CERVICAL CANCER DISPARITIES IN TEXAS

by

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ABSTRACT

As a preventable and curable cancer, cervical cancer incidence and mortality rates have declined due to the adoption of Human papillomavirus (HPV) vaccine as a prevention method, as well as the wide use of Pap smear tests as a screening tool. However, cervical cancer remains one of the most common cancers among females in the United States. Cervical cancer outcome disparities by race/ethnicity, socioeconomic status, and geographic location have been documented. One of the overarching themes of the American Cancer Society's (ACS) 2015 goals is to eliminate disparities in cancer burdens among different segments of the U.S. population.

Despite advances in knowledge about cancer during the last century, identifying factors associated with cervical cancer disparities remains a challenging task. An increasing number of studies revealed that health disparities are attributed to a wide range of factors that exist and operate on different levels (e.g., contextual and individual level). However, there are several research gaps in the literature on cervical cancer disparities. First, no research has taken into consideration individual-level factors (age, race/ethnicity, tumor characteristics, and type of treatment received) in conjunction with contextual-level factors (demographic factors, behavioral factors, health insurance expenditure, urbanization, and spatial access to health care) to study cervical cancer disparities. Second, no work has placed all the above factors in a spatial context and examined how they jointly contribute to geographic disparity in cancer. Third, no work

has examined how the racial disparity in cervical cancer varies spatially. Fourth, little work has analyzed geographic disparities in cervical cancer survival and examined impacts of multilevel factors on the geographic disparities.

Taking advantage of Geographic information science and spatial analysis techniques, this dissertation investigated cervical cancer disparities of state at diagnosis, survival and mortality in Texas based on data from 1995 to 2008 from three social domains: race/ethnicity, socioeconomic status (SES), and geographic location. Multilevel models were adopted to measure the impact of individual- and contextual-level factors on cervical cancer disparities. Spatial scan statistics were used to measure geographic variations of cervical cancer outcomes. The dissertation also used a population-weighted risk difference to measure geographic variations of racial/ethnic disparities of cervical cancer mortality.

This dissertation found statistically significant racial/ethnic and SES disparities of cervical cancer late-stage diagnosis and survival. African-American women had an elevated risk of late-stage diagnosis or mortality compared with their non-Hispanic white counterparts. Compared with women from census tracts with a higher SES, individuals from census tracts with a lower SES experienced elevated risk of late-stage diagnosis or mortality. The study did not observe any significant geographic disparities of late-stage diagnosis. However, it identified statistically significant geographic clusters of longer-than-expected or shorter-than-expected cervical cancer survival. This study also identified significant geographic variations in racial/ethnic disparities. Findings from this

study have several important implications for reducing cervical cancer disparities in Texas by providing information for developing effective cervical cancer intervention programs in Texas. This research found that contextual-level factors explained part of cervical cancer disparities. Therefore, it is important to ameliorate contextual effects in order to reduce disparities in cervical cancer survival. Intervention programs should be developed to target socially deprived areas (e.g., areas with lower SES, areas with higher percentage of African Americans, foreign-born women, or linguistic isolated households).

CHAPTER I

INTRODUCTION

Background

Cancer has become the second leading cause of mortality in the United States. About 1, 660, 290 new diagnosed cases and 580, 350 mortality cases have been estimated in the United States in 2013 according to the American Cancer Society (ACS) 2013(ACS 2013). There has been striking progress in the decrease of cancer mortality rates and the increase of survival rates since 1990. However, not all people benefit from such progress, nor do all people benefit equally.

There are unevenly distributed cancer-related burdens among people in the United States, including screening, incidence, diagnosis, treatment, survival, and mortality (Feresu et al. 2008; Ward et al. 2004). Minority groups such as African Americans and Hispanics, as well as individuals with lower socioeconomic status (SES) have persistently experienced higher cancer risks. There are also geographic variations, such as rural/urban differences, in cancer risks in the United States. There are unequal/disproportional cancer burdens in disadvantaged social groups compared to advantaged social groups. It has become one of the overarching themes of the ACS's 2015 goals to "eliminate disparities in the cancer burden among different segments of the US population defined in terms of socioeconomic status (income, education, insurance status, etc.), race/ethnicity, residence, sex, and sexual orientation." (Byers et al. 1999)

In the United States, cervical cancer is one of the most common cancers among women. The transmittable agent human papillomavirus (HPV) infection is well known as

the primary origin of cervical cancer. About 12, 340 new cases and 4, 030 mortality cases are estimated in 2013 according to the ACS 2013. Texas ranks second in the estimated number of new cases of cervical cancer, accounting for 1,110 new cases in 2013 (ACS 2013).

Although the overall incidence and mortality rates in cervical cancer have declined due to the adoption of HPV vaccine as a prevention method as well as the wide use of Pap smear tests as a screening tool (Byrd et al. 2013; Mitchell and Mccormack 1997), disparities of cervical cancer still exist among different population groups. Racial disparities exist between minority groups and whites in cervical cancer diagnosis, incidence, screening, and mortality. Hispanics experience the highest incidence rate, and African Americans have the second highest incidence rate of cervical cancer. However, African Americans have steadily experienced the highest documented mortality rate. Compared to whites, minorities have a higher probability of being diagnosed at a late stage (Coker et al. 2009). SES disparities in cervical cancer have been well documented, too. People with lower SES were found to have a lower cervical cancer screening rate (Daley et al. 2011). Females with lower SES have a higher probability of being diagnosed with late-stage cervical cancer compared to women with higher SES (McCarthy et al. 2010). Cervical cancer incidence, screening, and mortality vary across geographic regions (Horner et al. 2011). People from rural areas are less likely to receive cervical cancer screening than those from urban areas (Jackson et al. 2009). Residents from the US-Mexico border counties experienced higher cervical cancer incidence compared to those from non-border counties (Coughlin et al. 2008). These remaining disparities suggest sustained efforts are necessary in understanding factors associated with the

disproportionate burdens among ethnic minorities and socioeconomically disadvantaged groups toward the goal of eliminating disparities in cervical cancer.

Problem Statement

Despite advances in knowledge about cancer during the last century, identifying factors associated with cervical cancer disparities remains a challenging task. An increasing number of studies have revealed that health disparities are attributed to a wide range of factors that exist and operate on different levels (e.g., contextual and individual level) (Holmes et al. 2008). However, there are several research gaps in the literature on cervical cancer disparities. First, no research has taken into consideration individual-level factors (age, race/ethnicity, tumor characteristics, and type of treatment received) in conjunction with contextual-level factors (demographic factors, behavioral factors, health insurance expenditure, urbanization, and spatial access to health care) to study cervical cancer disparities. Second, no work has placed all the above factors in a spatial context and examined how they jointly contribute to geographic disparity in cancer. Third, no work has examined how the racial disparity in cervical cancer varies spatially. Fourth, little work has analyzed geographic disparities in cervical cancer survival and examined impacts of multilevel factors on the geographic disparities.

Objectives and Research Questions

The purpose of this study is to contribute to the theoretical literature on spatial epidemiology and cancer research by examining the cervical cancer disparities in Texas. More specifically, this study will investigate cervical cancer disparities in Texas from the stage at diagnosis, mortality and survival by several social domains: race/ethnicity, SES,

and geographic locations. Meanwhile, it will determine how individual- and contextual-level factors jointly contribute to the disparities.

The research aims to address the following questions:

1. Does the stage of cervical cancer at diagnosis vary by SES, race/ethnicity, and geographic locations in Texas?
2. How do individual-level factors in conjunction with contextual-level factors impact the occurrence of the stage at diagnosis and its geographic pattern?
3. Does cervical cancer survival vary by SES, race/ethnicity, and geographic locations in Texas?
4. How individual-level factors in conjunction with contextual-level factors impact cervical cancer survival and its geographic pattern?
5. Are there any geographic variations of racial/ethnic disparities of cervical cancer mortality in Texas? How do contextual-level factors contribute to the disparities?

The research proposes five hypotheses to answer the above research questions:

Hypothesis 1: The stage at diagnosis of cervical cancer varies by SES, race/ethnicity, and geographic locations.

Hypothesis 2: Individual- and contextual- level factors jointly impact the occurrence of the stage at diagnosis and its geographic pattern.

Hypothesis 3: Cervical cancer survival varies by SES, race/ethnicity, and geographic locations.

Hypothesis 4: Individual- and contextual- level factors jointly impact cervical cancer survival and its geographic pattern.

Hypothesis 5: There are statistically significant geographic variations of racial/ethnic disparities of cervical cancer mortality in Texas. These disparities could be explained by contextual-level factors.

CHAPTER II

LITERATURE REVIEW

Introduction

This chapter reviews literature related to cancer disparities. The chapter consists of four sections. Section 2.2 introduces definitions of health disparities. Section 2.3 introduces definitions of cancer disparities and summarizes literature on several social domains. Section 2.4 reviews methods used in cancer disparity research. The chapter concludes with a description of limitations in current research.

Health Disparities

The term "Health disparities" or "Health disparity" has appeared in public health literature that studies the differences in health among different social groups over the last three decades. Health disparity has been a developing concept all over the world. Since the early 1990s in Europe, health disparity has referred to health differences among socioeconomic groups that are "not only unnecessary and avoidable but, in addition, are considered unfair and unjust," because it is assumed that everyone has an equal opportunity to "attain their full health potential" (Whitehead 1992). However, there was no clear official definition in the United States until 1999 when the National Institutes of Health (NIH) defined health disparity as "the differences in the incidence, prevalence, mortality and burden of diseases and other adverse health conditions that exist among specific population groups in the United States" (NIH 1999). The research on health disparity initially focused on racial disparities and later expanded scope to incorporate other factors such as geographic location, education, and income (Krieger 2005).

The National Cancer Institute (NCI) defines health disparities as "differences in the incidence, prevalence, mortality, and burden of cancer and related adverse health conditions that exist among specific population groups in the United States." The population groups can be characterized by "race/ethnicity, age, gender, income, education, social class, disability, geographic location, or sexual orientation" (NCI 2004).

In spite of the various definitions, health disparity has often been considered an "unjust" or "unfair" difference that could be modified or prevented through policies (Krieger 2005; Braveman 2006). Not all differences in health are health disparity. Differences in health such as biological differences are not characterized as health disparity. This study will adopt the definition from Braveman (2006) that health disparity is a disparity where disadvantaged social groups persistently experience worse health than advantaged social groups. This study characterizes the social groups from perspectives of race/ethnicity, SES, insurance, geographic locations, socio-environmental factors, socio-cultural factors, and spatial access to health care. Therefore, this study considers health disparity as an unjust difference from the above aspects that could be amenable to interventions by policies. Pursuing health equality is pursuing the elimination of the above health disparities.

Cancer disparities

Cancer disparities are defined as "adverse differences in cancer incidence, prevalence, survivorship, mortality and cancer-related burden among specific population groups," (NCI 2012). Cancer rates have decreased in recent years. The remarkable decrease in cancer incidence is primarily due to the intervention in tobacco use from the early 1990's. The top five cancer sites in cancer disparities research are: breast, colon,

prostate, cervical, and lung cancer. The cancer outcomes in cancer disparities research, ranked by the number of studies conducted from the most to the least are: survival, screening, mortality, diagnosis, treatment, and incidence.

In order to better understand cancer disparities, this research systematically reviewed publications on cancer disparities. The review is conducted based on the "cancer disparities grid" developed by Krieger (2005) to summarize what is known and not known in cancer disparities research. The cancer disparities grid characterizes research based on several social domains (socioeconomic position, race/ethnicity, age, gender, language, disability, immigration status, literacy, insurance status, housing status, sexuality, and geography) and cancer continuums (incidence, prevention, screening, diagnosis, etiology, access to clinical trials, morbidity, treatment, survival, and mortality). This review aims to identify three areas: 1 areas where evidence of cancer disparities is well known and documented; 2 areas where evidence of cancer disparities is inconsistent, suggesting more research is encouraged in order to obtain a better understanding; and 3 areas where there is little or no evidence of cancer disparities, suggesting research needs to be done to address the research gap.

This research conducted a literature search in the database of Web of Science (ISI). The keywords used were 'cancer disparities,' and 'cancer disparity'. There were about 4,500 publications for the preliminary search and about 300 relevant papers were left after refinements. The cancer disparities grid was modified to incorporate race/ethnicity, SES, insurance, geography, access to health care, behavioral factors, socio-cultural factors (such as immigration status and language), and socio-environmental factors (such as the percentage of Hispanics and African Americans) within the domains

of social inequality. The review used incidence, screening, diagnosis, treatment, survival, and mortality as the cancer continuums. Through categorizing the research into the "grid" that is the intersection of social inequality and cancer continuum, this review found that most studies on cancer disparities have focused on race/ethnicity and SES within the domain of social inequality, and survival, screening, mortality, and diagnosis within the cancer continuum. A moderate amount of research has focused on insurance, socio-cultural factors, and geography within the domain of social inequality, as well as incidence and treatment within the cancer continuum. There is little work on socio-environmental factors, behavioral factors, and spatial access to health care from the domain of social inequality. Table 2.1 presents a cervical cancer disparities grid. Table 2.2 presents a list of cancer disparities research.

Table 2.1 Cervical cancer disparities grid

Domains of social inequality	Cancer continuum					
	Incidence	**Screening**	**Diagnosis**	**Treatment**	**Survival**	**Mortality**
Race/ethnicity	Coughlin et al. 2008; Hopenhayn et al. 2008; and McCarthy et al. 2010	Adams et al. 2007; De Alba and Sweningson 2006; and Wang et al. 2008	Coker et al. 2009; Coughlin et al. 2008; and Priest et al. 2010	Coker et al. 2009; and Leath et al. 2005	[a][Brookfield et al. 2009; Leath et al. 2005; and Lim and Ashing-Giwa 2011; and Singh et al. 2004]	Horner et al. 2011; McCarthy et al. 2010; and Singh et al. 2004
Socioeconomic status	Chu et al. 2007; Coughlin et al. 2008; McCarthy et al. 2010; Rodriguez et al. 2005; and Singh et al. 2004	Daley et al. 2011; Datta et al. 2006; and Lofters et al. 2010	McCarthy et al. 2010; and Patel et al. 2009	Brookfield et al. 2009; and Leath et al. 2005	Lim and Ashing-Giwa 2011; and Singh et al. 2004	Du et al. 2010; McCarthy et al. 2010; and Singh et al. 2004
Immigration status	McCarthy et al. 2010	Goel et al. 2003; McDonald and Neily 2011; and Rodriguez et al. 2005	McCarthy et al. 2010; and McDonald and Neily 2011	Du et al. 2010		McCarthy et al. 2010
Language		and Ponce et al. 2006				
Geography	Coughlin et al. 2008; Horner et al. 2011; and Patel et al. 2009	Goel et al. 2003; and Horner et al. 2011	Horner et al. 2011; and Patel et al. 2009			Horner et al. 2011
Insurance		Shi et al. 2011	Banerjee et al. 2007; and Leath et al. 2005	Leath et al. 2005	Leath et al. 2005; and Morgan et al. 1996	
Socio-environmental factors		Coughlin et al. 2008;				
Behavioral factors		McDonald and Neily 2011; and Welch et al. 2008				Du et al. 2010
Spatial access to health care						

[a] indicates contradictory conclusions.

Table 2.2 A review of selected publications on cancer disparities in the United States

Study	Purpose	Cancer Site(s), continuum, and study Period	Settings and scale	Domains of social inequality	Conclusion
Bradley et al. 2001	To examine the disparities in cancer diagnosis and survival between insured and uninsured people	Diagnosis and survival in breast, cervix, lung, prostate, and colon cancer, 1996-1998	Michigan, individual level	Race, SES, and insurance	Disparities existed in diagnosis and survival between insured and uninsured people.
Brookfield et al. 2009	To examine the racial and SES disparities in cervical cancer survival.	Cervical cancer survival and treatment, 1998-2003	Florida, individual level	Race and SES	Racial and SES disparities in survival could be explained by stage at diagnosis and treatment.
Byers et al. 2008	To examine the impact of SES on cancer survival.	Breast, Colon, and prostate cancer survival, 1997	Seven states in the United States, individual level	Race and SES	Low SES was associated with cancer mortality, which could be explained by late-stage at diagnosis and less treatment.
Chu et al. 2007	To investigate the trend of cancer mortality disparities in race and SES	The mortality of breast, colon, cervical, lung, and prostate cancer, 1990-2000	United States, County level	Race and SES	The change in the racial disparity by SES varied by cancer sites.
Coker et al. 2009	To investigate racial disparities in cervical cancer survival and exploratory factors in Texas	Cervical cancer survival, diagnosis, and treatment, 1998-2002	Texas, individual level	Race, SES, socio-cultural factors	Racial disparities in survival could not be explained by the factors.

Table 2.2-Continued

Coughlin et al. 2008	To examine the geographic disparities in cervical cancer incidence between the US-Mexico border region and other regions in the United States	Cervical cancer incidence and diagnosis, 1998-2003	US-Mexico Border counties, County level	Race, geography, SES, and immigration status	Hispanics had higher incidence in border counties than non-Hispanics in both border counties and nonborder counties. There were significant disparities in geography, race, migration status, and stage at diagnosis.
Du et al. 2007	To evaluate the impact of SES and treatment on racial disparities in colon cancer survival	Colon cancer treatment and survival, 1992-1999	11 geographic areas in the United States, National level	Race and SES	SES substantially explained racial disparities. SES and treatment were associated with colon cancer survival.
Du et al. 2011	To examine the impact of SES on racial disparities in cancer survival and treatment	Treatment, diagnosis, and survival of eight cancer sites , 1973-2003	Unites States, individual level	Race, SES, and insurance	Higher SES could explain the higher survival rate. Racial disparities persisted in breast and prostate cancer after adjusting for SES and treatment.
Feresu et al. 2008	To examine the racial disparities in breast and cervical cancer screening	Breast and cervical cancer screening, 1993–2004	Nebraska, individual level	Race and SES, insurance, and geography	There were significant racial disparities in cancer screening.
Goel et al. 2003	to examine the disparities in cancer screening by race and birthplace	Screening of cervical, breast, and colon cancer , 1998	United States, individual level	Race, immigration, geography, SES, and behavioral factors	Immigration status explained a portion of racial disparities.
Goovaerts et al. 2007	To examine spatial variations of racial disparities	Prostate and lung cancer mortality, 1970-1994	688 counties of the Southeastern Unites States, county level	SES and geography	Counties with significant racial disparities were identified.

Table 2.2-Continued

Grann et al. 2005	To examine racial and geographic disparities in breast cancer mortality	Breast cancer diagnosis and mortality, 1990-2001	United States, Individual level	Race, geography, and insurance	Disparities existed in mortality by race, geography, and SES. Racial disparities persisted after adjusting for SES. Insurance partially explained racial disparities.
Haas et al. 2008	To examine how the racial segregation influence the breast cancer disparities in care and mortality	Breast cancer mortality and diagnosis, 1992-2002	United States, individual level	Race and socio-environmental factors	Segregation accounted for part of the racial disparities in cancer care, but it did not explain the mortality disparities.
Hsu et al. 2007	To examine the Geographic disparities in prostate cancer	prostate cancer mortality, 1980-2001	Texas, County level	Geography and race	Prostate cancer mortality varied by race/ethnicity in Texas.
Huang et al. 2007	To detect spatial clusters in colon and lung cancer survival	Colon and lung cancer survival, 1988-2002	California and the County of Los Angeles, county level	Race, geography, SES, and insurance	Clusters of significant survival differences were identified.
Jackson et al. 2009	To investigate the impact of distance, geography, and other factors on breast cancer screening rates	Breast cancer screening, 2003-2005	California, multiple geographic scales	Race, SES, spatial access to health care, and language	Distance and geography did not explain the breast cancer screening disparity.
Kandula et al. 2006	To determine the factors contributing to racial disparities in colon, cervical, and breast cancer screening	Colon, cervical, and breast cancer screening, 2001	California, individual level	Race, immigration status, language, and spatial access to health care	Social demographic factor, years in the United States, language explained the disparities.

Table 2.2-Continued

Krieger et al. 2006	To investigate if SES disparity in breast cancer incidence has decreased and the impact of race on the disparity	Breast cancer incidence, 1978-2002	California and Massachusetts, individual level	Race and SES	The change in the SES disparity varied by race.
Kuo et al. 2010	To examine whether differences in late-stage breast cancer diagnosis vary spatially	Breast cancer diagnosis, 2000-2005	California, Medical Service Study Area	Race, SES, geography, and immigration status	Significant geographic disparities in stage at diagnosis have been identified.
Lian et al. 2011	To examine the geographic disparities in CRC survival and the contributing factors	Colon cancer survival , 1995-2003	United States. individual level	Race, SES, geography, and behavioral factors	Significant overall geographic variation was found. SES did not explain the disparities.
Luo et al. 2010	To investigate the influence of spatial aggregation error on the disparity in late-stage diagnosis	Breast cancer diagnosis, 1998-2002	Illinois, zip code and census block levels	Race, SES, and spatial access to health care	Spatial aggregation error could significantly modify the disparities.
McCarthy et al. 2010	To evaluate how race and SES affect cervical cancer incidence and mortality	Cervical cancer diagnosis, incidence, and mortality, 1995-2006	New York City, individual level	Race, SES, and immigration status	Race was associated with late-stage diagnosis and mortality. SES was associated with mortality.
Meliker et al. 2009	To examine how racial disparities change at different geographic scales, and the factors that have contributed to it	Breast and prostate cancer survival, 1985- 2002	Michigan, three different scales	Race, SES, and geography	SES contributed to the racial disparities at larger scales.

Table 2.2-Continued

Robbins et al. 2010	To examine the contribution of insurance and other factors in cancer survival	colon cancer diagnosis, treatment, and survival, 1998-2002	United States, Individual level	Race, SES, and insurance	Insurance, stage at diagnosis, and treatment explained the disparity
Russell et al. 2011	To examine the impact of residential segregation and spatial access on breast Cancer mortality	Breast Cancer Mortality, 1999-2003	Georgia, individual level	Race, SES, and spatial access to medical services	Racial disparities in the mortality could not be explained by the spatial access.
Schootman et al. 2009	To investigate the factors contributing to geographic distribution of breast cancer survival	Breast cancer survival, 1991-1999	United States, census tract level	Race, SES, geography, and socio-cultural factors	Stage at diagnosis and SES explained the geographic disparities in breast cancer survival.
Shi et al. 2011	to examine the impact of race and insurance on cancer screening	Cervical, breast, and colon cancer screening, 2000-2008	United states, individual level	Race and insurance	Cancer screening was associated with race and insurance status.
Singh et al. 2004	To investigate the temporal trends of SES disparities in cervical cancer diagnosis, incidence, survival, and mortality	Cervical Cancer diagnosis, incidence, survival, and mortality, 1975 to 2000	United States, County and census tract levels	Race and SES	SES disparities have persisted.
Tian et al. 2010	To examine how the geographic scale impact racial disparities in breast cancer mortality	Breast cancer mortality, 1995-2005	Texas, census tract, zip code and county levels	Race, SES, and geography	Racial disparities varied by geographic scales.
Ward et al. 2004	To examine cancer disparities by race and SES	Incidence, screening, diagnosis, survival, mortality, and treatment of cancer, 1975-2000	United States, National level	Race and SES	Disparities in race and SES existed for all cancer combined.

Race/ethnicity

Racial disparities between minorities, such as African Americans, Hispanics, and Asians, and non-Hispanic Whites have been well documented. Cancer incidence and mortality are acknowledged to vary by race/ ethnicity. For African Americans, incidence and mortality rates are higher in colon, liver, prostate, stomach, and cervical cancer, and their survival rate is lower for almost every cancer (Ward et al. 2004). Hispanics experienced the highest incidence rate in cervical cancer. Asian Americans have been reported with higher risks of stomach and liver cancer.

Cancer screenings also vary by race/ethnicity. Significant racial disparities in screening have been found in breast and cervical cancer (Feresu et al. 2008; Rodriguez et al. 2005). Race is also associated with late-stage of diagnosis in several cancer sites (Underwood et al. 2006; Deshpande et al. 2009). Treatment differences between African Americans and Whites have been widely documented, as well. African Americans have been reported less likely to receive treatment (Coker et al. 2009; Du et al. 2010).

Temporal change has been reported in racial disparities. Chu et al. (2007) have reported growth in racial disparities of breast, colon cancer, and prostate cancer mortality from 1990-1994 to 1995-2000. DeLancey et al. (2008) found that from 1975-2004, racial disparities have decreased for tobacco related cancer but remained for cancer related to treatment and screening.

Racial differences can be accounted for by multiple factors. Mortality and survival differences by race could be partially attenuated by SES (Du et al. 2007; Haas et al. 2011), treatment (Byers et al. 1999), stage of cancer at diagnosis (Coughlin et al. 2008; Brookfield et al. 2009), insurance (Robbins et al. 2010), and language (Fiscella et

al. 2002). The differential occurrence of stage at diagnosis by race has been found to be related to insurance, SES, and behavioral factors (O'Malley et al. 2006; Xiao et al. 2011).

Racial differences in cervical cancer between racial minority groups and whites have been documented. Hispanics experience the highest incidence rate, and African Americans have the second highest incidence rate of cervical cancer. However, African Americans steadily experienced the highest mortality rate documented in the past years (ACS 2012). Significant differences in cervical cancer screening among different racial groups have been reported (De Alba and Sweningson 2006; Feresu et al. 2008). A lower screening rate was observed in Asians compared to whites (Wang et al. 2008). Screening differences have decreased between African Americans and whites, while remained between Hispanics and whites (Adams et al. 2007). Compared to whites, minorities bear higher risks of late-stage cervical cancer. For example, one study shows that the late-stage diagnosis rate in cervical cancer was higher in African Americans and Hispanics (Coker et al. 2009). Some studies found the disparities persisted after adjusting for age and SES. Furthermore, racial disparities in treatment were also reported. African Americans have been reported less likely to receive treatment (Coker et al. 2009). There is contradictory evidence in the survival differences by race. Although several studies identified considerable disparities of cervical cancer survival among racial groups (Brookfield et al. 2009; Coker et al. 2009; Lim and Ashing-Giwa 2011), Leath et al. (2005) failed to observe the above disparities.

