Hispanic), tumor grade (Well differentiated, moderately differentiated, poorly differentiated, undifferentiated and unknown), age at diagnosis and year of diagnosis.

Racial residential segregation was measured using the isolation index because the aim of this study was to measure the possibility of contact between an African American resident in an area to a White resident in the same area.[16, 17, 40] The isolation index ranged from 0 (no segregation) to 1 (greatest segregation).

Information on PCPs' practice addresses was derived from the Texas Medical Board Physician database. Using the Texas A&M University Department of Geography geocoding software[41] addresses of the practices were assigned latitude and longitude coordinates. Only PCP whose licenses were active between January 1995 and December 2012 and whose practices were located in Texas were included in the analyses. For the purpose of this study, physician specialties that were regarded as PCPs included family medicine, family practice, general practice, general preventive medicine, geriatric medicine, gynecology, internal medicine and preventive medicine. Final sample size of physicians was 21,606. Distance to the closest facility from a given patient's residence was then derived using the network analyst of ArcGIS.[42]

Analytic methods

Descriptive statistics for select independent variables were conducted. Maps depicting spatial distribution of rural-urban designation and residential segregation and

CT poverty levels of the census tracts were generated. Since the dependent variable of interest was binary, logistic regression equations were estimated. Bivariate and multivariate multilevel logistic regression equations were estimated; individuals were nested within CTs, and CTs nested within counties. Bivariate models were estimated for residence, census tract poverty level, travel distance and residential segregation. However, due to model non-convergence only bivariate results for residence and residential segregation are reported. The final sample size consisted of 190,525 individuals nested within 4,358 census tracts, nested within 254 counties.

The general form of the three-level logistic regression was:

$$\mathbf{Y_{ijk} = \gamma 00 + \gamma 01 X_{ijk} + \gamma 02 CT_{jk} + \gamma 03 C_{k} + U_{jk} + R_{k}}$$

Where Y_{ijk}=log of late-stage probability divided by early stage probability for person *i* in census tract *j* in county *k*,

γ_{00}=overall intercept for the two level model

i= indexes the individual level

j= indexes the CT level

k= indexes the county level

X= A vector of the individual level variables (race, ethnicity, tumor grade, age, and year of diagnosis),

CT= A vector of the census tract level variables (poverty estimates, travel distance to nearest provider)

C= A vector of the county level variables (residence, residential segregation)

U_{jk} = error term at the census tract level

R_k = error term at the county level

Exponents of the coefficients (odds ratios) and 95% confidence interval are reported. Two way interactions between residence and residential segregation, poverty level and travel distance to the nearest PCP were explored. Adjusted predicted probabilities of rural-urban trends in late-stage diagnosis by CT poverty levels were derived. All statistical tests were two-sided, and findings were considered statistically significant at $p < 0.05$. All analyses were conducted using Stata 13.1[33] and ArcGIS.[42]

3.4 Results

Table 3-1 shows results of the descriptive analyses. Whites and African Americans comprised of 88.67% and 11.33% of the study population, respectively. About 83% of the study population where non-Hispanics while 16.68% were Hispanics. With regards to residence, residents of urban metropolitan areas accounted for 85.92% of the study population, 12.99% were residents of urban non-metropolitan areas and 1.09% were residents of rural areas. A majority of the study population were residents of low poverty census tracts (48.60%), residents of middle poverty census tracts accounted for 30.42% of the study population while 20.99% of the study population were residents of high poverty census tract.

Table 3-1 Descriptive Statistics of Texas Women Diagnosed with Breast Cancer between 1995 and 2012 (n=190,525)

		Freq.	Percent
Race			
	White	168,948	88.67
	African Americans/Black	21,577	11.33
Ethnicity			
	Non-Hispanic	158,742	83.32
	Hispanic	31,783	16.68
Residence			
	Urban metro	163,708	85.92
	Urban non-metro	24,740	12.99
	Rural	2,077	1.09
Poverty			
	low	92,588	48.60
	middle	57,955	30.42
	high	39,982	20.99
Tumor grade			
	Well differentiated	28,163	14.78
	Moderately differentiated	63,627	33.40
	Poorly differentiated	63,825	33.50
	Undifferentiated	3,372	1.77
	Unknown	31,538	16.55
Year of diagnosis			
	1995	7,643	4.01
	1996	7,968	4.18
	1997	8,613	4.52
	1998	9,171	4.81
	1999	9,582	5.03
	2000	10,028	5.26
	2001	10,234	5.37
	2002	10,493	5.51
	2003	10,393	5.45
	2004	10,505	5.51
	2005	10,943	5.74
	2006	11,196	5.88
	2007	11,950	6.27

Table 3-1: continued

		Freq.	Percent
Year of diagnosis			
	2008	12,144	6.37
	2009	12,811	6.72
	2010	12,410	6.51
	2011	12,223	6.42
	2012	12,218	6.41

Figure 3-2 shows the spatial distribution of urban metropolitan, urban non-metropolitan and rural counties, isolation index of counties and census tract poverty estimates of our sample. There were no clear spatial patterns observed between the three variables.

Figure 3-2: Rural-urban county classification, county isolation index and census tract poverty estimates

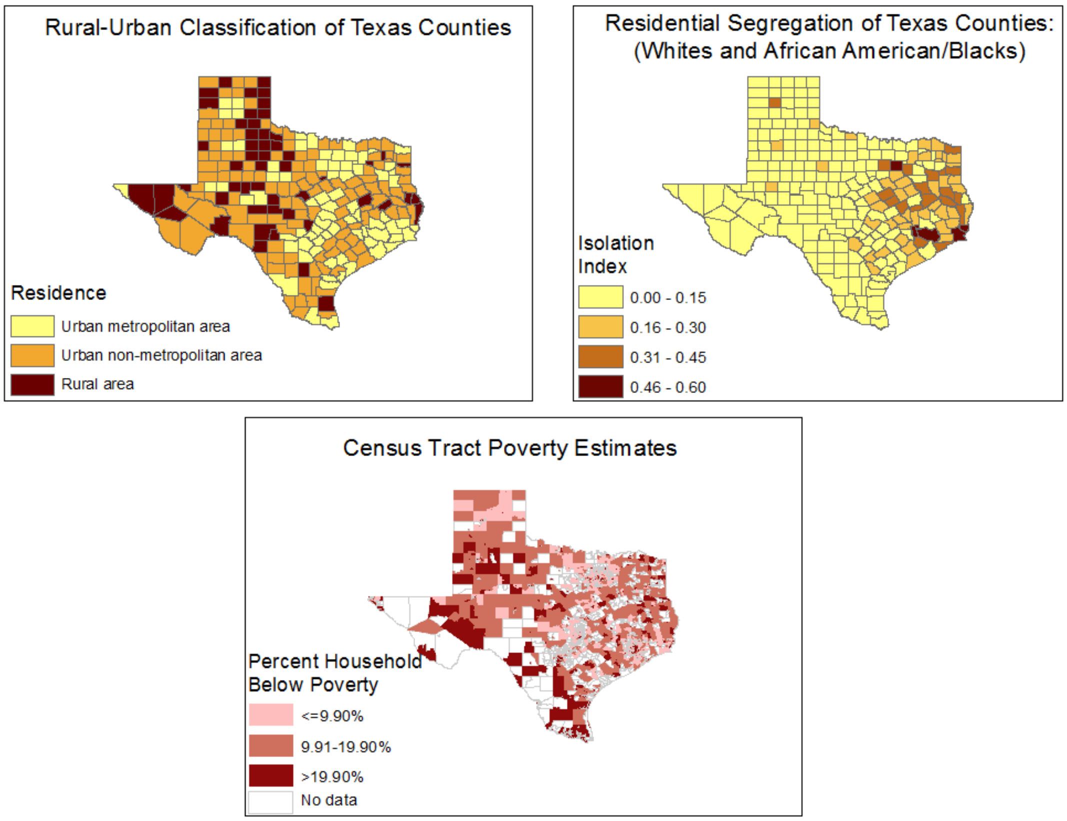


Table 3-2 shows results of the bivariate and multivariate analyses. On bivariate analysis (Model 1), there was no statistically significant association between rural residence and late-stage diagnosis; residents of urban non-metropolitan areas had an increased likelihood (OR=1.09; 95% CI=1.05-1.14) of receiving a late-stage diagnosis compared to residents of urban residents. There was a decreased likelihood of receiving a late-stage diagnosis with increasing (OR=0.86; 95% CI=0.78-0.96) racial residential segregation.

Table 3-2 (Model 2) shows that controlling for the covariates, compared to urban metropolitan residents, urban non-metropolitan (OR=1.18; 95% CI=1.14-1.23) and rural residents (OR=1.14; 95% CI=1.03-1.27) had higher likelihood of receiving a late-stage diagnosis. African Americans had a higher likelihood (OR=1.46; 95% CI=1.41-1.50) of receiving a late-stage diagnosis compared to Whites. Hispanics had an increased likelihood (OR=1.39; 95% CI=1.35-1.43) of late-stage diagnosis compared to non-Hispanics. Compared to those diagnosed in 1995, those diagnosed between 1997 and 2012 had a significantly decreased likelihood of receiving a late-stage diagnosis.

Controlling for poverty (Table 3-2, model 3), residents of urban non-metropolitan areas continued to have a significantly increased likelihood of late-stage diagnosis (OR=1.11; CI= 1.07-1.16) compared to urban residents while the association between rural residence and stage at diagnosis was no longer significant. Compared to residents of low-poverty CTs, there was an increased likelihood of late-stage diagnosis among residents of middle poverty (OR=1.17; 95% CI=1.14-1.21) and high poverty CTs (OR=1.26; 95% CI=1.22-1.30).

Controlling for poverty, residential segregation and travel distance (Table 3-2, model 4), residents of urban non-metropolitan areas continued to have a significantly increased likelihood of late-stage diagnosis (OR=1.08; CI= 1.03-1.13) compared to urban residents while the association between rural residence and stage at diagnosis was no longer significant. Compared to residents of low-poverty CTs, there continued to be an increased likelihood of late-stage diagnosis among residents of middle poverty (OR=1.17; 95% CI=1.14-1.20) and high poverty CTs (OR=1.26; 95% CI=1.22-1.30). There was a decreased likelihood of late-stage diagnosis with increasing residential segregation (OR=0.67; 95% CI=0.60-0.76). There was no significant association between travel distance and late-stage diagnosis.

