Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Sari De'Ann Hopson Date

A Population-Based Study of Colon Cancer Treatment Quality in Georgia: Race, Residential Segregation and Rural-Urban Residence

By

Sari De'Ann Hopson
Doctor of Philosophy
Epidemiology

_____
Michael Goodman, MPH, MD
Advisor

_____
David Kleinbaum, PhD
Committee Member

_____
Joseph Lipscomb, PhD
Committee Member

_____
Sheree Marshall-Williams, MS, PhD
Committee Member

_____
Kevin Ward, CTR, MPH, PhD
Committee Member

Accepted:

_____
Lisa A. Tedesco, Ph.D.
Dean of the James T. Laney School of Graduate Studies

_____

Date

A Population-Based Study of Colon Cancer Treatment Quality in Georgia: Race, Residential Segregation and Rural-Urban Residence

By

Sari De'Ann Hopson
B.S.P.H & B.A., University of North Carolina, Chapel Hill, 2003
M.S.P.H., Emory University, 2005

Advisor: Michael Goodman, MPH, MD

An abstract of
A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in Epidemiology

2012

Abstract

A Population-Based Study of Colon Cancer Treatment Quality in Georgia: Race, Residential Segregation and Rural-Urban Residence

By Sari De'Ann Hopson

Prognosis of colorectal cancer, the third most common invasive malignancy in the US, depends on timely diagnosis and on the receipt of appropriate treatment. Clinical factors strongly influence treatment; however, studies also demonstrate the impact of non-clinical factors. This dissertation examined the role of non-clinical factors (patient race and residential characteristics) in the receipt of quality colon cancer treatment. Treatment quality was assessed in terms of surgeon training and experience and the receipt and completion of adjuvant chemotherapy.

Three questions motivated this project:

1. Are the qualifications of colon cancer surgeons associated with characteristics of their Medicare patient population?
2. Do patient race and/or rural-urban residence influence the receipt of adjuvant chemotherapy among Medicare patients with stage III colon cancer; if so, are these associations explained by residential segregation?
3. Is patient race associated with the receipt and completion of adjuvant chemotherapy among stage III colon cancer patients in predominantly rural Southwest Georgia (SWGA)?

For question one, we found that percentages of black patients were higher for less qualified surgeons and lower for most qualified surgeons. The patients of most qualified surgeons resided in less racially segregated census tracts. These findings indicate that non-clinical patient factors may affect the quality of colon cancer care among Medicare patients.

For question two, neither patient race nor residential segregation measures were associated with receipt of adjuvant chemotherapy among Georgia Medicare colon cancer patients. Receipt of chemotherapy was less common among patients who were older, non-married and had co-morbid illnesses. These findings suggest that receipt of chemotherapy is more strongly influenced by possible contraindications to chemotherapy (advanced age and comorbidities) than by social factors.

For question three, race was not a significant predictor of chemotherapy receipt among Southwest Georgia colon cancer patients; however, white patients completed adjuvant chemotherapy less often than black patients. Chemotherapy receipt was higher among younger patients and those receiving therapy at accredited cancer facilities. Chemotherapy completion was more common among married patients and those with private insurance. The observed racial disparity in treatment completion may be explained by differences in chemotherapy tolerance, toxicity and patient support.

A Population-Based Study of Colon Cancer Treatment Quality in Georgia: Race, Residential Segregation and Rural-Urban Residence

By

Sari De'Ann Hopson
B.S.P.H & B.A., University of North Carolina, Chapel Hill, 2003
M.S.P.H., Emory University, 2005

Advisor: Michael Goodman, MPH, MD

A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in Epidemiology

2012

Acknowledgements

I am thankful to my mentors, family and friends for believing in me and encouraging me to fulfill this dissertation. I appreciate the perspectives and diverse insight my committee members offered to this project and my learning. I will always be grateful for my advisor, Dr. Michael Goodman, for making me accountable and providing invaluable support to my research.

Table of Contents

List of Tables

List of Figures

Introduction

Study Motivation

Currently, colorectal cancer (CRC) is the third most commonly diagnosed cancer and the third most common cause of cancer-related death in the U.S [1]. It is the only major cancer to affect men and women almost equally. Colon cancer's treatment is most strongly influenced by cancer stage and location [2]. However, population-based studies have shown that non-clinical factors also influence treatment [3-7]. These non-clinical factors need to be addressed to increase quality of colon cancer care.

The non-clinical factors of interest include, among others, patient residential segregation, rural-urban residence and race [8-13]. The majority of studies evaluating the effect of community characteristics on quality of cancer care or access to colorectal cancer specialists have used coarse community characteristics such as residential racial composition and income level [8, 14-16]. These factors serve as proxies for some known or unknown community characteristics that affect health care delivery. The use of more refined community factors, such as residential racial and economic segregation measured by the dissimilarity and/or isolation indices, is a burgeoning area of research [14, 15]. These measures describe processes known to affect the distribution of health and social resources in the community [17, 18]. However, the effect of these measures on the quality of colon cancer care has yet to be examined.

Rural-urban residence and patient race are additional non-clinical factors expected to affect the quality of colon cancer treatment [9-13, 19]. Rural-urban and racial disparities in the receipt of colon cancer adjuvant therapy typically remain after controlling for other potential confounders [10, 13]. Few studies have sought to explain the perpetuation of these disparities among cancer patients. Residential racial and economic segregation have been shown to disproportionately

affect black and rural populations as well as affect the distribution and possibly quality of health care resources in communities [20-22].

These observations suggest that residential segregation is a relevant factor whose influence on the observed rural-urban and racial disparities affecting the quality of treatment for colon cancer must be assessed. Specifically the assessment should address its effect on the current most common measure of treatment quality used in colon cancer outcomes research, receipt of adjuvant chemotherapy among stage III colon cancer patients, which has been shown to affect disease prognosis [23, 24].

In addition to the type of therapy received, residential segregation, rural-urban residence, and patient race may be also related to factors associated with other aspects of cancer care, such as the characteristics of the treating physician. Studies have shown that level of physician training and/or experience may determine the quality of cancer care [25-27]. The distribution of these physician characteristics may differ across patient populations. No studies to date have examined the associations between physician training and/or experience and the demographic and residential characteristics of colon cancer patients.

Studying the clinical treatment of colon cancer in the United States (U.S.) is made possible through the development of state-wide cancer surveillance programs and the ability to link surveillance data to insurance claims. Obtaining accurate assessments of the quality of clinical treatment in the U.S. is of great concern among researchers using this data. Validation studies of cancer registry data have indicated that adjuvant chemotherapy is underreported in the database [28-30]. An assessment of bias in chemotherapy data from the combined cancer registry-Medicare databases has not been performed in recent years nor has it been evaluated in the state of Georgia. This assessment is necessary to ensure the quality of this clinical treatment data.

Research Goals and Specific Study Questions

The long-term goals of this dissertation are to enhance our understanding of non-clinical factors that influence colon cancer treatment and to explore the use of linked Georgia Cancer registry and Medicare data for colon cancer treatment research. These long-term goals are achieved through the following three specific research questions, each addressed in a separate study:

Study I: Addresses the question: Is the level of training and/or experience of colon cancer surgeons associated with characteristics of their patient population? Data sources for this study came from stage I-III colon cancer patients included in the Georgia Cancer Registry (GCR) – Medicare linkage file for the years 2001-2005 and supplemented with additional information from the Medicare Physician Identification and Eligibility Registry (MPIER), the U.S. Census, the United States Department of Agriculture (USDA) Economic Research Service (ERS) and the SEER-Medicare Hospital file.

Study II: Addresses the question: Is there evidence indicating racial and/or rural-urban disparities in the receipt of adjuvant chemotherapy (the current most common measure of treatment quality) in stage III colon cancer patients; and if so, are these disparities explained, at least in part, by residential neighborhood racial and economic segregation? The data to address this question was obtained from the GCR-Medicare linkage file, but pertaining only to stage III colon cancer patients, and supplemented with data from the SEER-Medicare Hospital file, the U.S. Census and the United States Department of Agriculture (USDA) Economic Research Service (ERS).

Study III: Addresses the question: Is there evidence of racial differences in the receipt and completion of adjuvant chemotherapy among stage III colon cancer patients in Southwest Georgia? This last question will be addressed by utilizing data collected as part of the Southwest Georgia Cancer Care Study (SWGCCS), which is considered the "gold standard" database in this study with respect to data completeness and accuracy and supplemented with data from the U.S.

Census and the United States Department of Agriculture (USDA) Economic Research Service (ERS).

Chapter 1: Understanding Colorectal Cancer

Epidemiology of Colorectal Cancer

Colorectal Cancer in the United States

In the U.S., colorectal cancer (CRC) accounts for 10-percent of the cancer incidence among men and women and 8-percent of cancer mortality among men and 9% among women in the U.S. [1]. Currently, it is the third most common cancer and the third leading cause of cancer-related death nationwide [1]. It is the only major cancer to affect men and women almost equally. Incidence rates are declining in the United States; this decrease partially reflects the increase in the detection and removal of precancerous lesions through endoscopic polypectomy [31, 32]. Within the US, racial groups vary in colorectal cancer incidence [33]. The cumulative incidence for black men and women are 5.60 and 4.22 percent, respectively, and 4.98 and 3.38 percent for white men and women, respectively [32]. Based on the 2000-2004 data, blacks have the highest incidence of CRC in the U.S. (72.6 and 55.0 per 100,000 people for men and women respectively) [1]. The corresponding incidence rates are lower for whites (60.4 for men and 44.0 for women) and lower still for other racial/ethnic groups including Asian Americans/Pacific Islanders, American Indians/Alaska Natives and Hispanic/Latinos.