Racial inequalities in cervical cancer could be attributable to several factors. Late-stage diagnosis was found to be a major cause of mortality disparities among racial groups (Priest et al. 2010). Among cervical cancer survival studies, there is contradictory

evidence in contributing factors of racial disparities. For example, several studies found racial disparities of survival could be attributed to stage at diagnosis, screening, and treatment (Brookfield et al. 2009; Hicks et al. 2006). However, the above findings were not identified by Coker et al. (2009). After adjusting for other factors, several studies found disparities in survival still persisted (Howell et al. 1999). However, the disparities were eliminated when covariates were adjusted for in some studies.

Socioeconomic status

SES disparities across cancer continuums have been widely documented. SES can be measured from various perspectives, including poverty, income, education, occupation, and employment (Krieger et al. 1997). Area-level SES is commonly used because of the unavailability of individual SES in most research. Associations between SES and cancer outcomes vary by cancer sites and cancer outcome. Lower SES was acknowledged to be related to an elevated hazard of late-stage diagnosis and mortality, as well as lower survival rates in most cancer cases (Singh et al. 2003; Ward et al. 2004). Although people from more affluent areas have a higher risk of breast cancer, people with lower SES experience a higher risk of diagnosis at a late stage (Clegg et al. 2009). Low SES was found associated with cancer mortality in breast, colon and prostate cancer survival (Byers et al. 2008). Higher SES could explain the higher survival rate for several cancers (Du et al. 2011). SES also contributes to the disparities in cancer treatment (Haas et al. 2011). No consistent pattern was found in the role of SES in cancer screening for several cancers in a review conducted by Pruitt et al. (2010).

There is a large body of work on the associations between SES and other social factors, as well as their impact on cancer. The relationship between SES and

race/ethnicity has been widely documented in cancer disparities research. SES and race/ethnicity often impact each other. For example, SES was found to be an important predictor of racial disparities (Krieger et al. 2006; Niu et al. 2010). SES could substantially explain colon cancer survival differences among African Americans and whites (Du et al. 2007). Racial disparities persisted in breast and prostate cancer after adjusting for SES (Du et al. 2011). Oliver et al. (2006) found SES did not account for the disparities in incidences of prostate cancer among racial groups. SES disparities can be ascribed to several factors. For example, SES disparities in mortality and survival have been related to late-stage diagnosis and treatment received in several different types of cancer (Byers et al. 2008).

SES disparities in cervical cancer have been documented from different aspects of cancer continuums. Associations between cervical cancer screening and SES have been widely studied. A correlation between lower SES and lower cervical cancer screening rates was found (Daley et al. 2011; Datta et al. 2006; Lofters et al. 2010). Studies have found significant associations between SES and cervical cancer diagnosis. Females of lower SES had a higher risk of late-stage cervical cancer compared to women of higher SES (McCarthy et al. 2010; Patel et al. 2009). A few researchers examined the role of SES in cervical cancer mortality and survival. They found SES significantly impacted mortality and survival (Brookfield et al. 2009; Ueda et al. 2006). Studies on temporal trends of SES disparities have concluded that SES disparities have continued in cervical cancer from 1975 to 2000 (Singh et al. 2004).

The relationship between SES and race/ethnicity across cervical cancer continuums has been examined. Racial disparity in cervical cancer screening is higher

among people with higher SES than that among people with lower SES (O'Malley et al. 2012). However, another study found people with lower SES had a similar screening rate in spite of racial differences (Katz et al. 2007). Studies examining the role of race/ethnicity in SES disparities in the stage in diagnosis have failed to identify a relation.

Geography

The research question of whether geographic location is a factor of cancer risk has captured the interest of scholars. It has been well documented that cancer outcomes are not evenly distributed spatially. Geographic distribution of cancer has been studied across cancer sites and cancer continuums. A large body of studies have reported significant geographic variations in breast, cervical, colon, and prostate cancer (Grann et al. 2005; Hsu et al. 2007; Kuo et al. 2010; Xiao et al. 2011). A few studies have examined whether cancer screening and survival vary spatially (Huang et al. 2007; Lian et al. 2008; Lian et al. 2011; Schootman et al. 2009).

In the literature, the term "scale" is used to refer to two different categories of scales. The first category is the "phenomenon scale", at which a spatial process operates. The second category is the "analysis scale", at which data are aggregated for analysis. The latter is adopted in the research. This research considers a scale as large if the sample size of data is large enough for direct estimates with precision. Large scale includes country, state, metropolitan area, and urban/rural level. This research considers a scale as small if the sample size is small and direct estimates with precision cannot be produced. It also uses the terms "finer scale" or "small area" to represent small scales of analysis. Finer scale or small area includes county, census tract, census block, and so on.

Most of the existing work on geographic disparities has focused on rural/urban differences. A growing body of studies has started to examine the small-area of disparities in cancer at finer scales. For example, small-area geographic disparities in colon cancer incidence and mortality were investigated by Schootman et al. (2011). Another study has evaluated the small-area disparities in prostate cancer survival. These studies on small areas have provided detailed information on cancer disparities.

There is a growing body of work on the associations between geography and other social factors, as well as their impact on cancer continuums. Several studies have investigated the interaction between race/ethnicity and geography. For example, there has been research on how racial disparities vary across space (Goovaerts et al. 2007; Meliker et al. 2009; Tian et al. 2011). Geographic disparities in cancer were associated with several factors, including race/ethnicity, SES, socio-cultural and socio-environmental factors. However, there are inconsistent results on the associations, primarily due to the aggregated geographic scale. For example, Meliker et al. (2009) found SES explained geographic disparities of breast and prostate cancer at a larger scale (the federal House legislative districts), and failed to find the above associations at smaller scales such as state House legislative districts and community-defined neighborhoods. However, Oliver et al. (2006) found SES could not explain racial disparities at census-tract and county level.

Only a few studies have focused on how cervical cancer outcomes vary spatially. Those outcomes include incidence, screening and mortality. For example, Horner et al. (2011) have observed the above disparities across space. A higher cervical cancer risk was observed in urban areas compared to rural areas (Sung et al. 1997). No work has

evaluated the geographic disparities in cervical cancer survival. Race, immigration status, and screening rate have been found associated with geographic patterns of cervical cancer. However, the impacts of other factors, including insurance, access to health care, and SES have been seldom assessed. Most of the existing work on geographic disparities in cervical cancer was conducted at large scales, such as state, and urban/rural (Coughlin et al. 2008; Hopenhayn et al. 2008; Sung et al. 1997). No work has been conducted at finer scales such as the census tract.

Insurance

Significant disparities in cancer outcomes were reported between insured and uninsured people. Enrollment in health insurance was a contributing factor to late-stage diagnosis, lower screening rate, and higher mortality rate (Grann et al. 2005; Shi et al. 2011; Xiao et al. 2011). Previous research has reported that mortality in breast and cervical cancer was disproportionately higher among uninsured or underinsured women. The differences in the impact of different insurance plans on cancer outcomes have been evaluated as well. For example, it has been found that the late-stage diagnosis rate among people with Medicaid is higher than those enrolled in commercial insurance plans (Bradley et al. 2001; McDavid et al. 2003). One study compared the late-stage diagnosis rate among people enrolled in different commercial insurance plans, and did not observe any significant difference.

Studies have shown that insurance interacts with other factors such as race/ethnicity and SES when explaining cancer disparities, because insurance status often varies by SES and race/ethnicity in the Unites States. Racial minorities have a lower insurance rate compared to whites. Insurance status could partially explain racial

disparities in cancer diagnosis and mortality (Grann et al. 2005). One study found that insurance status impacted colon cancer survival differences among different racial groups (Robbins et al. 2010). Studies have suggested that the associations between health insurance and cancer screening vary across racial groups. Previous research suggests that insurance status can serve as a substitution of SES to study cancer disparities.

The impact of health insurance status on cervical cancer has been documented in the literature. Uninsured people less frequently received a cervical cancer screening (Shi et al. 2011). Enrollment in private insurance has been observed as an indicator of cervical cancer screenings. In a few studies, the diagnosis at late stages in cervical cancer was found related to the lack of insurance (Banerjee et al. 2007; Leath et al. 2005). Research also found that insurance is a strong predictor of cervical cancer survival (Morgan et al. 1996). Consistent evidence has been found on the positive influence of private insurance on cervical cancer.

Socio-cultural factors

Socio-cultural factors reflect characteristics of a homogeneous population group (Singer 2012), including immigration status, language proficiency, and cultural beliefs. The impact of socio-cultural factors on cancer outcome has been widely documented in the literature. This research reviews two important socio-cultural factors: immigration status and language.

Immigration status

The impact of immigration status in the United States (whether or not born in the United States) on cancer outcomes has been examined in several studies across cancer continuums. Immigration status was found to be an explanatory factor of cancer

incidence, screening, diagnosis, and mortality rates in several studies. Kuo et al. (2010) established a relationship between foreign birth and the late-stage diagnosis of breast cancer. McCarthy et al. (2010) found immigration status also accounted for cancer incidence and mortality.

Most studies have focused on how immigration status influences cancer screening. A lower screening rate of colon cancer was found associated with foreign birth (Shih et al. 2008). Foreign-born Hispanic Americans bear the highest risk of never receiving breast and cervical cancer screenings (Rodriguez et al. 2005).

Immigration status impacts other factors, such as race/ethnicity, SES, access to health care and insurance status. Immigration status partially explains racial disparities in screening of several cancers (Goel et al. 2003). One study found after adjusting for insurance and whether or not having a source of care, screening disparities in breast cancer by immigration status was attenuated (Echeverria and Carrasquillo 2006).

For cervical cancer, the differences in screening between immigrants and US-born women have been well presented. Immigrants have been observed less frequently to be screened than US-born females (Goel et al. 2003; Rodriguez et al. 2005). Immigration status has been found to impact cervical cancer incidence, diagnosis, and mortality. Vietnamese and Hispanic Americans bear incidence rates higher-than-whites (McCarthy et al. 2010). In spite of the overall decrease in cervical cancer mortality, mortality rates among immigrants have remained. Foreign-born Hispanic Americans experience a higher mortality rate than those born in the United States.

Studies have observed that immigration status interacted with other factors, such as race/ethnicity SES, language, and insurance, when explaining cancer disparities. For

example, among immigrants, higher SES, English proficiency, insurance coverage are associated with increased screening. Some studies have concluded that SES impacted the association between immigration status and cervical cancer outcomes. For example, disparities in screening by immigration status were eliminated after adjusting for SES (Rodriguez et al. 2005). However, research conducted by Echeverria and Carrasquillo (2006) concluded that cervical cancer screening differences have remained after taking into account SES.

Language

The impact of language on cancer outcome has been examined in several studies. Language has been related to breast, colon and cervical cancer screening (Jackson et al. 2009; Jerant et al. 2008; Kandula et al. 2006). A language barrier was observed associated with treatment by surgeons and oncologists in breast cancer (Karliner et al. 2011).

For cervical cancer, there is very little research on how language has impacted cancer outcomes. Previous research has focused on the impact of language on screening (Kandula et al. 2006; Ponce et al. 2006). It has been observed as a barrier to screening for Hispanics with low English proficiency (De Alba and Sweningson 2006). No research has been conducted on the impact of language on cervical cancer diagnosis, treatment, mortality, or survival.

Previous research on cervical cancer disparities has related language to immigration status. Among immigrants, English proficiency is associated with increased cervical cancer screening. Language also interacts with other factors such as

race/ethnicity and SES. One study found language, together with SES and years in the United States, explained the racial disparities of screening (Kandula et al. 2006).

Socio-environmental factors

A growing body of work has started to incorporate environmental settings in cancer research. Social environment indicates social and physical environment of communities where individuals, including racial composition (such as percentage of African-Americans in a community) and geographic factors (Coughlin et al. 2008).

Several socio-environmental factors, including the percentage of black and Hispanic populations, have been examined. Studies have assessed the contribution of socio-environmental factors in cancer screening, diagnosis, mortality, and survival (Haas et al. 2008; Haas et al. 2011; Lim et al. 2011; Russell et al. 2011).

Studies have explored the interaction among socio-environmental factors and other roles including race/ethnicity and SES. One study found that socio-environmental factors explained racial disparities in cancer (Haas et al. 2008). Another study found socio-environmental factors could be considered as a proxy of SES. Socio-environmental factors exhibited a persistent impact on breast cancer mortality after adjusting for other factors (Russell et al. 2011).

There is very little research examining how socio-environmental factors influence cervical cancer outcomes. Coughlin et al. (2008) found the percentage of female population of African Americans at county level was an indicator of cervical screening rate. Lim and Ashing-Giwa (2011) examined the association between socio-environmental factors and cervical cancer survival. They found females residing in

neighborhoods with a higher percentage of African Americans experienced a higher risk of mortality.

Behavioral factors

Behavioral factors (sometimes recorded as lifestyle factors) have been examined in cancer disparities research. Behavioral factors include diet, physical activity, as well as tobacco and alcohol consumption. The impact of behavioral factors has been documented in breast, prostate, lung, and cervical cancer.

It has been well documented that diet and exercise impact the risk of breast cancer. The relationship between smoking and risk of lung cancer has been well documented in the literature. Studies found diet and exercise accounted for a small segment of racial disparities of breast cancer. However, it was concluded that smoking and alcohol use could not explain the racial differences of survival in one study. Smoking and sexual behaviors were documented as risk factors of cervical cancer diagnosis.

Behavioral factors also interact with other factors like SES in cancer disparities research. For example, it has been found that risk-promoting factors, including poor nutrition, smoking, physical inactivity and obesity, were associated with lower SES. Therefore, those factors could partially explain SES disparities in cancer outcomes.

For cervical cancer, the impact of behavioral factors on screening has been studied (McDonald and Neily 2011; Welch et al. 2008). Studies on the association between behavioral factors and mortality have identified a significant relationship between tobacco use and mortality (Du et al. 2010). Few have studied the impact of behavioral factors on cervical cancer diagnosis, treatment and survival.

Access to health care

Access to health care is measured by the ease of obtaining health care services (such as screening and treatment). Access to health care is categorized into two groups: non-spatial and spatial access. Non-spatial accessibility is impacted by non-spatial factors, while spatial accessibility is impacted by spatial factors. Spatial factors include spatial location, travel time, and travel distance, while non-spatial factors include health insurance, SES and other factors that might impact access. In this research, access to health care is defined as spatial access.

Spatial access to health care has been increasingly examined to measure cancer disparities. Several studies have discovered significant disparities in spatial access experienced by different social groups characterized by race, SES, and residential region (Wang et al. 2008; Wan et al. 2012). It has been documented that people from disadvantaged communities might bear a long waiting time and travel long distances to access facilities that provide cancer services. The impact of spatial access on cancer screening, diagnosis, treatment, and mortality has been examined. Studies did not detect any screening differences in breast cancer due to spatial accessibility (Engelman et al. 2002; Jackson et al. 2009). Several studies have reported significant relations between spatial accessibility and cancer stages (Huang et al. 2009; Wang et al. 2008). However, research on how spatial accessibility impacts survival is rare.

For cervical cancer, one study in New Zealand evaluated associations between travel distance to health care and racial/ethnic disparities in cervical cancer mortality.[34] However, no similar work has been conducted in the United States. Previous studies have focused on non-spatial access. For example, the impact of whether having a regular

source of care on cervical cancer outcomes has been investigated (Kandula et al. 2006). Du et al (2010) assessed the impact of the number of hospitals and physicians per 10,000 people on cervical cancer mortality.

Studies of cancer disparities elimination

There have been increasing efforts to address cancer disparities. To address disparities is to eliminate risk factors in a specific underserved social group (such as African Americans, Asians, and Hispanics). Disparity elimination programs have been enhancing the use of cancer preventive, screening, and treatment services among the underserved groups. Programs including community based participatory research, community network program, and patient navigation program have been developed to address cancer disparities.

Methods for cancer disparities research

Cancer disparities measurement

How to choose a measurement of health disparity may affect the size and direction of the result of disparities. According to Keppel et al. (2005), several issues need to be considered in order to select a health disparity measurement:

(1) Choosing a reference point. A reference point is a quantity of health status to which the difference is measured. Different reference groups can be used such as the best group rate and mean group rate. It is important to choose an appropriate reference point as well as to state clearly the reason for the choice. Generally the best group is chosen as the reference point when disparities are evaluated between two groups.

(2) Whether to measure disparities using the absolute or relative method. The absolute difference is the simple difference between a specific group for which the disparity is measured and a reference group. The relative difference is the rate ratio between the specific group and the reference group. When measuring the disparities at a single point using both of the two methods, the results from the absolute measure and the relative measure might be correlated. However, when measuring disparities change over time, contradictory results might be obtained in both the size and direction. One of the advantages of using relative measure is that the results are adjusted for the original rates In addition, it can be used for comparison among different indicators because it is a unit-free measurement. However, it might lose magnitude of change information from the original rates. Both absolute and relative methods should be incorporated in order to get a better understanding of disparities, especially when measurement over time and space is conducted.

(3) Whether to measure disparities using pair-wise or summary measure. A pair-wise measure is used when a specific group is the focus in the measurement. Summary measure is used when the domain is the focus, and comparisons are made over time, space, and different indicators. Pair-wise measure only measures the disparity between two groups and does not measure disparities among more than two groups. One of the flaws of summary measure is that it might lose information. A summary measure should be used together with pair-wise measure to comprehensively measure disparities.

(4) Whether to weight the population size of groups for summary measure. Whether to weight or not depends on the purpose of the summary measurement. Weighted measurement allocates greater weight to groups with a larger population and

corrects for small number problems for minority groups with less population in small geographic areas. However, it may mask the higher-rate group with a small number of populations.

(5) Choosing summary measures for ordered categories. Measuring disparities for ordered categories often lays interests on the measurement of disparities across the entire domain instead of particular groups. Population weighted methods might be appropriate for ordered categories in that it can compensate for any inaccuracy from arbitrary cutting points. The regression based method and the concentration based method are the most commonly used methods for ordered categories.

Table 2.3 presents a summary of health disparities measurement methods from the above perspectives based on Harper and Lynch (2006).

Table 2.3 Health disparity measures

Disparity Measure	Definition	Absolute or Relative	Reference group	pair-wise or summary measure	Social group weighting
Absolute Difference (AD)	$AD = r_1 - r_2$, where r_1 and r_2 represent the health indicators in two social groups.	Absolute	Best	pair-wise	No
Relative Difference (RD)	$RD = r_1/r_2$, where r_1 and r_2 represent the health indicators in two social groups.	Relative	Best	pair-wise	No
Regression-Based Relative Effect (RRE)	$y_i = \beta_0 + \beta_1 X_i$, where y_i represent the transformed (e.g. logarithmic) health indicator for individual i, X_i represents social group i, β_1 is a relative summary indicator of disparity, and β_0 represents the health indicator when X_i is 0.	Relative	Best	summary	No
Regression-Based Absolute Effect (RAE)	$y_i = \beta_0 + \beta_1 X_i$, where y_i represent the untransformed health indicator for individual i, X_i represents social group i, β_1 is an absolute summary indicator of disparity, and β_0 represents the health indicator when X_i is 0.	Absolute	Best	summary	No
Index of Disparity (ID_{isp})	$ID_{isp} = \left(\sum_{j=1}^{J-1} \lvert r_j - r_{ref} \rvert / J\right) / r_{ref} \times 100$, where r_j is the health indicator in the jth group, r_{ref} represents the health indicator in the reference population, and J indicates the total number of social groups compared.	Relative	Best	summary	No
Index of Dissimilarity (ID)	$ID = \frac{1}{2}\sum_{j=1}^{J} \lvert d_j - p_j r_{pop} \rvert$, where d_j and p_j indicate the number of disease cases and the population in the jth group, and r_{pop} represents the disease rate in the total population.	Absolute	Average	summary	Yes

Table 2.3-Continued

Index of Dissimilarity% (ID%)	$ID\% = \frac{1}{2}\sum_{j=1}^{J}\lvert s_{jh} - s_{jp}\rvert$, where s_{jh}represents the jth social group's share of health, and $s_{jp}$is the population share in jth social group.	Relative	Average	summary	Yes
Relative Concentration Index (RCI)	$RCI = \frac{2}{\mu}\left[\sum_{j=1}^{J} p_j \mu_j R_j\right] - 1$, where p_j and μ_j are the population share and average health of jth social group, R_j represents the socioeconomic group j's relative rank defined as: $R_j = \sum_{j=1}^{J} p_\gamma - \frac{1}{2}p_j$, p_γ indicates the cumulative proportion of the population up to group j, and p_j is the population share in group j.	Relative	Average	summary	Yes
Absolute Concentration Index (ACI)	$ACI = \mu RCI$, where μ is the mean health indicator in the population.	Absolute	Average	summary	Yes
Between-Group Variance (BGV)	$BGV = \sum_{j=1}^{J} p_j\left(y_j - \mu\right)^2$, Where p_j and y_j are the population size and average health of group y_j, and μ is the mean health indicator in the entire population.	Absolute	Average	summary	Yes
Theil Index (T)	$T = \sum_j p_j\, r_j \ln\left(r_j\right)$, where p_j is population share for an individual, and r_j is the ratio of the health indicator of the individual to the average health indicator.	Relative	Average	summary	Yes
Mean Log Deviation (MLD)	$MLD = \sum_j p_j \ln\left(\frac{1}{r_j}\right)$, where p_j is population share for an individual, and r_j is the ratio of the health indicator of the individual to the average health indicator.	Relative	Average	summary	Yes
Variance of Logarithms (VarLog)	$VarLog = \sum_j p_j\left[\ln r_j - \sum\left(\ln r_j\right)\right]^2$, where p_j is population share for an individual, and r_j is the ratio of the health indicator of the individual to the average health indicator.	Relative	Average	summary	Yes

Measurement of disparities by multiple factors

Regression-based measures have been widely used to evaluate health disparities when multiple covariates are considered. Using regression, one can measure how cancer outcomes are associated with covariates. The regression method provides statistical inference with statistical power. Compared with the traditional health disparities measures that fail to provide statistical significance of the results, regression is capable of identifying statistically significant disparities that do not occur by chance. Moreover, regression is capable of taking into account multiple factors that cannot be done by the previous methods. For example, when assessing the SES disparities in cancer outcomes, we also incorporate several covariates into the regression such as race and insurance to rule out their influence on SES disparities. Traditional regression methods used in health disparities research include linear regression and logistic regression.

Multivariate logistic regression has been used to measure associations between a categorical dependent variable and independent variables. It is capable of taking any input values, and the output is always between 0 and 1. Therefore, it has been widely used to analyze cancer outcomes that are categorical, such as the stage at diagnosis, vital status, and so on. According to Hosmer and Lemeshow (2000), a multivariate logistic regression can be defined as follows:

$$\boldsymbol{logit}[\boldsymbol{\pi}(\boldsymbol{x})] = \boldsymbol{\beta_0} + \sum_{\boldsymbol{i=1}}^{\boldsymbol{N}} \boldsymbol{\beta_i}\, \boldsymbol{x_i} \qquad 2.1$$

where $\pi(x) = \frac{e^{\beta_0+\sum_{i=1}^{N}\beta_i x_i}}{1+e^{\beta_0+\sum_{i=1}^{N}\beta_i x_i}}$ is the probability of being a case ("1"), β_i is the coefficient of the ith independent variable, and β_0 is the linear intercept in the regression. The coefficient of the variables is estimated through the maximum likelihood procedure. Logistic regression provides the significance of the coefficient and odds ratio.

An odds ratio is the ratio of odds of one event that occur in one group to the odds that occur in another group. It can be computed as e^{β}. In cancer disparities research, a logistic regression with the stage at diagnosis as dependent variable and SES as independent variable computes the ratio of odds of cancer at a late stage occurring in a high SES group to that in a low SES group. Covariates can be adjusted in regression to account for confounding independent variables.

However, the traditional multivariate logistic regression is a single-level model which fails to take into account correlations among individuals within the same neighborhood and (the) random effect caused by geographic variation. A growing number of studies have adopted multilevel logistic regression, which will be described in detail in chapter 3.

Measurement of Geographic disparities

There are three traditions in spatial epidemiology: disease mapping, disease clustering, and geographical analysis of the correlations between disease and risk factors. These traditions also play important roles in geographic studies of cancer. Exploratory studies in spatial variation of cancer involve mapping cancer data and spatial cluster analysis of cancer.

As one of the traditions of spatial epidemiology, disease mapping has served as an effective tool to visualize disease information, for descriptive purposes, to generate a hypothesis, and to aid policy formation. In cancer disparities research, disease mapping summarizes the spatial variation of cancer outcomes in order to quantify the geographic disparities (Best et al. 2005). However, there have been several challenges in disease mapping. One of the major challenges is the small-number problem. This problem occurs

when studies are conducted on small areas (such as census tracts) where cancer cases or population at risk are sparse (Pickle and White 1995).The raw disease rate yields spurious estimates for small populations and thus is not stable for disease mapping. The standardized mortality ratio (SMR) has been used to measure the relative risk of disease incidence and mortality in large geographical regions (Clayton and Kaldor 1987). The SMR is defined by the ratio of the observed number of deaths to the expected number of fatalities. The major drawback of the SMR is that the varying background population size is not considered in the geographical region. Therefore, the estimated SMRs for small areas might be extreme in the map and dominate the spatial pattern. In order to address the above problem caused by population variability, smoothing methods have been proposed. The smoothed- estimated rate is produced by combining the rate in each small area and that from the surrounding areas. Smoothing is usually carried out through the spatial hierarchical models in the framework of Bayesian statistics. Let Y_{ij} and N_{ij} indicate the number of cases and population at risk in stratum j (such as age, sex, and so on) and area i. For rare diseases such as cancer according to Wakefield et al. (2000), the Poisson model is used:

$$\mathbf{Y_{ij} \sim Poisson\left(N_{ij} \times P_{ij}\right)} \qquad \mathbf{2.2}$$

where $P_{ij}$is the probability (risk) of disease. According to the proportionality assumption, P_{ij} can be expressed as:

$$\boldsymbol{P_{ij} = \theta_i \times P_j} \qquad 2.3$$

where θ_i is the relative risk of disease in area i, θ_i is estimated through a regression based on a $k \times 1$ vector of explanatory variables X_i, and the model is expressed as:

$$\boldsymbol{log\,\theta_i = \alpha + X_i^T \beta} \quad 2.4$$

where β is the regression coefficient of the explanatory variable X_i, and α is the offset. θ_i can be estimated via the maximum likelihood method. However, for small areas, the estimates could be highly unstable because of sparse data. One way to address this problem is to utilize a multivariate probability distribution of θ that considers both unstructured and structured variability. According to Besag et al. (1991), the hierarchical spatial model can be then defined by:

$$\boldsymbol{log\,\theta_i = \alpha + X_i^T \beta + U_i + V_i} \quad 2.5$$

where V_i is the unstructured variability that can be explained as the residual log odds ratio in area i after adjusting risk factors, and $U_i$is the spatially structured variability that reflects the spatial dependence (Besag et al. 1991). The parameter estimation can be carried out via Empirical Bayesian or fully Bayesian methods (Best et al. 2005). The difference in the two methods lies in the estimates of the posterior distribution. The fully Bayesian method has been proven to perform better that the Empirical Bayesian.