Table 3-2: Bivariate and Multivariate Analysis of Stage at Diagnosis of Breast Cancer among Female Residents of Texas: 1995 and 2012 (n=190,525)

	Unadjusted	**Adjusted**		
	Model 1	Model 2	Model 3	Model 4
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Residence				
Urban metropolitan area	Ref.	Ref.	Ref.	Ref.
Urban non-metropolitan area	**1.09 (1.05-1.14)**	**1.18 (1.14-1.23)**	**1.11 (1.07-1.16)**	**1.08 (1.03-1.13)**
Rural area	0.98 (0.88-1.10)	**1.14 (1.03-1.27)**	1.08 (0.97-1.19)	1.02 (0.91-1.13)
Isolation Index	**0.86 (0.78-0.96)**			**0.67 (0.60-0.76)**
Census Tract Poverty Level				
Low poverty (≤9.90% below FPL)			Ref.	Ref.
Middle poverty (9.91% - 19.90% below FPL)			**1.17 (1.14-1.21)**	**1.17 (1.14-1.20)**
High poverty (≥19.90% below FPL)			**1.26 (1.22-1.30)**	**1.26 (1.22-1.30)**
Travel Distance to Nearest Primary Care Provider				
<5 miles				Ref.
> 5 miles & <=10 miles				1.03 (0.99-1.08)
> 10 miles & <=15 miles				1.01 (0.94-1.09)
>15 miles & <=20 miles				1.05 (0.94-1.18)
>20 miles				1.10 (0.94-1.29)
Race				
White		Ref.	Ref.	Ref.
Black		**1.46 (1.41-1.50)**	**1.36 (1.32-1.41)**	**1.37 (1.33-1.42)**

*Bold font indicates statistical significance

Table 3-2 Continued

	Unadjusted	**Adjusted**		
	Model 1	Model 2	Model 3	Model 4
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Ethnicity				
Non-Hispanic		Ref.	Ref.	Ref.
Hispanic		**1.39 (1.35-1.43)**	**1.32 (1.28-1.36)**	**1.32 (1.28-1.36)**
Tumor grade				
Well differentiated		Ref.	Ref.	Ref.
Moderately differentiated		**2.13 (2.06-2.21)**	**2.13 (2.06-2.21)**	**2.13 (2.06-2.21)**
Poorly differentiated		**3.21 (3.10-3.32)**	**3.20 (3.09-3.32)**	**3.20 (3.09-3.31)**
Undifferentiated		**2.28 (2.11-2.47)**	**2.27 (2.10-2.45)**	**2.27 (2.10-2.45)**
Unknown		**1.77 (1.71-1.85)**	**1.77 (1.70-1.84)**	**1.77 (1.70-1.84)**
Age at Diagnosis		0.99 (0.99-0.99)	0.99 (0.99-0.99)	0.99 (0.99-0.99)

*Bold font indicates statistical significance

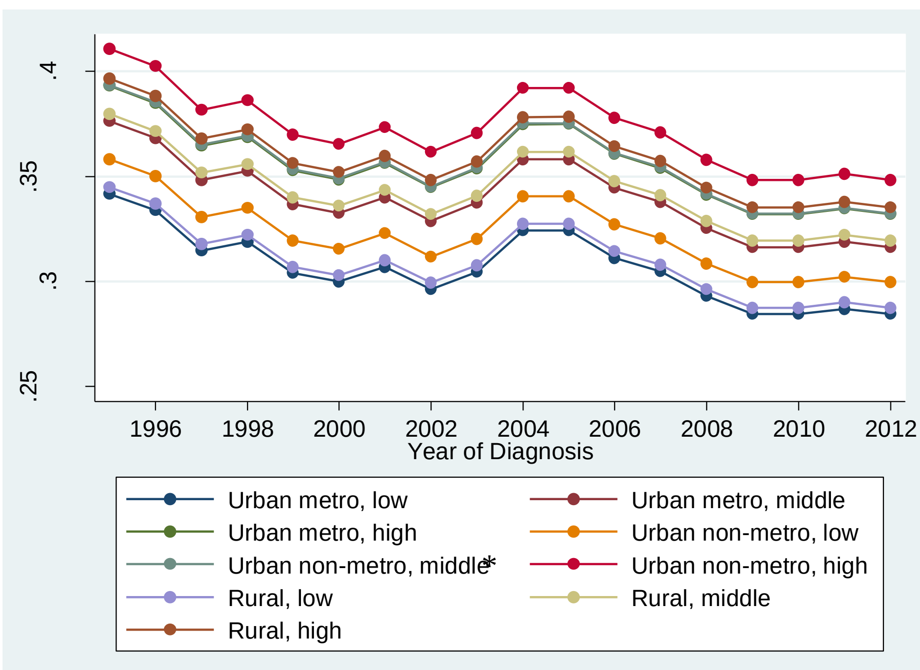
Table 3-2 Continued

	Unadjusted	Adjusted		
	Model 1	Model 2	Model 3	Model 4
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Year of Diagnosis				
1995		Ref.	Ref.	Ref.
1996		0.96 (0.90-1.03)	0.97 (0.90-1.03)	0.96 (0.90-1.03)
1997		**0.88 (0.82-0.94)**	**0.88 (0.83-0.94)**	**0.88 (0.83-0.94)**
1998		**0.90 (0.84-0.96)**	**0.90 (0.84-0.96)**	**0.90 (0.84-0.96)**
1999		**0.83 (0.78-0.89)**	**0.84 (0.78-0.89)**	**0.84 (0.78-0.89)**
2000		**0.81 (0.76-0.87)**	**0.82 (0.77-0.87)**	**0.82 (0.77-0.87)**
2001		**0.84 (0.79-0.90)**	**0.85 (0.80-0.91)**	**0.85 (0.80-0.90)**
2002		**0.80 (0.75-0.85)**	**0.81 (0.76-0.86)**	**0.81 (0.76-0.86)**
2003		**0.83 (0.78-0.88)**	**0.84 (0.79-0.89)**	**0.84 (0.79-0.89)**
2004		**0.91 (0.86-0.97)**	**0.92 (0.87-0.98)**	**0.92 (0.87-0.98)**
2005		**0.91 (0.86-0.97)**	**0.92 (0.87-0.98)**	**0.92 (0.87-0.98)**
2006		**0.85 (0.80-0.91)**	**0.87 (0.82-0.92)**	**0.87 (0.81-0.92)**
2007		**0.83 (0.78-0.88)**	**0.84 (0.79-0.89)**	**0.84 (0.79-0.89)**
2008		**0.78 (0.73-0.83)**	**0.79 (0.75-0.84)**	**0.79 (0.74-0.84)**
2009		**0.75 (0.70-0.79)**	**0.76 (0.71-0.81)**	**0.76 (0.71-0.81)**
2010		**0.75 (0.70-0.79)**	**0.76 (0.71-0.81)**	**0.76 (0.71-0.81)**
2011		**0.76 (0.71-0.80)**	**0.77 (0.72-0.82)**	**0.77 (0.72-0.82)**
2012		**0.75 (0.70-0.79)**	**0.76 (0.71-0.81)**	**0.76 (0.71-0.81)**

*Bold font indicates statistical significance

Using estimates from the fully adjusted model, the predicted probabilities of late-stage diagnosis were estimated. A decline in the probability of late stage diagnosis between 1995 and 2012 (data not shown) across all levels of residence and county poverty levels was seen. Figure 3-3 shows that across all years, the probability of late-stage diagnosis was highest for urban non-metropolitan high poverty CT residents followed by rural high poverty CT residents, while it was lowest for urban metropolitan low poverty CT residents. Residents of UNM middle poverty and urban metropolitan high poverty CTs had the similar probability of late-stage diagnosis across all years.

Figure 3-3: Trends in Predicted Probability of Late-Stage Diagnosis of Breast Cancer



*Superimposed over urban metropolitan high CT poverty values

3.5 Discussion

In this study, CT poverty level and residential isolation index explained the association between rural residence and late-stage diagnosis but not the association between urban non-metropolitan residence and late-stage diagnosis. There was no statistically significant association between travel distance to the nearest PCP and stage at diagnosis of breast cancer.

<u>Residence</u>

There have been inconsistencies in the reported association between late-stage diagnosis and rural residence; however, a meta-analysis comprised of 21 studies and a sample size of 879,660 found that rural residents had a higher likelihood of being diagnosed with late-stage breast cancer compared to urban residents.[11] In this study, there was no significant association between rural residence and late-stage diagnosis on bivariate analysis. After controlling for race, ethnicity, tumor grade, age and year of diagnoses, the association between rural residence and stage at diagnosis of breast cancer became statistically significant. Adjusting for CT poverty and residential segregation the association between rural residence and stage at diagnosis was no longer statistically significant but the association between stage and diagnosis and UNM residence remained statistically significant. This finding suggests that among our study population, CT poverty level and racial residential segregation explained disparities associated with rural residence but not UNM residence. These results suggest that in the state of Texas, interventions to reduce disparities in stage at diagnosis of breast cancer are needed among residents of urban non-metropolitan.

It has been suggested that increased cancer control interventions in rural areas are responsible for the lack of significant association between late-stage breast cancer diagnosis and rural residence.[13] It might therefore be necessary to identify cancer control measures or interventions that have been resulted in decreased incidence of late-stage diagnosis in order to implement them in urban non-metropolitan areas in Texas

Residential segregation

In this study, residents of areas that had high racial residential segregation were found to have a decreased likelihood of late-stage diagnosis compared to residents of less segregated areas. In contrast to this study findings, a California study found no significant association between residential segregation and late-stage diagnosis; they however, reported that black women living in areas with low percentage of black women and white women living in areas of high percentage of black women had an increased odd of late-stage diagnosis.[43] Another study comprised of individuals ages 65 and older reported that disparities in late-stage diagnosis between blacks and whites were less among blacks living in highly segregated areas compared to blacks living in low segregation areas.[44] In agreement with our study, Mobley and colleagues found that residents of highly segregated areas had decreased odds of being diagnosed with late-stage breast cancer.[36] The finding of decreased association between late-stage diagnosis and increasing racial residential segregation could be indicative of increased social support among such individuals[36] ultimately leading to improved health-seeking behavior. A study that focused on residents of metropolitan areas found that blacks living in areas with high black residential segregation were more likely to be diagnosed with late-stage diagnosis.[17] It is therefore possible that the association between racial residential segregation and late-stage breast cancer diagnosis is dependent on whether the area is metropolitan, non-metropolitan or rural; however, in this study interaction terms between residence and residential segregation were not significant.