Using U.S. data from the years 2000 to 2004, the annual age-standardized death rate from CRC was 49,960 per 100,000 people making it the third leading cause of cancer-related deaths [1]. Black men have the highest mortality rate from CRC in the U.S. with a rate of 32.7 per 100,000 people [1]. Black women and white men have the second highest mortality rate from CRC, both with rates of 22.9 per 100,000 people [1]. The lowest mortality rate is among Asian American/Pacific Islander and Hispanic/Latino women with rates of 10.3 and 11.1, respectively [1].

Age-adjusted CRC death rates are variable in the U.S. from state to state with the highest annual rates in California (5,070 per 100,000 people) and the lowest rates in Alaska (70 per 100,000 people) [1]. The five-year survival for persons with CRC in the United States is 65.2% for men and 62.4% for women [31]. When detected at an early stage, the five-year survival rate increases to 90% [31]. Survival from colon and rectal cancer has increased from 1975 to 2003: colon cancer survival rates for all races increased from 51% to 65%, for blacks from 46% to 55%, for whites from 52% to 66%; rectal cancer survival rates for all races increased from 49% to 66%, for African Americans from 45% to 58%, for whites from 49% to 66% [1].

Colorectal Cancer in the State of Georgia

As in the rest of the U.S., CRC is the third most common cancer diagnosed and the third leading cause of cancer-related deaths among men and women in Georgia. Each year from 1999-2003, over 3,500 colorectal cancers were diagnosed among the residents of the state [34]. The annual incidence of CRC in Georgia is higher among black men (72 per 100,000) than white men (60 per 100,000) and is also higher among black women (53 per 100,000) compared to white women (41 per 100,000). According to the 1999-2003 statewide data, the average annual CRC incidence rate for rural white men (65 per 100,000) were higher than that for urban white men (58 per 100,000) [34]. Incidence rates for rural white women (42 per 100,000) and urban white women (41 per 100,000) were similar. Rural black men and urban black men had incidence rates of 67 per 100,000 and 74 per 100,000, respectively; however the difference was not statistically significant. The incidence rate for rural and urban black women (51 per 100,000 and 54 per 100,000, respectively) were comparable [34].

Data for 2000-2004 indicate that CRC was responsible for 1,315 deaths in the state of Georgia. Mortality rates from colorectal cancer were higher among blacks than among whites: 32 per 100,000 for black men versus 22 per 100,000 for white men and 24 per 100,000 for black women versus 14 per 100,000 for white women [34]. During this same period mortality rates from

colorectal cancer were higher for rural white men (24 per 100,000) than for urban white men (21 per 100,000) [34]. The differences in mortality rates were similar for urban and rural black men (32 per 100,000 and 32 per 100,000, respectively), for urban and rural black women (24 per 100,000 and 23 per 100,000) and for urban and rural white women (16 per 100,000 and 14 per 100,000, respectively) [34].

Etiology of Colorectal Cancer

The accumulation of genetic and epigenetic alterations of cellular and tissue functions in the large intestine trigger the development of colorectal cancer. The adenoma-carcinoma sequence hypothesized by Vogelstein is the archetypical pathogenic pathway. It describes the stepwise progression from normal cell to dysplastic epithelium to carcinoma which is associated with an accumulation of genetic and epigenetic alterations in oncogenes and tumor suppressors [35, 36]. The adenoma-carcinoma sequence (also called APC-*β-catenin* pathway is thought to be responsible for most CRC cases. Other colorectal carcinogenesis pathways that are responsible for a relatively small proportion of new cases include: Hereditary Nonpolyposis Colorectal Cancer (HNPCC) pathway, ulcerative colitis dysplasia–carcinoma sequence, and hypermethylation silencing of the estrogen receptor gene pathway [37].

Colorectal cancer is inherited in about 5% of cases [32]. Inherited genetic mutations and a personal or family history of CRC and/or polyps strongly increase the risk of disease [38, 39]. Chronic inflammatory conditions, such as ulcerative colitis, Crohn's disease and other inflammatory bowel diseases, also predispose patients to colorectal cancer [40-42]. The majority of cases are sporadic rather than inherited. Exogenous factors including modifiable lifestyle factors, such as obesity, physical inactivity, smoking, heavy alcohol consumption, a diet high in red and processed meat, and inadequate intake of fruits and vegetables have been found to be associated with increased incidence of colorectal cancer, however most associations reported to date have

been modest and inconsistent across studies [43-52]. Incidence may be reduced with nonsteroidal anti-inflammatory drugs, such as, aspirin and with hormone replacement therapy, which includes estrogen and progestin [53-57].

Anatomy and Physiology of the Large Intestine

Colorectal cancer originates in the large intestine which is formed by the colon and the rectum. The large intestine is divided into five segments based on its vascular supply and location outside or behind the peritoneal cavity [58]. This structure is shown in Appendix Figure 1. The five segments of the large intestine include the cecum (with appendix) and the ascending colon, the transverse colon, the descending colon, the sigmoid colon and the rectum. The proximal (right) colon includes the cecum, ascending and transverse colon; the distal (left) colon includes the descending colon and sigmoid colon [58]. The rectum segment comprises the rectum proper and the rectosigmoid junction. The first 4 to 5 feet of the large intestine is the colon, whereas the rectum represents only the last 4 to 5 inches. Colon length varies within the population and is estimated to range from 91 to 125 cm. Within the colon, the luminal diameter varies. The diameter is widest at the cecum (approximately 8.5 cm) and most narrow at the distal sigmoid (approximately 2.5 cm). The frequent presentation of obstructive symptoms among patients with annular cancers have been attributed to the above described change in colon luminal diameter and the consistency of formed fecal content in the descending and sigmoid colon [59].

The main function of the colon is to absorb water and electrolytes from partially processed food received from the ileum of the small intestine. After the absorption of 90% of the fluid, the partially processed food becomes semisolid feces [60]. The colon serves as a storage place for this waste before it is sent to the rectum to be excreted [61]. The waste moves from the colon to the rectum, and is eliminated through the anus [60].

The wall of the colon and rectum is comprised of several layers of tissue. Colorectal cancer starts in the mucosal epithelium, which is the innermost layer of the colon, and can grow through some or all of the other layers. The stage of CRC depends, in part, on how deeply the primary tumor grows into these layers (Figure 1). In addition to localized tumor extension, CRC stage depends on its spread to regional or distant lymph nodes and on the presence of metastases in other organs [62]. An understanding of colon anatomy, structure, location and vascular supply is critical to perform safe and effective CRC surgery. The extent of colon resection is dependent on vascular supply and the need to remove regional draining lymph nodes [58]. An illustration of colon cancer stages is shown in Appendix Figure 2.

Cancers of the colon and rectum have many shared features. These cancers develop slowly over several years. Most of these cancers begin as an adenomatous polyp—a pre-malignant lesion, which also originates in the colorectal mucosa, but does not penetrate other layers and does not metastasize [63, 64]. The slow development of colorectal cancer makes it an ideal cancer for screening. Early detection of cancer through screening has been found to increase survival and removal of precancerous adenomas has been found to decrease CRC incidence [65-69].

Diagnosis and Staging of Colorectal Cancer

Diagnosis

Signs and symptoms of colorectal cancer include anemia, fatigue, blood in stool, rectal bleeding, increased frequency of bowel dysfunction, such as constipation, diarrhea or vague abdominal discomfort [59]. Right-sided lesions are associated with symptoms of fatigue and anemia and left-sided lesions produce symptoms such as rectal bleeding, constipation, and abdominal pain [59]. Among symptomatic and asymptomatic cases, colonoscopy performs well in terms of colorectal cancer diagnosis [70]. Colonoscopy provides visualization of the colon, determination of the location of tumors, and provides the opportunity for histologic examination of tumor tissue.

Staging

Cancer staging is a measuring system of the progression or severity of cancer based on the extent of the original tumor and the extent of spread in the body. The TNM Staging System is among the most commonly used [71]. It was developed and maintained by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) [71]. TNM cancer staging is based on the extent of the tumor (T); the extent of spread to the lymph nodes (N); and presence of metastasis (M) [62, 71]. The definitions of the TNM stages are given in Appendix Table 1.

There are 2 types of AJCC stages. The clinical stage (cTNM) is based on physical examination and some imaging studies done before surgery [71]. The clinical stage is used to decide which, if any, operations should be performed [71]. After colorectal surgery, the pathologic stage (pTNM) is determined by examining the tissue, including lymph nodes, that has been removed [71]. The pathologic stage is used to decide which patients with colon and rectal cancer should receive adjuvant treatment and, if so, exactly which treatment should be used [71].

Colon Cancer Treatment

Although the etiology and the risk factors for cancers of colon and rectum are sufficiently similar to allow combining the two sites into a single CRC category, the therapeutic approaches for carcinomas of the colon are different from those used to treat rectal cancers. As the focus of this dissertation is on quality of colon cancer care, the following section is limited to colon (as opposed to colon and rectum) cancer treatment.

The standard for curative therapy of the colon cancer is radical resection of the bowel segment bearing the tumor [59]. This means that wide surgical margins and removal of the lymphatic drainage of the tumor are typically performed. Tumor size, grade, location and stage

determine the extent of the resection. Limited segmental resections as opposed to radical resection are indicated for palliative surgery in the case of metastatic disease (stage IV cancers).

Adjuvant therapy is usually indicated for stage III disease; while stage IV patients often receive palliative care, which may include surgery, chemotherapy and/or radiation. The inclusion of adjuvant therapy for stage III colon cancer after surgical intervention is an indicator of quality care [72]. Adjuvant therapy is designed to eliminate or prevent the growth of cancerous cells that may not have been surgically removed. Clinical trials have shown that adjuvant chemotherapy increases 5-year survival rates and decreases cancer recurrence rates among stage III colon cancer patients [23, 73, 74]. The North Central Cancer Treatment Group conducted a clinical trial finding a 12% survival benefit among stage III colon cancer patients receiving surgery and adjuvant chemotherapy compared to those receiving surgery alone [75]. Other trials have shown that stage III colon cancer patients receiving surgery and adjuvant chemotherapy have improved disease-free and overall survival compared to patients receiving only surgery [24]. Guideline treatment for stage II colon cancer is not well established and the added benefit of adjuvant chemotherapy among these patients is currently being evaluated in clinical trials [76]. Appendix Table 2 shows a summary of treatment by colon cancer stage.