Cluster was defined as "a geographically bounded group of occurrences of sufficient size and concentration to be unlikely to have occurred by chance" (Knox 1989). Spatial cluster analysis comprises clustering-detection and cluster-detection methods. The clustering-detection method examines the general geographic patterns globally and determines if there is any global clustering in the entire study area. The cluster-detection method examines if there is any clustered distribution and identifies areas with an excess of a certain event through statistical techniques. Different approaches have been proposed for spatial cluster analysis including distance, area, moving window, and risk surface estimation method. Distance methods identify clusters based on locations of individual events. Approaches that are based on distance include the nearest neighbor index, K-

function, and so on. The nearest neighbor method compares the average distance between the nearest neighbors with that under an expected random distribution (Cuzick and Edwards 1990). The K-function evaluates clustering over a range of distance and employs the Monte Carlo method to conduct significance testing (Ripley 1977). The distance method can evaluate clustering at any scale and is free from the modifiable areal unit problem (MAUP). However, it has several drawbacks. First, it is challenging to adjust for the spatial variation of the risk population. Second, it might cause overcomputation because it tends to evaluate the same subset of events multiple times. Area methods analyze health events that are aggregated at a neighborhood scale. There are several area methods including Moran's I, Getis's G* and Geary's C (Getis and Ord 1992; Moran 1950). The area method is preferred when data are aggregated to area units such as census units. Moreover, the socio-cultual information from the area units can be employed for geographic analysis of association between clusters and related factors. The major limitation in the area method is that it is subject to the MAUP.

Moving window methods employ a series of circular regions as moving windows to analyze spatial clustering. Clusters will be detected through the significance test of the number of health events that fall inside the circular window. Spatial cluster analysis methods that employ the moving window method include Openshaw et al. (1987), Besag and Newell (1991), Fotheringham and Zhan (1996), the spatial scan statistic (Kulldorff 1997), and so on. The methods define the moving window differently. Openshaw et al. (1987) defined the circular region based on the distance between health events. Besag and Newell (1991) defined the circle according to the number of health events, and the spatial scan statistic defines it in terms of the population size.

The risk surface estimation method implements spatial cluster analysis through the estimation of the underlying spatial residual risk surface after accounting for unmeasured confounding factors. Related approaches include kernel methods, generalized additive models, and geostatistical methods. One of the merits of risk surface estimation methods is that they take covariates into account in the model. In the meantime, they can be routinely applied to a large database.

Measurement of spatial access to health care

There are three primary factors that exhibit impact on the measurement of spatial access to health care: supply of health services, demand for health services, and the travel cost between them. There have been several methods that measure spatial access to health services: the regional availability method, kernel density models, and gravity-based models (Luo and Wang 2003).

The regional availability method, as one of the traditional methods to measure spatial access, compares the supply of health services with the demand within a defined area. It could be carried out via Geographic Information System (GIS) functions such as buffering and overlay analysis. It has been adopted to identify medically underserved areas or social groups. However, it has been criticized due to two limitations. First, it assumes that people only seek health care within the predefined area and do not go beyond the boundary; second, it assumes that people from the same area have equal health care accessibility.

The kernel density model has also been employed to evaluate spatial access. It generates a density surface based on points using the kernel density function. To measure spatial accessibility, it generates a supply surface based on the medical services sites, and

a demand surface based on the population centroids. Then it computes the supply-to-demand ratio through dividing the supply surface by the demand surface. The kernel density method could address the problems in the regional availability method by using a distance-decay function. People are not restricted to the predefined area to seek health care. However, it still suffers two limitations. It calculates the density surfaces using a straight line distance that does not always reflect the real situation. Second, when estimating the supply and demand surfaces, it fails to consider the population distribution and the land use type of the real world. For example, non-residential areas, such as forests, might be also assigned medical services.

The gravity-based model has been widely used to evaluate the spatial accessibility of medical services (Hansen 1959). It considers the communication between the demand and supply among different geographic areas based on distance-decay. Spatial access to health services according to the gravity-based method is defined as follows:

$$A_i^G = \sum_{j=1}^{m} \frac{S_j d_{ij}^{-\beta}}{\sum_{k=1}^{n} P_k d_{kj}^{-\beta}} \qquad 2.6$$

where A_i^G is the spatial accessibility at population location i, P_k is the population size at location k, S_j indicates the supply capacity of the location j that provides health service, d_{ij} and d_{kj} are the distance or travel cost, n and m are the total number of population locations and medical service locations, and β represents the impedance coefficient that reflects the degree of distance-decay.

This method considers the competition of the available health care sites among the demanding population. Spatial access to medical care for a population site is the accumulative supply-to-demand ratio of all the available medical service locations. It is conceptually more complete compared to the previous methods. However, it is difficult to

interpret. It was further improved by Luo and Wang (2003a, b). The implementation of the 2SFCA method consists of two steps. First, for each medical service location j, search all the population locations k within a travel time (d_0) from j, and calculate the supply-to-demand ratio R_j. The travel time (d_0) from j is defined as the catchment j. R_j is expressed as:

$$\boldsymbol{R_j = \frac{S_j}{\sum_{k\in\{d_{kj}\le d_0\}} P_k}} \quad 2.7$$

where S_j represents the health care capacity of j, P_k represents the size of the population of k whose centroid is within catchment j ($d_{kj} \le d_0$), and d_{kj} is the travel cost between j and k. Second, search all the medical service locations j within a threshold travel time (d_0) from each population location i (catchment area i), and sum up the supply-to-demand ratio R_j computed from the first step. The second step can be defined by:

$$\boldsymbol{A_i^F = \sum_{j\in\{d_{ij}\le d_0\}} R_j = \sum_{j\in\{d_{ij}\le d_0\}} \frac{S_j}{\sum_{k\in\{d_{ij}\le d_0\}} P_k}} \quad 2.8$$

where A_i^F is the spatial accessibility of population location i, R_j represents the supply-to-demand ratio at location j, and d_{ij} represents the travel cost between i and j.

The two steps in the 2SFCA method are intuitive to interpret and implement. It has been applied in a growing number of studies to evaluate spatial access to care (Albert and Butar 2005; Wang et al. 2008). However, it still suffers two drawbacks: (1) it assumes that the population within the catchment area has equal access and (2) population locations outside the catchment area do not have any access. In order to address these problems, Luo and Qi (2009) proposed the enhanced two-step floating catchment area method (E2SFCA). This method applies distance-based weights to

differentiate catchment areas and thus divides the catchment areas into subzones. This method will be presented in detail in chapter 3.

Survival analysis

In survival analysis, relative and cause-specific survival is used to analyze net survival – an indicator of survival after correction for the impacts of covariates. Cause-specific survival measures deaths from the cancer of interest, and considers deaths that are due to other causes to be censored. Relative survival measures deaths of all causes and estimates the ratio of the observed to the expected survival of an external comparison population. Cause-specific survival is acknowledged as a standard in etiology such as clinic studies.

Cause-specific survival measures mortality only using deaths that are caused by the cancer of interest. It uses follow-up information that is collected from the date of the cancer at its diagnosis, to the date of death, loss-to-follow-up or the end of the study period. Patients will be censored when they die from other causes, are lost to follow-up or did not die during the study period. Cause-specific survival for a given time period is commonly measured using the Kaplan-Meier estimator or the Cox proportional hazard regression. One of the advantages of the Kaplan-Meier method is it takes into account censored cases. Let $S(t)$ indicate the probability of a case having a lifetime T longer than t, $t\big(S(t) = P_r(T > t)\big)$, the observed time of a sample with size N sample is defined as: $0 \leq t_1 \leq t_2 \leq t_3 \leq \cdots t_N$, and $S(t)$ can be estimated as follows:

$$\widehat{\boldsymbol{S}}(\boldsymbol{t}) = \prod_{\boldsymbol{t_j<t}} \frac{\boldsymbol{n_j - m_j}}{\boldsymbol{n_j}} \qquad 2.9$$

where m_j indicates the total number of deaths at time t_j, and n_j represents the total number alive prior to t_j. In the scenario of no censoring, n_j represents the total

number of alive cases prior to time t_j. When there is censoring, n_j represents the difference between the total number of alive cases and censored cases (Kaplan and Meier 1958). One of the limitations of the Kaplan-Meier method is that it estimates survival based on a single factor.

The Cox proportional hazard model has been widely used to analyze survival and takes into account multiple covariates. The hazard function can be modeled as:

$$\boldsymbol{h_j(t) = h_0(t)e^{X_j\beta}} \quad 2.10$$

where $h_j(t)$ is the instantaneous risk of death of the jth observation at the time t, $h_0(t)$ is the baseline hazard function at time t, X_j is the covariate vector (also known as explanatory variables) of the jth individual, and β is the model parameter that can be estimated using maximum partial likelihood (Cox 1972). One of the advantages of the Cox proportional hazard model is that it does not make any assumptions on the shape of the underlying hazard. However, it suffers one major limitation in that it assumes the impact of the covariates on hazard remain constant during the study period.

One of the limitations of the traditional Cox proportional hazard model is that it is a single-level model which fails to take into account correlations among individuals within the same neighborhood and random effect caused by geographic variation. A growing number of studies have adopted multilevel survival model (Schootman et al. 2009), which will be described in detail in chapter 3.

Limitations in cancer disparities research

A growing body of literature has examined cancer disparities in several cancer sites. Significant racial and SES disparities have been reported across cancer

continuums. However, no consensus has been reached across several domains of cancer disparities. There are several research gaps in the literature on cancer disparities.

Limitations in measuring cancer disparities

There has been no consensus on which measurement should be employed to assess cancer disparities. Measurements such as rate ratio, rate difference, regression-based indicators (such as relative risk, odds ratio, and hazard ratio) have been widely used in cancer disparities research. There have been several guidelines discussed above on which choices of measurement methods are justified. For example, the pair-wise method should be used in conjunction with the summary method; relative measurement should be used together with absolute measurement; and population groups should be weighted (Keppel et al. 2005; Harper and Lynch 2006). However, most studies have focused on a single measurement that might fail to capture the disparity from different perspectives (Harper and Lynch 2006). Only a few studies have combined and compared several measurements (Harper et al. 2008; Chu et al. 2007). Moreover, problems have arisen from evaluating cancer disparities in small areas due to sparse samples in small areas and a lack of statistical power. In order to address these problems, new methods are needed to measure the spatial variation of cancer disparities in different social classes, races, genders, and so on. There are only a few studies that have evaluated the spatial variation of racial and SES disparities (Goovaerts et al. 2007; Tian et al. 2010). Therefore, a research gap exists in how to measure the spatial variation of cancer disparities from different perspectives.

Limitations in measuring single factor

SES

Due to the lack of socioeconomic data at the individual level, areal-based SES indicators have been widely employed as a proxy of individual-level SES. The areal-level SES indicators are often aggregated at various geographic scales (such as census tract and census block). The adoption of the areal-level SES inevitably suffers a few limitations. First, there has been no consensus among researchers on which SES indicator should be chosen to measure cancer disparities. In the literature, a large number of studies have adopted a single variable to measure SES such as income or poverty. However, it has been pointed out that no single variable is capable of capturing all of the socioeconomic characteristics (Krieger et al. 1999; Krieger et al. 2003). In order to address the problem, researchers have adopted composite indicators that are extracted from the various SES variables, such as income, education, poverty, and housing conditions, to better represent different domains of SES (Krieger et al. 2002; Lian et al. 2011; Liu et al. 1998; Singh et al. 2002). However, there is no significant difference between the composite indicators and single indicators in measuring SES disparities (Krieger et al. 2006). Due to the unavailability of true individual SES, the use of areal-level SES might yield misclassification and thus lead to wrong conclusions of the measurement of SES disparity. Second, areal-level SES might lead to "ecology (ecological) fallacy" when cancer disparities results at the population level are applied at the individual level. Furthermore, areal-level SES at different geographic scales can produce different results of disparities. In order to mitigate such uncertainty, the smallest unit is recommended. The rationale is that the smaller the units, the more homogeneous in SES are its

population. In summary, how to choose variables for SES is critical in cancer disparities research.

Geographic location

Geography provides two distinct perspectives: space and place. The spatial pattern of cancer serves a monitoring purpose and provides information on cancer prevention. Place facilitates the explanation of cancer disparities. Studies on geographic disparity are often conducted at large geographic scales, such as state level, which has been criticized because of the coarse resolution for cancer disparities research (Krieger et al. 2002). There has been a growing number of studies on disparity in small areas. However, such studies suffer an inherent problem — the small-number problem. The use of crude rates from small areas in disease mapping or geographic analysis leads to spurious estimates. Moreover, when taking into account geographic location, researchers should be aware of spatial dependence, that nearby observations tend to be similar. The above two problems have been recognized in spatial epidemiology literature. However, there has been little attention on them in cancer disparities research.

Spatial access to health care

Regular screening by health care professionals can help detect and remove precancerous growths, as well as diagnose early-stage treatable cancers. It has been proven that early detection of breast, cervix, colon, and rectum cancer could help reduce mortality. Cancer treatment might have an impact on cancer outcomes such as survival. Therefore, spatial access to cancer screening and treatment has captured researchers' interests. Several studies have been conducted to analyze the relation between cancer and spatial access to screening and treatment (Huang et al. 2009; Wang et al. 2008; Wan et al.

2011). However, there has been no consistent conclusion on the relationship between cancer outcomes and spatial access. There is little research that has examined the relationship between cervical cancer outcomes and spatial access to medical services. These existing studies have not focused on access from the spatial perspective. Moreover, previous studies have focused on cancer screening facilities. Research on spatial access to other preventive services such as primary care is rare. Because the Pap smear test is typically provided by primary care physicians (PCPs), access to PCPs plays an important role in the prevention of cervical cancer. It has been documented that the Pap smear screening was statistically associated with the contact with PCPs.

Limitations in measuring multiple factors

A substantial number of studies have been dedicated to investigating cancer disparities from the perspectives of race/ethnicity and SES. There are three research gaps in the literature. An increasing number of studies have revealed that health disparities are attributed to a wide range of factors that exist and operate on different levels (e.g., contextual and individual level) (Holmes et al. 2008). However, there are several research gaps in the literature on cervical cancer disparities. First, no research has taken into consideration individual-level factors (age, race/ethnicity, tumor characteristics, and type of treatment received) in conjunction with contextual-level factors (demographic factors, behavioral factors, health insurance expenditure, urbanization, and spatial access to health care) to study cervical cancer disparities. Second, no work has placed all the above factors in a spatial context and examined how they jointly contribute to geographic disparity in cancer. Third, there has been contradictory evidence on certain cancer disparities. For example, no consensus has been reached on how cervical cancer survival

is impacted by race adjusting for both individual- and contextual- level factors. Last but not least, most previous studies only adopted a single-level model to measure disparities, which failed to take into account correlations among patients within the same neighborhood and random effect caused by geographic variation.

CHAPTER III

DATA SOURCES AND METHODOLOGY

Introduction

This chapter describes the study area, data sources, and methodology of this dissertation. The first section describes the study area of this dissertation. The second section describes data sources, including cervical cancer incidence data, cervical cancer health care data, census-tract-level data, and treatment data. The third section describes how permission to perform human-subject research was obtained and how the rights and safety of human subjects were protected. The last section provides a review of methods used in this dissertation.

Study area

The state of Texas in the United States was selected as the study area for several reasons. First, Texas is the largest state in the 48 contiguous United States, with the second largest population (26.1 million) in the United States. Second, Texas has a racially/ethnically diverse population, with the second largest Hispanic population and foreign born population in the United States. Third, Texas shares a 1,000-mile United States border with Mexico. Border regions have predominantly Hispanic population with lower SES. It was reported that people from Texas-Mexico border counties experienced a lower cervical cancer screening rate than their counterparts from non-border counties. The characteristics mentioned above provide a suitable template and environment to examine cervical cancer disparities and factors contributing to these disparities. This

template can be extended to other regions (e.g., the rest of the United States and other counties).

Data sources

This dissertation uses several data sources, including cervical cancer incidence data, cervical cancer health care data, census-tract-level data, and treatment data (Table 3.1)

Cervical cancer incidence data

Cervical cancer incidence data of Texas from 1995-2008 was collected from the Texas Cancer Registry (TCR). The collected dataset included diagnosed cervical cancer cases. Information includes race/ethnicity, sex, residential address, date of diagnosis, year of diagnosis, age at diagnosis, stage at diagnosis, tumor grade, vital status, vital status follow up source, date of last contact, and cause of death. Stage at diagnosis of cervical cancer will be categorized into localized, regional, and distant stages based on the classification method from the Surveillance Epidemiology and End Results (SEER) program from the National Cancer Institute (NCI). SEER provides the fundamental staging system to categorize cancer stage. Stage at diagnosis in this research will be recoded as two general categories based on clinical and pathological information: early and late stage. The former includes localized stages; the latter includes regional and distant stages.

Cervical cancer medical service data

Cervical cancer medical service data include preventive and treatment service data collected from Texas Department of State Health Services (TDSHS). The preventive

services data were represented by PCPs in Texas in 2000. Primary care physicians were analyzed because people typically receive cervical cancer screening services such as Pap smears from their PCPs (Weinstein et al. 2009). A total of 14,268 PCPs with 6,372 primary practicing addresses were analyzed, including obstetrician, gynecologists, family physicians, general practice physicians, and general internists. Cervical cancer treatment service data were represented by oncologists in 2000, including surgical, radiation, medical, and gynecologic oncologists. The number of oncologists in 2000 was 205 with 121 primary practicing addresses.

Census demographic data

Census-tract level demographic data were extracted from Census 2000 datasets. This study used 16 variables to represent three domains: socioeconomics, socio-culture, and socio-environment. Socioeconomics were represented by several variables, including poverty rate, median household income, unemployment rate of female, median home value, percentage of female with high school education, percentage of female with college education, percentage of female living in crowed housing, and percentage of households without a car derived from census 2000 Summary File 3 (SF3). Poverty rate, income, employment rate, and education have been widely used to represent SES in the literature (Bradley et al. 2001; Chu et al. 2007; Du et al. 2007; Krieger et al. 2006; Ward et al. 2004). Housing, financial and occupancy characteristics as well as vehicle information have been examined to measure SES disparity in several studies (Coughlin et al. 2006; Haas et al. 2011; Lian et al. 2011).Socio-culture was represented by percentage of linguistic isolated households, percentage of never-married females, percentage of divorced females, and percentage of females living alone extracted from SF3; and

percentage of foreign born females from Census 2000 Summary File 4 (SF4). Language, immigration status, and marriage status have been widely used to examine cancer disparities. Several studies have used percentage of linguistic isolated household, foreign-born population, never-married females, and divorced females at the county level to measure social-cultural factors (Coughlin et al. 2008; Haas et al. 2011). Socio-environment is represented by female population by age and race/ethnicity, percentage of Hispanics, percentage of African Americans, and percentage of female-householder households extracted from Census 2000 Summary File 1 (SF1). The above variables have been examined in several studies (Haas et al. 2008; Haas et al. 2011).

Health insurance expenditure data

Census-tract level health insurance expenditure was obtained from Simplymap developed by Geographic Research Inc. Simplymap derives data from the Easy Analytic Software Inc. (EASI), a commercial developer of demographic data. Simplymap estimates data at various geographic levels using two data sources: demographic and socio-economic data from the U.S. Census, and the Consumer Expenditure Survey (CEX) data from the Bureau of Labor Statistics (EASI 2010). It first estimates data at the block-group level using a disaggregation technique, and then uses the block-group level data to obtain data at other geographic levels such as census tracts. Data estimated from EASI follows standard demographic techniques and are considered of high accuracy. The comparison among data from EASI and other sources such as the U.S. Census has shown that the difference is within two percent in general and 0.005 percent in denser population areas (EASI 2010). Health insurance expenditure variables include average household

health insurance expenditure, and average household commercial health insurance expenditure.

Treatment data

Individual-level treatment data are derived from the cervical cancer incidence data from the TCR. Type of first course of treatment included: 1) only surgery; 2) radiation and chemotherapy; 3) radiation/chemotherapy; 4) radiation, chemotherapy, and surgery; 5) radiation/chemotherapy and surgery; 6) no treatment; 7) unknown treatment.

Behavioral data

Area-level behavioral data were collected from Simplymap using consumer survey data from Experian Simmons. Experian Simmons conducts an annual consumer survey to measure over 200 Designated Market Areas (DMS) in the United States. The average population sample per market is about 30,000. Representative samples from each census block are selected through alert letters. Respondents recruited for data collection receive mail and telephone surveys. Simmons data and other sources (e.g., CDC, Census, MapInfo, and infoUSA) are used to estimate values of different variables at the census block level. Data are further estimated at the state, county, zipcode, census tract and block group level. Variables used in this research include: percentage of non-smoking population, percentage of people who eat healthy, percentage of people who exercise regularly, and percentage of nonalcoholic population.

Table 3.1 Data sources

Dataset	Source	Variables	Geographic area units	Year of data
Cervical cancer incidence / mortality/survival data	Texas Cancer Registry (TCR), Texas Department of State Health Services (TDSHS)	Race/ethnicity Sex Residential address Date of diagnosis Age at diagnosis Stage at diagnosis Vital status Date of last contact Cause of death	Individual	1995-2008
Cervical cancer medical service data	TDSHS	Primary care physicians (PCPs) Oncologists	Individual	2000
Demographic data	Census 2000	Poverty rate Unemployment rate of females % females with college education % females with high school education % females living in crowed housing % households without a car Median home value Median household income % linguistic isolated households % never-married females % divorced females % female living alone % foreign born females	Census tract	2000

Table 3.1-Continued

		Female population by age and race/ethnicity % Hispanics % African Americans % female-householder households		
Health insurance data	Simplymap by Geographic Research Inc using the Consumer Expenditure Survey from U.S. Department of Labor as the data source	Average household health insurance Expenditure Average household commercial health Insurance expenditure	Census tract	2000
Treatment data	TCR	First course treatment received	Individual	1995-2008
Behavioral data	Simplymap by Geographic Research Inc using the Consumer Expenditure Survey from U.S. Department of Labor as the data source	% people who eat healthily % people who exercise regularly % non-smoking population % nonalcoholic population	Census tract	2000

Protection of Human Subjects

The use and analysis cervical cancer incidence data in this research have been approved by TDSHS Institutional Review Board (IRB). The IRB review involved an agreement between TCR and data users to ensure the confidentiality of the human subjects. According to the agreement, the following provisions were required during the processing and analyses of the cervical incidence data.

a). The cancer registry data are treated as strictly confidential.

b). During the study, a password-protected computer with up-to-date antivirus software is used to store and analyze the confidential data. A cabinet with access limited only to the data users is used to lock up the computer when not in use.

c). The presentation and publication of results may not include specific individual case information or make any case identifiable.

d). The confidential dataset will be destroyed one year after the research is finished. A non-confidential dataset will be created and maintained.

Methodology

This research consists of four parts. The first part examines disparities of stage at diagnosis of cervical cancer in Texas by SES, race/ethnicity, and geographic locations. It analyzes how individual- and contextual-level factors impact the occurrence of cervical cancer stage at diagnosis and its geographic pattern using multilevel logistic regression. Geographic disparities of cervical cancer late-stage diagnosis are measured using spatial scan statistics. The second part of the study examines disparities of cervical cancer survival in Texas by SES, race/ethnicity, and geographic locations. It analyzes how

individual- and contextual-level factors impact cervical cancer survival and its geographic pattern using a multilevel survival model. Exponential spatial scan statistics are used to measure geographic disparities of cervical cancer survival. The third part examines geographic variations of racial/ethnic disparities of cervical cancer mortality in Texas using population-weighted risk difference and risk ratio. Multivariate logistic regression is used to measure the impact of contextual-level factors on these geographic variations. A review of methods used in this research are presented below, including the relative spatial access presentation method, multilevel logistic regression, the multilevel survival model, the spatial scan statistic method, and the population-weighted risk difference and risk ratio.

The relative spatial access presentation method

A relative spatial access presentation method (Wan et al. 2012) was used to measure spatial access to healthcare in Texas. This method incorporates a concept of spatial access ratio (SPAR) to describe levels of relative spatial access based on the enhanced two-step floating catchment area (E2SFCA) method (Luo and Qi, 2009). Specifically, it first computes a spatial access index (SPAI) for each census tract using the E2SFCA method, then it uses a ratio of SPAI in each census tract to the average SPAI of the entire region to represent the level of relative spatial access.

This study implemented the E2SFCA method in two steps to compute the SPAI. First, it defined a 60-minute travel-time zone (catchment) for each healthcare location i, and divided the travel-time zone into four subzones $D_t(t$ =1, 2, 3, 4): less than 10 minutes, between 10 and 20 minutes, between 20 and 30 minutes, and between 30 and 60

minutes (Wan et al. 2012). Then, it computed the supply-to-demand ratio R_i for each PCP location i. The first step could be expressed as:

$$\mathbf{R_i} = \frac{\mathbf{S_i}}{\sum_{\mathbf{i}\in\{\mathbf{d_{ki}}\in\mathbf{D_t}\}} \mathbf{P_k W_t}} \quad \mathbf{3.1}$$

Where S_i represents the count of health care capacities at location i, P_k represents the population size of any census tract k within subzone D_t, d_{ki} indicates the shortest travel time between i and census tract k, and W_t represents the impedance weight for D_t based on the Gaussian function (Wan et al. 2012). Second, it summed up the weighted supply-to-demand ratio of all the healthcare locations I within the 60 minutes travel-time zone of each census tract j. The second step could be expressed as:

$$\mathbf{A_j^F} = \sum_{\mathbf{I}\in\{\mathbf{d_{jI}}\in\mathbf{D_t}\}} \mathbf{R_I W_t} \quad \mathbf{3.2}$$

where A_j^F is the SPAI of any census tract j, R_I represents the supply-to-demand ratio for any healthcare location I within the 60 minutes travel-time zone of each census tract j, and jI represents the shortest travel time between j and I.