Poverty

In this study, there was an independent association between increasing CT poverty and late-stage diagnosis. The fully adjusted model showed that residents of middle and high poverty CTS had a 17% and 26% higher odds of being diagnosed with late-stage breast cancer diagnosis, respectively. Previous studies have also reported an association between increased area poverty level and late-stage breast cancer diagnosis.[4,13,18, 19] In contrast to this study however, Henry and colleagues found that CT poverty explained the association between rural residence and late-stage diagnosis.[13] It has been suggested that increased likelihood of late-stage presentation among residents of high poverty areas could be attributed to inadequate access to health insurance, screening facilities and lack of information.[34] In their study however, Hahn et al., did not find any significant association between screening using mammography, poverty and late-stage diagnosis.[45] Another study that reported decreased odds of annual screening mammogram among residents of areas with 5-9.9% and 10% living below poverty level compared to residents of areas with 0-4.9% living in poverty[46] did not find any significant association between poverty level and late-stage breast cancer diagnosis among the same population. There is therefore a need to continue to explore and identify factors that contribute to the observed increase in the risk of late-stage diagnosis among residents of middle or high poverty areas. Variations in the association between area poverty and late-stage diagnosis have been previously reported across states[34] highlighting the importance of state-based studies.

Travel distance

There was no significant association between travel distance to the nearest PCP and late-stage diagnosis in this study. Other studies have also reported no significant association between proximity to diagnostic facilities and stage at diagnosis of breast cancer.[9,20] These findings imply that proximity to a primary care practice or breast cancer diagnosing facility does not guarantee early-stage diagnosis.[9] This finding also suggests that it might be more beneficial for interventions to reduce disparities in stage at diagnosis of breast cancer to focus on other access to health care measures that have been associated with late-stage disease such as lack of health insurance.[7,8,47]

Trends

In their study, Hausauer and colleagues reported that patterns of invasive breast cancer were similar for residents of urban and sub-urban counties but different for rural residents with rural residents having a higher incidence rate.[48] Hausesur and colleagues did not find any difference in the incidence of invasive cancer incidence by county poverty level.[48] This is in contrast to this study in which probability of late-stage diagnosis varied by residence and CT poverty levels, with residents of urban non-metropolitan high poverty CTs having the highest probability across all years. This difference could be because Hauser and colleagues were assessing incidence while this study was assessing probability of receiving a late-stage diagnosis. The difference could also be because the study by Hausaeur et. al was a multistate study which used county level estimates while this study focused on only residents of Texas and used CT estimates. Hauser et al reported a decline in late-stage diagnosis;[48] we also saw a decline in the predicted probabilities of late-stage diagnosis between 2004 and 2012. A study reported that although survival for breast cancer increased across all poverty levels between 1973 and 2007, mortality rates were still highest among residents of high poverty census tracts.[49] In this study, analyzing trends in probability of late-stage diagnosis by residence and CT poverty level also highlighted the importance of considering these two factors when developing strategies to mitigate late-stage breast cancer diagnosis.

3.6 Limitations and Strengths

This study has some limitations. The TCR data is limited to the state of Texas, thus this study findings may not be generalizable to the entire United States population. Another limitation is that information on factors such as actual physician visitation or number of visitation which might further explain the association between healthcare provider availability and stage at diagnosis of breast cancer was not available and therefore, not included in the analyses. Information about insurance status was not available across all the years of interest; therefore this variable which has been previously reported to be associated with stage at diagnosis of breast cancer was not included in the analyses.

This study also has a number of strengths. A unique strength of this study is that the data spanned across seventeen years allowing us to observe variations in late-stage breast cancer diagnosis across the years of analyses. Another unique strength is the use of three-level models which allowed us to account for variations across CTs and counties. The use of CT also enabled analyses at a more granular geographical level. The ability to also use the Texas Medical Board physician database to establish proximity to PCPs also provided new insights in factors associated with disparities in stage at diagnosis. Ability to explore variations in late-stage diagnosis by residence and poverty levels also enabled identification of subpopulations at increased risk for late-stage diagnosis in the state of Texas.

This study suggests that interventions to improve early stage diagnosis are needed most among residents of urban non-metropolitan high poverty CTs in Texas.

4. GEOGRAPHICAL DISPARITIES IN TREATMENT OF EARLY-STAGE BREAST CANCER DIAGNOSIS AMONG FEMALE RESIDENTS OF TEXAS

4.1 Introduction

Treatment of breast cancer is dependent on the stage at which the tumor was diagnosed.[21] Moreover, adequate and early treatment increases the chances of survival.[50] Surgical treatment using either breast conserving surgery or mastectomy is recommended for early stage tumors.[21] Radiation following mastectomy is dependent on whether tumor cells were found in the axillary lymph nodes; however, whole breast radiation therapy following breast conserving surgery, also known as adjuvant radiotherapy is recommended regardless of axillary lymph node involvement.[21] Randomized control trials have shown that individuals diagnosed with early stage tumors who received breast conserving surgery and radiation had equal chances of survival when compared to women who received mastectomy.[51,52] There has also been shown to be less than a five percent recurrence rate of breast cancer ten years post-diagnosis among patients treated with breast conserving treatment and radiation therapy.[52] Women who do not receive radiation therapy following breast conserving surgery have been found to have about 14-15% higher recurrence rates;[53, 54] Higher odds of mortality (1.67-2.34) has also been reported among those who do not receive adjuvant radiotherapy.[50, 55, 56]

Although researchers noted an initial decline in mastectomy rates after it was established that breast conserving surgery with adjuvant radiotherapy had comparable survival rates with mastectomy, recent studies have reported a gradual increase in mastectomy rates.[57,56] Although type of surgical treatment is usually individualized and dependent on various factors such as patient preference[57] and tumor characteristics,[51] studies suggest that rural residents are more likely to be treated using mastectomy compared to their urban counterparts.[58] Rural residents have also been reported to be less likely to receive adequate treatment following a diagnosis of breast cancer compared to urban residents[22,59] This disparity in type of surgical treatment is worsened with increasing rurality.[58] Rural residents have also been reported to be less likely to receive radiotherapy compared to urban residents.[4]

There are inconsistencies about the association between poverty and receipt of surgical treatment. A Georgia study reported that residents of lower socioeconomic census tracts were less likely to receive surgical treatment following breast cancer diagnosis[4] while a study comprised of residents of the Detroit area found no association between census tract poverty level and receipt of surgical treatment.[26] Living in a high poverty census tract has also been associated with decreased likelihood of receiving breast conserving surgery and radiation therapy.[26, 4, 27]

A study that comprised of only Medicare insured patients, reported that racial disparities in receipt of adequate treatment was mediated by residential segregation.[44] This highlights a need to explore whether racial residential segregation moderates other factors that have been associated with treatment of early-stage breast cancer.

There is a gap in literature about the independent association between residence, CT poverty, residential segregation and treatment of early-stage breast cancer. Further analyses are also needed to determine whether rural-urban disparities in breast cancer treatment are explained by CT poverty level and residential segregation. Understanding the interplay between these factors will provide clarification as to populations that have the greatest of need for interventions aimed at ensuring appropriate breast cancer treatment.

The aim of this study was to analyze:

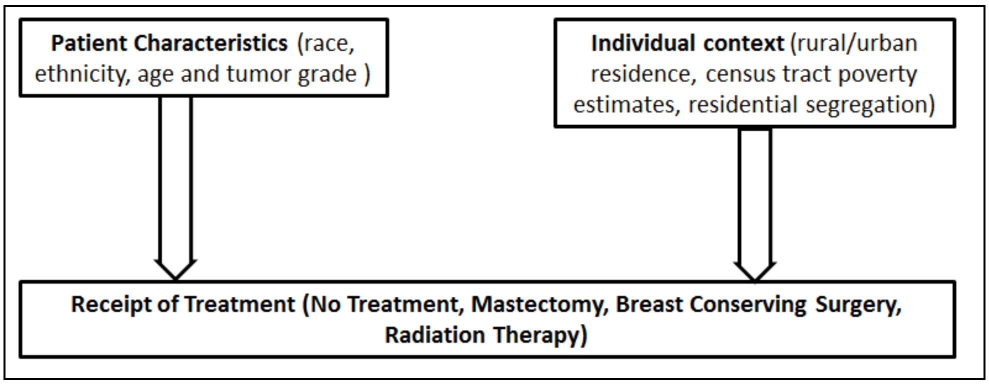
1. The independent association between residence, CT poverty and residential segregation and surgical treatment, type of surgical treatment and receipt of radiation therapy following early stage diagnosis of breast cancer.
2. Whether CT poverty and residential segregation explained rural-urban disparities in surgical treatment, type of surgical treatment and receipt of radiation therapy following early stage diagnosis of breast cancer.
3. Trends in probability of receiving surgical treatment, type of surgical treatment and receipt of radiation therapy among female residents of Texas diagnosed between 1995 and 2012.

To our knowledge, this is the first study that sequentially explores disparities in cancer treatment across the treatment continuum controlling for residence, census tract poverty and residential segregation.

4.2 Conceptual Framework

The conceptual framework (Fig. 4-1) is a modified version of the model of access to cancer care.[60] Our framework identifies two constructs that would influence early-stage breast cancer treatment: 1) patient characteristics (race, ethnicity, age and tumor grade) and the individual context (rural/urban residence, CT poverty estimates and residential segregation). We expect that these constructs will influence receipt of treatment as well as type of treatment received.

Figure 4-1. Conceptual Model of Access to Cancer Care



4.3 Methods

Study population

The TCR was used for this study. The study population consisted of all females ages 18 and older diagnosed with early-stage breast cancer between 1995 and 2012 who had only one primary tumor. Due to small sample size and model non-convergence, analyses were limited to only those who were Whites or African Americans/Blacks. The study was approved by the Texas A&M University Institutional Review Board.

Variables

There were three dependent variables of interest: 1) whether a patient was treated surgically (0=No 1= Yes); 2) What type of surgical treatment was used (0=breast conserving surgery 1=mastectomy) and 3) Whether a patient received radiation therapy following breast conserving surgery (0=No 1=Yes). The final sample size for receipt of surgical treatment was 124,821 individuals nested in 4,349 census tracts, the final sample size for type of surgical treatment was 94,390 individuals nested within 4,341 CTs while the final sample size for receipt of radiotherapy following breast conserving surgery was 12,899 individuals nested in 3,633 CTs. The independent variables of interest were residence, census tract poverty level and racial residential segregation. The census tract poverty level was derived from by the Texas Cancer Registry from the United States Decennial Census 2000 for those diagnosed between1995 and 2005 and Census 2010 for those diagnosed between 2006 and 2012. Covariates included race (White, Black), ethnicity (Hispanic, Non-Hispanic), age at diagnosis, year of diagnosis and tumor grade. Tumor grade was classified as low grade (well/moderately differentiated), high grade (poorly/undifferentiated) and unknown grade.

Racial residential segregation was measured using the isolation index. The isolation index measures the possibility of contactor exposure between an African American resident in an area to a White resident in the same area[16,17,40] The residential segregation index ranged from 0 (no segregation) to 1 (greatest segregation).

<u>Analytic methods</u>

Descriptive statistics for selected independent variables of interest were conducted. The dependent variables of interest were binary; therefore, logistic regression equations were estimated. Bivariate and multivariate two-level logistic regression equations were estimated; individuals were nested within CTs.