Chapter 2: Measures and Determinants Of Treatment Quality: A Literature Review

Evaluating Health Care Quality

Quality of health care – "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge"---Institute of Medicine [77]

Providing patients with appropriate services for the improvement of their condition is a key indicator of good quality care. The overuse, underuse, and misuse of treatments are three problems that may occur within the US health care system.

Donabedian, one of the pioneers of health care quality research, states in his classic article that health care quality can be evaluated based on either the assessment of structure, outcomes, or process of health care [78]. Structural quality assesses the characteristics of the medical environment or setting in which the health care takes place [78, 79] . Outcome quality assesses the health status of the patient following medical care [78, 79]. Process quality assesses the health care procedures performed by the physician and whether "good" health care has been provided based on current professional knowledge [78, 79].

The feasibility of studies investigating quality of care depends on the availability of data. These data must be "easily, sometimes routinely, measurable and reasonably valid" [78]. There is also a need for the identification of disparities in quality of care and the assessment of explanations for these disparities. Appropriate evidence-based actions cannot be made to reduce and/or eliminate disparities in health care until we understand who is at risk for poor quality care and what determines this risk. Health care quality varies by community and patient race. The following discussion will define and discuss community and racial factors that may be associated with quality of health care.

Residential Segregation

Community characteristics have been associated with health and health care outcomes in many studies. However, few studies have assessed the role of racial segregation in health care disparities and none have evaluated the association between economic segregation and health care. Segregation is the physical separation of groups (racial or economic) in residential contexts. Racial segregation was historically enforced by law, backed by major economic institutions and housing policies, and encouraged by racism and racial discrimination [80, 81]. Restrictive covenants limited housing options for blacks to least desirable residential areas [80, 82]. Although, the Civil Rights Act of 1968 made discrimination in housing sale and rental illegal, there is evidence of the persistence of this discrimination even today [83]. The political and economic processes of racial segregation affect quality of social resources, such as health and education, received by the marginalized group. These processes not only segregate groups from one another but also separate certain populations from social resources. Racial segregation has been deemed the "fundamental cause" of health disparities [84].

Williams asserts that "the roots of black-white differences in health are not due to differences in biology or beliefs… [but] are driven by fundamental societal inequalities" [84]. Blacks in both urban and rural settings are more likely to live in racially segregated communities than whites [21, 85]. Racial residential segregation is associated with economic inequality between racial groups. As a result the worst urban poverty in which whites reside is considerably better than the average economic context of black communities [20, 22, 86].

Economic segregation may affect quality of health and health care due to its effect on social resources in a community. Increased concentration of poverty transforms a neighborhood into a physically deteriorated area, characterized by high crime, poor schools and excessive mortality [22]. Massey postulates that poverty concentration in racial segregated areas result from the interaction between the level of racial segregation and changes in the structure of the income

distribution [22]. This occurs because generally minorities experience a higher poverty rate than whites. As communities become composed of more minority members, their high poverty rate is compounded and poverty becomes concentrated [22]. Kawachi theorizes that higher levels of income inequality in a community lead to a decline in community involvement and attachment resulting in deleterious material consequences [87]. Communities with income inequalities may experience a disinvestment in health-promoting human capital such as education and medical care [88].

Measures of Segregation

Segregation can be measured several ways; however, for purposes of this dissertation, discussion will be limited to the two most widely used dimensions: the dissimilarity index and the isolation index [89]. Higher values on both indices signify greater segregation.

The dissimilarity and isolation indices measure different aspects of segregation. The dissimilarity index (D) measures the extent to which groups are segregated from each other [89, 90]. It represents the percent of group X members that would have to change their area of residence to achieve an even distribution of group X in relation to group Y residents within each subareal unit within the area being examined (e.g. subareal unit is city and area is county) [89]. This means that one subareal unit does not have a different percent of group X relative to group Y residents than another subareal unit within the area being examined, e.g. each census tract within a county has a 20% black American population and an 80% white American population. This index ranges from 0 to 1, where D=1 indicates complete segregation (the two groups live in completely different neighborhoods) and D=0 means complete integration (the two groups are distributed exactly the same way across the neighborhoods). When assessing black-white segregation of a given census tract, the D value of 0.66 indicates that 66 percent of blacks must move from the census tract so that the distribution of blacks and whites will be equal in the census tract. Values greater than 0.6

are considered a level of high segregation [21]. This index is invariant to relative size of groups. The actual calculation of the dissimilarity index is provided in Appendix Formula 1.

The isolation index measures the extent by which group members are exposed to one another rather than to members of another group [89, 91]. It can be used to calculate the probability that a randomly selected member of Group X will come in contact with another member of Group X in the same residential area [90]. The isolation index may not only measure the isolation of the disadvantaged populations (e.g., blacks or poor) from the more advantaged population (e.g., whites or non-poor), but may also measure the isolation of disadvantaged groups from social mobility and resources [17]. This index ranges from 0 to 1 and can be interpreted as the probability that a randomly selected member of Group X will come in contact with another member of Group X in the same residential area [90]. The calculation of the isolation index is presented in Appendix Formula 2.

The dissimilarity and isolation indices have been regarded as unsatisfactory measures of economic segregation because they do not allow continuous variables such as income to be placed in the formulas [20]. The main criticism of these indices as measures of economic segregation is that continuous variables such as income must be arbitrarily categorized (e.g. poor (those below the federal poverty line) versus not poor (those above the federal poverty line)). The neighborhood sorting index (NSI), the ratio of the standard deviations of mean neighborhood income and mean household incomes in the neighborhood, is deemed a more appropriate measure of economic segregation; however, variables needed to calculate this measure are not available for the entire population in the U.S. Census [20].

Geographic units of measurement

Traditionally, the census tract (average population 5,000) has been the areal unit used to approximate a neighborhood. Recent discussion has been centered on the use of a smaller areal unit, the census block group (average population 1,100), to better approximate a neighborhood,

due to the unit's increased population homogeneity when compared to the census tract [90]. Too few studies have been conducted to adequately determine the best areal unit to assess residential neighborhood affect on health care. Studies assessing the affect of community characteristics on health care have predominately used zip code and county level data [8, 16, 92], which are clearly too heterogeneous to allow meaningful area-based analyses. Only some studies have used census tracts [15].

Segregation and Cancer Care

Racial Segregation

Black-white disparity in early stage CRC diagnosis is most pronounced in low racially segregated (based on the isolation index) / low income areas [14]. A recent study showed as the county-level black population percentage increased there was a decrease in the supply of gastroenterologists and radiation oncologist and a trend toward a decrease in the number of colorectal surgeons in a given county [8]. This finding shows that racial residential segregation affects the geographic distribution of physicians. This association may indirectly affect the quality of CRC care and may explain the observed racial disparity since blacks are more likely than whites to reside in a racially segregated community [21].

No studies to date have assessed the role of racial segregation on racial disparities specifically in colon cancer care. One study, however, has evaluated the role of racial segregation on disparities in breast cancer care [15]. This study found that blacks were less likely than whites to receive adequate care [OR=0.72, 95% CI (0.65-0.78)]. After adjusting for racial segregation, the black-white disparity decreased [OR=0.78, 95% CI (0.71-0.86)]. As black segregation increased patients were less likely to receive adequate breast cancer care [OR=0.73, 95% CI (0.64-0.82)].

Economic Segregation

Research on the relation of economic segregation to health and health care is scant. No studies to date have assessed the role of economic segregation on racial disparities in cancer care. Several studies have examined the role of area-based measures of socioeconomic status (SES), namely census tract based median household income, on racial disparities in CRC adjuvant therapy [5, 6, 93, 94]. This measure is typically used as a surrogate of individual SES level. It has been reported that area-based measures of SES are independently associated with receipt of adjuvant therapy in several studies. These findings may indicate that community based economic characteristics act as determinants of the quality of health care delivered to that community. It is also important to recognize that census tract-level median household income is associated with race in some studies, which makes this area-based measure of SES a potential confounder and possible explanatory factor of the racial disparity in CRC adjuvant therapy.

Defining Rural-Urban Status for Epidemiology Research

Studies evaluating rural-urban differences have used various definitions of rural and urban status. Health access studies using a dichotomous rural-urban variable have found that outcome heterogeneity among very rural populations was masked by this overly broad grouping [95, 96]. Studies have also shown that use of large geographic areas, such as counties or cities, as the level of rural-urban classification also masks heterogeneity in outcomes. Smaller delineations of rural-urban status, such as at the census-tract level, have shown to unmask heterogeneity in rural classifications and may more accurately capture the socio-cultural context in which disease occurs and health care is received [97]. Hall et al states that choice of rural-urban definition in research should take into consideration the aspect of rural-urban residence that is suspected to influence the outcome [95]. The proximity of residence to health care facilities is one aspect of rural-urban residence that influences quality and/or receipt of health care [11].

Rural Urban Commuting Area (RUCA) codes divide areas into communities based on the size and direction of resident commuting flow to places of employment. This classification may also indicate the commuting flow to areas of health care delivery. The codes are based on the same theoretical concepts as those used by the Office of Management and Budget (OMB) to define county level metropolitan and micropolitan areas. RUCA codes were developed and are provided by the researchers at the United States Department of Agriculture in collaboration with the Health Resources Service Administration, Office of Rural Health Policy and the Washington, Wyoming, Alaska, Montana, and Idaho (WWAMI) Rural Health Research Center [95].