The multilevel logistic regression

Multilevel regression models are statistical models to analyze hierarchical or clustered data at different levels (e.g., patient-level and census tract-level), taking account of the variability associated with each level of the hierarchy. A multilevel logistic model can be applied to data with a binary outcome variable (Dai et al. 2001).

$$\mathbf{y_{ij}} = \boldsymbol{\pi}_{\mathbf{ij}} + \mathbf{e_{ij}} \quad \mathbf{3.3}$$

$$\mathbf{logit}(\boldsymbol{\pi}_{\mathbf{ij}}) = \mathbf{log}\frac{\boldsymbol{\pi}_{\mathbf{ij}}}{\mathbf{1}-\boldsymbol{\pi}_{\mathbf{ij}}} = \boldsymbol{\alpha}_{\mathbf{j}} + \boldsymbol{\beta}\mathbf{x_{ij}} \quad \mathbf{3.4}$$

$$\boldsymbol{\alpha}_{\mathbf{j}} = \boldsymbol{\alpha} + \mathbf{u_j} \quad \mathbf{3.5}$$

where y is a binary outcome variable, i is the patient level indicator, j is the census tract level indicator, $\pi_{ij} = \frac{\exp(\alpha+\beta x_{ij})}{1+\exp(\alpha+\beta x_{ij})}$ is the probability of late-stage diagnosis for patient i in census tract j, and e_{ij} is patient-level random error. The logit function assumes that each census tract has its own intercept α_j measuring census-tract level effects. α_j is a linear combination of a grand mean α and a deviation u_j from that mean. Therefore, the hierarchical model has both fixed effects (α, β) and random effects u_j.

The multilevel survival model

Multilevel survival models are statistical models to analyze correlated failure times (e.g., clustered decease). It is critical to take into account correlation of the failure times within the same cluster (census tract) in order to avoid bias. Frailty models are successful tools in the analysis of correlated failure times data (Liu and Huang 2007).

Suppose there are $i = 1, 2, \dots, n$ census tracts, where each census tract has $j = 1, 2, \dots, n_i$ patients. Each patient within census tract i has an event (decease) time T_{ij} which is the clustered (correlated) time. The observed time for a patient is X_{ij} which is the minimum of the event time T_{ij} and the censoring time D_{ij}. Z_{ij} is a covariate vector which represents fixed effects for each patient. v_i is the unobserved random effect (frailty) for the ith census tract with a density f_θ, which is assumed to follow a Gamma distribution. δ_{ij} is an event indicator function. The hazards for failure (decease) $\lambda_{ij}^{T}(t)$ and censoring $\lambda_{ij}^{D}(t)$ are given by

$$\boldsymbol{\lambda_{ij}^{T}(t) = \exp\left(\beta^{T} Z_{ij} + v_i\right)\lambda_0^{T}(t)} \quad \textbf{3.6}$$

$$\boldsymbol{\lambda_{ij}^{D}(t) = \exp\left(\alpha^{T} Z_{ij} + \gamma v_i\right)\lambda_0^{T}(t)} \quad \textbf{3.7}$$

The likelihood for census tract i is given by

$$\mathbf{L_i} = \int \left[\prod_{\mathbf{j=1}}^{\mathbf{n_i}} \mathbf{L_{ij}^T L_{ij}^D} \right] \mathbf{f_\theta}(\mathbf{v_i}) \mathbf{d_{v_i}} \quad \textbf{3.8}$$

where

$$\mathbf{L_{ij}^T} = \left[\mathbf{exp}\left(\boldsymbol{\beta}^{\mathbf{T}} \mathbf{Z_{ij}} + \mathbf{v_i}\right) \boldsymbol{\lambda}_{\mathbf{0}}^{\mathbf{T}}(\mathbf{x_{ij}}) \right]^{\boldsymbol{\delta}_{\mathbf{ij}}} \mathbf{exp}\left[- \int_{\mathbf{0}}^{\mathbf{x_{ij}}} \mathbf{exp}\left(\boldsymbol{\beta}^{\mathbf{T}} \mathbf{Z_{ij}} + \mathbf{v_i}\right) \boldsymbol{\lambda}_{\mathbf{0}}^{\mathbf{T}}(\mathbf{t}) \mathbf{dt} \right] \quad \textbf{3.9}$$

$$\mathbf{L_{ij}^D} = \left[\mathbf{exp}\left(\boldsymbol{\alpha}^{\mathbf{T}} \mathbf{Z_{ij}} + \boldsymbol{\gamma} \mathbf{v_i}\right) \boldsymbol{\lambda}_{\mathbf{0}}^{\mathbf{D}}(\mathbf{x_{ij}}) \right]^{\mathbf{1} - \boldsymbol{\delta}_{\mathbf{ij}}} \mathbf{exp}\left[- \int_{\mathbf{0}}^{\mathbf{x_{ij}}} \mathbf{exp}\left(\boldsymbol{\alpha}^{\mathbf{T}} \mathbf{Z_{ij}} + \boldsymbol{\gamma} \mathbf{v_i}\right) \boldsymbol{\lambda}_{\mathbf{0}}^{\mathbf{D}}(\mathbf{t}) \mathbf{dt} \right] \quad \textbf{3.10}$$

The spatial scan statistic method

The spatial scan statistic was adapted to measure geographic disparities of cervical cancer outcomes. This method was selected because it implemented tests of significance to identify geographic regions (clusters) with increased risks compared to other regions. The Poisson model assumed the number of cases followed a Poisson distribution and the expected number of cases was proportional to risk population when there were no covariates. A circular window was used to scan the area. For each scanning window, the alternative hypothesis is that there is an increased risk within the scanning window compared with areas outside the window. The likelihood function for a specific scanning window is proportional to (Kulldorff 2009):

$$\left(\frac{\mathbf{c}}{\mathbf{E(c)}}\right)^{\mathbf{c}} \left(\frac{\mathbf{C-c}}{\mathbf{C-E(c)}}\right)^{\mathbf{C-c}} \mathbf{I}() \quad \textbf{3.11}$$

Where C is the total number of cases in a study area, c is the observed number of cases within the scanning window, and I() is an indicator function. When there is no covariate, $\mathrm{E(c)}$ is the expected number of cases within the scanning window defined as $\mathrm{E(c)} = \mathrm{p} * \mathrm{C/P}$, where p is the population within the scanning window, C and P are the total number of cases and population in the study area. The expected number of cases with covariates adjustment is defined as $\mathrm{E(c)} = \sum_i \mathrm{E(c_i)} = \sum_i \mathrm{p_i} * \mathrm{C_i/P_i}$, where $\mathrm{p_i}$ and $\mathrm{c_i}$

represent population and number of cases for covariate category i within the scanning window, P_i and C_i are population and total cases for covariate category i in the study area.

Exponential spatial scan statistic was used to measure geographic disparities of cervical cancer survival. The method identifies geographic regions (clusters) with shorter-than-expected or longer-than-expected survival compared with other regions. It assumes survival times follow an exponential distribution, and compares mean survival time within a geographic region with that outside the region.

The maximum likelihood estimation method was used to calculate the likelihood of each scanning window. The most likely cluster is a window with the maximum likelihood. Monte Carlo simulations were implemented to derive p-values and evaluate the statistical significance of candidate clusters with high risks.

The population-weighted risk difference

The population-weighted risk difference (RD) has strong statistical power and fewer false-positive results(Goovaerts et al. 2007). It is calculated as follows:

$$\boldsymbol{RD(a_i) = \frac{r_1(a_i) - r_2(a_i)}{\sqrt{\bar{r}(a_i)\,(1-\bar{r}(a_i))\left[\frac{1}{p_1(a_i)}+\frac{1}{p_2(a_i)}\right]}}} \qquad \textbf{3.12}$$

Where $\bar{r}(a_i)$ is the population-weighted average cervical cancer late-stage diagnosis or mortality rate in a census tract defined as follows:

$$\mathbf{\bar{r}(a_i) = \frac{p_1(a_i)r_1(a_i)+p_2(a_i)r_2(a_i)}{p_1(a_i)+p_2(a_i)}} \qquad \textbf{3.13}$$

In equations 3.12 and 3.13, $RD(a_i)$ represents the risk difference, $RD(a_i)$ represents the risk ratio, a_i is a census tract, $r_1(a_i)$ and $p_1(a_i)$ represent cervical

cancer rate and population size of a group in question in this census tract, $r_2(a_i)$ and $p_2(a_i)$ represent cervical cancer rate and population size of a reference group in question in this census tract.

The null and alternative hypotheses to test whether the risk difference is significant are as follows:

$$\begin{aligned} \boldsymbol{H_0}&\boldsymbol{: |RD(a_i)| = 0} \\ \boldsymbol{H_1}&\boldsymbol{: |RD(a_i)| \neq 0} \end{aligned} \qquad \textbf{3.14}$$

CHAPTER IV

RACIAL/ETHNIC, SOCIOECONOMIC, AND GEOGRAPHIC DISPARITIES OF CERVICAL CANCER LATE-STAGE DIAGNOSIS IN TEXAS

Introduction

Late-stage detection is a primary cause of mortality among patients diagnosed with cervical cancer (Brookfield et al. 2009; Priest et al. 2010). There has been a consistent decrease in late-stage diagnosis in the United States, due to the wide use of Pap smear screening as an early detection tool (ACS 2013). However, this benefit was not uniformly shared among different population groups. Significant gaps have been documented in cervical cancer late-stage diagnosis by race/ethnicity, socioeconomic status (SES) and geographic locations (Mitchell and Mccormack 1997; Saraiya et al. 2007; Coughlin et al. 2008; Watson et al. 2008; Barnholtz-Sloan et al. 2009). Hispanics and African-Americans have an increased risk of late stage cervical cancer diagnosis, compared with non-Hispanic whites in the United States (Schwartz et al. 2003; Patel et al. 2009; Leath et al. 2005; Eggleston et al. 2006; McCarthy et al. 2010). Individuals with lower SES experienced elevated risks of late-stage diagnosis, compared with those with higher SES (McCarthy et al. 2010; Patel et al. 2009). Cervical cancer patients residing in rural areas and areas along the US-Mexico border had higher risks of being diagnosed at a late stage (Coughlin et al. 2008; Jackson et al. 2009).

Failure of timely screening was a well-recognized cause of late-stage diagnosis in cervical cancer (Janerich et al. 1995). Understanding factors associated with screening and stage at diagnosis could help policymakers develop and implement more appropriate public health policies. The existing literature has documented several individual and

contextual (neighborhood or community-level) factors contributing to screening and the stage at diagnosis. Individual-level factors include: age, race/ethnicity, SES (e.g., education and income), socio-cultural factors (e.g., immigration status and language proficiency), and access to healthcare (e.g., whether or not having a regular doctor) (Banerjee et al. 2007; Coker et al. 2009; De Alba and Sweningson 2006).

Contextual factors include SES, socio-cultural factors, socio-environmental factors, and access to healthcare (Daley et al. 2011; Documét et al. 2008; Downs et al. 2008; Katz et al. 2007; Wells and Horm 1998). Contextual SES include community-level poverty rate, high school and college graduation rate, unemployment rate, to name a few (Daley et al. 2011; Datta et al. 2006). Contextual socio-cultural factors reflect characteristics of a homogeneous population group (Singer 2012). Socio-environmental factors included racial composition (such as percentage of African-Americans in a community), and geographic factors (Coughlin et al. 2008). Contextual access to healthcare could be impacted by both non-spatial factors (e.g., health service resources in a community) and spatial factors measured by geographic features (e.g., travel distance to the closest screening facility). An increasing number of studies have found that spatial access to healthcare of a community played an important role in cancer screening, diagnosis, treatment, and survival (Brewer et al. 2012; Wang et al. 2008; Wan et al. 2012; Wan et al. 2013).

Although previous studies have established the impact of individual and contextual factors on late-stage diagnosis of cervical cancer, evidence of effects of individual factors on racial/ethnic, SES, and geographic disparities of cervical cancer late-stage diagnosis was inconclusive and inconsistent (Brewer et al. 2012; Wang et al.

2008; Wan et al. 2012; Wan et al. 2013; Drain et al. 2002; Islami et al. 2013; Leath et al. 2005; O'Malley et al. 2006; Patel et al. 2009; Schwartz et al. 2003). For contextual factors, evidence of their effects on the disparities mentioned above was limited in cervical cancer. In a broader field of cancer research, several studies have suggested that some contextual variables, such as percentage of African-Americans and foreign-born population in a community, were associated with racial disparities of late-stage diagnosis in breast, prostate and colorectal cancer (Haas et al. 2008; Shebl et al. 2012). One study revealed that spatial access to healthcare explained a small portion of racial/ethnic disparities of late-stage cervical cancer in New Zealand (Brewer et al. 2012). However, until now, no reported study has examined the impact of spatial access to healthcare on cervical cancer in the United States. Studies on the effects of contextual factors on SES and geographic disparities are even sparse.

This chapter investigates disparities of cervical cancer late-stage diagnosis in Texas based on data from 1995-2008 from three social domains: race/ethnicity, SES, and geographic location. Meanwhile, it examines the role of both individual and contextual factors in these disparities. This is the first attempt to examine effects of both individual and contextual factors on late-stage cervical cancer disparities by race/ethnicity, SES, and geographic location in the United States. By looking at multiple-level influences on race/ethnicity, SES, and geographic location when explaining cervical cancer outcomes, this study enhances knowledge about factors associated with cervical cancer disparities of late-stage diagnosis. It is hoped that results from this study will provide multiple-level information for developing more effective cervical cancer intervention programs in Texas.

Materials and Methods

Study population

Cervical cancer cases in Texas between 1995 and 2008 were obtained from the Texas Cancer Registry (TCR) within Texas Department of State Health Services (TDSHS). There were 15,370 incidences of cervical cancer between 1995 and 2008. Cervical cancer stage at diagnosis was categorized into localized, regional, and distant stages according to the Surveillance Epidemiology and End Result (SEER) program from the National Cancer Institute (NCI). Based on clinical and pathological information, localized stage was grouped as early stage, while the regional and distant stages were grouped as late stage. The number of early, late, and unknown stage cases was 7,365 (48%), 6,057 (39%), and 1,948 (13%) respectively. Cases with unknown stages were excluded from the study. The use and analysis of the cervical cancer data has been approved by the Institutional Review Board (IRB) of TDSHS.

Study variables

Individual variables in this study included age at diagnosis, race/ethnicity, tumor grade, and stage at diagnosis. Adopting stage at diagnosis as an outcome variable in this study, the study categorized the age at diagnosis into five groups (<34, 34-44, 45-54, 55-64, and >64). Because Asian, Native American, and other racial groups only accounted for a small portion of total cases (3%), only Hispanic, African-American, and non-Hispanic white groups were included in the analysis of this study. Tumor grade represented the degree of abnormality of cancer cells and was categorized to well differentiated, moderately differentiated, poorly differentiated, and undifferentiated based on the International Classification of Diseases for Oncology Third Edition (ICD-O-3).

Contextual variables included census demographic variables, census-tract level health insurance expenditure variables, and cervical cancer healthcare data. This study used twelve census-tract level demographic variables from Census 2000 datasets. These variables included: percentage of females without college education, percentage of females without high school education, percentage of foreign-born females, percentage of linguistic isolated households, percentage of African-Americans, percentage of Hispanics, percentage of females living in crowed housing, median household income, percentage of households without a car, poverty rate, median home value, and unemployment rate of females. These variables reflected several domains: socioeconomics, socio-cultural context, and social environment, which were selected based on suggestions in previous research that examined the association between contextual factors and cancer outcomes (Coughlin et al. 2006; Haas et al. 2011; Krieger et al. 2006; Lian et al. 2011; Schootman et al. 2009).

Factor analysis was used to reduce the dimension of census-tract demographic variables mentioned above. Three factors that explained 75% of the overall variance were extracted (Table 4.1). The first common factor explained 43.5% of the total variance. Five variables had high factor loadings (factor loading coefficient > 0.60) on this factor, including poverty rate, percentage of households without a car, percentage of females without college education, percentage of females living in crowed housing, and percentage of Hispanics in a census tract. These five variables exhibited a high internal consistency (Cronbach's alpha = 0.88) and were used to construct SES. The second common factor explained 20% of the total variance. Three variables had high factor loadings (factor loading coefficient > 0.60) on this factor, including percentage of

linguistically isolated households, percentage of females without high school education, and percentage of foreign-born females in a census tract. These three variables also exhibited a good internal consistency (Cronbach's alpha = 0.74) and were used to construct the socio-cultural factor. The third common factor explained 11.5% of the variance and only the percentage of African Americans in a census tract had a factor loading coefficient greater than 0.60. Therefore, the study used the percentage of African Americans in a census tract as a single factor in the analysis.

Two census-tract level health insurance expenditure variables were collected from Simplymap: average household health insurance expenditure, and average household commercial health insurance expenditure. These two variables were standardized for the factor analysis. A single health insurance expenditure factor was extracted.

This study used PCPs data as cervical cancer healthcare data in Texas because PCPs were primary providers of screening services for cervical cancer (Weinstein et al. 2009). It was reported that Pap smear screening was statistically associated with the contacts of primary care providers. A total of 14,268 PCPs with 6,372 primary practicing addresses in 2000 was obtained from TDSHS. These primary practicing addresses were geocoded using ArcGIS 10.0 (ESRI 2011) and the number of PCPs at each practicing address was counted.

Table 4.1 Factor loadings and the percentage of variance explained by each factor

Variables	Factors		
	Socioeconomic status	**Socio-cultural factor**	**Percentage of African Americans**
Poverty rate	**0.84**	−0.12	0.26
Unemployment rate of females	0.48	−0.12	0.45
Median home value	−0.59	0.56	0.34
Median household income	−0.74	0.49	0.16
Females without high school education (%)	−0.04	**0.74**	0.41
Females without college education (%)	**0.67**	−0.37	−0.25
Linguistically isolated households (%)	0.48	**0.80**	−0.10
Females living in crowed housing (%)	**0.86**	0.32	−0.05
Households without a car (%)	**0.68**	−0.18	0.45
African Americans (%)	0.20	−0.49	**0.64**
Hispanics (%)	**0.78**	0.37	−0.27
Foreign-born females (%)	0.64	**0.65**	−0.04
Cumulative proportion of total variance explained by the factor	43.49%	63.71%	74.87%

Methods

A relative spatial access presentation method (Wan et al. 2012) was adopted to measure spatial access to PCPs in Texas. This method considers the competition of the available healthcare sites among the demanding population. The spatial access to healthcare for a population site is accumulative supply-to-demand ratio of available healthcare locations. The method first computes a spatial access index for a census tract

using the E2SFCA method (Luo and Qi 2009) implemented in Visual Basic for Applications in ArcGIS 10.0 (ESRI 2011), then it adopts spatial access ratio (SPAR) to describe levels of relative spatial access. SPAR is defined as a ratio of spatial access index in a census tract to the average spatial access index of the entire region. A SPAR greater than one indicates higher-than-average spatial access. Detail of this method can be found elsewhere (Wan et al. 2012).

Disparities of cervical cancer late-stage diagnosis by race/ethnicity and SES were measured using multilevel logistic regression. SAS PROC GLIMMIX procedure was adopted to fit the multilevel logistic regression. Three regression models were built to evaluate race/ethnic, and SES disparities respectively. Stage at diagnosis was adopted as the dependent variable in these regression models. To measure late-stage diagnosis disparities by race/ethnicity, the first model (Model I) included age group, tumor grade, and race/ethnicity as independent variables. The second model (Model II) included age group, tumor grade, race/ethnicity, and SES. In order to examine the impact of contextual factors on racial/ethnic disparities, a third model (Model III) included all the variables in Model II with the addition of contextual factors, including socio-cultural factors, percentage of African Americans in a census tract, insurance expenditures, and spatial access to PCPs. To measure late-stage diagnosis disparities by SES, the first model (Model I) included age group, tumor grade, and SES. The second model (Model II) included age group, tumor grade, SES, and race/ethnicity. The third model (Model III) included all the variables in Model II with the addition of contextual factors.

This study measured geographic disparities of cervical cancer late-stage diagnosis using a spatial scan statistic. The study adopted the Poisson model that assumed the

number of late-stage diagnosis cases followed a Poisson distribution and the expected number of cases was proportional to risk population when there were no covariates. The study used a circular window to scan the study area and adopted 50% of risk population as the maximum scanning window size. 9999 Monte Carlo simulations were implemented to derive p-values and evaluate the statistical significance of candidate clusters with high risks. The spatial scan statistical analysis was conducted in the SaTScan (v.8.2.1) software (Kulldorff 2009). The study conducted four separate spatial scan statistic tests to identify geographic clusters of late-stage cervical cancer. The first test was adjusted for age; the second test was adjusted for age and race/ethnicity; the third test was adjusted for age, race/ethnicity, and SES; the fourth test was adjusted for all covariates in the third test with the addition of percentage of African Americans in a census tract. Non-overlapping clusters with p-values less than 0.05 were reported in this study.

Results

Spatial access to healthcare

Figure 4.1 presents unequally distributed spatial access to PCPs in Texas. Urban areas (displayed as areas around population centers in Figure 4.1), where PCPs were more concentrated, had higher levels of spatial access to PCPs, compared with rural areas. Results in Figure 4.1 also reveal that a moderate portion of western and southern Texas experience a lower level of spatial access to PCPs.

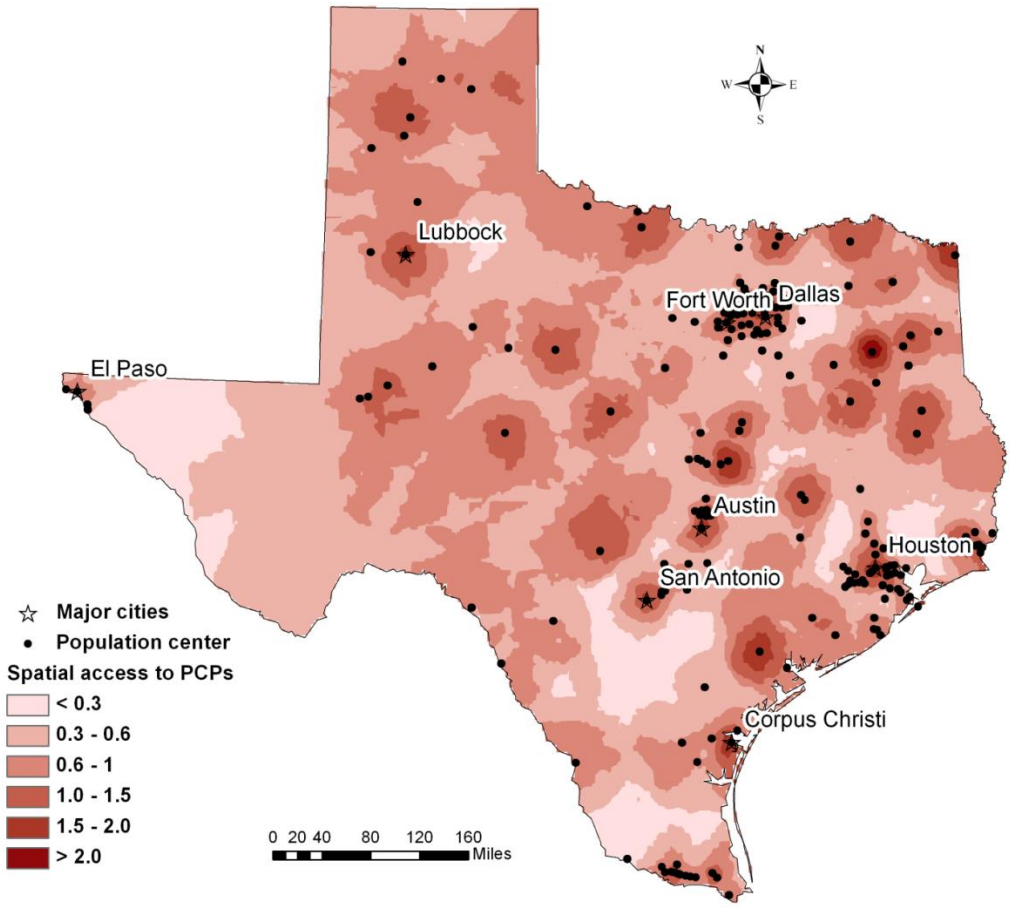

Figure 4.1 Spatial access to primary care physicians (PCPs)

(Note: A value greater than one on the map represents a higher-than-average spatial access; A value less than one on the map represents a lower-than-average spatial access.)

Racial/ethnic and SES disparities

Distributions of selected characteristics, including both individual and contextual-level characteristics between early and late-stage diagnosed groups, is presented in Table 4.2. According to Chi-Square tests, there were statistically significant differences between early and late-stage cases in terms of age, race/ethnicity, and SES. A larger proportion of late-stage patients were diagnosed at an older age, compared with early-stage patients. There were a higher proportion of late-stage patients who were Hispanics (37.2%) and African-Americans (15.4%), compared with their early-stage counterparts.

A larger proportion of late-stage patients were from census tracts with the lowest SES, compared with the early-stage patients. Chi-Square tests did not identify significant differences in other contextual variables, including socio-cultural factors, percentage of African Americans in a census tract, and spatial access to PCPs.

Table 4.3 presents cervical cancer late-stage diagnosis disparities by race/ethnicity and SES. There are statistically significant racial/ethnic disparities of cervical cancer late-stage diagnosis. Compared with non-Hispanic white cervical cancer patients, African-American patients had an elevated risk of late-stage diagnosis (odds ratio [OR], 1.46; 95% confidence interval [CI], 1.31–1.63). Hispanic patients also experienced a higher risk of late-stage diagnosis (OR, 1.35; 95% CI, 1.25–1.46) (Model I). After adjusting for SES, the risk was reduced by 14% and 15% respectively for African-Americans (OR, 1.32; 95% CI, 1.18–1.48) and Hispanics (OR, 1.20; 95% CI, 1.10–1.31) (Model II). However, the risk remained the same for African-Americans (OR, 1.32; 95% CI, 1.15–1.51) and only decreased slightly for Hispanics (OR, 1.18; 95% CI, 1.08–1.30) after adjusting for contextual factors (Model III).