The general form of the three-level logistic regression was:

$$\mathbf{Y_{ij} = \gamma 00 + \gamma 01 X_{ij} + \gamma 02 CT_j + U_j}$$

Where Y_{ij}=log of probability surgical treatment/mastectomy/adjuvant radiotherapy divided by probability of probability no surgical treatment/BCS/no adjuvant radiotherapy for person *i* in census tract *j*,

γ_{00}=overall intercept for the two level model

i= indexes the individual level

j= indexes the CT level

X= A vector of the individual level variables (race, ethnicity, age, and year of diagnosis),

CT= A vector of the census tract level variables (residence, residential segregation, poverty estimates)

U_j = error term at the census tract level

Exponents of the coefficients (odds ratios) and 95% confidence interval are reported. Two way interactions between residence and residential segregation and poverty level were explored. Adjusted predicted probabilities of rural-urban trends in late-stage diagnosis by census tract poverty levels were derived. All statistical tests were two-sided, and findings were considered statistically significant at $p < 0.05$.

Following multivariate regression analyses, Bayes estimates of the posterior means of random effects were estimated.[61] In line with the cancer registry requirement, to protect patient confidentiality, census tracts with less than 16 observations were not used to generate the maps. All analyses were conducted using Stata 13.1[33] and ArcGIS.[42]

4.4 Results

Table 4-1 shows descriptive statistics for the study population. About 90% of the study population were whites and 9.96% were African Americans/Blacks. Hispanics comprised 15% of the population while non-Hispanics comprised 85%. Residents of urban metropolitan, urban non-metropolitan and rural areas comprised of 86.3%, 12.61% and 1.09% of the study population, respectively. Residents of low poverty CTs comprised about 50.89% while residents of middle and high poverty CTs comprised 29.87% and 19.24% of the study population respectively.

Table 4-1 Descriptive Statistics of Texas Women Diagnosed with Early-Stage Breast Cancer between 1995 and 2012 (n=124,821)

	Freq.	Percent
Race		
White	112,388	90.04
Black	12,433	9.96
Ethnicity		
Non-Hispanic	106,093	85.00
Hispanic	18,728	15.00
Residence		
Urban metro	107,721	86.3
Urban non-metro	15,743	12.61
Rural	1,357	1.09
County Poverty level		
low	63,521	50.89
middle	37,280	29.87
high	24,020	19.24

Table 4-1 Continued

	Freq.	Percent
Tumor Grade		
Low	65,145	52.19
High	37,742	30.24
Unknown	21,934	17.57
Year of Diagnosis		
1995	4,777	3.83
1996	5,042	4.04
1997	5,609	4.49
1998	5,919	4.74
1999	6,287	5.04
2000	6,404	5.13
2001	6,726	5.39
2002	7,005	5.61
2003	6,810	5.46
2004	6,644	5.32
2005	6,862	5.5
2006	7,168	5.74
2007	7,695	6.16
2008	7,977	6.39
2009	8,747	7.01
2010	8,512	6.82
2011	8,319	6.66
2012	8,318	6.66

Surgical treatment

Table 4-2 shows results of the bivariate and multivariate analysis of receipt of surgical treatment. On bivariate analysis (model 1), compared to urban metropolitan residents, urban non-metropolitan (OR=1.69; 95% CI=1.55-1.85) and rural residents (OR=1.44; 95% CI=1.12-1.84) were more likely to receive surgical treatment. Compared to residents of low poverty CTs, residents of middle poverty CTs (OR=1.25; 95%

CI=1.18-1.34) were more likely to be surgically treatment; there was no statistically significant association between living in a high poverty area and receipt of surgical treatment. There was increased likelihood of not being treated surgically with increasing residential isolation (OR=0.36; 95% CI=0.31-0.43).

Adjusting for residence and the control variables (race, ethnicity, tumor grade, age, year of diagnosis), urban non-metropolitan residents (OR=1.60; 95% CI=1.46-1.74) and rural residents (OR=1.29; 95% CI=1.00-1.65) continued to be significantly more likely to receive a surgical treatment compared to urban metropolitan residents. African Americans had a significantly decreased odds (OR=0.78; 95% CI=0.73-0.83) of receiving surgical treatment compared to Whites. Those whose tumor grades were unknown had a significantly decreased likelihood (OR=0.49; 95% CI=0.47-0.52) of receiving surgical treatment compared to those who had low grade tumors. Compared to those diagnosed in 1995, those who were diagnosed between 1996 and 2005 had statistically significant higher likelihood of being surgically treated while those diagnosed between 2006 and 2012 were significantly less likely to receive surgical treatment.

Adjusting for residence, the control variables and CT poverty, urban non-metropolitan residents (OR=1.57; 95% CI=1.44-1.72) continued to have a significantly higher likelihood of being treated surgically compared to urban metropolitan residents. The significant association between rural residence and surgical treatment was eliminated. Compared to residents of low poverty CTs, there was an increased likelihood of being treated surgically among residents of middle poverty CTs (OR=1.09; 95%

CI=1.02-1.16) while residents of high poverty CTs had decreased odds (OR=0.89; 95% CI=0.83-0.96) of being treated surgically.

Adjusting for residence, the control variables and racial residential segregation, urban non-metropolitan residents (OR=1.41; 95% CI=1.29-1.54) continued to have a significantly higher likelihood of being treated surgically compared to urban metropolitan residents; the effect size of urban non-metropolitan residence decreased by 19%, compared to the model adjusted for only the control variables. The significant association between rural residence and surgical treatment was eliminated.

The fully adjusted model showed that urban non-metropolitan residents continued to have a higher likelihood (OR=1.39; 95% 1.27-1.53) of being surgically treated compared to urban metropolitan residents; rural residence was no longer significantly associated with receipt of surgical treatment. Residents of middle poverty CTs continued to be significantly more likely to receive surgical treatment (OR=1.08; 95% CI=1.01-1.15) compared to residents of low poverty CTs; residents of high poverty CTs still had significantly lower odds of being surgically treated (OR=0.87; 95% CI=0.82-0.94). Increasing residential isolation continued to be associated with decreased likelihood of receiving a surgical treatment (OR=0.42; 95% CI=0.36-0.50).

Table 4-2: Bivariate and Multivariate Analysis of Surgical Treatment among Female Residents of Texas Diagnosed with Early-Stage Breast Cancer: 1995-2012 (n=124,821)

	Unadjusted	**Adjusted**			
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Odds Ratio (95% CI)	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**
Residence					
Urban metropolitan area	Ref.	Ref.	Ref.	Ref.	Ref.
Urban non-metropolitan area	**1.69 (1.55-1.85)**	**1.60 (1.46-1.74)**	**1.57 (1.44-1.72)**	**1.41 (1.29-1.54)**	**1.39 (1.27-1.53)**
Rural area	**1.44 (1.12-1.84)**	**1.29 (1.00-1.65)**	**1.26 (0.98-1.62)**	1.09 (0.85-1.41)	1.08 (0.84-1.38)
Census tract poverty level					
Low poverty (≤9.90% below FPL)	Ref.	Ref.	Ref.	Ref.	Ref.
Middle poverty (9.91% - 19.90% below FPL)	**1.25 (1.18-1.34)**		**1.09 (1.02-1.16)**		**1.08 (1.01-1.15)**
High poverty (≥19.90% below FPL)	0.98 (0.91-1.04)		**0.89 (0.83-0.96)**		**0.87 (0.81-0.94)**
Isolation index	**0.36 (0.31-0.43)**			**0.43 (0.37-0.51)**	**0.42 (0.36-0.50)**
Race					
White		Ref.	Ref.	Ref.	Ref.
Black		**0.78 (0.73-0.83)**	**0.80 (0.74-0.85)**	**0.83 (0.77-0.88)**	**0.85 (0.80-0.91)**

*Bold font indicates statistical significance

Table 4-2 Continued

	Unadjusted	Adjusted			
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Odds Ratio (95% CI)	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**	**Odds Ratio (95% CI)**
Ethnicity					
Non-Hispanic		Ref.	Ref.	Ref.	Ref.
Hispanic		0.97 (0.91-1.03)	1.01 (0.94-1.07)	**0.93 (0.87-0.98)**	0.96 (0.90-1.03)
Tumor grade					
Low		Ref.	Ref.	Ref.	Ref.
High		0.99 (0.94-1.04)	0.99 (0.94-1.04)	0.98 (0.94-1.03)	0.98 (0.94-1.03)
Unknown		**0.49 (0.47-0.52)**	**0.49 (0.47-0.52)**	**0.49 (0.47-0.52)**	**0.49 (0.47-0.52)**
Age at diagnosis		1.01 (1.01-1.01)	1.01 (1.01-1.01)	1.01 (1.01-1.01)	1.01 (1.01-1.01)