RUCA codes are available at the census tract level from the 1990 and 2000 U.S. Census estimates [98]. Census tracts provide a finer level of analysis than cities and counties to examine rural homogeneity in health outcomes [95, 98]. These codes delineate metropolitan, micropolitan, small town, and rural commuting areas based on population density, urbanization and daily commuting. There are 10 primary (referring to primary commuting destination) and 30 secondary (referring to secondary flow) codes in the classification. The 10 primary codes offer a clear-cut delineation from metropolitan to rural settlement based on the size and direction of the primary commuting flows [98]. The numerous primary and secondary codes offer flexibility in aggregating the codes into smaller categories. The RUCA codes and RUCA code categorization schemes are shown in Appendix Table 3 and Appendix Table 4, respectively.

There are several potential RUCA code categorization schemes, but three of these schemes (titled as A, B and C) are used most frequently [99]. These three categorization schemes are proposed by researchers at the WWAMI, Rural Health Research Center. Categorization scheme A aggregates RUCA codes into four categories: urban, large rural city/ town, small rural town, and small isolated rural town [99]. This scheme is used most often in health related analyses. The advantage of this definition is that it divides urban and rural areas at the sub-county level in a similar way as the OMB Metro definition. The division of rural into the three categories is

relevant for health research in terms of the potential differences in availability or access to health providers and resources in these communities. Categorizations B and C divide RUCA codes into three and two categories respectively, B: urban, large rural city/town and small isolated rural town and C: urban and rural [99].

Rural-Urban Disparities in Colon Cancer Care

Rural patients tend to receive lower quality of and/or access to health care than urban patients. Evidence of this disparity is found in studies showing that rural patients present with more advanced CRC stages than urban patients [10, 100]. The literature on rural-urban disparities in colon cancer care is sparse. A study of colorectal and lung cancer patients in Scotland assessed the effect of deprivation and rural residence on treatment [11]. This study found that rural-urban residence (defined by distance to treatment center in kilometers) was associated with the receipt of radiotherapy among CRC patients. Patients living further away were less likely to receive treatment than those living closer to the treatment center. In a study conducted in France, Launoy et al, found that rural residence was associated with treatment at specialized centers, advanced stage at diagnosis and poor prognosis for CRC [9]. Investigators found that the observed rural-urban difference is primarily explained by the distance between patients' residence and treatment centers. A U.S. study assessed CRC treatment among rural residents in North and South Carolina with no urban comparison. This study found that adjuvant therapy was not frequently given to rural patients with colorectal cancer [101].

Black-White Racial Disparity in Receipt of Colorectal Cancer (CRC) Adjuvant Therapy

Racial disparities in health care -- "racial or ethnic differences in the quality of healthcare that are not due to access-related factors or clinical needs, preferences, and appropriateness of intervention"--- Institute of Medicine [102]

Many studies have shown that adjuvant chemotherapy is less likely to be given to black colon cancer patients than white patients [12, 13, 103-106]. The cause of this disparity remains unclear. Considering the above definition of racial disparity, the following review will discuss factors in addition to race that were considered in each study.

Surveillance Epidemiology End-Results (SEER) and Medicare Populations

Many of the studies in the SEER-Medicare population adjusted for several potential confounders and several previously unrecognized covariates, such as area-based SES measures, post-operative morbidity, rural versus urban residence, physician and hospital characteristics, as well as certain individual measures of SES. Racial disparities persisted in this population after controlling for potential confounders.

Sundararajan et al used SEER-Medicare data from patients diagnosed in 1992 to 1996 to assess variations in adjuvant chemotherapy among stage III colon cancer patients. Among these patients, chemotherapy was given to 51% of whites and 41% of blacks. After adjusting for covariates and potential confounders such as, education, number of lymph nodes involved at diagnosis, residence in urban setting, and SEER site, the racial disparity remained. The adjusted odds ratio (OR) and 95% confidence interval (CI) for receipt of chemotherapy for blacks versus whites was OR=0.46 (0.36-0.59) [12]. This indicated that black stage III colon cancer patients are 44% less likely to receive adjuvant chemotherapy than their white counterparts.

Gross et al assessed trends in racial disparities in cancer therapy from 1992 to 2002 by using linked SEER-Medicare data [19]. Analyses controlled for year, patient demographic factors, census tract based median household income, state buy-in of Medicare coverage (a measure of

poverty), and physician access before cancer diagnosis. For stage III colon cancer, 52.1% of black patients and 64.1% of white patients received adjuvant therapy, OR =0.76 (0.68-0.83).

The overall rates of adjuvant therapy increased over the years, but the racial disparity in care did not change. In 1992-1994, the adjusted percentages of stage III colon cancer patients that received adjuvant chemotherapy were 46.2% for blacks and 61.9% for whites. The corresponding adjusted percentages in 2000-2002 were 57.6% and 72.0% for whites and blacks, respectively.

Baldwin et al conducted one of few studies that specifically set out to explain racial differences in the receipt of treatment for colon cancer patients [13]. Data were used from the linked SEER-Medicare database for patients diagnosed with stage III colon cancer during the years 1992 to 1996. Patient- and provider-related factors including length of hospital stay following resection and readmission to an acute care hospital within six weeks of resection, RUCA codes, census tract-based median income, census tract based race-specific percentage of patients age 25 years or older with a high school education, physician characteristics, and hospital characteristics included in the models and assessed for their role in explaining the racial disparity. The black-white disparity in chemotherapy decreased with age. There was no statistically significant difference between racial groups with respect to receipt of chemotherapy for patients aged 80 years and over. The largest disparity was found among patients age 66 to 70 years, which is the youngest group of patients in the analysis with an OR of 0.88 (0.77-0.98) in the full model. The associations between race and treatment initially found among those aged 71 to 75 and those aged 76 to 80 appeared to be confounded by other demographic characteristics. Other studies have shown that older patients are less likely to receive adjuvant therapy regardless of race [94, 107, 108]. A study examining the affect of age on chemotherapy use showed not only a decrease in the chemotherapy rate as age increases, but also a decrease in the differences in chemotherapy rates among blacks and whites as age increases [94].

In contrast to previously discussed studies, White et al found a racial disparity in the receipt of standard therapy that was no longer evident after adjustment for confounders. The SEER-Medicare data were used for patients diagnosed in 1991 to 2002 with stage I, II, or III CRC [103]. Patient factors including number of positive lymph nodes removed, census tract based SES, urban/rural residence and SEER site were included in the multivariate model. Standard therapy was received by 73.7% of blacks and 77% of whites, $p < 0.001$. Radiation therapy was received by 15.9% of blacks and 17% of whites, $p=0.043$. Chemotherapy was received by 25.7% of blacks and 29.3% of whites, $p<0.001$. The racial disparity seen in the receipt of standard therapy [OR=0.84 (0.78-0.90)] was no longer statistically significant after tumor stage, grade, number of positive lymph nodes, and comorbidities age, marital status, sex, and SES were included in the model [OR= 0.94 (0.87-1.02)].

One potential explanation for the differences in the findings reported by Sundararajan and White is Sundararajan only focused on Stage III disease while White analyzed receipt of stage specific standard care collectively among stage I-III colon cancer patients and stage II and III rectal cancer patients. A racial disparity found in stage III colon cancer patients may have been washed out by a lack of disparity in standard therapy for stage II or I colon cancer patients. This explanation is supported by one previous study using SEER data that found no disparities in receipt of treatment for stage II colon cancer patients [109]. Another potential explanation for the discrepancy in the two studies may be the different time periods examined. Racial disparities present in the early half of the 1990s as reported in Sundararajan's study may have narrowed by the end of the 1990s, although another recent study by Gross et al did not find this to be true [19].

Cancer Registry Only Populations

Cases obtained from the cancer registries differ from the SEER-Medicare population in that chemotherapy data are not augmented by Medicare claims. Studies have shown that use of only cancer registry data to assess chemotherapy may be inappropriate. Also, these studies

typically include colon cancer patients younger than age 65, who may face differing barriers to chemotherapy, since they are perceived to better handle the treatment compared to older patients [110-112].

Potosky et al. used SEER data for CRC patients age 20 or older diagnosed from 1987 through 1995 and contacted the treating physicians to verify the use of chemotherapy and radiation for each patient [113]. Receipt of adjuvant therapy in this study was defined as treatment offered, recommended, or administered. After controlling for comorbid illnesses and census tract-based race-specific income 58% of white and 47% of black patients (adjusted percentages) with stage III colon or stage II/III rectal cancer received standard adjuvant therapy; OR=1.75 (1.09-2.83). The difference in receipt of standard therapy between white and black patients was less pronounced for those aged <55 years than those aged 65 to 80 years. This finding contrasts with the results reported by Baldwin et al who found that within the Medicare (≥ age 65) population, the youngest patients had larger racial disparity in receipt of adjuvant therapy than older patients and as age increased the disparity narrowed [13].

Roetzheim et al used data from the state of Florida cancer registry to assess racial disparities in CRC care among patients diagnosed in 1994 [5]. Investigators used hospital discharge abstract data and cancer registry data on first course of treatment to assess patient receipt of radiation and chemotherapy. No racial disparities in the receipt of adjuvant therapy were found in crude or adjusted analyses (controlling for health insurance type, census-derived measures of income and education, and rural/urban residence). Receipt of radiation and chemotherapy may have been underestimated since these treatments are typically administered on an outpatient basis and may have not been captured in this study.