Table 4.3 also reveals statistically significant SES disparities of cervical cancer late-stage diagnosis. There was a significant pattern that the risk of late-stage diagnosis increased as SES decreased. Cervical cancer patients from census tracts with the lowest SES were 77% more likely to be diagnosed at a later stage (OR, 1.77; 95% CI, 1.57–2.00) adjusted for age and tumor grade (Model I). Model II shows that this elevated risk for individuals from census tracts with the lowest SES was reduced after including race/ethnicity (OR, 1.56; 95% CI, 1.37–1.77). However, the risk was only slightly

reduced with the adjustment of contextual factors (OR, 1.54; 95% CI, 1.29–1.85) (Model III).

Table 4.2 Selected characteristics of cervical cancer stage at diagnosis in Texas, 1995-2008

Characteristics	Early Stage (n = 7,365)		Late Stage (n = 6,057)	
	Cases	%	Cases	%
Age*				
< 35	1,663	22.6	669	11.0
35-44	2,353	31.9	1,429	23.6
45-54	1,539	20.9	1,499	24.7
55-64	840	11.4	1,023	16.9
> 64	970	13.2	1,437	23.7
Race/Ethnicity*				
Non-Hispanic White	3,821	51.9	2,725	45.0
Hispanic	2,393	32.5	2,254	37.2
African American	845	11.5	931	15.4
Socioeconomic Status*				
First quartile (High)	1,083	14.7	595	9.8
Second quartile	1,497	20.3	1,065	17.6
Third quartile	2,479	33.7	1,965	32.4
Fourth quartile (Low)	2,306	31.3	2,432	40.2
Socio-cultural factor				
First quartile (High)	1,696	23.0	1,486	24.5
Second quartile	1,881	25.5	1,492	24.6
Third quartile	1,894	25.7	1,500	24.8
Fourth quartile (Low)	1,894	25.7	1,579	26.1
Percentage of African Americans				
First quartile (High)	1,799	24.4	1,540	25.4
Second quartile	2,066	28.1	1,634	27.0
Third quartile	1,856	25.2	1,486	24.5
Fourth quartile (Low)	1,644	22.3	1,397	23.1
Spatial access to primary care physicians				
First quartile (High)	1,598	21.7	1,479	24.4
Second quartile	1,813	24.6	1,497	24.7
Third quartile	2,043	27.7	1,646	27.2
Fourth quartile (Low)	1,911	25.9	1,435	23.7

* Chi-Square tests for the distribution of the factors between early and late-stage diagnosed groups were significant ($p<0.001$).

Table 4.3 Odds ratio of cervical cancer late-stage diagnosis by race/ethnicity and contextual socioeconomic status (SES)

	Odds ratio of Model I (95% CI)	Odds ratio of Model II (95% CI)	Odds ratio of Model III (95% CI)
Race/Ethnicity			
Non-Hispanic White	1 (Referent)	1 (Referent)	1 (Referent)
Hispanic	1.35 (1.25–1.46)*	1.20 (1.10–1.31)*	1.18 (1.08–1.30)*
African-American	1.46 (1.31–1.63)*	1.32 (1.18–1.48)*	1.32 (1.15–1.51)*
Socioeconomic status			
First quartile (High)	1 (Referent)	1 (Referent)	1 (Referent)
Second quartile	1.26 (1.11–1.44)*	1.23 (1.08–1.41)*	1.19 (0.99–1.42)
Third quartile	1.38 (1.22–1.55)*	1.30 (1.15–1.47)*	1.27 (1.07–1.52)*
Fourth quartile (Low)	1.77 (1.57 – 2.00)*	1.56 (1.37–1.77)*	1.54 (1.29–1.85)*

*p<0.005
Model I is adjusted for age and tumor grade. Model II is adjusted for age, tumor grade, race/ethnicity, and SES. Model III is adjusted for all factors of Model II, with addition of contextual factors, including socio-cultural factors, percentage of African Americans, insurance expenditures, and spatial access to primary care physicians.

Geographic disparities

Figure 4.2a shows geographic clusters of cervical cancer late-stage diagnosis adjusted for age. The most likely cluster was observed in the western tip of Texas with a relative risk of 1.77. Three secondary clusters covered southern Texas (secondary cluster 1), the Bryan/College Station area (secondary cluster 2), and central Houston (secondary cluster 3) with relative risks of 1.27, 3.07 and 1.93 respectively. Other characteristics of the above clusters, including the number of census tracts and p-values, are presented in Table 4.4.

Table 4.4 SaTscan statistics for geographic clusters of late stage-diagnosis in Texas

SaTScan statistics	Most likely Cluster	Secondary Cluster1	Secondary Cluster2	Secondary Cluster3	Statewide
Number of Census Tracts	89	608	36	57	4,388
Observed number of late-stage diagnosis cases	261	997	46	107	6,057
Expected number of late-stage diagnosis cases	150	814	15	56	6,057
Relative Risk	1.77	1.27	3.07	1.93	1
P-Value	0.0001	0.0001	0.0001	0.0002	-

Table 4.5 presents the distribution of selected individual and contextual-level characteristics within the geographic clusters shown in Figure 4.2a. The distribution of age was similar among four geographic clusters. The distribution of several characteristics, including race/ethnicity, SES, socio-cultural factors, and percentage of African Americans, was different among the clusters. For example, the most likely cluster, as well as secondary clusters 1 and 3 had a higher percentage of Hispanic patients and census tracts with the lowest SES compared with secondary cluster 2. Similar patterns were observed for the socio-cultural factor. The most likely cluster, as well as secondary clusters 1 and 3 had a higher percentage of census tracts within the lowest socio-cultural factors quartile, which primarily represented a higher percentage of foreign-born people and language isolated households, compared with secondary cluster 2. In terms of the percentage of African Americans, secondary clusters 2 and 3 had a higher percentage of census tracts with a higher percentage of African-Americans in a census tract, compared with other clusters.

Table 4.5 Selected characteristics of geographic clusters of cervical cancer late-stage diagnosis in Texas, 1995-2008

Individual-level Characteristics	Most likely Cluster (n = 261)	Secondary Cluster1 (n = 997)	Secondary Cluster2 (n = 46)	Secondary Cluster3 (n = 107)
Age				
< 35	9.3%	11.7%	11.3%	10.1%
35-44	18.9%	22.1%	25.4%	27.3%
45-54	18.6%	22.1%	22.5%	24.5%
55-64	23.2%	16.4%	16.9%	21.6%
> 64	30.0%	27.6%	23.9%	16.5%
Race/Ethnicity				
Non-Hispanic White	6.1%	18.4%	74.6%	4.3%
Hispanic	92.9%	78.4%	12.7%	56.8%
African American	1.1%	3.1%	12.7%	38.8%
Contextual-level Characteristics	**Most likely Cluster (n = 89)**	**Secondary Cluster1 (n = 608)**	**Secondary Cluster2 (n = 36)**	**Secondary Cluster3 (n = 57)**
Socioeconomic status				
First quartile (High)	1.1%	6.3%	13.9%	3.5%
Second quartile	4.5%	10.9%	35.6%	1.8%
Third quartile	27.0%	27.6%	25.0%	14.0%
Fourth quartile (Low)	67.4%	55.3%	25.6%	80.7%
Socio-cultural factor				
First quartile (High)	2.2%	5.1%	80.6%	33.3%
Second quartile	2.2%	27.8%	11.1%	7.0%
Third quartile	22.5%	33.1%	5.6%	17.5%
Fourth quartile (Low)	73.0%	34.0%	2.8%	42.1%
Percentage of African Americans				
First quartile (High)	37.1%	35.7%	22.2%	10.5%
Second quartile	37.1%	34.0%	38.9%	17.5%
Third quartile	12.4%	22.0%	19.4%	15.8%
Fourth quartile (Low)	13.5%	8.2%	19.4%	56.1%

For age and race/ethnicity, percentage in the table represents the proportion of late stage diagnosis cases within each group. For other variables, percentage in the table is the proportion of census tracts within each quartile.

Figure 4.2b presents two geographic clusters of late-stage diagnosis after adjusting for age and race/ethnicity. Secondary clusters 1 and 3 presented in Figure 4.2a were eliminated. Area of the most likely cluster and secondary cluster 2 was substantially

reduced. A closer examination of the most likely cluster in Figure 4.2b revealed that 88% of census tracts had the lowest SES. The remaining secondary cluster only covered one census tract, located in Huntsville, Texas. This census tract was found with a higher SES. The percentage of African-Americans and Hispanics in this census tract were 25.9% and 12.7% respectively. It was also found that 31% females aged 18 years and older were single according to Census 2000.

After adjusting for age and race/ethnicity with the addition of SES, the most likely cluster in the western tip of Texas was eliminated, suggesting an association between SES and a higher risk of late-stage diagnosis in this cluster (Figure 4.2c). After controlling for the above factors with the addition of the percentage of African Americans, the only cluster in city of Huntsville, Texas was eliminated (Figure 4.2d), which suggests that the percentage of African Americans in a census tract might explain the high risk of late-stage diagnosis in this cluster.

To further explore whether geographic location was an independent predictor of cervical cancer late-stage diagnosis, this study modeled odds ratio of late-stage diagnosis risk using multilevel logistic regression (Table 4.6). Compared with patients residing outside geographic clusters in Figure 4.2a, individuals within these clusters had an elevated risk of late-stage diagnosis after adjusting for age (OR, 1.30; 95% CI, 1.19–1.41) (Model I). After adjusting for age and race/ethnicity, the risk of late-stage diagnosis was reduced for patients within the clusters (OR, 1.19; 95% CI, 1.08–1.30) (Model II). After adjusting for age, race/ethnicity, and SES, the risk decreased substantially and was marginally significant (OR, 1.10; 95% CI, 1.00–1.21) (Model III). The risk became insignificant after adjusting for all of the factors mentioned above with the addition of the

percentage of African Americans in Model IV. Geographic disparities of late-stage diagnosis were explained by race/ethnicity, SES, and the percentage of African Americans in this study.

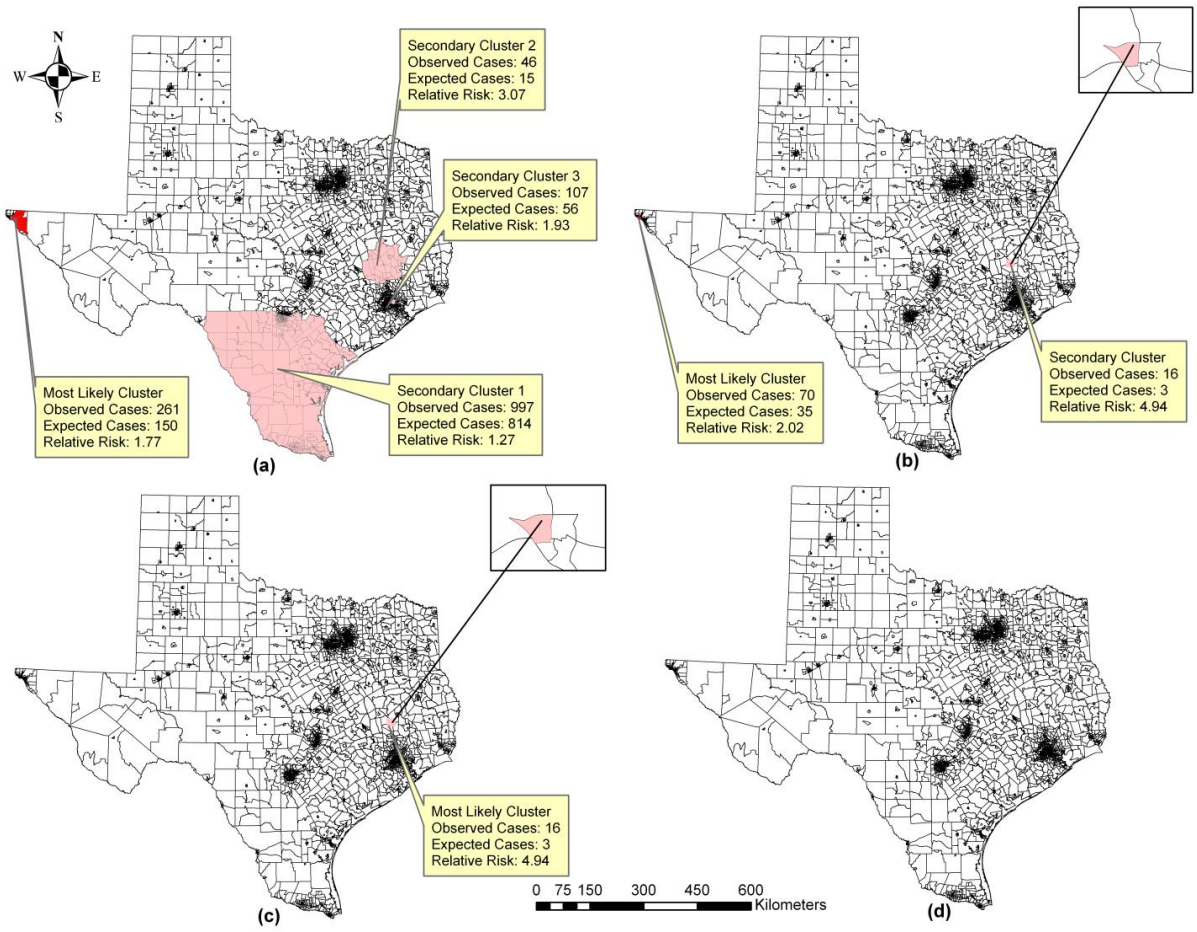

Figure 4.2 Geographic clusters of cervical cancer late-stage diagnosis in Texas

(a) adjusted for age; (b) adjusted for age and race/ethnicity; (c) adjusted for age, race/ethnicity, and SES; (d) adjusted for age, race/ethnicity, SES, and the percentage of African Americans in a census tract.

Table 4.6 Odds ratio of cervical cancer late-stage diagnosis by geographic locations

	Odds ratio of Model I (95% CI)	Odds ratio of Model II (95% CI)	Odds ratio of Model III (95% CI)	Odds ratio of Model IV (95% CI)
Geographic locations				
Noncluster	1 (Referent)	1 (Referent)	1 (Referent)	1 (Referent)
High-risk clusters	1.30 (1.19–1.41)**	1.19 (1.08–1.30)*	1.10 (1.00–1.21)	1.10 (0.99–1.21)

*p<0.05
**p<0.001
Model I is adjusted for age. Model II is adjusted for age, and race/ethnicity. Model III is adjusted for age, race/ethnicity, and SES. Model IV is adjusted for all the factors in Model III with the addition of the percentage of African Americans in a census tract.

Discussions and conclusions

This study found statistically significant racial/ethnic and SES disparities of cervical cancer late-stage diagnosis. Race/ethnicity and SES were independent predictors of the stage of diagnosis of cervical cancer. Hispanic and African-American patients had an elevated risk of late-stage diagnosis even after adjusting for other factors, including both individual and contextual factors, compared with their non-Hispanic white counterparts. Compared with patients from census tracts with a higher SES, individuals from census tracts with a lower SES experienced elevated risk of late-stage diagnosis even after adjusting for other factors.

This study did not observe any significant geographic disparities after adjusting for several factors, including age, race/ethnicity, SES, and the percentage of African Americans in a census tract.

Persistent racial/ethnic disparities reported in this study corroborate previous findings that race/ethnicity could serve as an independent predictor of cervical cancer

stage of diagnosis. Several studies have found that Hispanics and African-Americans have a higher chance of experiencing late-stage diagnosis in Texas even after controlling for covariates (Eggleston et al. 2006; Leath et al. 2005). The reduction of risk after adjusting for contextual SES in this study suggests that SES could partially explain racial/ethnic disparities. The interaction between SES and race/ethnicity could be attributed to the fact that minorities, such as Hispanics and African-Americans, tended to reside in communities with lower SES (McCarthy et al. 2010). The adjustment of other contextual factors slightly reduced the elevated risk in Hispanics. However, the impact of these contextual factors on racial/ethnic disparities of cervical cancer has rarely been analyzed in the literature. An examination of a broader field of cancer disparity research revealed that socio-cultural factors and the percentage of African Americans in a census tract could partially explain racial/ethnic differences in stage at diagnosis in cancer (Haas et al. 2008; Shebl et al. 2012).

This study reported statistically significant SES disparities of cervical cancer late-stage diagnosis. Similarly, one study found that patients from communities with a lower SES in Texas were more likely to experience late-stage diagnosis even after controlling for age, race/ethnicity, and place of residence (Eggleston et al. 2006). The adjustment of contextual factors only slightly reduced the elevated risk for individuals from census tracts with the lowest SES in this study. The unexplained SES disparities in this study might be attributed to other unmeasured individual-level factors. Several studies suggest that insurance status is a strong predictor of cervical cancer screening and stage at diagnosis (Echeverria and Carrasquillo 2006).

Differences in spatial access did not explain racial/ethnic and SES disparities of cervical cancer late-stage diagnosis in this study. A similar study in New Zealand implied that spatial access to healthcare only explained a small portion of racial/ethnic disparities of cervical cancer late-stage diagnosis (Brewer et al. 2012). However, until now, no reported research has examined the impact of spatial access to healthcare on cervical cancer in the United States. In the broader field of cancer research, one study revealed that spatial access to healthcare was a significant predictor of breast cancer stage at diagnosis (Wang et al. 2008). Another study found that although spatial access to healthcare was associated with stage at diagnosis of colorectal cancer, it did not explain racial/ethnic and SES disparities (Wan et al. 2013). This research is the first attempt to examine the role of spatial access to healthcare in cervical cancer late-stage diagnosis disparities by race/ethnicity and SES in the United States, thus, results from this preliminary study need to be confirmed by further research.

The results suggest that late-stage diagnosis differences by geographic locations might reflect race/ethnicity, SES and other social differences across Texas. A similar study suggested that demographic characteristics (e.g., race/ethnicity and SES) might explain a higher risk of late-stage diagnosis experienced by individuals from US-Mexico border counties, compared with their counterparts from non-border counties (Coughlin et al. 2008). Another study found geographic disparities of cervical cancer late-stage diagnosis in the United States could be explained by race/ethnicity and screening differences (Horner et al. 2011). This study found a substantial decrease in geographic disparities after adjusting for race/ethnicity, which implied that the major underlying

cause of unequal distribution of late-stage diagnosis in Texas was patients' race/ethnicity rather than geographic location.

Several limitations needed to be considered in this study. First, as stated earlier, failure of timely screening was a major cause of cervical cancer late-stage diagnosis (Janerich et al. 1995; Shy et al. 1989). Therefore, disparities by race/ethnicity, SES, and geographic location in the study might reflect cervical cancer screening differences. Lacking relevant screening data, this study employed individual and contextual-level proxy of cervical cancer screening. Previous research has reported associations between these individual factors and cervical cancer screening (Carrasquillo and Pati 2004; Shi et al. 2011). Future studies should focus on whether contextual factors studied in the paper were associated with cervical cancer screening. Second, the remaining racial/ethnic and SES disparities even after adjusting for other factors in the study might be attributed to unmeasured individual factors: immigration status, language, insurance status, marital status, smoking history, and so on. Further research is needed to include these factors in order to disentangle racial/ethnicity and SES disparities of cervical cancer late-stage diagnosis.

Implications for practice and policy

The findings have important implications for developing effective cervical cancer screening and control programs. Traditional cervical cancer screening programs have only adopted individual characteristics to identify who should be selected (Wells and Horm 1998). This study implies that both individual and contextual characteristics should be used to guide screening in order to address cervical cancer disparities. The findings also suggest that geographic disparities in cervical cancer late-stage diagnosis in Texas

can be eliminated if racial/ethnic and SES disparities are addressed. Policymakers should make efforts to address cervical cancer disparities in late-stage diagnosis in Texas through more effective cervical cancer screening, targeting racial/ethnic minority groups, as well as individuals from communities with lower SES, higher percentage of foreign-born and African-American population.

CHAPTER V

RACIAL/ETHNIC, AREA SOCIOECONOMIC AND GEOGRAPHIC DISPARITIES OF CERVICAL CANCER SURVIVAL IN TEXAS

Introduction

Cervical cancer is one of the most commonly diagnosed cancers among women in the United States (Parkin et al. 2005). Although the overall incidence and mortality rates of cervical cancer have declined due to more effective interventions, disparities in cervical cancer survival have persisted (ACS 2013) particularly among African-American women (Samelson et al. 1994; Grigsby et al. 2000; Coker et al. 2009; Eggleston et al. 2006; Morgan et al. 1996) and those with lower SES (Coker et al. 2009; Eggleston et al. 2006; Morgan et al. 1996; Mundt et al. 1998). Although it is well documented that cervical cancer survival disparities are associated with several individual-level factors, such as age, tumor characteristics, type of treatment received, health behaviors, and access to healthcare (Brewster et al. 1999; Eggleston et al. 2006; Coker et al. 2009; Farley et al. 2001), an increasing number of studies have revealed that health disparities are attributed to a wide range of contextual-level factors beyond the individual level (Holmes et al. 2008). Several contextual-level factors have been examined including SES, racial composition, geographic access to healthcare, and other geographic characteristics (e.g. urbanization) (Brewer et al. 2012; Coughlin et al. 2008; Downs et al. 2008; Daley et al. 2011; Du et al. 2011; Lim and Ashing-Giwa 2011; Ashing-Giwa et al. 2009; Lin and Zhan 2013), but evidence of the effects of these factors on cervical cancer survival has been inconclusive and inconsistent.

There are three major literature gaps in cervical cancer survival disparity research. First, there are contradictory findings with regard to racial/ethnic disparities (Garner and Newmann 2012). For example, several studies found that Hispanic women were less likely to die of cervical cancer (Coker et al. 2009; Eggleston et al. 2006), while other studies have reported no such survival difference between Hispanics and non-Hispanic whites (Armstrong et al. 2003; Mundt et al. 1998; Brewster et al. 1999). These inconsistent findings suggest that more research is needed to obtain a better understanding of this issue. Second, studies examining small-area variations of cervical cancer survival were scarce (Walters et al. 2011; Du et al. 2010). Third, no reported study has examined impacts of both individual- and contextual-level variables on small-area variations of cervical cancer survival. This study investigated disparities in cervical cancer survival in Texas using individual and contextual data from 1995-2008 from three social domains: race/ethnicity, census-tract-level SES, and geographic location. The large geographic area and diverse population make Texas ideally suited to examine cervical cancer disparities. These findings will provide opportunities for developing and implementing effective intervention focused on modifiable factors aimed at reducing cervical cancer disparities.

Materials and Methods

Study population

This study used the population-based, statewide Texas Cancer Registry (TCR) about 12,144 women diagnosed with invasive cervical cancer between 1995 and 2005. The Texas Department of State Health Services Institutional Review Board approved the use of these data. The study excluded 932 women who 1) were unable to be geocoded to

street location; 2) have a survival time of 0 months (i.e., death certificate only cases and those lost to follow-up after diagnosis); or 3) were not Hispanics, African-Americans, or non-Hispanic whites. Of the remaining 11,212 women, 5,648 (50.4%) were non-Hispanic white, 3,979 (35.5%) were Hispanic, and 1,585 (14.1%) were African American.

Study variables

Outcome variables

Five-year cervical cancer specific mortality was the main outcome variable, measured in months from the date of diagnosis to the date of death, or to the date of last follow-up. The last possible day of follow-up was December 31, 2010, which allows at least 5 years of follow-up for all women. Women who were lost to follow-up, remained alive at the last day of the five-year period, or died of other causes were censored.

Individual-level variables

Based on previous work (Schootman et al. 2009), individual-level variables included three different groups of factors: patient characteristics (age at diagnosis, race/ethnicity, and year of diagnosis), tumor characteristics (stage at diagnosis and tumor grade), and type of treatment received. Age at diagnosis was categorized into five groups: <34, 35-44, 45-54, 55-64, and >64. For analysis purposes, stage at diagnosis was categorized as early (localized), late (regional and distant), or unknown stage. Tumor grade was categorized as well differentiated, moderately differentiated, poorly differentiated, undifferentiated, or unknown. Type of first course of treatment included: 1) only surgery; 2) radiation and chemotherapy; 3) radiation/chemotherapy; 4) radiation, chemotherapy, and surgery; 5) radiation/chemotherapy and surgery; 6) no treatment; 7) unknown treatment.

Contextual-level variables

Based on previous work (Coughlin et al. 2008; Haas et al. 2011; Lian et al. 2011; Schootman et al. 2009), contextual variables reflected the three social domains of socioeconomics, socio-cultural context, and social environment and included census tract-level demographic variables, health insurance expenditure, behavioral variables, urbanization, and spatial access to primary care physicians. Demographic variables included 12 census tract variables analyzed in chapter 4.

This study selected six census-tract variables from Simplymap: average household health insurance expenditure, and average household commercial health insurance expenditure, percentage of non-smoking population, percentage of people who eat healthily, percentage of people who exercise regularly, and percentage of nonalcoholic population.

Urbanization was measured using the nine categories of the Rural Urban Commuting Area Code (RUCA) at the census tract-level. This study recategorized census tracts into urban, large town, small town, and rural.

Spatial access to PCPs has been computed in Chapter 4 and was categorized as quartiles with the first quartile representing the highest spatial access.

Statistical analyses

Three demographic factors constructed in chapter 4 were used here: area socioeconomic status, socio-cultural factors, and percentage of African Americans. Using factor analysis, two factors were constructed from the six census-tract variables: health insurance expenditure and the behavioral factor. All factors were categorized into quartiles for statistical analyses.

This study adopted the Kaplan Meier method with log-rank test to calculate five-year survival differences according to race/ethnicity, age at diagnosis, tumor grade, census-tract-level SES, type of treatment received, and contextual-level factors. Five-year survival rates stratified by stage at diagnosis (early, late, and unknown stage) according to the above factors were also calculated.

A multilevel survival model using the NLMIXED procedure in the SAS system was used to estimate cervical cancer mortality risk by race/ethnicity and census-tract-level SES while adjusting for confounding factors. Three adjusted multilevel survival models were constructed focused on the effect of race/ethnicity or census-tract-level SES on cervical cancer survival including year of diagnosis, age at diagnosis, tumor grade, stage at diagnosis, type of treatment received, and contextual-level factors as confounders. Models 1 and 2 were adjusted for individual-level factors. Model 3 was adjusted for individual- and contextual-level factors.