*Bold font indicates statistical significance

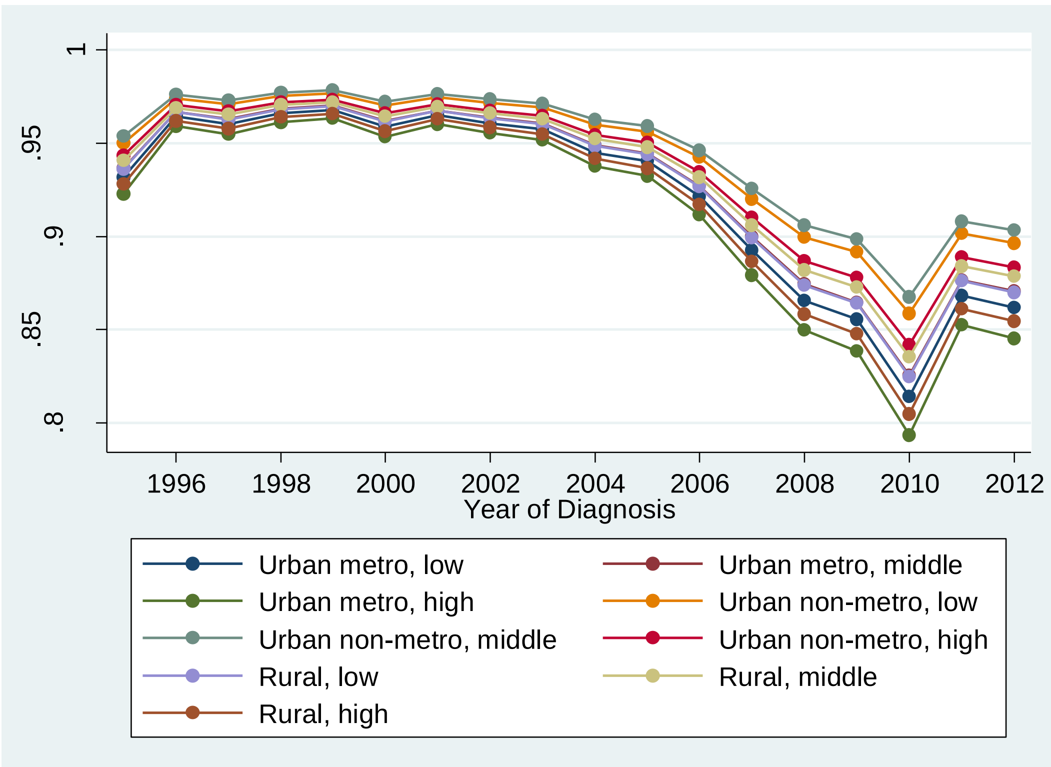
Table 4-2 Continued

	Unadjusted	Adjusted			
	Model 1	Model 2	Model 3	Model 4	Model 5
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Year of diagnosis					
1995		Ref.	Ref.	Ref.	Ref.
1996		**1.98 (1.66-2.37)**	**1.99 (1.66-2.37)**	**1.98 (1.66-2.36)**	**1.98 (1.66-2.36)**
1997		**1.77 (1.50-2.09)**	**1.77 (1.50-2.09)**	**1.77 (1.49-2.09)**	**1.77 (1.50-2.09)**
1998		**2.10 (1.76-2.49)**	**2.10 (1.76-2.49)**	**2.09 (1.75-2.48)**	**2.09 (1.75-2.48)**
1999		**2.21 (1.86-2.63)**	**2.21 (1.86-2.64)**	**2.20 (1.85-2.63)**	**2.20 (1.85-2.63)**
2000		**1.73 (1.47-2.03)**	**1.73 (1.47-2.03)**	**1.72 (1.46-2.02)**	**1.72 (1.46-2.02)**
2001		**2.03 (1.72-2.40)**	**2.03 (1.72-2.40)**	**2.03 (1.72-2.40)**	**2.03 (1.71-2.39)**
2002		**1.81 (1.54-2.12)**	**1.81 (1.54-2.12)**	**1.80 (1.53-2.11)**	**1.80 (1.53-2.11)**
2003		**1.66 (1.42-1.95)**	**1.66 (1.41-1.94)**	**1.66 (1.41-1.94)**	**1.65 (1.41-1.94)**
2004		**1.27 (1.09-1.47)**	**1.26 (1.09-1.47)**	**1.26 (1.08-1.47)**	**1.26 (1.08-1.46)**
2005		**1.16 (1.00-1.35)**	**1.16 (1.00-1.34)**	**1.16 (1.00-1.34)**	1.15 (0.99-1.33)
2006		**0.87 (0.75-1.00)**	**0.86 (0.75-0.99)**	**0.86 (0.75-0.99)**	**0.86 (0.75-0.98)**
2007		**0.61 (0.54-0.70)**	**0.61 (0.53-0.69)**	**0.61 (0.53-0.69)**	**0.60 (0.53-0.69)**
2008		**0.47 (0.42-0.54)**	**0.47 (0.42-0.54)**	**0.47 (0.41-0.53)**	**0.47 (0.41-0.53)**
2009		**0.43 (0.38-0.49)**	**0.43 (0.38-0.49)**	**0.43 (0.38-0.49)**	**0.43 (0.38-0.48)**
2010		**0.32 (0.28-0.36)**	**0.32 (0.28-0.36)**	**0.32 (0.28-0.36)**	**0.31 (0.28-0.36)**
2011		**0.48 (0.43-0.55)**	**0.48 (0.43-0.55)**	**0.48 (0.42-0.54)**	**0.48 (0.42-0.54)**
2012		**0.46 (0.40-0.52)**	**0.46 (0.40-0.52)**	**0.45 (0.40-0.51)**	**0.45 (0.40-0.51)**

*Bold font indicates statistical significance

Figure 4-2 shows that among individuals diagnosed with early-stage breast cancer between 1995 and 2012, the lowest probability of being surgically treated was seen among those living in urban metropolitan, high poverty CT areas who were diagnosed in year 2010. Residents of urban non-metropolitan middle poverty census tracts had the highest probability of being surgically treated across all years of analyses.

Figure 4-2: Trends in Predicted Probability of Surgical Treatment by Residence and Census Tract Poverty.



Type of surgical treatment

Table 4-3 shows results of the bivariate and multivariate analysis of type of surgical treatment received (breast conserving surgery versus mastectomy). On bivariate analysis (unadjusted), compared to urban metropolitan residents, urban non-metropolitan (OR=1.35; 95% CI=1.28-1.41) were more likely to be treated with mastectomy; there was no significant association between rural residence and mastectomy. Compared to residents of low poverty CTs, there was increased likelihood of being treated with mastectomy among residents of middle poverty CTs (OR=1.25; 95% CI=1.18-1.34) and high poverty CTs (OR=1.37; 95% CI=1.31-1.43). There was decreased likelihood of being treated with mastectomy with increasing residential isolation (OR=0.62; 95% CI=0.56-0.68).

Adjusting for residence and the control variables (race, ethnicity, tumor grade, age, year of diagnosis), urban non-metropolitan residents (OR=1.32; 95% CI=1.25-1.39) continued to be significantly more likely to be treated with mastectomy compared to urban metropolitan residents; there was no significant association between rural residence and type of surgical treatment. African Americans had significantly increased odds (OR=1.32; 95% CI=1.25-1.39) of being treated with mastectomy compared to Whites. There was increased likelihood of being treated with mastectomy among individuals who had high (OR=1.32; 95% CI=1.25-1.39) or unknown tumor grade (OR=1.24; 95% CI=1.19-1.30), compared to those who had low grade tumors. Compared to those diagnosed in 1995, those who were diagnosed between 1998 and 2001 had statistically significant higher likelihood of being treated using mastectomy while those diagnosed between 2003 and 2012 were significantly less likely to be treated with mastectomy.

Adjusting for residence, the control variables and CT poverty, urban non-metropolitan residents (OR=1.25; 95% CI=1.19-1.32) continued to have a significantly higher likelihood of being treated with mastectomy compared to urban metropolitan residents. There was no significant association between rural residence and type of surgical procedure used. Compared to residents of low poverty CTs, there was an increased likelihood of being treated with mastectomy among residents of middle poverty CTs (OR=1.11; 95% CI=1.07-1.16) and high poverty CTs (OR=1.19; 95% CI=1.13-1.25).

Adjusting for residence, the control variables and racial residential segregation, urban non-metropolitan residents (OR=1.23; 95% CI=1.17-1.30) continued to have a significantly higher likelihood of being treated with mastectomy compared to urban metropolitan residents; the effect size of urban non-metropolitan residence decreased by 9%, compared to the model adjusted for only the control variables. There was no significant association between rural residence and type of surgical treatment.

Table 4-3: Bivariate and Multivariate Analysis of Surgical Treatment using Breast Conserving Surgery versus Mastectomy among Female Residents of Texas Diagnosed with Early-Stage Breast Cancer: 1995-2012 (n=94,390)

	Unadjusted	**Adjusted**			
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Residence					
Urban metropolitan area	Ref.	Ref.	Ref.	Ref.	Ref.
Urban non-metropolitan area	**1.35 (1.28-1.41)**	**1.32 (1.25-1.39)**	**1.25 (1.19-1.32)**	**1.23 (1.17-1.30)**	**1.18 (1.12-1.25)**
Rural area	1.15 (0.99-1.32)	1.10 (0.94-1.28)	1.04 (0.90-1.22)	1.01 (0.86-1.17)	0.96 (0.83-1.13)
Census tract poverty level					
Low poverty (≤9.90% below FPL)	Ref.		Ref.		Ref.
Middle poverty (9.91% - 19.90% below FPL)	1.25 (1.21-1.30)		1.11 (1.07-1.16)		1.11 (1.06-1.15)
High poverty (≥19.90% below FPL)	1.37 (1.31-1.43)		1.19 (1.13-1.25)		1.17 (1.12-1.23)
Isolation index	0.62 (0.56-0.68)			0.63 (0.56-0.70)	0.64 (0.57-0.72)

*Bold font indicates statistical significance

Table 4-3 Continued

	Unadjusted	Adjusted			
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Race					
White		Ref.	Ref.	Ref.	Ref.
Black		1.32 (1.25-1.39)	1.25 (1.19-1.32)	1.23 (1.17-1.30)	1.18 (1.12-1.25)
Ethnicity					
Non-Hispanic		Ref.	Ref.	Ref.	Ref.
Hispanic		**1.32 (1.25-1.39)**	**1.25 (1.19-1.32)**	**1.23 (1.17-1.30)**	**1.18 (1.12-1.25)**
Tumor grade					
Low		Ref.	Ref.	Ref.	Ref.
High		**1.32 (1.25-1.39)**	**1.25 (1.19-1.32)**	**1.23 (1.17-1.30)**	**1.18 (1.12-1.25)**
Unknown		**1.24 (1.19-1.30)**	**1.24 (1.19-1.29)**	**1.24 (1.19-1.29)**	**1.24 (1.19-1.29)**
Age at diagnosis		1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)

*Bold font indicates statistical significance

Table 4-3 Continued

	Unadjusted	Adjusted			
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Year of diagnosis					
1995		Ref.	Ref.	Ref.	Ref.
1996		**1.32 (1.25-1.39)**	**1.25 (1.19-1.32)**	**1.23 (1.17-1.30)**	**1.18 (1.12-1.25)**
1997		1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.01 (0.91-1.12)
1998		**2.52 (2.22-2.85)**	**2.52 (2.22-2.86)**	**2.51 (2.21-2.85)**	**2.51 (2.21-2.85)**
1999		**2.45 (2.16-2.77)**	**2.45 (2.16-2.78)**	**2.44 (2.16-2.77)**	**2.45 (2.16-2.77)**
2000		**2.35 (2.07-2.66)**	**2.35 (2.08-2.67)**	**2.34 (2.06-2.65)**	**2.34 (2.07-2.65)**
2001		**1.70 (1.52-1.91)**	**1.71 (1.53-1.92)**	**1.70 (1.51-1.90)**	**1.70 (1.52-1.91)**
2002		0.98 (0.88-1.08)	0.98 (0.89-1.09)	0.97 (0.88-1.08)	0.98 (0.88-1.09)
2003		**0.23 (0.21-0.25)**	**0.23 (0.21-0.25)**	**0.22 (0.21-0.25)**	**0.23 (0.21-0.25)**
2004		**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**
2005		**0.20 (0.18-0.22)**	**0.20 (0.18-0.22)**	**0.20 (0.18-0.22)**	**0.20 (0.18-0.22)**
2006		**0.20 (0.18-0.22)**	**0.20 (0.18-0.22)**	**0.20 (0.18-0.22)**	**0.20 (0.18-0.22)**
2007		**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**
2008		**0.21 (0.19-0.23)**	**0.21 (0.19-0.23)**	**0.20 (0.19-0.22)**	**0.21 (0.19-0.23)**
2009		**0.21 (0.19-0.23)**	**0.22 (0.20-0.24)**	**0.21 (0.19-0.23)**	**0.21 (0.20-0.23)**
2010		**0.23 (0.21-0.25)**	**0.23 (0.21-0.25)**	**0.22 (0.20-0.24)**	**0.23 (0.21-0.25)**
2011		**0.21 (0.20-0.24)**	**0.22 (0.20-0.24)**	**0.21 (0.20-0.23)**	**0.22 (0.20-0.24)**
2012		**0.22 (0.20-0.24)**	**0.22 (0.20-0.24)**	**0.21 (0.20-0.23)**	**0.22 (0.20-0.24)**