McGory et al assessed the association between race/ethnicity and the underuse of appropriate adjuvant therapy for CRC among patients in the California Cancer Registry who were diagnosed with stage III colon or stage II/III rectal cancer from 1994 to 2001.[93] Investigators

adjusted for patient demographic factors including type of insurance, year of diagnosis and census tract based SES measure (percentage of person living below the 200 percent poverty threshold in the patient's census tract). For stage III colon cancer, there was no statistically significant association between race and receipt of chemotherapy; the OR for blacks versus whites was 1.11 (0.88-1.42).

Only one study used hospital based cancer registry data to assess racial disparity in CRC adjuvant therapy. Jessup et al assessed trends in adjuvant chemotherapy use from 1990 to 2002 using the National Cancer Data Base [111]. They found that a lower percentage of blacks than whites received chemotherapy in years 1990 to 1991 and in 1995 to 1996, $p<0.001$, but not in 2001 to 2002; however, no analyses for this outcome controlled for potential confounders.

Veterans Affairs and Military Medical Center Population

One study utilized Veteran's Affairs or military medical center data to assess black-white racial disparities in adjuvant therapy of CRC patients. Among military populations which are considered to have "equal access" to care, the study found no evidence of black-white racial disparities. Using health care data from a national database of Veterans Affairs Medical Centers and outpatient clinic files, Dominitz et al found no racial disparities in colorectal cancer treatment [104]. Patients were black and white male veterans who were discharged with a diagnosis of CRC in the year 1989. Analyses controlled for patient demographic factors including eligibility of hospitalization in the VA medical center and geographic location of the hospital. Twenty-three percent of blacks and 23% of whites received chemotherapy, adjusted OR (95% CI) for blacks versus whites was 0.99 (0.78-1.24). In 1989, the year analyzed in this study, adjuvant therapy was not yet established as the standard of care for stage III colon patients and stage II/III rectal cancer patients. It was not until 1990 with the release of the National Institutes of Health Consensus Conference recommendations on adjuvant therapy that adjuvant chemotherapy for stage III colon cancer patients and combined adjuvant chemotherapy and radiation for stage II and III rectal

cancer patients were recommended as standard of care [114]. It is difficult to interpret the lack of a racial disparity found in this population, since a disparity in guideline recommended therapy was not assessed.

Summary of findings

Studies assessing racial disparities in colon cancer adjuvant therapy in the U.S. are inconsistent. The studies that found evidence of racial disparities in therapy tended to use larger more nationally representative samples of older population subgroups; while those finding no evidence in support of racial disparities were smaller, included younger cases or were based on data from institutions considered to have "equal-access" to care. It should be noted that the majority of studies included in this review assessed racial disparities among patients diagnosed with CRC during the 1990s. For this reason, studies assessing disparities in the more recent years are necessary to provide insight into the current pattern of racial disparities in CRC therapy.

Clinical and Non-Clinical Determinants of Adjuvant Therapy for Colon Cancer

Several factors have been found to independently predict the receipt of adjuvant therapy among colon cancer patients. These factors will be briefly examined with the purpose of selecting covariates for multivariate analyses of rural-urban and racial disparities in the proposed dissertation.

Patient characteristics

In addition to race (reviewed in the previous section), other patient-related factors shown to be associated with the receipt of adjuvant chemotherapy include age, gender, marital status, and co-morbidities. Increasing age predicts a decreased likelihood of receipt of adjuvant therapy as reported in multiple studies [5, 6, 12, 93, 94, 101, 104, 108, 113, 115-120]. Increased number of comorbid conditions and the presence of medical contraindications to adjuvant therapy are also associated with a decreased likelihood of adjuvant care [5, 12, 93, 94, 104, 108, 113, 116-118, 120]. Women have been

reported to be less likely to receive chemotherapy than males in some studies [93, 94]; however other studies have found an association in the opposite direction [5, 113]. It has been consistently reported that married patients are more likely to receive chemotherapy than their single, widowed or divorced counterparts [5, 113, 116, 120]. Other studies have found lower SES to predict a lower likelihood of receipt of chemotherapy among CRC patients [5, 6, 93, 94].

Tumor related factors

Stage of disease predicts receipt of adjuvant therapy [5, 6, 108, 113, 117, 120]. Specifically, the presence of distant metastases has been found to increase the likelihood of receipt of chemotherapy [104]. The greater the number of positive lymph nodes was also associated with the higher the likelihood of receipt of chemotherapy [12, 94, 113, 116, 118]. The histologic grade of the tumor is associated with the use of adjuvant therapy; patients with less differentiated tumors are more likely to receive adjuvant therapy than those with well differentiated tumors [113].

Insurance- and provider-related factors

Patients treated at hospitals with cancer programs approved by the Commission on Cancer of the American College of Surgeons (COC hospitals) are more likely to receive adjuvant therapy than patients attending non-COC hospitals [115]. Patients at teaching hospitals receive lower rates of adjuvant therapy than patients attending non-teaching hospitals [108]. Those with private health insurance receive better access to and better quality of health care when compared to those on government insurance and the uninsured [6]. Nevertheless, some studies have shown a decreased likelihood of receipt of adjuvant therapy among those with private insurance when compared to those with Medicare [93]. Among CRC patients without Medicare, those with private HMO insurance are less likely than those with private fee-for-service insurance to receive adjuvant therapy [5]. CRC patients with Medicare are more likely to receive adjuvant therapy than Medicaid recipients [108].

Time-trends and geographic differences

Use of adjuvant therapy has been found to increase from the late 1980s to the 1990s following recommendations released by the NIH consensus conference and continued to increase through the early 2000s [12, 93, 94, 113, 116]. Regional location has been shown to be associated with chemotherapy use [104, 113, 120]. Treatment rates vary by region of the U.S. , state, county and other geographic locations. Studies have shown that urban residence increases the likelihood of receipt of chemotherapy when compared to nonurban residence [5].

Physician Characteristics, Residential Characteristics and Patient Demographics

Physician Characteristics and Community Socioeconomic Status (SES)

A study based in New York City compared physician characteristics in a relatively wealthy community to those in a lower SES community [121]. This study showed that physicians in the lower SES community were more likely to be salaried, graduate from a foreign medical school, be without hospital admitting privileges, have a large percentage of minority patients, and have a lower number of years in practice than physicians in the upper SES community.

Physician Practices and Community Socioeconomic Status

Community level factors and conditions are seldom examined for their association with variations in cancer care and for their association with physician factors. In a previously discussed study in New York City, investigators found that physician practices in the lower SES community were more likely to receive patients with Medicaid or uninsured and had more black and Latino patients and a higher mean number of patient contacts per week than practices in the upper SES community [121]. Gastroenterology practices in the upper SES community were more likely to perform flexible sigmoidscopies and colonoscopies as CRC screening tests than corresponding practices in the lower SES community. Similar findings were reported for other cancer sites. For example, Nattinger et al found that breast cancer patients living in more affluent zip codes had an increased likelihood of having a more experienced surgeon [122].

Physician Characteristics and Rural-Urban Residence

Thompson et al characterized general surgeons based on the U.S. rural-urban environments in which they worked [123]. It was shown that the number of general surgeons per 100,000 varied by location with 6.53 in urban areas, 7.71 in large rural areas, and 4.67 in small isolated rural areas. Compared to urban areas, small isolated rural areas were more likely to have male physicians (92.7% versus 88.3%), surgeons age 50 + (51.6% versus 42.1%), surgeons who were international medical school graduates (25.2% versus 20.1%) and less likely to have surgeons who were not board certified in general surgery (2.3% versus 5.3%). Large rural areas compared to urban areas were more likely to have male surgeons, surgeons age 50 +, surgeons who were U.S. or Canadian medical school graduates, and surgeons who were board certified in general surgery. Differences were also seen among physicians in large rural and small isolated rural areas.

Physician Characteristics and Race of Cancer Patient

Baldwin et al found that oncologist characteristics differed for black and white colon cancer patients [13]. Compared to whites, blacks were less likely to have an oncologist who was board certified in internal medicine and an oncologist with ≥ 5 CRC chemotherapy consultations in a year. Blacks were more likely than whites to have black or Asian/Pacific Islander oncologists than whites. Diehr et al performed a study of a community hospital and showed that physicians of black and white breast cancer patients differed in specialty and years of practice [124]. Black patients were less likely to have a board certified surgeon (78.8% versus 83.3%) and a board certified radiation oncologist (10.6% versus 12.6%) but more likely to have a medical oncologist who was board certified (36.9% and 30.6%) compared to white patients. Black patients were more likely to have a surgeon with 1-10 years (20.8% versus 12.7%) and 11-20 years (32.0% versus 30.4%) in practice than white patients. White patients were more likely to have a surgeon with 21-30 years (28.6% versus 22.4%) and 31-40 years (28.4% versus 24.8%) in

practice than black patients. Nattinger et al found that white breast cancer patients were more likely than black patients to have a high volume surgeon [122].

Physician Characteristics, Cancer Treatment and Outcomes

Receipt of guideline recommended treatment among cancer patients was found to be associated with physician characteristics. Using SEER-Medicare data for breast cancer patients diagnosed between 1991 and 2002, Hershman et al showed that women who received chemotherapy compared to those who did not were more likely to have an oncologist who graduated after 1975 and who was employed in a private practice and less likely to have an oncologist who was trained in the U.S. [125]. Among patients at low risk of breast cancer recurrence (stage II), oncologist case volume during the study period was an additional physician characteristic associated with receipt of adjuvant chemotherapy [125]. Surgeon characteristics, including case volume, location of training (U.S. versus foreign), medical school affiliation, gender and years since medical graduation influenced patient receipt of adjuvant radiotherapy, breast conserving surgery and care adherent to guideline recommendations among breast cancer patients [26, 27, 126].