This study measured geographic disparities of cervical cancer survival using the spatial scan statistic, which identifies geographic regions (clusters) with shorter-than-expected or longer-than-expected survival compared with other areas. It assumes survival time follows an exponential distribution, and compares mean survival time within a geographic region with that outside that region. A circular window with a maximum size of 50% of cervical cancer cases was adopted in the study area. The study implemented 9999 Monte Carlo simulations to measure the statistical significance of candidate clusters in the SaTScan (v.8.2.1) software. The study reported statistically significant clusters with p values smaller than 0.05. Several characteristics of clusters were reported: observed deaths, expected deaths, the ratio of observed/expected deaths (O/E), as well as

patient and census tract-level characteristics. The expected number of deaths was based on comparing an individual time (survival or censoring time) against the mean survival time in a region.

This study constructed ten multilevel survival models to examine contributions of both individual- and contextual- level factors on geographic clusters (longer-than-expected survival, shorter-than-expected survival, or areas outside clusters).Areas outside clusters were used as the reference group. Factors included patient characteristics (age at diagnosis, year of diagnosis, race/ethnicity), tumor factors, type of treatment received, and contextual-level factors (census demographic factors, insurance expenditure, behavioral factors, urbanization, and spatial access to PCPs).

Results

Descriptive results

Table 5.1 presents five-year survival rates by individual- and contextual- level factors. Hispanic and African-American women have lower five-year survival rates compared with non-Hispanic white women. However, among women diagnosed with late-stage cervical cancer, Hispanics have higher survival rates (38.1%) than African-Americans (30.0%) and non-Hispanic whites (35.5%). Five-year survival rates decreased as census-tract-level SES decreased. For example, the overall five-year survival rates were 51.8% for women from census tracts with the lowest SES quartile and 62.8% for women from census tracts with the highest SES quartile. Five-year survival rates for all stages also varied by age, type of treatment, tumor grade, the socio-cultural factor, percentage of African Americans in a census tract, insurance expenditure, and spatial access to PCPs (Table 5.1).

Table 5.1 Five-year cervical cancer survival rates (%) by selected characteristics

Variables	All stages (n= 11,212)	Early stage (n= 5,505)	Late stage (n=4,472)	Unknown stage (n=1,235)
Individual-level factors				
Race/Ethnicity				
Non-Hispanic White	59.3	79.7	35.5	66.0
Hispanic	53.4	70.7	38.1	60.5
African American	51.3	76.4	30.0	46.9
P value	< 0.001	< 0.01	<0.001	<0.01
Age (years)				
< 34	57.4	73.4	31.0	69.0
35-44	56.3	76.1	31.7	60.8
45-54	54.3	78.2	33.3	63.8
55-64	56.8	80.6	38.2	59.6
>64	56.8	75.6	42.4	56.2
P value	< 0.005	0.31	0.61	< 0.001
Tumor grade				
Well differentiated	73.6	87.6	43.4	61.2
Moderately differentiated	55.7	72.8	38.8	56.5
Poorly differentiated	45.8	67.1	32.0	52.1
Undifferentiated	43.3	64.4	31.1	46.8
P value	< 0.001	< 0.001	< 0.001	<0.05
Type of Treatment				
No treatment	40.7	48.3	25.1	56.7
Radiation, chemotherapy, and	46.4	61.3	37.3	57.1
Radiation/chemotherapy and	54.7	69.0	44.4	73.3
Radiation and chemotherapy	31.5	48.7	27.0	24.4
Radiation/chemotherapy	33.5	53.7	26.4	30.8
Surgery	81.3	89.0	55.7	82.1
Unknown	46.7	63.3	32.7	54.6
P value	< 0.001	< 0.001	< 0.001	< 0.001
Contextual factors				
Socioeconomic status				
First Quartile (High)	62.8	81.0	39.9	64.0
Second Quartile	57.8	77.9	33.8	68.4
Third Quartile	55.4	75.9	35.7	60.8
Fourth Quartile (Low)	51.8	73.3	34.3	54.9
P value	< 0.001	< 0.05	0.09	0.21
Socio-cultural factor				
Table 5.1-Continued				
First Quartile (High)	53.5	75.8	33.0	55.1
Second Quartile	56.2	76.4	32.9	66.6

Table 5.1-Continued

Third Quartile	58.3	77.6	39.6	59.0
Fourth Quartile (Low)	57.6	77.7	37.3	64.0
P value	< 0.005	0.56	< 0.001	<0.05
Spatial access to PCPs				
First Quartile (High)	54.5	79.0	30.9	63.0
Second Quartile	54.1	75.5	34.6	52.4
Third Quartile	58.2	74.3	39.6	66.9
Fourth Quartile(Low)	58.2	78.9	36.8	61.1
P value	< 0.005	0.22	<0.005	<0.05
Percentage of African Americans				
First Quartile (Low percentage)	55.8	76.0	35.0	68.0
Second Quartile	59.1	78.0	39.2	63.6
Third Quartile	55.3	75.0	36.0	57.7
Fourth Quartile (High percentage)	54.7	78.2	31.8	56.4
P value	< 0.05	0.61	< 0.05	0.22
Behavioral factor				
First Quartile (High)	56.5	79.2	36.1	59.6
Second Quartile	55.7	76.8	33.9	66.1
Third Quartile	58.0	74.7	39.6	67.6
Fourth Quartile (Low)	57.4	78.0	34.5	57.6
P value	0.72	0.65	0.37	0.09
Insurance expenditure				
First Quartile (High)	60.7	81.7	35.1	79.4
Second Quartile	59.6	77.6	41.8	57.6
Third Quartile	56.2	74.8	35.8	70.3
Fourth Quartile(Low)	51.8	75.2	31.8	53.0
P value	< 0.001	0.13	<0.01	<0.001

Racial/ethnic and SES disparities

Table 5.2 presents cervical cancer-specific mortality by race/ethnicity and census-tract-level SES adjusted for other factors. African-American women were 38% more likely to die after adjusting for individual-level factors compared with non-Hispanic white women (Hazard Ratio [HR], 1.38; 95% confidence interval [CI], 1.21–1.57) (Model 1). After adjusting for SES (Model 2), the mortality risk among African-American women was reduced by 10% (HR, 1.28; 95% CI, 1.11–1.47). The risk was

further reduced to 1.19 (95% CI, 1.03–1.38) after including contextual factors (Model 3). However, no statistically significant survival differences were found between Hispanic and non-Hispanic women after adjusting for the above factors (Models 1, 2, and 3). Table 5.2 also revealed that there was no statistically significant racial difference among women diagnosed with cervical cancer at an early stage after adjusting for covariates. However, among late-stage cervical cancer women, Hispanics had a survival advantage over non-Hispanic whites even after adjusting for other factors (HR, 0.8; 95% CI, 0.69–0.94). No survival differences were observed between African American and non-Hispanic white women diagnosed at a late stage after adjusting for covariates. Among unstaged cases, African-Americans had an elevated mortality risk (HR, 1.72; 95% CI, 1.08–2.75); while Hispanic women had similar survival to non-Hispanic whites.

Table 5.2 also shows that risk of death is increased with decreasing SES. Compared with women from census tracts with the highest SES (Model 1), women from census tracts with the lowest SES were 42% more likely die from cervical cancer after adjusting for individual-level factors (HR, 1.42; 95% CI, 1.22–1.66). The risk remained elevated after adjusting for race/ethnicity (Model 2). However, after taking into account contextual-level factors (Model 3), the HR was further reduced (HR, 1.31; 95% CI, 1.09–1.57).

Geographic disparities

Figure 5.1a displays geographic clusters of cervical cancer survival in Texas. Two clusters of shorter-than-expected survival were found in San Antonio and a central Houston area with a O/E of 1.66 and 2.53 respectively. Two clusters of longer-than-

expected survival were observed in central Texas and another central Houston area with a O/E of 0.58 and 0.24 respectively.

Table 5.2 Hazard Ratios (HRs) of cervical cancer-specific mortality by stage, race/ethnicity, and census-tract socioeconomic status

	Hazard Ratio of Model 1 (95% CI)	Hazard Ratio of Model 2 (95% CI)	Hazard Ratio of Model 3 (95% CI)
All stages (n= 11,212)			
Race/Ethnicity			
Non-Hispanic White	1 (Referent)	1 (Referent)	1 (Referent)
Hispanic	1.06 (0.95–1.18)	0.95 (0.84–1.08)	1.01 (0.89–1.16)
African-American	1.38 (1.21–1.57)	1.28 (1.11–1.47)	1.19 (1.03–1.38)
Socioeconomic status			
First quartile (Highest)	1 (Referent)	1 (Referent)	1 (Referent)
Second quartile	1.27 (1.08–1.5)	1.27 (1.08–1.49)	1.14 (0.95–1.36)
Third quartile	1.34 (1.14–1.57)	1.30 (1.1–1.52)	1.15 (0.96–1.38)
Fourth quartile (Lowest)	1.42 (1.22–1.66)	1.42 (1.2–1.68)	1.31 (1.09–1.57)
Late stage (n=4,472)			
Race/Ethnicity			
Non-Hispanic White	1 (Referent)	1 (Referent)	1 (Referent)
Hispanic	0.81 (0.71–0.93)	0.77 (0.67–0.90)	0.80 (0.69–0.94)
African-American	1.26 (1.08–1.48)	1.22 (1.03–1.43)	1.14 (0.96–1.36)
Unknown stage (n=1,235)			
Race/Ethnicity			
Non-Hispanic White	1 (Referent)	1 (Referent)	1 (Referent)
Hispanic	1.21 (0.84–1.74)	1.14 (0.68–1.93)	1.21 (0.77–1.91)
African-American	2.29 (1.50–3.48)	2.07 (1.33–3.23)	1.72 (1.08–2.75)

Model 1 is adjusted for age at diagnosis, year of diagnosis, stage at diagnosis, tumor grade, and type of treatment received. Model 2 is adjusted for all factors in Model 1 and SES or race/ethnicity. Model 3 is adjusted for all factors of Model 2 and other contextual factors, including socio-cultural factors, percentage of African Americans, insurance expenditure, behavioral factors, urbanization, and spatial access to PCPs.

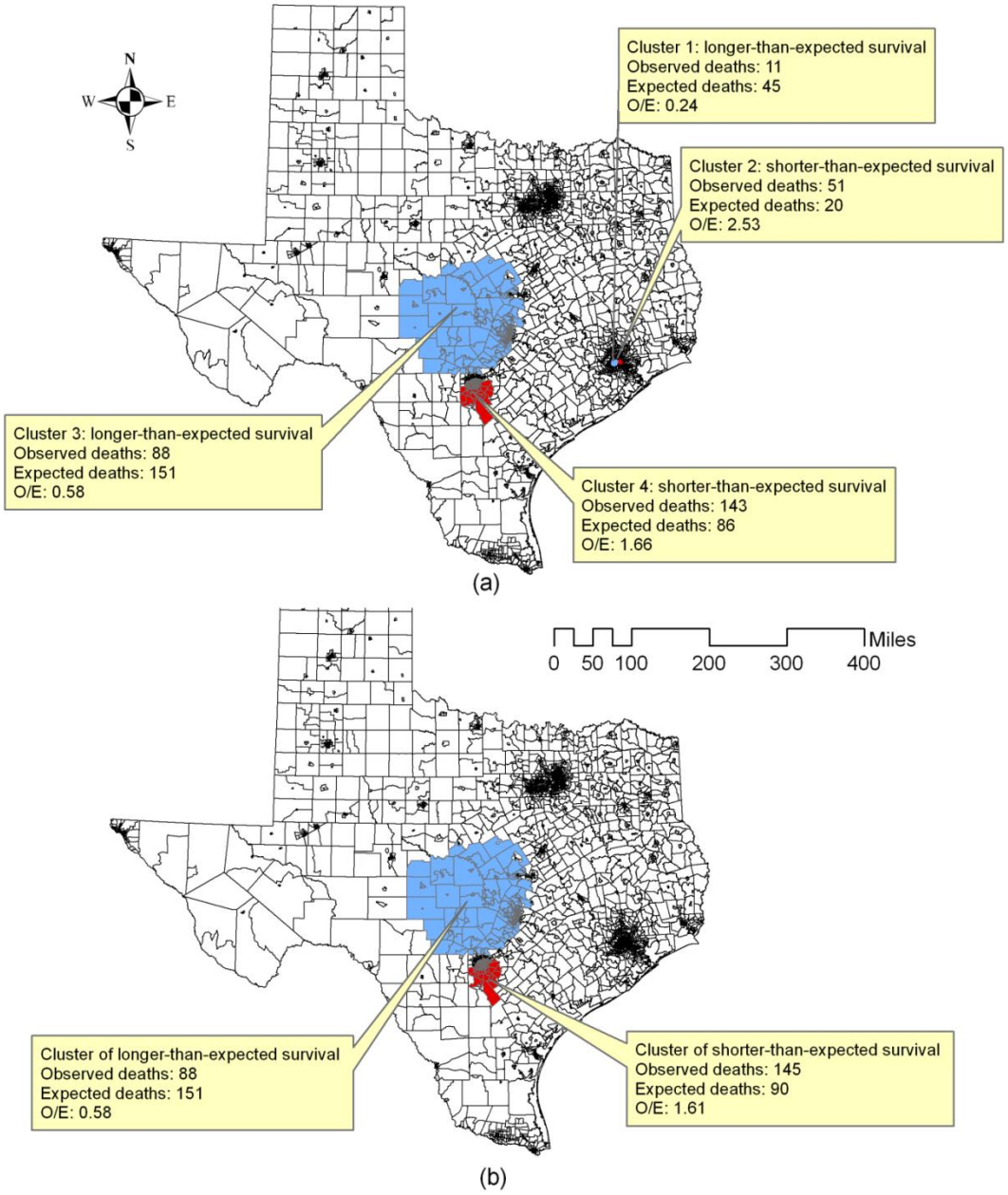

Figure 5.1 Geographic clusters of five-year cervical cancer survival in Texas, 1995-2005

(a) no adjustment; (b) adjusted for both individual- (age at diagnosis, year of diagnosis, tumor grade, stage at diagnosis, type of treatment received) and contextual-level factors (SES, socio-cultural factors, percentage of African Americans, insurance expenditure, behavioral factors, urbanization, and spatial access to PCPs)

Table 5.3 presents selected individual- and census tract-level characteristics of three geographic regions: cluster of shorter-than-expected survival, cluster of longer-than-expected survival, and areas outside clusters. Five-year survival rates were 40.1%, 72.2%, and 56.1% for these areas, respectively. Clusters of shorter-than-expected survival were characterized by a higher percentage of women who: 1) were diagnosed at a late stage; 2) were Hispanics; or 3) received only radiation or chemotherapy compared with other areas. Additionally, these clusters have a higher percentage of census tracts with lower SES. In contrast, clusters of longer-than-expected survival have a higher percentage of women who: 1) were non-Hispanic whites; 2) were diagnosed at an early stage; or 3) only received surgery.

Table 5.4 revealed that women residing in clusters of shorter-than-expected survival were 79% more likely to die from cervical cancer (HR, 1.79; 95% CI, 1.45–2.22) compared with those living in areas outside clusters (Model 1). Women residing in clusters with longer-than-expected survival had a survival advantage (HR, 0.47; 95% CI, 0.36–0.62) (Model 1). The study added several variables to Model 1, including race/ethnicity, age, year of diagnosis, tumor grade, census-tract-level SES, stage at diagnosis, type of treatment, and other contextual-level factors. SES reduced the HR for women in the cluster of shorter-than-expected survival from 1.79 in Model 1 to 1.64 (95% CI, 1.32, 2.03) in Model 5. After adjusting for all factors in the table (Model 10), HR for women in the cluster of shorter-than-expected survival remained significant, although it was reduced (HR, 1.61; 95% CI, 1.31-1.98).

Table 5.3 Selected characteristics of geographic clusters of cervical cancer survival in Texas, 1995-2005

Characteristics	Cluster of shorter-than-expected survival	Cluster of longer-than-expected survival	Geographic areas outside cluster
Individual-level Characteristics			
Cervical cancer cases, no. (%)	631 (5.6)	612 (5.5)	9969 (88.9)
5-year survival rate, %	40.1	72.2	56.1
Stage at diagnosis, no. (%)			
early	265 (42.0)	350 (57.2)	4890 (49.1)
late	304 (48.2)	200 (32.7)	3968 (39.8)
unknown	62 (9.8)	62 (10.1)	1111 (11.1)
Race/Ethnicity, no. (%)			
Non-Hispanic White	128 (20.3)	421 (68.8)	5099 (51.1)
Hispanic	428 (67.8)	158 (25.8)	3393 (34.0)
African American	75 (11.9)	33 (5.4)	1477 (14.8)
Type of treatment, no. (%)			
No treatment	15 (2.4)	14 (2.3)	265 (2.7)
Radiation, chemotherapy, and surgery	16 (2.5)	20 (3.3)	273 (2.7)
Radiation/chemotherapy and surgery	52 (8.2)	45 (7.4)	794 (8.0)
Radiation and chemotherapy	29 (4.6)	29 (4.7)	640 (6.4)
Radiation/chemotherapy	124 (19.7)	86 (14.1)	1498 (15.0)
Surgery alone	216 (34.2)	312 (51.0)	4068 (40.8)
Unknown	179 (28.4)	106 (17.3)	2431 (24.4)
Contextual-level Characteristics			
Census tracts, no. (%)	228 (5.2)	366 (8.3)	3794 (86.5)
Socioeconomic status, no. (%)			
First quartile (High)	15 (6.6)	183 (50.0)	903 (23.8)
Second quartile	21 (9.2)	76 (20.8)	1006 (26.5)
Third quartile	69 (30.3)	58 (15.8)	961 (25.3)
Fourth quartile (Low)	123 (53.9)	49 (13.4)	924 (24.4)
Socio-cultural factor, no. (%)			
First quartile (High)	29 (12.7)	23 (6.3)	1052 (27.7)
Second quartile	72 (31.6)	62 (16.9)	956 (25.2)
Third quartile	89 (39.0)	109 (29.8)	908 (23.9)
Fourth quartile (Low)	38 (16.7)	172 (47.0)	878 (23.1)

Table 5.4 Hazard Ratios (HRs) of cervical cancer-specific mortality by geographic locations

Model	Adjustment variables	Cluster of shorter-than-expected survival	Cluster of longer-than-expected survival
		Hazard Ratio (95% CI)	**Hazard Ratio (95% CI)**
1	No adjustment	1.79 (1.45–2.22)	0.47 (0.36–0.62)
2	Age at diagnosis, year of diagnosis, and race/ethnicity	1.71 (1.41–2.09)	0.5 (0.39–0.65)
3	Stage at diagnosis, and tumor grade	1.75 (1.42–2.17)	0.52 (0.40–0.68)
4	Type of Treatment	1.79 (1.46–2.2)	0.48 (0.37–0.62)
5	Socioeconomic Status (SES)	1.64 (1.32–2.03)	0.51 (0.39-0.67)
6	Contextual factors (socio-cultural factors, percentage of African Americans, areal-level health insurance expenditure, behavioral factors, spatial access to PCPs, and urbanization)	1.71 (1.37–2.12)	0.48 (0.36–0.63)
7	Age at diagnosis, year of diagnosis, race/ethnicity, stage at diagnosis, and tumor grade	1.68 (1.37–2.05)	0.55 (0.43–0.71)
8	Age at diagnosis, year of diagnosis, race/ethnicity, stage at diagnosis, tumor grade, and type of treatment	1.67 (1.40–2.00)	0.55 (0.43–0.70)
9	Age at diagnosis, year of diagnosis, race/ethnicity, stage at diagnosis, tumor grade, type of treatment, and SES	1.63 (1.32–2.00)	0.57 (0.44–0.73)
10	All of the above factors	1.61 (1.31–1.98)	0.58 (0.45–0.75)

Figure 5.1b shows geographical clusters after adjusting all factors in this study. Clusters in central Houston areas in Figure 5.1a were eliminated. However, a cluster of shorter-than-expected survival and longer-than-expected survival remained. Results

suggest that individual- and contextual-level factors in the study could explain some portion of geographic disparities.

Discussion

This study found statistically significant racial/ethnic and census tract SES disparities of cervical cancer survival in Texas. African-American women had an elevated mortality risk compared with non-Hispanic whites even after adjusting for other factors in the study. This risk was even higher among African-American women with unknown stage information. Among women diagnosed at a late stage, Hispanics were statistically less likely to die compared with their non-Hispanic white counterparts. Women with cervical cancer from census tracts with the lowest SES experienced an elevated risk of death compared with those from census tracts with the highest SES even after adjusting for other factors. The research also identified statistically significant geographic clusters of longer-than-expected or shorter-than-expected cervical cancer survival. Only a small portion of these disparities were explained by individual- and contextual-level factors in this study.

Prior Findings about race/ethnicity disparities in cervical cancer survival have been inconsistent. The finding addressed two studies focused on racial disparities in Texas; African American women had a higher risk to die, while Hispanic women were less likely to die (Coker et al. 2009; Eggleston et al. 2006). It has been puzzling that Hispanics have similar cervical cancer survival compared with their non-Hispanic white counterparts despite lower SES among Hispanics. Among late-stage patients, the study found that Hispanics had a survival advantage even after adjusting for treatment and contextual factors. Previous studies on racial disparities have suggested that this

'Hispanic Paradox' might be explained by selective return migration toward the end of life (e.g., immigrants who return to Mexico might be lost to follow-up) , social network, community support, comorbid conditions, smoking status, religion, and cultural factors (Coker et al. 2009; Eggleston et al. 2006; Coker et al. 2009; Markides and Eschbach 2005).

This research found that African-Americans had higher mortality risk, which is consistent with several studies in the literature (Eggleston et al. 2006; Samelson et al. 1994; Singh et al. 2004). It also found higher mortality risk among African-Americans with unknown stage information, which is similar to a previous finding (Coker et al. 2009).The study found that older women (>64) ($p<0.05$), women living in census tracts with lower SES or higher percentage of African Americans ($p<0.05$), or women with unknown grade information or treatment information were more likely to have missing stage information. A prior study suggests that the missing stage might be due to poor health status of patients rather than by chance (Coker et al. 2009).The remaining mortality risk among African-Americans might be attributed to factors not analyzed in this study, such as socioeconomic factors, insurance status, comorbid conditions, marital status, smoking status, and social barriers to health care (Coker et al. 2009; Farley et al. 2001; Johnson et al. 2004; Schwartz et al. 2003). According to the Behavioral Risk Factor Surveillance System (BRFSS), African-Americans had a persistently higher percentage of people who had no health insurance than non-Hispanic whites in Texas during 2002-2010. Two studies found that equal access to healthcare could eliminate survival differences between African-Americans and non-Hispanic white women (Coker et al. 2009; Farley et al. 2001).

Findings that women who lived in census tracts with lower SES had poorer cervical cancer survival corroborated previous work (Singh et al. 2004; Du et al. 2011; Morgan et al. 1996; Mundt et al. 1998; Johnson et al. 2004). The great reduction in racial disparities after adjusting for census tract SES in this study implied that contextual factors played an important role in the association between race/ethnicity and cervical cancer survival. SES explained survival differences between Hispanic and non-Hispanic white women diagnosed at an early stage, which is consistent with findings from previous work (Eggleston et al. 2006). Additionally, SES together with other contextual-level factors explained elevated mortality risk among African-Africans diagnosed with late-stage cervical cancer. Therefore, it is important to ameliorate contextual effects in order to reduce racial/ethnic disparities in cervical cancer survival. Intervention programs should be developed to target socially deprived areas (e.g., areas with lower SES, areas with higher percentage of African Americans, foreign-born women, or linguistic isolated households).

Only a small portion of geographic disparities of cervical cancer survival could be explained since a large portion of clusters remained unexplained. Although previous studies suggested that census tract SES might explain geographic disparities (Schootman et al. 2009); findings from this research failed to confirm this. Other individual-level factors, including patients' comorbid conditions, health insurance status, and access to healthcare might also explain geographic disparities in the study. According to the BRFSS 2002-2010, the San Antonio area (the cluster of shorter-than-expected survival) had a higher percentage of people without health insurance compared with the cluster of longer-than-expected survival. Previous studies have also suggested that smoking was

associated with poor cervical cancer survival (Waggoner et al. 2006). but these data were not available in the study. According to the 2002-2010 BRFSS data for women 18 years and older, the San Antonio area had a higher percentage of women who smoked compared with the cluster of longer-than-expected survival. Future studies could add these individual-level factors in an attempt to examine their effect on geographic disparities in cervical cancer survival.

This study has a number of strengths. First, it used a population-based cancer registry with a large sample size (n=12,144), which reduces the potential for selection bias relative to hospital-based studies. Second, this is the first study in the United States to examine geographic variation in cervical cancer survival. Understanding such disparities and their associated factors will help develop more effective and targeted intervention programs to reduce disparities. Third, this is the first study to examine the impact of multilevel factors, including individual- and contextual-level variables, on cervical cancer survival by race/ethnicity, SES and geographic locations, taking into account correlations among women within the same neighborhood.

Findings from this research should be considered in light of two limitations. First, available treatment data reflected the first treatment women received and women may have received additional treatment. This is unlikely to have affected geographic and racial disparities since further treatment is unlikely to have varied by race/ethnicity and geographic location. Second, the remaining racial/ethnic and geographic disparities might be attributed to other unmeasured individual-level factors, such as womens' comorbid conditions, smoking status, marital status, and access to healthcare, which merits future investigations.

Findings from this study have important implications for developing effective cervical cancer intervention programs. The effect of census tract SES and other contextual-level factors on racial/ethnic and geographic disparities suggest that contextual-level characteristics should be used together with individual-level characteristics to guide intervention programs. Intervention programs should be developed to target African-American women, women of lower SES and socially deprived areas in order to reduce disparities in cervical cancer survival. Because it remains unclear which factors have contributed to the cluster of shorter-than-expected survival observed in San Antonio, it is too early to derive conclusions on which interventions should be implemented in this area. Future studies are needed to further understand underlying factors that contribute to the higher risk of mortality among females in the region.

CHAPTER VI

GEOGRAPHIC VARIATIONS OF RACIAL/ETHNIC DISPARITIES OF CERVICAL CANCER IN TEXAS

Introduction

Cervical cancer is one of the most common cancers among females in the United States (Parkin et al. 2005; Howe et al. 2006). It is estimated that there will be about 12,340 newly diagnosed and 4,030 mortality cases in 2013 (ACS 2013). The persistent incidence and mortality reflect enormous social disparities among females suffering from cervical cancer because cervical cancer can be prevented and cured (Mitchell and Mccormack 1997; Downs et al. 2008; Byrd et al. 2013). Hispanics and African Americans persistently experience higher mortality rates in cervical cancer compared with non-Hispanic whites (Howe et al. 2006; ACS 2013).