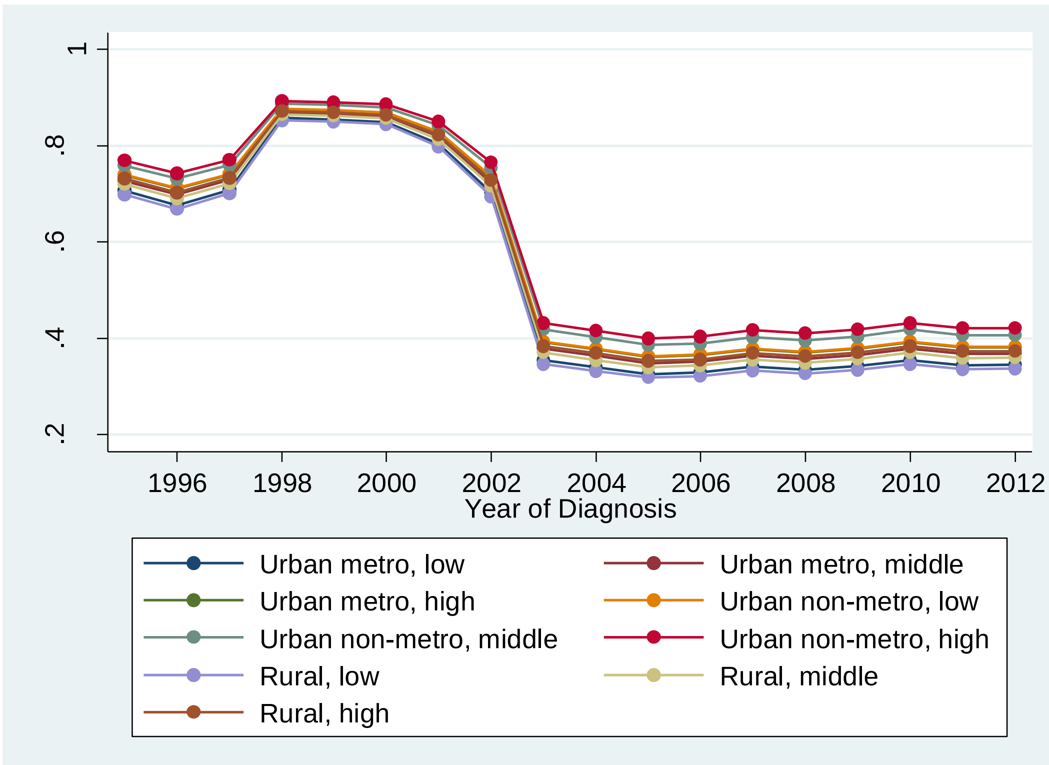
*Bold font indicates statistical significance

The fully adjusted model showed that urban non-metropolitan residents continued to have a higher likelihood (OR=1.18; 95% 1.12-1.25) of being treated using mastectomy compared to urban metropolitan residents; the effect size of urban non-metropolitan residence decreased by 14%, compared to the model adjusted for only the control variables. Rural residence was still not significantly associated with type of surgical treatment. Residents of middle poverty (OR=1.11; 95% CI=1.06-1.15) and high

poverty (OR=1.17; 95% CI=1.12-1.23) CTs continued to be significantly more likely to be treated with mastectomy compared to residents of low poverty CTs. Increasing residential isolation continued to be associated with decreased likelihood of being treated using mastectomy (OR=0.64; 95% CI=0.57-0.72).

Figure 4-3 shows a sharp decline in mastectomy between 2002 and 2003 across all levels of residence and census tract poverty. Residents of urban non-metropolitan high poverty census tracts had the highest probabilities of being treated using mastectomy across all years of analyses.

Figure 4-3: Trends in Predicted Probability of Treatment using Mastectomy by Residence and Census Tract Poverty



Radiation therapy

Table 4-4 shows results of the bivariate and multivariate analysis of radiation therapy following breast conserving surgery. On bivariate analysis (unadjusted), compared to urban metropolitan residents, rural residents (OR=1.52; 95% CI=1.05-2.20) were more likely to receive adjuvant radiotherapy; there was no significant association between urban non-metropolitan residence and adjuvant radiotherapy treatment. Compared to residents of low poverty CTs, there was decreased likelihood of receiving radiotherapy among residents of high poverty CTs (OR=0.84; 95% CI=0.76-0.94); there was no significant association between living in a middle poverty CT and receipt of radiation therapy. There was significantly increased likelihood of adjuvant radiotherapy treatment with increasing residential isolation (OR=1.43; 95% CI=1.12-1.81).

Adjusting for residence and the control variables (race, ethnicity, tumor grade, age, year of diagnosis), rural residents (OR=1.57; 95% CI=1.07-2.30) continued to be significantly more likely to be treated with radiotherapy compared to urban metropolitan residents; there was no significant association between urban non-metropolitan residence and treatment with adjuvant radiotherapy. There was a significantly decreased likelihood of radiotherapy treatment among Hispanics (OR=0.72; 95% CI=0.65-0.80) compared to non-Hispanics. There was also a decreased likelihood of receiving radiotherapy among individuals who had high (OR=0.87; 95% CI=0.79-0.95) or unknown tumor grade (OR=0.61; 95% CI=0.54-0.68), compared to those who had low grade tumors. Compared to those diagnosed in 1995, those who were diagnosed between 2010 and 2012 had statistically significant higher likelihood of being treated with radiotherapy.

Adjusting for residence, the control variables and CT poverty, rural residents (OR=1.47; 95% CI=1.00-2.16) continued to have a significantly higher likelihood of being treated with radiotherapy compared to urban metropolitan residents. There was no significant association between urban non-metropolitan residence and receipt of adjuvant radiotherapy. Compared to residents of low poverty CTs, there was a significantly increased likelihood of radiotherapy among residents of middle poverty CTs (OR=1.15;

95% CI=1.04-1.27); the association between high poverty CT residence and radiation therapy was no longer significant.

Adjusting for residence, the control variables and racial residential segregation, rural residents (OR=1.77; 95% CI=1.20-2.60) continued to have a significantly higher likelihood of being treated with radiotherapy compared to urban metropolitan residents. The association between urban non-metropolitan residence and receipt of adjuvant radiotherapy became significant (OR=1.22; 95% CI=1.07-1.40). There was increasing odds of receipt of radiotherapy with increasing racial residential segregation (OR=1.86; 95% CI=1.43-2.43).

The fully adjusted model showed that urban non-metropolitan residents (OR=1.16; 95% 1.01-1.34) and rural residents (OR=1.65; 95% CI= 1.12-2.44) continued to have a higher likelihood of being treated with radiation therapy compared to urban metropolitan residents. Residents of middle poverty (OR=1.15; 95% CI=1.06-1.15) continued to be significantly more likely to be treated with radiation therapy compared to residents of low poverty census tracts; there was no significant association between living in a high poverty census tract and receipt of radiation therapy . Increasing residential isolation continued to be associated with increased likelihood of being treated using radiation therapy (OR=1.86; 95% CI=1.42-2.43).

Table 4-4: Bivariate and Multivariate Analysis of Adjuvant Radiotherapy among Female Residents of Texas Diagnosed with Early-Stage Breast Cancer: 1995 and 2012 (n=12,899)

	Unadjusted	**Adjusted**			
	Model 1	Model 2	Model 3	Model 4	Model 5
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Residence					
Urban metropolitan area	Ref.	Ref.	Ref.	Ref.	Ref.
Urban non-metropolitan area	1.12 (0.98-1.27)	1.12 (0.99-1.28)	1.07 (0.94-1.23)	**1.22 (1.07-1.40)**	**1.16 (1.01-1.34)**
Rural area	**1.52 (1.05-2.20)**	**1.57 (1.07-2.30)**	**1.47 (1.00-2.16)**	**1.77 (1.20-2.60)**	**1.66 (1.12-2.44)**
Census tract poverty level					
Low poverty (≤9.90% below FPL)	Ref.		Ref.		Ref.
Middle poverty (9.91% - 19.90% below FPL)	1.09 (0.99-1.19)		**1.15 (1.04-1.27)**		**1.15 (1.05-1.27)**
High poverty (≥19.90% below FPL)	**0.84 (0.76-0.94)**		0.96 (0.85-1.09)		0.98 (0.87-1.10)
Isolation index	**1.43 (1.12-1.81)**			**1.86 (1.43-2.43)**	**1.86 (1.42-2.43)**
Race					
White		Ref.	Ref.	Ref.	Ref.
Black		0.94 (0.83-1.07)	0.94 (0.83-1.07)	0.89 (0.78-1.01)	0.89 (0.78-1.01)

*Bold font indicates statistical significance

Table 4-4 Continued

	Unadjusted	**Adjusted**			
	Model 1	Model 2	Model 3	Model 4	Model 5
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Ethnicity					
Non-Hispanic		Ref.	Ref.	Ref.	Ref.
Hispanic		**0.72 (0.65-0.80)**	**0.73 (0.65-0.82)**	**0.75 (0.67-0.83)**	**0.75 (0.67-0.85)**
Tumor grade					
Low		Ref.	Ref.	Ref.	Ref.
High		**0.87 (0.79-0.95)**	**0.87 (0.79-0.95)**	**0.87 (0.80-0.95)**	**0.87 (0.79-0.95)**
Unknown		**0.61 (0.54-0.68)**	**0.61 (0.54-0.68)**	**0.61 (0.54-0.68)**	**0.61 (0.54-0.68)**
Age at diagnosis		0.99 (0.99-1.00)	0.99 (0.99-1.00)	0.99 (0.99-1.00)	0.99 (0.99-1.00)