Physician characteristics have also been shown to affect outcomes, such as mortality and morbidity following cancer treatment. Mortality and morbidity following colorectal surgery was reduced when patients' surgeon was board certified by the American Board of Surgeons and mortality decreased when years of experience since board certification increased [127]. Among colorectal cancer patients, non-colorectal trained surgeons and surgeons with low case volumes were associated with higher local cancer recurrence rates following surgery [128]. Mortality rates among colorectal cancer patients were decreased as surgeon procedure volume increased [129, 130]. Among lung cancer patients receiving surgery mortality rates were lower for those receiving

surgery from a specialist (thoracic surgeon) compared to a general surgeon after adjusting for case-mix [131, 132].

Hospital Characteristics, Patient Characteristics, Cancer Care and Outcomes

Hospital characteristics have been shown to influence cancer care received by patients as well as outcomes following cancer treatment. Hospital characteristics may also be associated with patient demographics as well. Zhang et al found that among patients receiving surgery for colorectal cancer, black patients and patients living in less affluent communities were more likely than whites and those living in more affluent communities, respectively, to receive surgery at hospitals with above-average mortality rates. Also, patients living in less affluent communities were less likely than those living in more affluent communities to receive surgery at a high-volume hospital [133]. Based on another study, type of facility where care is received is associated with outcomes following cancer treatment. Among rectal cancer patients, local recurrence and mortality rates after radiotherapy treatment was lower for patients receiving care at university hospitals compared to community hospitals [134]. It has also been shown that hospital accreditations and recognitions are associated with patient receipt of optimal cancer treatment and outcomes. Receipt of care at a hospital accredited by the Commission on Cancer of the American College of Surgeons (ACOS) was found to increase the likelihood of receipt of chemotherapy among ovarian cancer patients and optimal surgery type (sphincter sparing surgery) among rectal cancer patients [135, 136]. Patients receiving surgery at National Cancer Institute (NCI) designated facilities had lower post-surgery mortality rates than those receiving care at control (non-designated) hospitals [137].

Quality of Adjuvant Chemotherapy Data Reported by Cancer Registries Medicare

There is a need for the validation of chemotherapy data in the linked tumor registry-Medicare data file. Information on chemotherapy is difficult to obtain owing to the treatment

delivery in outpatient settings. This challenge may result in inaccurate or incomplete chemotherapy information reported to tumor registries. This chemotherapy data may be enhanced by supplementing the data with Medicare claims; however the quality of the linked tumor registry-Medicare data has not been assessed in recent years.

Cress et al augmented registry treatment information by surveying physicians and reviewing medical office records of patients in Northern California diagnosed during 1996 to 1997. The authors used this information to assess the completeness of the Northern California regional cancer registry data on chemotherapy and radiation among CRC patients [29]. The original registry data had chemotherapy information for 82% of the patients. Completeness of chemotherapy reporting in the cancer registry varied by patient and hospital characteristics. Complete chemotherapy information was more likely to be found for younger patients compared to older patients; cases of stage II or III rectal cancer compared to colon cancer cases; in HMO hospitals compared to non-HMO non-ACOS (hospitals with tumor registries not accredited by the American College of Surgeons Commission on Cancer) hospitals; and, in non-teaching hospitals compared to teaching hospitals.

McClish et al compared treatment data from the Virginia Cancer Registry with Medicare claims (MEDPAR file) data for patients diagnosed with colorectal, breast, prostate, or lung cancer during the years 1986-1989 [28]. In this study, CRC patients receiving only chemotherapy or radiation as reported in the Virginia Cancer Registry, were less likely to be identified in Medicare data than patients who were reported as not receiving any treatment [OR=0.43, 95% CI (0.32-0.59)]. The same was true for breast, prostate and lung cancer patients; however, the estimate was not statistically significant for lung cancer patients.

Warren et al assessed the ability of SEER (Surveillance, Epidemiology and End Results program) linked with Medicare claims data to identify chemotherapy use [30]. Chemotherapy data captured in SEER-Medicare was compared to data from the Patterns of Care (POC) studies,

which collects more detailed treatment data than SEER. For colon cancer, there was an observed agreement of 88% between Medicare and POC in reporting of chemotherapy use. The adjusted agreement (kappa statistic) was 0.73 and the sensitivity of Medicare in capturing chemotherapy data reported in POC was 90%. This reported kappa statistic denotes substantial agreement beyond chance [138]. The sensitivity was 88% for breast cancer, 95% for rectal cancer, and 93% for ovarian cancer. The kappa statistic for chemotherapy use for these cancers ranged from 0.81 to 0.88 (almost perfect agreement).

In two studies by Du et al, medical charts of patients diagnosed and treated in New Mexico were reviewed and used as the gold standard of treatment reporting. The first study assessed the completeness of Medicare claims for chemotherapy among breast cancer patients [139]. Among patients reported to have received chemotherapy in the Medicare data, treatment receipt was confirmed by a medical records in only 60% of cases. Of those reported to not have received chemotherapy in Medicare, 99% were confirmed in medical chart reviews. The observed agreement between Medicare and medical chart reviews was 94% with a kappa of 0.69 (95% CI: 0.63-0.76). Du et al conducted another study comparing chemotherapy information reported in the New Mexico Tumor Registry to the data from medical record reviews [140]. The agreement between the two sources of data was 96% with a kappa of 0.72 (95% CI: 0.64-0.79) and a sensitivity of 70.7%. Kappa statistics differed by patient age, source of medical chart, tumor stage, year of diagnosis, and vital status at time of review. Other studies support the finding that outpatient treatment data, such as chemotherapy, for breast cancer patients are underreported in tumor registries [141, 142].

This evidence indicates that the quality of cancer treatment data reporting, especially CRC, in Medicare and in cancer registries is variable. The evidence also suggests that more up–to-date analyses of the completeness and accuracy of cancer registry-Medicare linked data are warranted. The latest analysis in this review assessed data from 1996 to 1997. Studies have shown an

increase in receipt of chemotherapy and radiation from the 1990s through the 2000s [19, 143, 144]. This increase in treatment receipt may also affect the quality of treatment reporting.

Chapter 3: Source Population

The State of Georgia provides the source population for this dissertation. Georgia population estimates and distributions of the exposures of interest are discussed below. These estimates are based on the data from the 2000 U.S. Census and from the later U.S. Census Current Population Surveys (CPS).

Residential Segregation

Beginning in the 1890s and ending with the Voting Rights Act of 1965, Georgia and other southern states issued legislation that mandated racial segregation of public facilities under what was termed Jim Crow laws [145]. Under Jim Crow, blacks experienced discrimination in housing and employment that resulted in residential racial segregation. The Civil Rights Act of 1968 ended legal discrimination in housing sales and rentals. Although de jure segregation was outlawed in the 1960s, many Georgians still reside in racially segregated areas. A recent examination of the extent of racial segregation in U.S. cities showed that Georgia has cities ranking amongst the most and the least racially segregated [90]. Employing the dissimilarity index, Atlanta, Georgia ranked fourth among U.S. cities with the highest dissimilarity indices, D=0.83, meaning that 83% of blacks must leave Atlanta in order to equalize the distribution of whites and blacks in Atlanta. Hinesville, Georgia ranked 12th among U.S. cities with the lowest dissimilarity indices, D=0.17. Levels of economic segregation in Georgia have not been assessed.

Rural-Urban Residence

According to the USDA Economic Research Service (ERS), the rural population of Georgia (defined by RUCA codes calculated from the 2000 U.S. Census) is two million, which accounts for 24.7% of the population of the state [146]. In comparison, 20.5% of the U.S. population lives in rural areas. Eighteen percent of the Georgian rural population lives in

households below the poverty line versus 14.8% of the U.S rural population. The percent of persons age 65 or greater (age of our Medicare study population) living in rural areas is 12.7% which is lower than the 14.8% estimate for the U.S. rural population,

Racial Distribution

The U.S. Census reports in 2008 that 30.0 % of Georgians are black and 65.4 % are white [147]. In comparison blacks and whites constitute 12.8 % and 79.8 % of the U.S. population, respectively. Using data from the 2008 and 2009 U.S. Census Bureau's Current Population Survey, the Kaiser Family Foundation reported that the poverty rate is 31.9 % among black Georgians and 11.5 % among white Georgians [148]. These percentages compare to the corresponding estimates of 33.2 % and 12.3 % for U.S. blacks and whites, respectively.

Chapter 4: Overview of Data Sources

Because the following three chapters are stand-alone manuscripts the relevant methods for each study are reviewed in each chapter. For clarity the data sources are summarized below.

Data Sources:

Five data sources are used in this dissertation: (1) the Georgia Cancer Registry (GCR)-Medicare linked data file, including the Surveillance and Epidemiology End-Results (SEER)-Medicare Hospital file, (2) the Medicare Physician Identification and Eligibility Registry (MPIER), (3) the U.S. Census Summary Files, (4) the Rural Urban Commuting Area (RUCA) file from the United States Department of Agriculture (USDA) Economic Research Service (ERS) and (5) the Southwest Georgia Cancer Care Study (SWGCCS).

Data from the linked GCR-Medicare file includes tumor characteristics; first course of treatment including surgery, chemotherapy and radiation therapy, as well as, patients' demographic information. The primary sources of GCR data are medical records from hospitals with additional cases obtained from pathologists, oncologists, and radiotherapists. The Medicare claims included in the linked GCR-Medicare file report diagnoses and procedures provided during hospitalization. Carrier claims also included in this linked file contain all physician and supplier bills for medical procedures.

In addition to patient-, treatment- and disease-related variables, the Medicare claims also contains the unique physician identification numbers (UPINs) which can be used to determine physician characteristics. Each doctor's UPIN is used to link the GCR-Medicare data to the MPIER file. The MPIER file is maintained by the Centers for Medicare and Medicaid Services (CMS) a US federal agency which administers Medicare, Medicaid, and the Children's Health Insurance Program. Information for the MPIER file is provided to CMS quarterly from Transamerica Occidental Life Insurance Company, which maintains the national registry of

physicians [149]. This file contains information on a variety of physician characteristics including specialty, board certification, year of graduation, and location (country) of medical school.