Late-stage diagnosis, as well as failure of timely screening and treatment, was believed to be major causes of high mortality rates in cervical cancer among racial/ethnic minority groups (Brookfield et al. 2009; Priest et al. 2010). Based on findings from research that examined social domains, racial/ethnic disparities of mortality could be attributed to several factors: SES, insurance, access to health care, socio-cultural factors, and socio-environmental factors (Morgan et al. 1996; Wells and Horm 1998; Katz et al. 2007; Coughlin et al. 2008; Daley et al. 2011; Du et al. 2011; Lim and Ashing-Giwa 2011). Social demographics reflect socio-cultural characteristics of a homogeneous population group, including immigration status, language proficiency, and cultural beliefs

(Singer 2012). Social environment indicates social and physical environment of communities where individuals resided.

Despite established associations between racial/ethnic disparities in cervical cancer and factors previously stated, other factors, including behavioral factors, language, and spatial access to health care, were seldom examined. For spatial access to health care, one study in New Zealand evaluated associations between travel distance to health care and racial/ethnic disparities in cervical cancer mortality (Brewer et al. 2012). However, no similar work was conducted in the United States. Moreover, previous studies have focused on cancer screening facilities. Research on spatial access to other preventive services such as primary care is rare. Because the Pap smear test is typically provided by primary care physicians (PCPs), access to PCPs plays an important role in the prevention of cervical cancer (Weinstein et al. 2009).

This chapter aims to investigate geographic variations of racial/ethnic disparities of cervical cancer mortality based on analyses using data geo-referenced to the census tract level. Meanwhile, it will determine how census demographic factors, racial/ethnic disparities in late-stage diagnosis, the health insurance factor, behavioral factors, and spatial access to health care affect the racial/ethnic disparity. This study will enhance the understanding of cervical cancer disparities and thus have important implications for developing more effective cervical cancer intervention programs. Traditional programs have adopted individual characteristics such as race/ethnicity and age to identify who should be selected to receive certain health services (Wells and Horm 1998). In contrast, this study will identify geographic areas with significant racial/ethnic disparities and census-tract level factors associated with these disparities.

Material and Methods

Data sources

Cervical cancer data

The population-based, statewide Texas Cancer Registry (TCR) was used to identify women diagnosed with invasive cervical cancer between 1995 and 2008. Attributes of each case used in this study include race/ethnicity, age at diagnosis, stage at diagnosis, vital status, and residential address. Stage at diagnosis of cervical cancer was categorized into localized (coded as 1), regional (coded as 2-5), and distant stage (coded as 7) based on the classification method from the Surveillance Epidemiology and End Results (SEER) program. Based on clinical and pathological information, stage at diagnosis in the study was recoded in two categories: early (localized) and late (regional and distant) stage. Cases with unknown stages were excluded from the analysis. Vital status (survived or deceased) was used to derive cervical cancer mortality data. The use and analysis of this cervical cancer database has been approved by the Institutional Review Board (IRB) of Texas Department of State Health Services (TDSHS).

Census-tract level variables

Census-tract level variables include demographic factors, health insurance expenditure and behavioral factors measured in Chapters 4 and 5.

Cervical cancer health care data

Cervical cancer health care data include preventive and treatment service data collected from TDSHS. The preventive services data were represented by PCPs in Texas in 2000. A total of 14,268 PCPs with 6,372 primary practicing addresses were analyzed.

Cervical cancer treatment service data were represented by oncologists in 2000, including surgical, radiation, medical, and gynecologic oncologists. The number of oncologists in 2000 was 205 with 121 primary practicing addresses.

Analyses

Measurement of spatial access to health care

Spatial access to PCPs was measured in chapter 4. For oncologists, this study implemented the same method but with a different setting for the travel-time zone. Instead of 60 minutes, a 180-minutes travel-time zone was defined and divided into four subzones $D_t(t$ =1, 2, 3, 4): less than 30 minutes, between 30 and 60 minutes, between 60 and 120 minutes, and between 120 and 180 minutes (Wan et al. 2012). The travel-time zone was larger for oncologists because of the fact that patients would not mind traveling a longer distance to seek treatment for cancer. The E2SFCA model was implemented in ArcGIS 10.0 with the Visual Basic for Applications (ESRI 2011). The study adopted the SPAR to measure relative spatial access to PCPs and oncologists by computing the ratio of A_j^F to the average A_j^F of the entire region.

Measurement of racial/ethnic disparities

The study used population-weighted risk difference (RD) with strong statistical power and fewer false-positive results to measure racial/ethnic disparities. Age-adjusted mortality and late-stage diagnosis rates were first computed in each census tract for non-Hispanic whites, Hispanics, and African Americans in ArcGIS 10.0 (ESRI 2011). These three racial/ethnic groups are mutually exclusive. African Americans in this study refer to non-Hispanic African Americans exclusively. The rate of Hispanics or African

Americans in a census tract was compared with the rate of non-Hispanic whites (reference group) in that census tract using the population weighted RD. Census tracts with zero cervical cancer cases or zero population were excluded from the analysis. A normality test was conducted, and Kolmogorov–Smirnov test showed that rates of three racial/ethnic groups were normally distributed with a significance value less than 0.0001.

In order to identify census tracts with statistically significant disparities, the significance (measured by the p-value) was evaluated through a comparison between the test statistic and the expected distribution with a critical α level of 0.05. However, there were 8776 individual comparisons (2 comparisons in each census tract) in this study. These independent tests under a significance level of 0.05 will lead to a nearly 100% probability (likelihood of having false positive = $1-(1-0.05)^{8776}\sim=1$) that at least one test is significant even if none of census tracts exhibit racial disparities. The likelihood under a significance level of 0.01 is also near 100%. Therefore, it is essential to correct false positives produced by multiple tests. The false discovery rate (FDR) (Benjamini and Hochberg 1995) approach was used in this study because it is less restrictive and more powerful than other approaches. This study implemented the significance test with FDR correction in the SpaceStat software (EASI 2010). A positive RD with statistically significant p-value indicates the population group in question has a higher risk than the reference group.

Regression analysis

Stepwise binary logistic regression was constructed for census tracts to examine the relationship between racial/ethnic disparities of mortality in each census tract and multiple other factors. The dependent variable for this logistic regression was a

dichotomous variable (an RD that is significantly greater than 0 or an RD of 0). Census tracts with an RD that is significantly less than 0 were excluded from the logistic regression analysis. Odds ratio in this study measures the likelihood of a census tract exhibiting significant racial/ethnic disparities. In the analysis, all records were divided into four quartiles based on the values of the factor in question.

Results

Demographic characteristics

Table 6.1 presents the characteristics of 15,370 cervical cancer cases in Texas between 1995 and 2008. The study cohort included 7,356 (47.92%) early- and 6,057 (39.41%) late-stage cases. By the last day of follow-up (December 31, 2010), 9,439 (61.41%) patients of this cohort had survived, and 5,931 (38.59%) patients had died of cervical cancer. Although non-Hispanic whites accounted for a half (49.08%) of total cases in this cohort, higher cervical cancer incidence and mortality rates were observed in Hispanics or African Americans than non-Hispanic whites. Based on statistics from ACS, the average annual incidence rates in cervical cancer were 8.1, 12.1, and 15.1 per 100,000 for non-Hispanic whites, African Americans, and Hispanics between 1995 and 2008 in Texas. The average annual cervical cancer-specific mortality rates were 2.6, 5.8, and 4.3 per 100,000 for non-Hispanic whites, African American, and Hispanics between 1995 and 2008 in Texas (ACS 2008).

Table 6.1 Characteristics of cervical cancer cases in Texas, 1995-2008

Variables	Cases	(%)
Age		
< 24	178	1.16%
24-44	6,701	43.60%
45-64	5,510	35.85%
>64	2,981	19.39%
Race/Ethnicity		
Non-Hispanic White	7,544	49.08%
Hispanic	5,286	34.39%
African American	2,052	13.35%
Asian	259	1.69%
Native American	19	0.12%
Other	131	0.85%
Unkown	79	0.51%
Stage at diagnosis		
Early (local)	7,365	47.92%
Late (regional or distant)	6,057	39.41%
Unkown	1,948	12.67%
Vital status		
Survived	9,439	61.41%
Deceased	5,931	38.59%

Spatial access to health care

Figures 6.1 show the smoothed spatial access ratio of oncologists. There was unevenly distributed spatial access to oncologists in Texas. The highest spatial access to oncologists was distributed in metropolitan areas including the Dallas-Fort Worth corridor, the Austin-San Antonio corridor, Houston, and Lubbock, which could be explained by the highly clustered oncologists located in these metropolitan areas. A large portion of southwestern Texas had limited spatial access to oncologists.

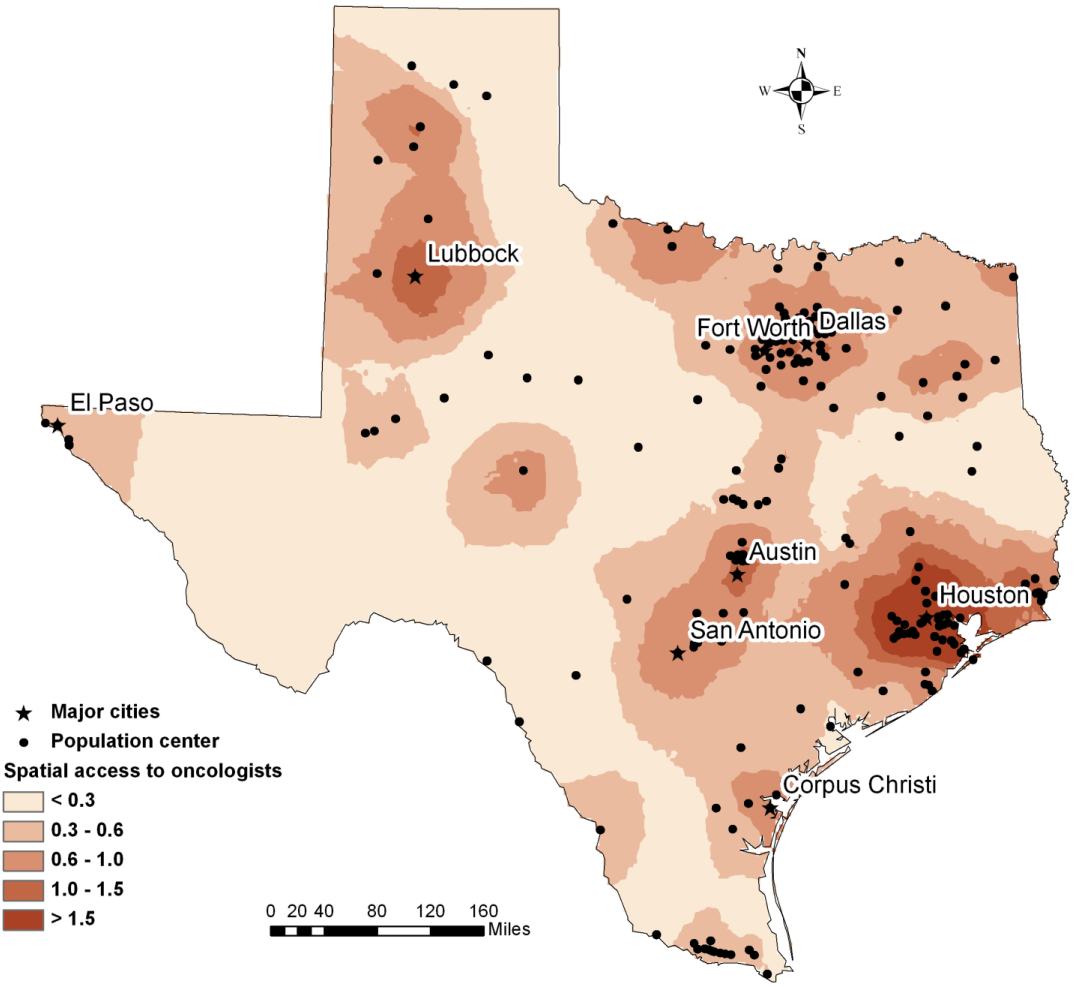

Figure 6.1 Spatial access to oncologists

(Note: A value greater than one on the map represents a higher-than-average spatial access; A value less than one on the map represents a lower-than-average spatial access.)

Racial/ethnic disparities in cervical cancer late-stage diagnosis

Figures 6.2 shows geographic variations of cervical cancer late-stage diagnosis disparities between African Americans and non-Hispanic whites based on RD statistic. There were 431 out of 4,388 census tracts experiencing significantly higher late-stage diagnosis rates in African Americans. These census tracts were observed in the metropolitan areas of Houston, Austin-San Antonio, and Dallas-Fort Worth. Several

census tracts in eastern Texas were identified with higher late-stage diagnosis rates in African Americans as well.

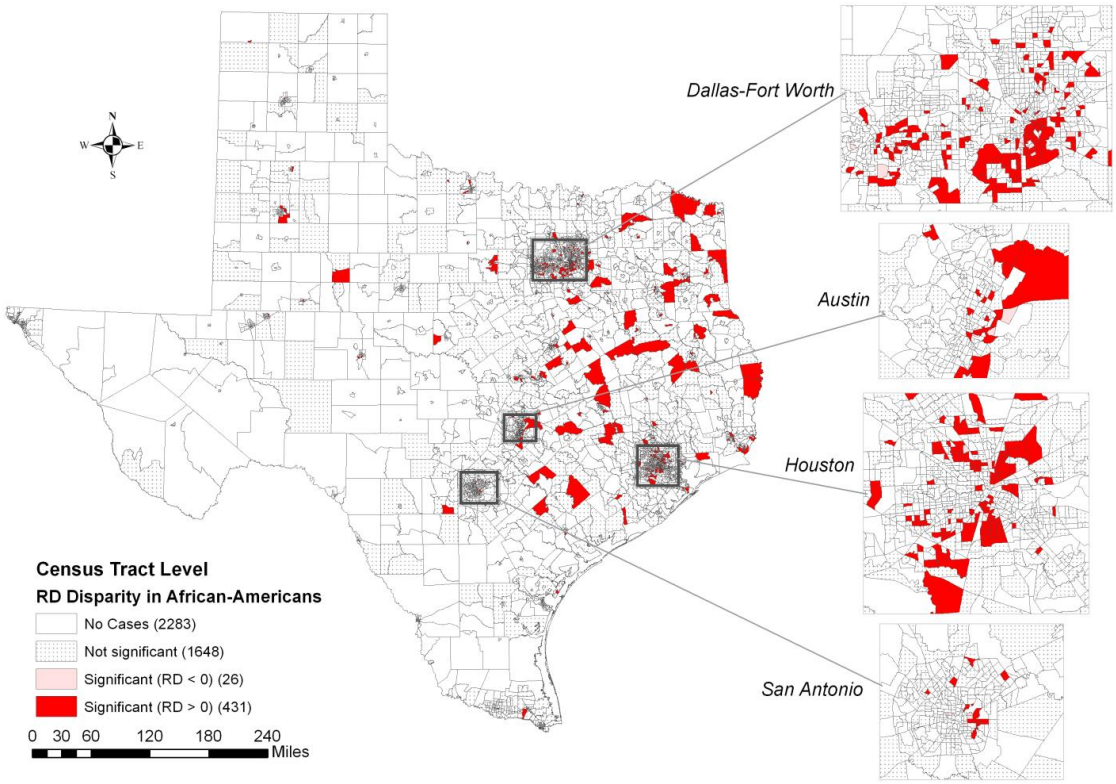

Figure 6.2 Cervical cancer late-stage diagnosis disparities between African Americans and non-Hispanic whites based on population-weighted risk difference statistic

(Note: Red census tracts are areas where African Americans have significantly higher late-stage diagnosis rates. Pink census tracts are areas where non-Hispanic whites have significantly higher late-stage diagnosis rates)

Figures 6.3 displays geographic variations of cervical cancer late-stage diagnosis disparities between Hispanics and non-Hispanic whites based on RD statistics. There were 481 census tracts with significantly higher late-stage diagnosis rates in Hispanics. These census tracts were observed in the metropolitan areas of Houston, Austin-San Antonio, and Dallas-Fort Worth. The southwest Texas-Mexico border areas exhibited a higher rate in Hispanics as well. Results also reveal that several census tracts have

displayed significantly lower late-stage diagnosis rates in Hispanics or African Americans than non-Hispanic whites. A closer examination to these census tracts suggest that there was a relatively small number of non-Hispanic whites residing in those areas.

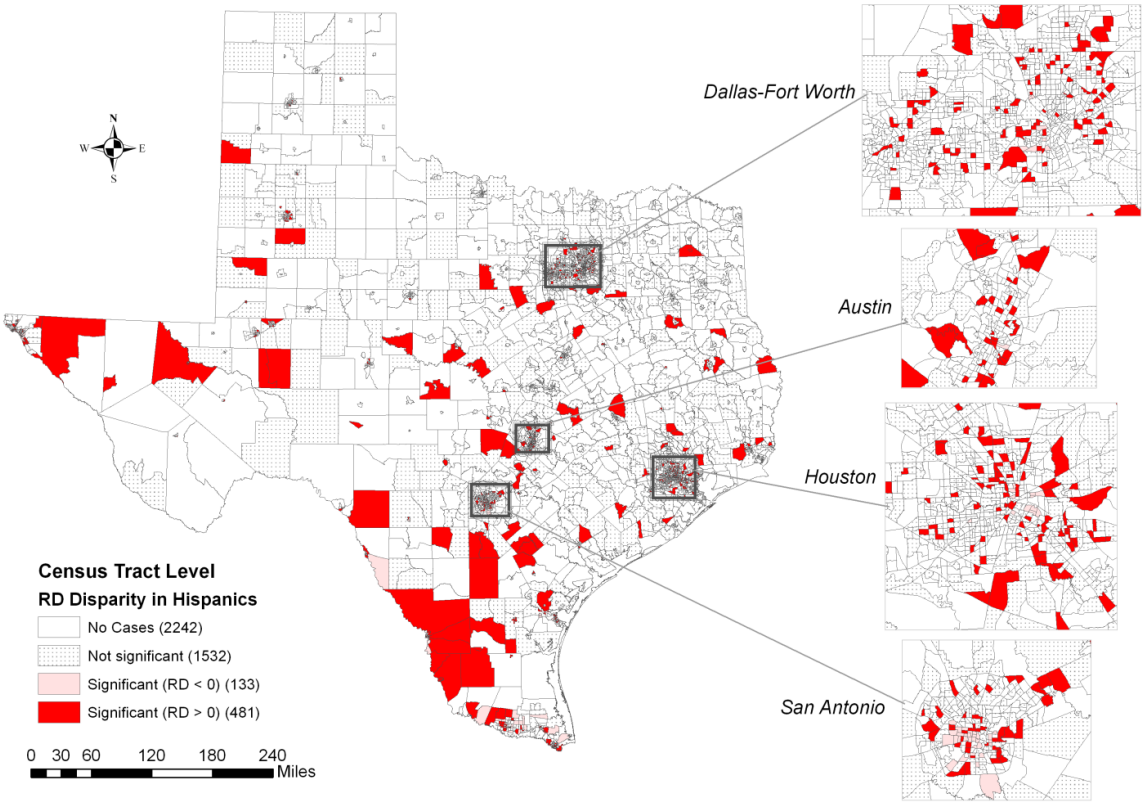

Figure 6.3 Cervical cancer late-stage diagnosis disparities between Hispanics and non-Hispanic whites based on population-weighted risk difference statistic
(Note: Red census tracts are areas where Hispanics have significantly higher late-stage diagnosis rates. Pink census tracts are areas where non-Hispanic whites have significantly higher late-stage diagnosis rates)

Racial/ethnic disparities in cervical cancer mortality

Figure 6.4 shows geographic variations of cervical cancer mortality disparities between African Americans and non-Hispanic whites. There were 418 out of 4,388 census tracts experienced significantly higher mortality rates in African Americans than non-Hispanic whites in those census tracts. These census tracts were located in the metropolitan areas of Houston, Austin-San Antonio, and Dallas-Fort Worth. Several

census tracts in eastern Texas were identified with high mortality rates in African Americans as well.

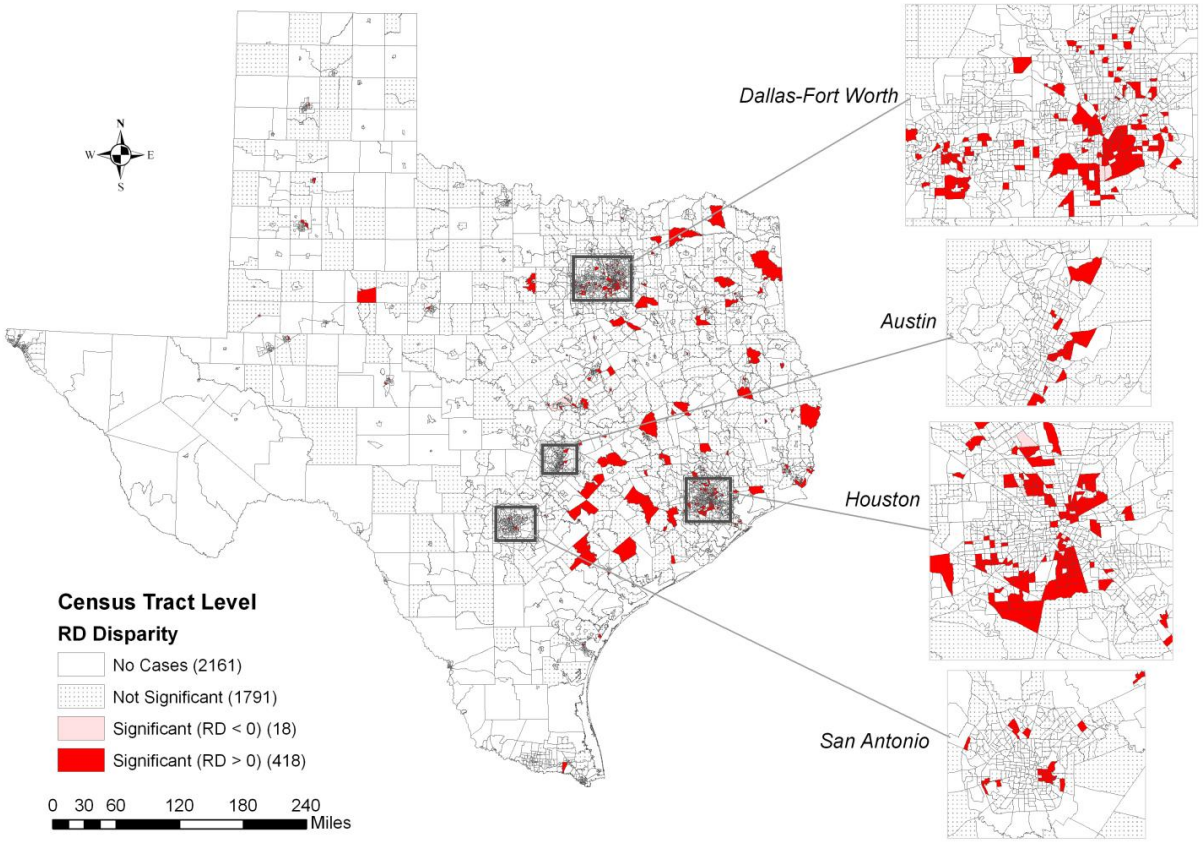

Figure 6.4 Cervical cancer mortality disparities between African Americans and non-Hispanic whites based on population-weighted risk difference statistic
(Note: Red census tracts are areas where African Americans have significantly higher mortality rates. Pink census tracts are areas where non-Hispanic whites have significantly higher mortality rates)

Figure 6.5 display geographic variations of cervical cancer mortality disparities between Hispanics and non-Hispanic whites. There were 751 census tracts with significantly higher mortality rates in Hispanics than non-Hispanic whites in those census tracts. These significant census tracts were found in the metropolitan areas of Houston, Austin-San Antonio, and Dallas-Fort Worth. The southwest Texas-Mexico border areas exhibited high mortality rates in Hispanics as well.