*Bold font indicates statistical significance

Table 4-4 Continued

	Unadjusted	**Adjusted**			
	Model 1	Model 2	Model 3	Model 4	Model 5
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Year of diagnosis					
1995		Ref.	Ref.	Ref.	Ref.
1996		1.23 (0.96-1.57)	1.23 (0.96-1.58)	1.23 (0.96-1.58)	1.23 (0.96-1.58)
1997		**1.43 (1.03-1.99)**	**1.42 (1.02-1.98)**	**1.43 (1.03-1.98)**	**1.42 (1.02-1.97)**
1998		0.94 (0.33-2.66)	0.91 (0.32-2.58)	0.95 (0.34- 2.67)	0.92 (0.33-2.59)
1999		1.66 (0.49-5.60)	1.65 (0.49-5.57)	1.65 (0.49-5.58)	1.64 (0.48-5.55)
2000		3.11 (0.78-12.41)	3.14 (0.79-12.57)	3.22 (0.80-12.87)	3.26 (0.81-13.05)
2001		**6.30 (1.67-23.74)**	**6.28 (1.66-23.70)**	**6.39 (1.69-24.09)**	**6.37 (1.68-24.06)**
2002		0.59 (0.20-1.78)	0.59 (0.20-1.75)	0.61 (0.20-1.83)	0.60 (0.20-1.81)
2003		0.60 (0.34-1.07)	0.61 (0.34-1.08)	0.59 (0.33-1.05)	0.60 (0.34-1.06)
2004		**4.75 (2.36-9.56)**	**4.80 (2.38-9.68)**	**4.85 (2.41-9.77)**	**4.90 (2.43-9.88)**
2005		**5.41 (2.63-11.15)**	**5.44 (2.64-11.21)**	**5.42 (2.63-11.17)**	**5.45 (2.65-11.23)**
2006		**3.31 (1.70-6.45)**	**3.33 (1.71-6.49)**	**3.34 (1.71-6.52)**	**3.36 (1.72-6.55)**
2007		**7.19 (3.83-13.51)**	**7.18 (3.82-13.48)**	**7.29 (3.88-13.71)**	**7.29 (3.88-13.70)**
2008		**5.19 (3.05-8.83)**	**5.25 (3.09-v)**	**5.27 (3.10-8.97)**	**5.34 (3.14-9.09)**
2009		**7.76 (5.79-10.41)**	**7.81 (5.82-10.48)**	**7.96 (5.93-10.67)**	**8.01 (5.97-10.75)**
2010		**3.33 (2.74-4.05)**	**3.35 (2.76-4.07)**	**3.38 (2.78-4.11)**	**3.40 (2.79-4.13)**
2011		**3.82 (3.15-4.63)**	**3.83 (3.16-4.65)**	**3.89 (3.21-4.72)**	**3.91 (3.22-4.74)**
2012		**4.21 (3.46-5.11)**	**4.23 (3.48-5.13)**	**4.31 (3.54-5.23)**	**4.33 (3.56-5.26)**

*Bold font indicates statistical significance

Figure 4-4 shows fluctuations in receipt of radiotherapy following BCS with a steep decline in seen in 2002 and a steep increase in 2004. Residents of rural middle poverty census tracts had the highest probability of receiving adjuvant radiotherapy across all years of analyses while residents of urban metropolitan low and high poverty counties had the lowest predicted probability of receiving radiotherapy across all years of analyses.

Figure 4-4: Trends in Predicted Probability of Treatment using Adjuvant Radiotherapy

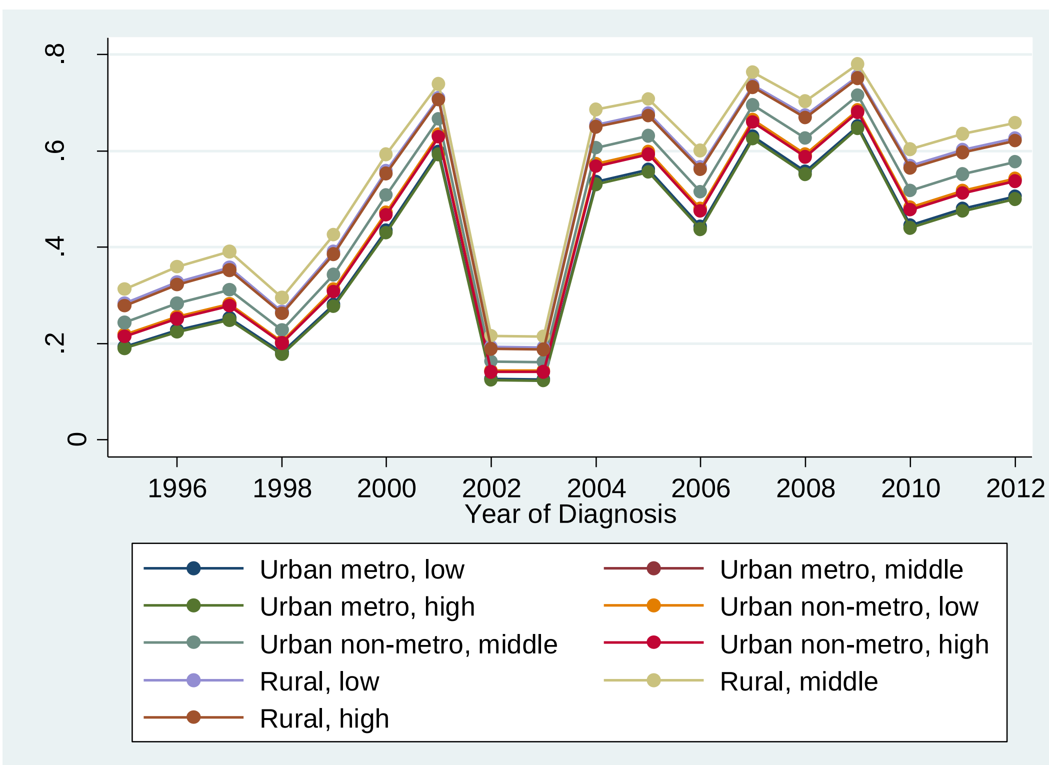
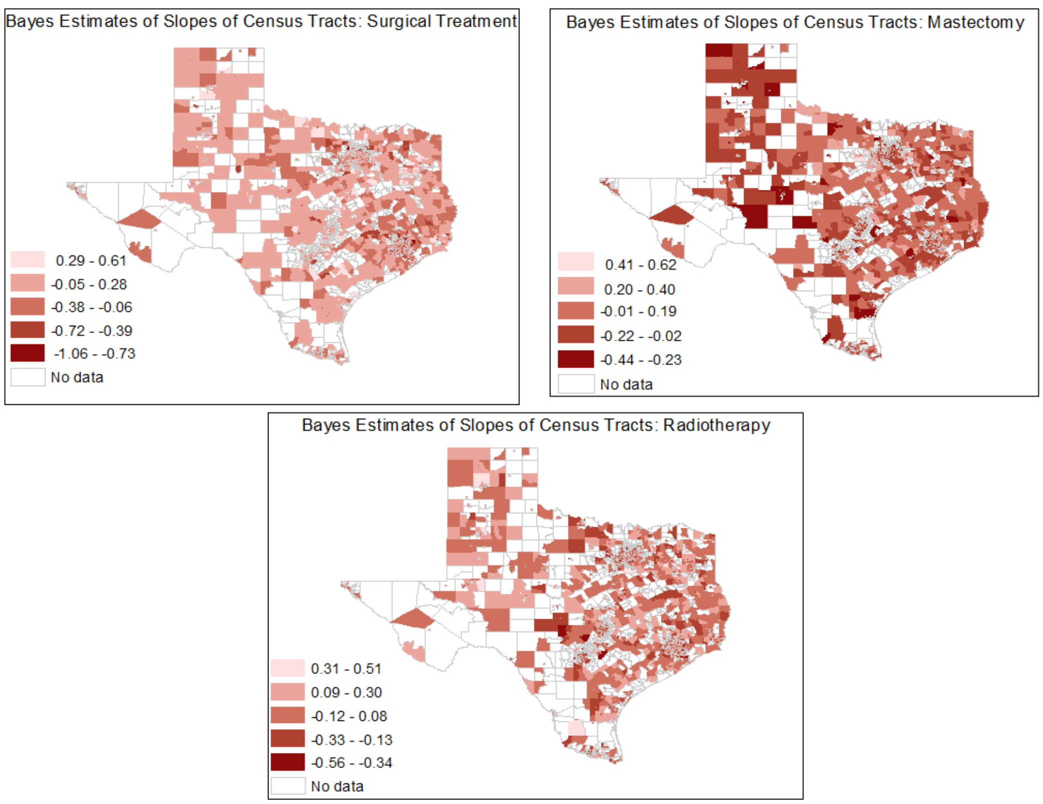


Figure 4-5 shows results of the Bayes estimates of the random intercepts of the models for surgical treatment, type of surgical treatment and receipt of adjuvant radiotherapy. Darker colors indicate census tracts with decreased likelihood of surgical treatment, breast conserving surgery or adjuvant radiotherapy.

Figure 4-5: Census Tract Bayesian Estimates of Slopes of Surgical Treatment, Mastectomy and Radiotherapy post-mastectomy after Early-Stage Breast Cancer Diagnosis.



4.5 Discussion

In this study, residential disparities in treatment of breast cancer among women diagnosed with early stage disease, and whether census tract poverty level and residential segregation explained these disparities were analyzed. Trends in probability of treatment between 1995 and 2012 were also analyzed.

Receipt of surgical treatment

With regards to receiving surgical treatment (mastectomy or breast conserving surgery) versus not receiving surgical treatment, there was a reversal in rural-urban disparities on bivariate analysis. Rural and urban non-metropolitan residents had an increased likelihood of receiving surgical treatment compared to urban metropolitan residents; this persisted after controlling for race, ethnicity, tumor grade and year of diagnosis. We however, found that census tract poverty levels and residential segregation eliminated the significant association between rural residence and receiving a surgical treatment but not the association between urban non-metropolitan residence and receipt of surgical treatment. A Georgia study also found no significant association between rural residence and receipt of surgical treatment.[22] In another study however, Markossian and colleagues found a significantly increased association between rural residence and receipt of surgical treatment[4] while a South Carolina study found that rural patients had a decreased likelihood of being surgically treated compared to the urban patients.[62] In the present study, residents of high poverty CTs were less likely to receive surgical treatment compared to residents of low poverty CTs. Interestingly, residents of middle poverty census tracts had an eight percent higher likelihood of being surgically treated compared to residents of low poverty census tracts. Markossian and colleagues also found that women who were living in high poverty CTs were less likely to receive surgical treatment.[4] Increasing levels of residential segregation was associated with a 58% decreased odds of receiving surgical treatment.