The third data element is the 2000 U.S. Census Summary Files which was used to obtain census block- and census tract-level information on community racial and income characteristics. This information provides the metrics used to calculate patient residential racial and economic segregation indices for each patient's residential neighborhood.

Data from the United States Department of Agriculture (USDA) Economic Research Service (ERS) is used to classify rural-urban residence in this dissertation. The USDA, ERS conducts a research program to inform public and private decision-making on economic and policy issues involving food, farming, natural resources, and rural development. Rural Urban Commuting Area (RUCA) codes are developed and provided by the USDA Economic Research Service. These codes are used to categorize patient residential census tracts into rural urban classifications.

The SWGCCS data contains detailed treatment information for patients newly diagnosed with various cancers (including cancers of the colon and rectum) during the years 2001-2003 and residing in Southwest Georgia, a large 33-county area with the population of approximately 700,000 [150]. All treatment data for SWGCCS were collected by trained local abstractors and included dates, doses and drugs delivered as part of the chemotherapy protocol as well as information on surgery and radiation [150]. Patient factors included age, race, gender, insurance status, rural-urban residence and co-morbid conditions. Tumor characteristics included cancer stage and grade.

Chapter 5: Is the level of training and/or experience of colon cancer surgeons associated with characteristics of their patient population?

Abstract:

Background: Treatment outcomes in colon cancer patients have been shown to be related to their surgeons' level of training and/or experience. Yet, little is known about the relation between the characteristics of physicians that perform colon cancer surgery and the social and demographic profile of their patients.

Methods: This study used linked data from the 2000 U.S. Census Summary Files, the Georgia Cancer Registry and Medicare pertaining to colon cancer patients diagnosed during the years 2001-2005. Training and experience measures for each surgeon were combined into a single summary score. Multivariate logistic regression analysis assessed the association between surgeons' scores and the individual and area-based characteristics of their patients. The area-based characteristics of primary interest included measures of racial and income segregation.

Findings: After accounting for social and demographic confounding factors, surgeons' with suboptimal training and experience (summary score ≤ 6 versus >6) were more likely to have high percentages of black patients. Conversely, surgeons with high levels of training and experience (summary score ≥ 9 versus <9) were more likely to care for colon cancer patient populations that included low percentage of blacks and those residing in less racially segregated census tracts.

Conclusion: Race and residential characteristics of patients are associated with surgeons' training and experience. The findings from this study indicate that non-clinical patient factors may affect the quality of colon cancer care among Medicare patients.

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy in the U.S. [1]. An estimated 90-92% of those with colon cancer receive surgery [151]. Access to and quality of surgical care and outcomes following surgery differ by racial and residential characteristics [8, 16, 152, 153]. Studies have shown that surgeon quality as measured by level of training and experience predicts multiple patient outcomes, such as mortality, post-surgery morbidity, cancer recurrence and delivery of optimal treatment [27, 126-128, 130, 134, 154]. By contrast, little is known about the association between racial and residential characteristics of a surgeon's patient population and characteristics of the surgeon. Factors such as patient race and residential characteristics have been found to play a part in access to care [8, 16, 92], but few studies have assessed the role of these factors in access to quality surgeons [6]. The aim of this study is to compare surgeons with optimal and sub-optimal levels of training and/or experience with respect to their patients' demographic and socioeconomic characteristics.

We hypothesize that sub-optimally trained and experienced surgeons will have higher percentages of black and urban patients as well as patients who reside in segregated areas (counties and census tracts). In addition, we hypothesize that the association between surgeons' medical training and experience and the percentage of black patients in their patient population may be confounded by patients' county and census tract residential segregation measures.

Methods

Data Sources:

Five data sources were used in this analysis: the Georgia Cancer Registry (GCR)-Medicare linked data file, including the SEER-Medicare Hospital file, the Medicare Physician Identification and Eligibility Registry (MPIER), the Georgia Composite Medical Board, the U.S. Census Summary Files, and the Rural Urban Commuting Area (RUCA) file from the United

States Department of Agriculture (USDA) Economic Research Service (ERS). The GCR-Medicare linked file was used to identify the cohort of surgically treated stage I-III colon cancer patients diagnosed between January 1, 2001 and December 31, 2005. Data from this file included patients' demographic information, tumor characteristics, and first course of treatment including surgery, chemotherapy and radiation therapy. The primary sources of GCR data were medical records from hospitals with additional information obtained from pathologists, oncologists, and radiotherapists. The Medicare claims reported diagnoses and procedures provided during hospitalization (MEDPAR-Medicare Provider Analysis and Review) along with physician and supplier claims for medical procedures (NCH-National Claims History).

In addition to patient-, treatment- and disease-related variables, the Medicare claims also contain the unique physician identification numbers (UPINs) which can be used to determine physician characteristics. Each doctor's UPIN was used to link the GCR-Medicare data to the MPIER file. The MPIER file is maintained by the Centers for Medicare and Medicaid Services (CMS), a US federal agency which administers Medicare**,** Medicaid and the Children's Health Insurance Program. Information for the MPIER file is provided to CMS quarterly from Transamerica Occidental Life Insurance Company, which maintains the national registry of physicians [149]. This file contains information on a variety of physician characteristics including specialty, board certification, year of graduation, and location (country) of medical school. These data were supplemented with the surgeon data from the Georgia Composite Medical Board (GCMB). The GCMB provides physician profile information that include board certification, specialty and location of medical school.

The third data source was the 2000 U.S. Census Summary Files that were used to obtain census tract-level information on community racial and income characteristics. These data were used to calculate racial and income measures and segregation indices for each patient's residential area (county and census-tract). Lastly, Rural Urban Commuting Area (RUCA) codes from the

United States Department of Agriculture (USDA) Economic Research Service (ERS) were used. These codes categorized patient residence (census tracts) into rural urban classifications.

Inclusion Criteria:

This study included surgeon information for all non-Hispanic white and black patients identified in the GCR-Medicare database who were age 66 years and older and diagnosed as having stage I, II or III colon cancer during the years 2001-2005. Those with lymphomas and sarcomas of the large intestine were excluded because these cancers are staged differently. Only patients with documented cancer-directed surgery (defined as colon resection or bypass based on International Classification of Diseases 9th Edition (ICD-9) procedure codes and Healthcare Common Procedure Coding System (HCPCS**)** codes) were considered in these analyses. A list of the codes used for this study is provided in Appendix A.

Cancer surgeon identification information was not documented in the GCR; therefore Medicare claims were searched to obtain this information and supplement the GCR data. For each eligible patient reported as having colon cancer surgery in the GCR (see appendix), Medicare claims within 6 months after the date of diagnosis were searched to identify surgical interventions that would ordinarily be performed as part of curative colon cancer treatment. This time period was chosen to ensure the treatment documented in the claims data pertained to the cancer of interest and not for a subsequent cancer. To account for inaccuracies in the registry's date of diagnosis, colon cancer surgeries reported up to three months prior to the reported date of colon cancer diagnosis from the registry were included if no post-diagnosis colon cancer surgery claims were found.

Patients were excluded if they did not have continuous coverage from both Medicare Part A and B for a year prior to colon cancer diagnosis and coverage up to six months after colon cancer diagnosis or until death, whichever occurred first. Coverage for at least a year prior to diagnosis ensures there is sufficient Medicare claims history to assess patient co-morbid illnesses

(which may affect receipt of cancer treatment) and to ensure patient had access to care prior to cancer diagnosis. Coverage up to six months after diagnosis ensures that there are adequate Medicare claims to assess care received following diagnosis. Patients were also excluded from the analysis if they were enrolled in a Medicare Health Maintenance Organization (HMO). Patients not continuously enrolled in Medicare Part A and B were excluded because claims may not be available to document surgical procedures and the surgeons providing those procedures. Members of Medicare Health Maintenance Organizations (HMO) were excluded because they do not typically bill Medicare for services, so their treatment information may also be missing within the claims data.

After applying the above inclusion and exclusion criteria, a total of 4,106 colon cancer patients were eligible for the analysis. Of these patients, 171were excluded for the following reasons: 1: Performing provider (Unique Physician Identification Number (UPIN)) was missing, 2: Date of surgery in NCH claims did not fall within 1 week of the date of surgery in MEDPAR claim or 3: Surgery claim reported in NCH claims did not match the pre-determined list of colon cancer surgery codes. Additionally, 14 patients had one or more colon or rectal cancers staged IV or unknown within 6 months of the date of the colon cancer diagnosis of interest (treatment among these patients is less likely to model typical care received among stage I-III colon cancer patients) ; 78 additional patients were excluded because they received care outside of the state of Georgia; 6 patients had missing census tract codes; 2 had missing comorbid illness information (which is necessary to assess patient case-mix among surgeons) and 44 patients had concurrent rectal cancer diagnosed at time of colon cancer diagnosis (surgery for rectal cancer will coincide with colon cancer surgery). The final patient population for this analysis was 3,964 colon cancer patients treated by 525 surgeons in the state of Georgia.

Dependent variables:

The dependent variable in these analyses was the surgeon's training and experience score. This score is the sum of ranked characteristics that serve as a marker of physician training or experience. A characteristic with a rank of 1 indicates sub-optimal training or experience; a rank of 2 indicates moderate level of training or experience; and a rank of 3 indicates optimal training or experience. The characteristics and their ranked classifications for these analyses included the number of surgeon's board certifications: none (1 point), one (2 points) and two (3 points); subspecialty training: general surgeon (1 point), colorectal surgeon (2 points), and colorectal surgical oncologist (3 points); location of surgeon's medical school: foreign (1 point), unknown (2 points), and U.S. (3 points); and surgeon's colon cancer case volume tertile during study period 2001-2005 (based on the total number of claims for colon cancer surgery among patients in this study during study period 2001-2005): first through third tertile assigned 1-3 points, respectively. Each of the score components has been linked to patient outcomes and/or delivery of optimal treatment in earlier studies [7, 9, 10-13,16, 17]. After the points assigned for each characteristic are summed, a summary score is obtained (possible range 4-12) with higher scores indicating increased quality of a surgeon's training and experience.