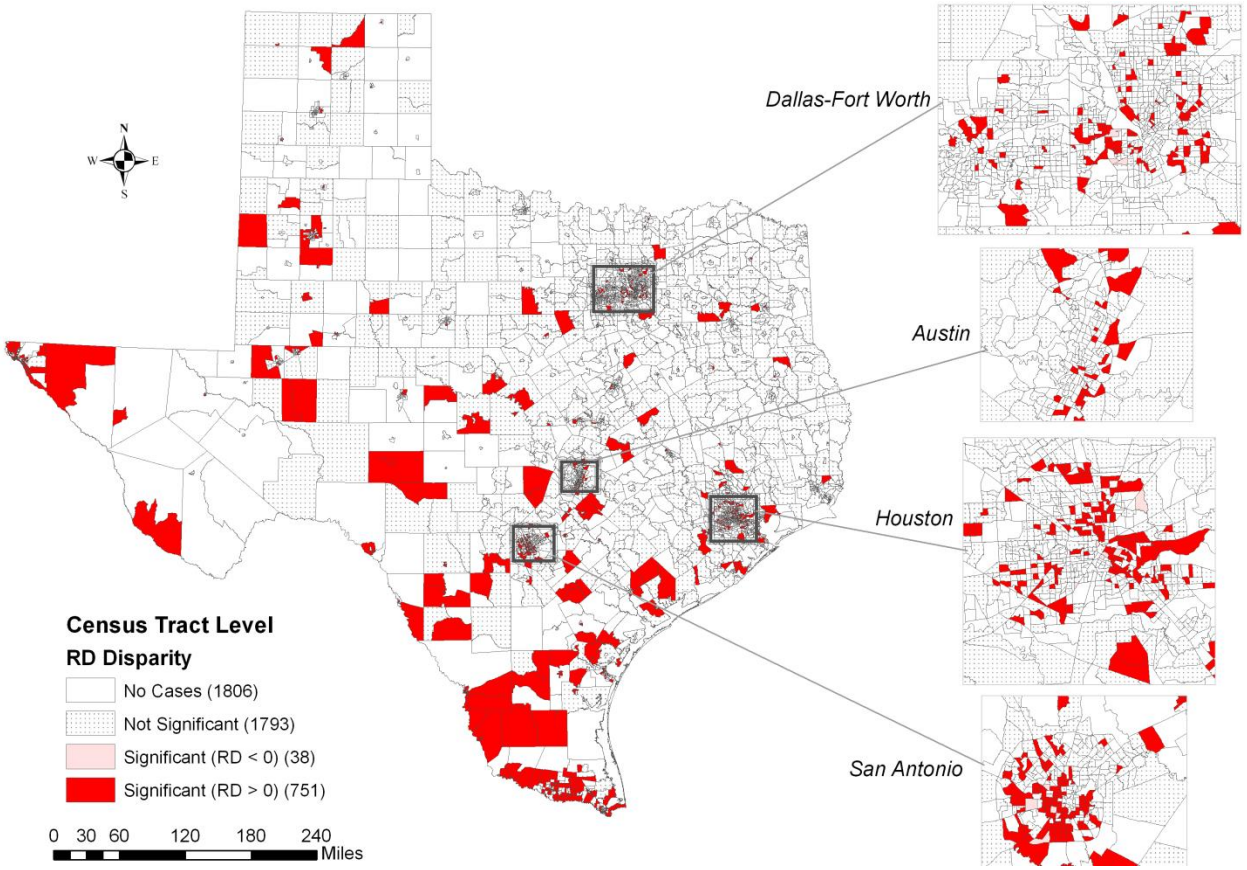

Figure 6.5 Cervical cancer mortality disparities between Hispanics and non-Hispanic whites based on population-weighted risk difference statistic
(Note: Red census tracts are areas where Hispanics have significantly higher mortality rates. Pink census tracts are areas where non-Hispanic whites have significantly higher mortality rates)

Regression analysis

Table 6.2 shows odds ratio of census tracts exhibiting significantly higher mortality rates in African Americans than non-Hispanic whites. Compared with a census tract with the highest SES, a census tract with the lowest SES was more likely to have a higher mortality rate in African Americans than non-Hispanic whites after adjusting for covariates (odds ratio [OR] = 4.19; 95% confidence interval [CI] = 2.18–8.07). The study observed an elevated risk of higher mortality rates in African Americans than non-Hispanic whites for a census tract with significantly high late-stage diagnosis rates in African Americans (OR=17.22; CI: 12.00-24.69) after adjusting for covariates. Results also revealed that a census tract with the highest percentage of African Americans was 10.81 times more likely to have a higher mortality rate in African Americans than non-Hispanic whites. However, the odds ratio significantly decreased to 1.92 after adjusting for other factors. Insurance expenditures also influenced racial/disparities of mortality rates in census tracts, although this effect was attenuated after adjusting for covariates. Factors including spatial access to oncologists, the socio-cultural factor, or the behavior factor did not explain the higher mortality rate in African Americans than non-Hispanic whites in census tracts.

Table 6.2 Odds ratios (OR) measuring the likelihood of census tracts exhibiting significantly higher mortality rates in African Americans than non-Hispanic whites

	Unadjusted Odds ratio of Model I (95% CI)	Adjusted Odds ratio of Model II (95% CI)
Socioeconomic status		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	1.35 (0.87–2.09)	0.75 (0.38 –1.48)
Q3	3.88 (2.63–5.73)*	1.75 (0.91–3.34)
Q4 (Low)	8.25 (5.58–12.2)*	4.19 (2.18–8.07)*
Racial/ethnic disparities in late-Stage diagnosis		
Not significant	1 (Referent)	1 (Referent)
Significant	25.34 (18.62–34.49)*	17.22 (12.00–24.69)*
Spatial access to oncologists		
Q1 (High access)	1 (Referent)	1 (Referent)
Q2	1.01 (0.77–1.33)	0.86 (0.55–1.34)
Q3	0.34 (0.25–0.45)	0.45 (0.28–0.72)
Q4 (Low access)	0.32 (0.23–0.45)	0.52 (0.29–0.90)
Socio-cultural factor		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	0.40 (0.30–0.52)	0.67 (0.42–1.08)
Q3	0.37 (0.28–0.51)	0.41 (0.24–0.70)
Q4 (Low)	0.41 (0.30–0.57)	0.43 (0.23–0.79)
Percentage of African Americans		
Q1 (Low percentage)	1 (Referent)	1 (Referent)
Q2	1.77 (1.11–2.81)*	1.54 (0.83–2.85)
Q3	2.93 (1.90–4.52)*	1.72 (0.95–3.11)
Q4 (High percentage)	10.81 (7.23–16.19)*	1.92 (1.00–3.68)*
Behavioral factor		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	0.64 (0.46–0.89)	0.57 (0.33–0.99)
Q3	0.61 (0.44–0.84)	0.66 (0.39–1.13)
Q4 (Low)	0.47 (0.34–0.66)	0.49 (0.28–0.86)
Insurance expenditure		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	1.96 (1.02–3.76)*	0.87 (0.36–2.12)
Q3	4.04 (2.21–7.37)*	1.22 (0.52–2.88)
Q4 (Low)	22.72 (12.96–39.84)*	1.49 (0.60–3.69)

*p<.001Model I includes seven univariate logistic regressions with a dichotomous dependent variable (an RD that is significantly greater than 0 or an RD of 0), and seven independent variables listed in the table. Model II is a multivariate logistic regression model adjusted for all the factors. For example, for SES, Model I includes the independent variable of SES. Model II is adjusted for all of the factors in the table with the addition of spatial access to PCPs.

Table 6.3 illustrates odds ratios of census tracts exhibiting significantly higher mortality rates in Hispanics than non-Hispanic whites. Compared with a census tract with the highest SES, a census tract with the lowest SES was more likely to have a higher mortality rate in Hispanics than non-Hispanic whites after adjusting for covariates (OR = 8.15; 95% CI = 5.27–12.61). The study observed an elevated risk of higher mortality rates in Hispanics than non-Hispanic whites for a census tract with significantly high late-stage diagnosis rates in Hispanics (OR = 5.49; 95% CI = 4.30–7.00), and the risk increased slightly after adjusting for other factors (OR = 5.93; 95% CI = 4.47–7.88). The socio-cultural factor, which represents the percentage of linguistically isolated households, percentage of foreign-born females, and percentage of female without high school education in a census tract, was a significant predictor of a census tract showing a higher mortality rate in Hispanics than non-Hispanic whites after adjusting for covariates. Factors including spatial access to oncologists, the percentage of African Americans, or the behavior factor did not explain the higher mortality rates in African Americans than non-Hispanic whites in census tracts.

Table 6.3 Odds ratios (OR) measuring the likelihood of census tracts exhibiting significantly higher mortality rates in Hispanics than non-Hispanic whites

	Unadjusted Odds ratio of Model I (95% CI)	Adjusted Odds ratio of Model II (95% CI)
Socioeconomic status		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	1.00 (0.70–1.41)	1.28 (0.80–2.05)
Q3	2.32 (1.69–3.18)*	2.47 (1.59–3.83)*
Q4 (Low)	11.10 (8.21–15)*	8.15 (5.27–12.61)*
Racial/ethnic disparities in late-stage diagnosis		
Not Significant	1 (Referent)	1 (Referent)
Significant	5.49 (4.30–7.00)*	5.93 (4.47–7.88)*
Spatial access to oncologists		
Q1 (High access)	1 (Referent)	1 (Referent)
Q2	0.67 (0.50–0.90)	0.66 (0.45–0.98)
Q3	1.02 (0.82–1.28)	1.43 (1.05–1.95)*
Q4 (Low access)	1.23 (0.97–1.56)	1.30 (0.90–1.87)
Socio-cultural factor		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	2.16 (1.59–2.93)*	1.75 (1.18–2.59)*
Q3	3.61 (2.68–4.86)*	2.37 (1.56–3.59)*
Q4 (Low)	7.08 (5.28–9.49)*	3.83 (2.46–5.96)*
Percentage of African Americans		
Q1 (Low percentage)	1 (Referent)	1 (Referent)
Q2	1.02 (0.82–1.28)	0.89 (0.65–1.22)
Q3	0.72 (0.57–0.91)	0.69 (0.49–0.98)
Q4 (High percentage)	0.69 (0.53–0.90)	0.71 (0.46–1.09)
Behavioral factor		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	0.95 (0.73–1.22)	1.17 (0.82–1.67)
Q3	0.65 (0.50–0.85)	1.04 (0.71–1.51)
Q4 (Low)	0.36 (0.27–0.49)	0.78 (0.51–1.18)
Insurance expenditure		
Q1 (High)	1 (Referent)	1 (Referent)
Q2	2.36 (1.75–3.17)*	0.93 (0.61–1.42)
Q3	2.38 (1.76–3.2)*	0.72 (0.46–1.14)
Q4 (Low)	2.24 (1.63–3.08)*	0.84 (0.49–1.45)

*p<.001. Model I includes seven univariate logistic regressions with a dichotomous dependent variable (an RD that is significantly greater than 0 or an RD of 0), and seven independent variables listed in the table. Model II is a multivariate logistic regression model adjusted for all the factors. For example, for SES, Model I includes the independent variable of SES. Model II is adjusted for all of the factors in the table with the addition of spatial access to PCPs.

Discussion

Using census tracts as the geographic area units, the study identified significant geographic variations in racial/ethnic disparities. SES, racial/ethnic disparities of late-stage diagnosis, the socio-cultural factor, and percentage of African Americans in a census tract were significant predictors of a census tract showing significant racial/ethnic disparities of cervical cancer mortality.

In this study, no significant relationship was found between spatial access and racial/ethnic disparities. In the literature, no consistent conclusion was reached on the role of spatial access to health care in cancer disparities. For example, a few studies have failed to detect any screening differences in breast cancer due to spatial accessibility (Engelman et al. 2002; Jackson et al. 2009) while several studies have found spatial access to health care could explain disparities in cancer (Wan et al. 2012; Wan et al. 2013). In addition, research on the impact of spatial access to health care on cervical cancer mortality was rare.

This study reported that socio-cultural factor was a significant predictor of a census tract showing a higher mortality rate in Hispanics than non-Hispanic whites, which can be explained by high cervical cancer mortality rates among immigrants or women with low English proficiency. A prior study suggest that foreign-born Hispanic Americans experienced higher mortality rates than those born in the United States (McCarthy et al. 2010). Previous research examined the impact of language on screening as well (Kandula et al. 2006; Ponce et al. 2006). A barrier has been observed for Hispanics with low English proficiency to receive screening, and the screening rate was a strong predictor of late-stage diagnosis and mortality rate in cervical cancer (De Alba and

Sweningson 2006). In the study, after adjusting for other factors, including SES, the odds ratio for the socio-cultural factor decreased. This decrease was due to the interaction with confounding variables. For example, among immigrants, English proficiency, insurance coverage, and a high SES were associated with increased screening, which contributed to the decreased mortality in immigrants (Kandula et al. 2006; Goel et al. 2003).

Census tracts with high percentage of African Americans had higher mortality rates in African Americans than non-Hispanic whites in this study. This observation is consistent with a previous finding (Coughlin et al. 2008). After adjusting for covariates, the study found that the odds ratio for the percentage of African Americans in a census tract significantly decreased. This decrease could be explained by the interaction between SES and the percentage of African Americans. For example, census tracts with a high percentage of African Americans tended to have lower SES (Haas et al. 2011).

This research has a number of strengths. First, this is the first study to examine geographic variations of racial/ethnic disparity in cervical cancer mortality at the census tract level and jointly take into account multiple factors. In addition, by identifying factors associated with racial/ethnic disparities at the census tract level, this study could allow cervical cancer intervention programs to more clearly identify areas in efforts to reduce disparity of cervical cancer outcomes.

There are several limitations in this study. First, it did not include the Pap smear rates in the study because of the lack of Pap smear rate data at the census tract level. According to data from the Behavioral Risk Factor Surveillance System (BRFSS) 2002-2010, compared with nationwide statistics, Texas had a high percentage of women aged 18 years or older who had not received a pap smear within three years. The percentage

was higher in Texas-Mexico border counties than nonborder counties. Therefore, the screening rate of cervical cancer might be an important factor to explain the high mortality rate of border counties for Hispanic populations.

Second, because the last day of follow-up of cohort in this study was December 31, 2010, it is likely that patients diagnosed after 2005 had a lower risk of mortality than those who have been observed for over 5 years. Nevertheless, cases diagnosed after 2005 were included in order to obtain a larger sample size to calculate cervical cancer mortality rates in a census tract.

Last, the adoption of FDR approach might fail to identify census tracts where significant racial/ethnic disparities occur because of the moderately conservative nature of FDR. However, unadjusted test showed that false positive is costly, with a large number of significant census tracts. The study have examined closely these census tracts and found that some of them exhibited higher rates in non-Hispanic whites than other two groups because of the small non-Hispanic white population. Therefore, an adjusted test using the FDR approach was adopted to deal with false positives. Adjusted results showed a decrease in the number of significant census tracts especially those exhibited the small number problem.

Conclusions

This study identified significant geographic variations of racial/ethnic disparities of cervical cancer mortality in Texas. The study found no significant association between spatial access to health care and racial/ethnic disparities in census tracts. SES, racial/ethnic disparities of late-stage diagnosis, the socio-cultural factor, and percentage

of African Americans in a census tract were significant predictors of a census tract showing significant racial/ethnic disparities of cervical cancer mortality. Results suggest that cervical cancer health intervention programs should increase efforts to address cervical cancer disparities by targeting census tracts (e.g., the major metropolitan areas, eastern Texas, and the southwest Texas-Mexico border) where significant racial/ethnic disparities were found in Texas. Additionally, resources should be devoted to target areas of lower SES, as well as areas with a high percentage of immigrants, African Americans, and linguistically isolated households.

CHAPTER VII

CONCLUSION

The concluding chapter consists of three sections. The first section recaps the research findings from this dissertation. The second section outlines contributions of this dissertation to cancer disparity research literature. The last section points out limitations in this research and suggests areas for future research.

Results and discussions

This research has three primary objectives: 1) to examine disparities of cervical cancer late-stage diagnosis in Texas from three social domains: race/ethnicity, SES, and geographic location; 2) to examine disparities of cervical cancer survival in Texas from the social domains mentioned above; and 3) to investigate geographic variations of racial/ethnic disparities of cervical cancer mortality in Texas and factors contributing to these disparities.

In order to achieve the first objective, this study examined the role of both individual and contextual factors for cervical cancer late-stage diagnosis, including age, tumor grade, race/ethnicity, as well as contextual SES, spatial access to healthcare, socio-cultural factors, socio-environmental factors, and insurance expenditures. Statistically significant racial/ethnic and SES disparities of cervical cancer late-stage diagnosis were identified. Hispanic and African-American patients had an elevated risk of late-stage diagnosis even after adjusting for other factors, including both individual and contextual factors, compared with their non-Hispanic white counterparts. Compared with patients from census tracts with a higher SES, individuals from census tracts with a lower SES

experienced elevated risk of late-stage diagnosis even after adjusting for other factors. The study did not observe any significant geographic disparities after adjusting for several factors, including age, race/ethnicity, SES, and the percentage of African Americans in a census tract.

In achieving the second objective, this study examined the role of both individual- and contextual- level factors in cervical cancer survival using a multilevel survival model. Individual-level factors include age of diagnosis, race/ethnicity, year of diagnosis, tumor grade, stage at diagnosis, and type of treatment received. Contextual-level factors include census tract- level demographic variables, insurance expenditure, behavioral factors, urbanization, and spatial access to PCPs. Statistically significant racial/ethnic and SES disparities of cervical cancer survival were found in Texas. African-American patients were more likely to die compared with non-Hispanic whites even after adjusting for other factors in the study. This risk was even higher among African-American patients with unknown stage information. Although Hispanic patients' overall five-year survival rates were similar to their non-Hispanic white counterparts, those diagnosed at a late stage were statistically less likely to die from cervical cancer. Cervical cancer patients from census tracts with the lowest SES have persistently experienced an elevated risk of death compared with those from census tracts with the highest SES even after adjusting for other factors. The study also identified statistically significant geographic clusters of longer-than-expected or shorter-than-expected cervical cancer survival. Only a small portion of these disparities were explained by individual- and contextual-level factors in this study.

The third objective of this study was to investigate geographic variations of racial/ethnic disparities of cervical cancer mortality in Texas and factors contributing to these disparities. Using population weighted rate difference and rate ratio as the measurement, this study identified significant geographic variations in racial/ethnic disparities. For African Americans, the study observed a higher cervical cancer mortality rate in eastern Texas as well as the metropolitan areas of Houston, Austin-San Antonio, and Dallas-Fort Worth. Socioeconomic status, racial/ethnic disparities in late-stage diagnosis, and the percentage of African Americans in a census tract explained the higher mortality rates in African Americans. For Hispanics, the study found a significantly higher cervical cancer mortality rate along the southwest Texas-Mexico border as well as in the metropolitan areas of Houston, Austin-San Antonio, and Dallas-Fort Worth. Socioeconomic status, racial/ethnic disparities in late-stage diagnosis, and the socio-cultural factor explained the geographic pattern of racial/ethnic disparity between Hispanics and non-Hispanic white females. No significant association was found between racial/ethnic disparities and spatial access to oncologists as well as the behavioral factor.

Findings from this study have several important implications for reducing cervical cancer disparities in Texas. First, this study provides information for developing effective cervical cancer intervention programs in Texas. Traditional programs have adopted individual characteristics such as race/ethnicity and age to identify who should be selected to receive certain health services such as screening (Wells & Horm, 1998). This study suggests that both individual and contextual characteristics should be used to guide intervention programs in order to address cervical cancer disparities. Policymakers should make efforts to address cervical cancer disparities in late-stage diagnosis and

survival in Texas through more effective cervical cancer screening, targeting racial/ethnic minority groups, as well as individuals from communities with lower SES, higher percentage of foreign-born and African-American populations.

Second, results from this study have important implications for reducing racial/ethnic disparities of cervical cancer in Texas. Racial/ethnic disparities account for a large portion of cancer disparities in the United States, which is an "unjust" or "unfair" difference that could be reduced or prevented through better policies. Although past decades have witnessed decreases in these unjust racial/ethnic disparities in cervical cancer due to more effective interventions, Hispanics and African Americans persistently experience higher mortality rates in cervical cancer compared with non-Hispanic whites. This study implied that SES and contextual-level factors played an important role in the association between race/ethnicity and cervical cancer outcomes. Therefore, it is critical to take into account SES and contextual-level factors which are modifiable in reducing/addressing racial/ethnic disparities.

By identifying census-tract level factors associated with racial/ethnic disparities at the census tract level, this study provides information for cervical cancer intervention programs to more clearly identify areas in Texas in its efforts to reduce cervical cancer disparity. This study suggests that efforts and resources should be directed to metropolitan areas in Texas where significantly higher mortality rates in Hispanics and African-Americans were found, despite adequate spatial access to healthcare in these areas. Additionally, healthcare resources should be directed to the southwest Texas-Mexico border region to reduce racial/ethnic disparities between Hispanics and non-Hispanic whites.

Third, this research also provides information for implementing existing cervical cancer intervention programs in Texas. Since 1991, the Breast and Cervical Cancer Services program (BCCS) in Texas has offered screening for breast and cervical cancer at no cost or low cost to women who are low-income, uninsured, or underinsured. Results from this study suggest that several counties (e.g., Brown, Fannin, Freestone, Grayson, Dewitt, and Starr) with higher cervical cancer risks are not covered by this program. Additionally, several counties, although covered by this program, encounter geographic barriers to access facilities included in the BCCS program in Texas. For example, for 128 counties in western Texas, there are only 70 BCCS facilities. In contrast, there are 127 facilities covering only 126 counties in eastern Texas. Women from western Texas might travel longer distances to access the screening services provided by the BCCS program. Therefore, there is an urgent need to relocate BCCS health resources in order to eliminate potential geographic barriers of access to healthcare.

Contributions

This study has a number of contributions. First, this study exemplifies how GIS and spatial analysis techniques can be utilized in health disparity studies. Traditional health disparity studies have only adopted individual characteristics such as race/ethnicity and age to identify who should be selected to receive certain health services such as screening. In contrast, GIS and spatial analysis techniques could be used to study spatial patterns of cancer in order to serve a monitoring purpose, provide information on cancer prevention, and facilitate explanations of cancer disparities. Using these techniques, this study for the first time in the literature examined geographic disparities of cervical cancer late-stage diagnosis and survival at a fine geographic scale. Additionally, this is the first

attempt to examine how racial/ethnic disparity in cervical cancer mortality varies geographically at the census tract scale. Results from this study could provide information for cancer intervention programs to more clearly identify areas in its efforts to reduce cervical cancer disparity.

Second, despite advances in knowledge about cancer during the last century, identifying factors associated with cancer disparities remains a challenging task. There has been inconsistent and inclusive evidence of risk factors contributing to cancer disparities. In order to address this literature gap, this study is the first attempt to examine the impact of multilevel factors, including individual- and contextual-level variables, on cervical cancer. Most existing work has merely examined the effect of individual-level variables, while studies on contextual-level impacts were few. Moreover, there is no research that has taken into account multilevel factors and examined how they could jointly explain the geographic disparities in cancer outcomes. A growing body of studies has focused on geographic disparities in cancer outcomes, from which several are descriptive without explaining why disparities exist. By looking into multiple-level influences on cervical cancer outcomes, this study enhanced knowledge about factors associated with cervical cancer disparities.

Third, this study is the first attempt to examine the association between spatial access to healthcare and cervical cancer outcomes in the United States. Regular screening by health care professionals can help detect and remove precancerous growths, as well as diagnose early-stage treatable cancers. There has been no consistent conclusion on the relationship between cancer outcomes and spatial access. There is little research that has examined the relationship between cervical cancer outcomes and spatial access to

medical services. Moreover, previous studies have focused on cancer screening facilities. Research on spatial access to other preventive services such as primary care is rare. Because the Pap smear test is typically provided by primary care physicians (PCPs), access to PCPs plays an important role in the prevention of cervical cancer. It has been documented that the Pap smear screening was statistically associated with the contacts of primary care providers.

In addition, this study used a multilevel survival model to take into account multilevel data structure in this study. Most previous studies only adopted a single-level survival model which failed to take into account correlations among patients within the same neighborhood and random effect caused by geographic variation.

Limitations and future work

There are several limitations in this study. First, this study did not examine the impact of HPV vaccination rates or Pap smear rates on cervical cancer mortality because of the lack of data at the census tract level. The HPV vaccine prevents HPV which often causes cervical cancer; therefore, the geographic pattern of the HPV vaccination in Texas would be a strong factor contributing to overall cervical cancer incidence and mortality. The use of Pap smears as a screening method of cervical cancer provides an effective tool, which reduces the chances of late-stage diagnosis and mortality rate of cervical cancer. According to data from the Behavioral Risk Factor Surveillance System (BRFSS) 2002-2010, compared with nationwide statistics, Texas had a higher percentage of women aged 18 years or older who had not received a Pap smear within three years. The percentage was higher in Texas-Mexico border counties than nonborder counties.

Therefore, the screening rate of cervical cancer might be an important factor to explain the high mortality rate of border counties for Hispanic populations.

Second, treatment data used in the study were the first treatment for patients, instead of complete treatment information. Additionally, treatment data provided by TCR did not undergo the same quality assessment procedure as other core data. Therefore, the completeness and accuracy of treatment data is not known. More accurate and complete treatment data might help explain remaining survival differences and increase the power of the study.

Third, the remaining racial/ethnic and geographic disparities might be attributed to other unmeasured individual-level factors: patients' comorbid conditions, smoking status, health insurance status, marital status, and access to healthcare, which merits future investigations through qualitative methods. According to the BRFSS 2002-2010, health insurance status varies by race/ethnicity and geographic area in Texas. For example, African-Americans have a higher percentage of women who have no health insurance compared with non-Hispanic whites. The cluster of shorter-than-expected survival had a higher percentage of people without health insurance compared with the cluster of longer-than-expected survival.

Fourth, it is worth noting that cervical cancer data quality and data processing might have an impact on the overall result in the study. About 1,830 cancer cases (12%) were geocoded at the zip code level instead of street level, which poses uncertainty in positional accuracy of theses addresses. It is necessary to validate the accuracy of geocoding through sampling. In addition, geocoding was conducted on addresses at diagnosis which might not reflect the actual address where cervical cancer patients live

for a lifetime. For 7,253 cancer cases (47%), follow-up was not performed. Further investigation is needed to find out if the incomplete follow-up has any impact on the survival disparity result in the study. With respect to data processing, age-adjusted cervical cancer late-stage diagnosis and mortality rates during 1995 and 2008 were calculated based on the US Census 2000 population, which might lead to inaccurate rates.

The fifth limitation is related to the modifiable areal unit problem (MAUP). This study conducted spatial analysis and explained results at the census tract level. However, results based on other aggregated levels (e.g., census block group) might be different from this study. Future research needs to investigate the research questions at different aggregation levels. It is also interesting to randomize the data in the study in order to find an optimal spatial unit for cervical cancer disparity research.

Last, the statistical power of the racial/ethnic disparity tests in this study is worth further examination because of the small population sample at the census tract level. The study identified several census tracts with significantly higher mortality rates in non-Hispanic whites than minority groups. A further investigation of these census tracts revealed there was a small number of non-Hispanic white population there.

Future Research

Future work is needed to disentangle the 'Hispanic paradox' in Texas. Although several studies have suggested that the 'Hispanic Paradox' might be explained by selective return migration toward the end of life, social network, comorbid conditions, smoking status, religion, and cultural factors among Hispanic group, it is worth further investigation to understand factors contributing to better survival among Hispanics despite their lower SES compared with non-Hispanic whites. A future study can be

conducted to survey cervical cancer survivors, which might reveal some unmeasured factors that protect Hispanic women from dying of cervical cancer.

Only a small portion of geographic disparities of cervical cancer survival were explained in this study. Future research is needed to understand factors contributing to the remaining clusters of shorter-than-expected survival or longer-than-expected survival. It might be helpful to conduct studies on these geographic clusters to reveal reasons underlying the geographic disparities. It will be interesting to conduct comparative studies in order to better understand cervical cancer disparities in the world. For example, a similar cervical cancer disparity study can be performed in another state to find out if similar or different patterns can be observed.

Future work should also include efforts in reducing and eliminating cervical cancer disparities in Texas. By identifying census-tract level factors associated with racial/ethnic disparities at the census tract level, this study provides information for cervical cancer intervention programs to more clearly identify areas in Texas. Cervical cancer elimination programs (e.g., Community-based participatory program) should be developed towards the goal of addressing cervical cancer disparities.

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