Type of surgical treatment

There was no significant association between rural residence and type of surgical treatment received while urban non-metropolitan residents had an 18% higher likelihood of being treated using mastectomy compared to urban metropolitan residents. This finding is in contrast to a Georgia study which found that rural residents were significantly more likely to be treated using mastectomy.[22] A study that utilized the Surveillance Epidemiology and Ends Result database, also found that rural women had an increased likelihood of receiving mastectomy compared to urban residents.[63] A Kentucky study also reported that rural residents were more likely to be treated using mastectomy; they also found that although the use of mastectomy decreased between 1998 and 2005, it increased back in 2007.[56] Another Kentucky study found that rural residents were more likely to receive mastectomy compared to their urban counterparts.[64] An Australian study also reported that residents of rural areas had an increased likelihood of receiving mastectomy compared to urban residents.[65]

Census tract poverty levels and residential segregation did not explain the association between urban non-metropolitan residence and treatment using mastectomy. Residents of residentially segregated areas had a significantly decreased likelihood of being treated using mastectomy. A study that comprised of only Medicare patients reported that residents of residentially segregated areas had a decreased likelihood of receiving adequate surgical treatment.[44] The increased likelihood of being treated using BCS among residents of residentially segregated areas in spite of the reduced likelihood of surgical treatment could imply that although residents of such areas could face barriers to surgically treatment, these barriers do not appear to influence type of surgical treatment used.

There was an increase in the likelihood of being treated using mastectomy with increasing CT poverty levels. In their study, Gorey and colleagues also found that Californian residents of impoverished neighborhoods were less likely to receive breast conserving surgery compared to residents of affluent poverty although they found no such associations among Canadians.[66] A study comprised of only Medicare patients, reported that residents of low poverty areas and urban areas were more likely to receive BCS compared to their counterparts.[67]

Radiation therapy

With regards to receipt of adjuvant radiation therapy, there was also a reversal in rural-urban disparities among this study population. Rural and urban non-metropolitan residents had a 16% and 65% higher likelihood of receiving radiotherapy treatment respectively, compared to urban metropolitan residents. This finding is in contrast to the studies by Markossian and colleagues which found that rural Georgia residents diagnosed with breast cancer had decreased odds of receiving radiation therapy.[4,22] Another study consisting of residents of Sacramento and 13 counties around Sacramento reported that rural residents and residents of areas close to metropolitan areas had a decreased likelihood of receiving radiation therapy following lumpectomy; however, their study was not restricted to only patients who had early-stage tumors.[68] A study which utilized the SEER data and focused on women diagnosed with breast cancer between 2000 and 2009 also found that rural residents were less likely to receive radiotherapy compared to urban residents.[69] These differences in findings could be because these studies included patients with all stages of breast cancer while this study was limited to patients who had early-stage breast cancer. However, a Kentucky study of patients diagnosed with early-stage breast cancer reported that rural residents had a decreased likelihood of receiving radiotherapy after breast conserving surgery.[56] Another Kentucky study which included only patients diagnosed with early-stage breast cancer also found that rural residents were less likely to receive radiation therapy after BCS.[64] Women who were treated in rural centers have also been reported to be less likely to receive radiotherapy following BCS.[70] The difference between our findings and the findings by Dragun et al. and Freeman et al. is highlights variations in disparities that could exist across states, and the importance of state-based studies. It is also possible that rural residents who opt to be treated with BCS do so because they have the means to pay for radiotherapy, thus, our study results.

Census tract poverty and residential segregation did not explain the association between receipt of radiation therapy and rural residence; however the association between urban non-metropolitan residence and receipt of radiation therapy became significant after the two variables were included in the model. Increasing residential segregation was associated with increased likelihood of receiving radiation therapy.

Residents of middle poverty census tracts had 15% higher likelihood of receiving radiation therapy compared to residents of low poverty CTs; there was no significant association between living in a high poverty area and receiving radiation therapy. In contrast to these findings, Markossian and colleagues reported that residents of middle and high poverty CTs were less likely to receive radiotherapy compared to residents of low poverty CTs.[4]

Trends in probability of receipt of surgical treatment, mastectomy and radiotherapy

There was a gradual decline in receipt of surgical treatment between 2001 and 2010. However, the lowest probability of receiving surgical treatment found among residents of urban metropolitan high poverty census tracts was 0.79. A steep decline in mastectomy rates was observed among those diagnosed with early-stage breast cancer between 2002 and 2003 across all levels of residence and CT poverty. It is possible that this decline be as a result of increased awareness of equal survival rates for mastectomy and BCS with adjuvant radiotherapy. In contrast to these findings, a study based upon data from the Mofitt cancer center that focused on patients diagnosed with breast cancer between 1994 and 2007 reported a gradual increase in mastectomy across a years of studies.[57] A Kentucky study also found that although the use of mastectomy decreased between 1998 and 2005, it increased back in 2007.[56] In contrast to the studies by Mcguire and Dragun, in the current study, probability of treated using mastectomy has plateaued since 2002. There were constant fluctuations in receipt of adjuvant radiotherapy could be an indication for a need to increase access to patients and implement interventions to ensure that providers adhere to best practices.

4.6 Limitations and Strengths

This study has some limitations. First, the TCR data only covers the state of Texas, thus study findings may not be generalizable to the entire United States population. This study was also limited to those who had early-stage diagnosis, thus the findings may not be generalized to patients who are diagnosed with late-stage breast cancer. Analyses were limited to individuals who identified their race as White or African American/Blacks and thus, study findings may not be generalizable to other racial groups. Information on patient preference of type of surgical treatment which could influence treatment options was not available and therefore not included in the analyses. Information on health insurance was also not available across all years of analyses therefore we were unable to control the association between health coverage and stage at diagnosis. The results of the radiation therapy analyses should also be interpreted with caution because of the smaller sample size and the large confidence interval of some of the estimates.

In spite of these limitations, this study has several strengths. First to prior to this study, to the best of our knowledge, only one study had previously explored the association between residential segregation and breast cancer treatment, and the study comprised of only Medicare patients while our study comprised of all adults. The use of multilevel models also allowed us to account for variations across CTs. The large number of years also provided a clearer picture about how treatment patterns have varied across the years of our analyses. Our use of GIS also enabled identification of particular census tracts that have a higher probability of inadequate treatment which in turn could provide guidance for stake holders in such CTs.

5. SUMMARY AND CONCLUSION

5.1 Summary

In this study, between the national and state cohorts, there were variations in residential disparities in stage at diagnosis of breast cancer. Among the national cohort, rural and urban non-metropolitan residents were more likely to receive a late-stage diagnosis compared to those who lived in urban metropolitan areas; county poverty level explained the association between UNM residence and late-stage diagnosis but not the association between rural residence and late-stage breast cancer. Women who lived in rural areas with high poverty levels were the most likely to have late-stage breast cancer across all years.

Among residents of the state of Texas, women who lived in urban non-metropolitan areas were more likely to receive a late-stage diagnosis compared to urban metropolitan residents. There was no association between rural residence and late-stage diagnosis. Increasing levels of residential segregation levels was associated with decreased likelihood of late-stage diagnosis. There was no significant association between travel distance to nearest health care provider and stage at diagnosis of breast cancer. Women who lived in census tracts with high poverty areas were more likely to have late-stage breast cancer compared to women who lived in low poverty census tracts. Women who lived in UNM high census tract poverty areas were the most likely to have late-stage breast cancer across all years.

Acceptable treatment of early-stage breast cancer includes mastectomy or breast conserving surgery accompanied by radiotherapy. Treatment using breast conserving surgery with adjuvant radiotherapy has been shown to have comparable survival benefits with treatment using mastectomy.[51] This advantage is lost if BCS is not accompanied by radiotherapy.[50, 55, 56]

The third analysis showed that residents of UNM and rural residents were more likely to receive any surgical treatment compared to urban metropolitan residents. Census tract poverty and residential segregation, explained the association between rural residence and surgical treatment but not the relationship between urban non-metropolitan residence and surgical treatment of breast cancer. Residents of urban non-metropolitan were more likely to be treated with mastectomy; there was no significant association between rural residence and type of surgical treatment. Rural residents were more likely to be treated with adjuvant radiotherapy. There was no association between UNM residence and stage at diagnosis of breast cancer. Across all years, residents of urban metropolitan high poverty CTs had the lowest probability of being treated surgically and the lowest probability of receiving radiotherapy after breast conserving surgery. Residents of UNM high poverty CTs had the highest probability of being treated using mastectomy across all years.

5.2 Policy and Practice Implications

The findings from this study have important policy and practice implications. The results reinforce the need to monitor trends in late-stage diagnosis nationally and the state level, as this could provide insights into gains that have been made with regards to reduction of disparities in late-stage diagnosis of breast cancer. The results also highlight the need for state-based interventions or modification of national policies and interventions in order to ensure that state needs are being met. For example, based upon results from the analyses of the national cohort, it would be logical to develop interventions or programs that focus on rural residents; however, the Texas–based analyses showed that rural residents were not more likely to have late-stage diagnosis. Associations between area poverty and late-stage diagnosis has also been found to vary across states.[34]

The persistent association between late-stage diagnosis and area poverty is an indication that concerted efforts are needed to identify factors or barriers that contribute to these disparities among residents of middle and high poverty areas. It is also necessary to develop and implement interventions targeting such factors or barriers among residents of poor communities.

The absence of statistically significant association between travel distance to the nearest PCP and stage at diagnosis of breast cancer could be good news for poorer communities that have fewer PCPs or primary care facilities due to financial constraints. This lack of association suggests that could be indicative of a need to explore other access to care measures such as patient navigation, care coordination, insurance status, and lack of knowledge, in order to identify the influence they have on breast cancer disparities, and develop interventions accordingly.

The inadequate treatment found among residents of highly racially segregated and urban metropolitan areas could also provide guidance to stakeholders working to eliminate early-stage breast cancer treatment disparities. This finding could be an indication that outreach programs and educational efforts are needed to raise awareness of disparities in breast cancer treatment among residents and health care providers in urban metropolitan and racially segregated areas. Strategies to increase access to adequate treatment should also be explored. It is also important to identify the reasons for the increased likelihood of mastectomy found among residents of UNM residents. This will provide insights about whether the higher odds of mastectomy are as result of patients' preference, or other factors such as inadequate knowledge about the comparable outcomes between mastectomy and BCS combined with radiotherapy or inadequate access.

The ability to identify specific groups that have higher risks of late-stage diagnosis and inadequate treatment, by levels of residence and area poverty level is also important because resources for interventions that aim to reduce disparities are usually limited. Identifying sub-groups that have such high risks could therefore ensure that such interventions are implemented in areas that have the most need. For example, this study shows that residents of urban non-metropolitan areas in Texas have the highest need for interventions aimed at increasing early-stage breast cancer diagnosis while residents of urban metropolitan high poverty census tracts have the most need for interventions to ensure adequate treatment of breast cancer.

5.3 Conclusion

In order to achieve the HealthyPeople 2020 objectives of reducing the incidence of late-stage breast cancer as well as mortality rates, it is important to consider geographical characteristics when developing and implementing interventions aimed at reducing disparities in stage at diagnosis and treatment of breast cancer.

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