Main Independent Variables:

The independent variables in these analyses included patient level characteristics aggregated to the surgeon level. The main categorical independent variables of interest were calculated as a percent (%). These included % non-Hispanic blacks and % urban residents among colon cancer patients that underwent surgery performed by a given surgeon. The main continuous independent variables of interest were area-based measures of racial and income segregation at both the county and the census tract level. These were expressed as the median value for each surgeon's patient population. County level measures serve as predictors of the quality of and access to community health care resources [5, 6] while census tract level measures serve as predictors of patient and neighborhood economic and social resources [155].

Prior to determining the median segregation indices for each surgeon's patient population (i.e., surgeon-level indices), we calculated residential segregation indices for each individual patient (i.e., patient-level indices) as follows: Each patient's home address was geo-coded to determine the location of his or her residential census block group, census tract and county.

Using this residential information, four segregation indices were calculated separately for each patient's census tract and county (8 total indices): census tract level (1) racial dissimilarity index, (2) income dissimilarity index (3) racial isolation index and (4) income isolation index and county level (1) racial dissimilarity index, (2) income dissimilarity index, (3) racial isolation index and (4) income isolation index. The racial segregation measures assess black-white segregation. The income segregation measures assess segregation of those living below the federal poverty line from those living at or above the federal poverty line. These measures were calculated using data from the 2000 U.S. Census.

The dissimilarity index (D) measures the extent to which groups are segregated from each other [89, 90]. It represents the percent of group X members that would have to change their area of residence to achieve an even distribution of group X in relation to group Y residents within each sub-areal unit within the area being examined (e.g. sub-areal unit is census tract and area is county) [89]. This index ranges from 0 to 1, where D=1 indicates complete segregation (the two groups live in completely different sub-areal units) and D=0 means complete integration (the two groups are distributed exactly the same way across each of the sub-areal units). When assessing black-white segregation of a given county, the D value of 0.66 indicates that 66 percent of blacks must move to a different census tract (sub-areal unit) so that the distribution of blacks in relation to whites will be equal across census tracts within the county. Values greater than 0.6 are considered a level of high segregation [21]. This index is invariant to relative size of groups.

Dissimilarity index calculation:

$$D = \left[\frac{1}{2}\sum_{i=1}^{N} \left|\frac{x_i}{X} - \frac{y_i}{Y}\right|\right] * 100$$

where,

x_i = the black population (when measuring black-white racial segregation) or those living below the federal poverty line (when measuring income segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total population living below the federal poverty line when measuring income segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

y_i = the white population (or those living at or above the federal poverty line, when measuring income segregation) of the i^{th} area

Y = the total white population (or the total population living at or above the federal poverty line when measuring income segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

The isolation index measures the extent by which group members are exposed to one another rather than to members of another group [89, 91]. This index ranges from 0 to 1 and can be interpreted as the probability that a randomly selected member of Group X will come in contact with another member of Group X in the same residential area [90]. The isolation index may not only measure the isolation of the disadvantaged populations (e.g., blacks or poor) from the more advantaged population (e.g., whites or non-poor), but may also measure the isolation of disadvantaged groups from social mobility and resources [17].

Isolation index calculation:

$$\mathrm{I_i} = xPx = \left[\sum_{i=1}^{N}\left(\frac{x_i}{X} * \frac{x_i}{T_i}\right)\right] * 100$$

where,

xPx is the usual notation of the Isolation index . It symbolizes that the index calculates the group x (e.g. black population) weighted average of the group x (e.g. black population) proportion in each areal unit (e.g. census tract).

x_i = the black population (when measuring black-white racial segregation) or those living below the federal poverty line (when measuring income segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total population living below the federal poverty line when measuring income segregation) of the large geographic entity for which the isolation index is being calculated.

T_i = the total population of the i^{th} area

Covariates/potential confounders:

The patient demographic and clinical based covariates aggregated to the surgeon level included surgeon's % female patients, % married patients, % with no co-morbid illness (based on the Deyo adaption of the Charlson Comorbidity Index), % with cancer in the proximal colon site, % with stage III colon cancer, % with high grade tumors and mean patient age. The patient area-based measures were also aggregated to the surgeon level. For each surgeon's patient population, we calculated the median value of the following measures at both the census tract and county level: percent black residents, percent residents living below the poverty line and percent residents age 65 and older living below the poverty line. The specific surgeon aggregated facility characteristic used in the models was surgeon's percentage of patients who received colon cancer surgery at a hospital in the top quartile of volume. Hospital volume was calculated as the number of claims among each hospital for colon cancer surgery for the study population. This

characteristic was then aggregated to the surgeon level to produce the surgeon-level characteristic.

Analysis:

The data analyses began with descriptive statistics to examine the distributions of the variables under study. For analysis, all variables were categorized based on the distribution of the variables' values e.g. tertiles or a priori categories (see appendix for categorization descriptions). Bivariate analyses, chi-square tests of association, were performed to assess the relation of the independent variables and covariates to the various outcome measures (i.e. surgeon characteristics) and to each other. Possible interactions among study variables were not suggested in previous literature and therefore did not warrant assessment in this current analysis.

Multivariate logistic regression analyses were conducted to assess the association between surgeons' training and experience and their aggregated patient-population characteristics, % black patients, % urban residing patients, and median residential segregation index values after controlling for aggregated patient, facility and area-based confounding variables and covariates. Due to the large number of exposures variables in this analysis (N=10), all potential confounders and covariates were placed in the initial model to account for potential confounding of each of the exposure-dependent variable associations. Backwards elimination was conducted only on the exposures of interest as suggested by Kleinbaum and Klein [156]. Exposure variables remained in the model if they maintained statistically significant associations with the dependent variable (surgeon score) in the multivariate model. The results of the regression analyses were expressed as multivariate adjusted odds ratios (ORs) with the corresponding 95% confidence intervals (CIs). The level of statistical significance was set at $\alpha=0.05$, two-tailed for analyses. All models were assessed for collinearity amongst independent variables (see appendix for modeling strategy). Analyses were performed using SAS statistical software system, version 9.2 for Windows (SAS Institute Inc., Cary, NC).

Results

There were 525 surgeons who performed surgery on the 3,964 colon cancer patients in this study. The mean number of patients per surgeon was 7.64. The majority of the surgeons (57.9%) graduated from medical school between 1970 and 1989, 88.4% graduated from a medical school in the United States, 90.6% had at least one board certification and 91.1% were general surgeons. There were 67 (12.8%) surgeons with a surgeon score of 6 or less (which was considered low), 297 (56.6%) surgeons with a score of 7 or 8, and 161 (30.1%) surgeons with a score of 9 or greater (which was considered optimal).

Table 1 presents the overall statistics (mean, standard deviation, range, median and inter-quartile range) of the surgeons' patient profiles. Several of these characteristics have a skewed distribution. Percent black patients, percent patients with high grade tumor, county median racial dissimilarity index (patient residence) and census tract median racial isolation index (patient residence) are skewed to the right (i.e., mean % much higher than median %), indicating that there are surgeons with high extreme values for these characteristics in comparison to other surgeons. Percent of patients with an urban residence and percent of patients receiving surgery at a hospital in the top quartile for volume are skewed to the left (i.e., mean % much lower than median %) indicating the presence of surgeons with extreme low percentages of urban populations as well as low percentages of patients receiving surgery at high volume hospitals compared to the rest of the study group.

Table 2 presents the association (odds ratios and 95% Confidence Intervals for statistically significant associations at α=0.05 level) between surgeons' characteristics and their patient profiles. Among the exposures of main interest the observed statistically significant associations were in the hypothesized direction for percent black patients and percent urban patients. Surgeons with either low or moderate percent black patients compared to high percent

black patients were more likely to be a specialist, U.S. trained, in the higher tertiles of patient volume and have board certifications. Surgeons with a low percentage of patients residing in urban areas (<10.0%, predominantly non-urban patients) compared to surgeons with at least 10.0% of patients residing in urban areas were less likely to have specialized training, be in a higher tertile with respect to the patient volume and have a board certification.

Some of the associations found for county- and census tract-level segregation indices were in the opposite direction from what was predicted. For example depending on the comparison (low segregation vs. high segregation or moderate segregation vs. high segregation) surgeons that took care of patients residing in counties with lower levels of racial segregation were less likely than surgeons with patients residing in counties with higher racial segregation to be specialists ; however, the opposite was true for census tract level segregation.

Table 3 shows the crude (unadjusted) and adjusted associations between surgeon score and the exposures of interest within this study, where all exposure variables are being treated as categorical variables. In unadjusted analyses, surgeons' patient profile characteristics: percent black patients, median county racial dissimilarity index and median census tract income isolation index were statistically significant predictors of both suboptimal (≤6 vs. >6) and optimal (≥9 vs. <9) summary score. In addition, median county racial isolation index was a statistically significant predictor of surgeon score (≤6 vs. >6), whereas median census tract racial dissimilarity index and median census tract income dissimilarity index were statistically significantly associated with surgeon score (≥ 9 vs. <9).

After adjusting for covariates and confounders, percent of black patients was associated with suboptimal surgeon score (≤6 vs. >6) although the result was statistically significant only for the moderate (15-30%) versus high (≥30%) comparison (aOR=0.15, 95% CI: 0.03-0.71) and none of the segregation measures were statistically significant predictors of suboptimal surgeon score

(≤6 vs. >6). In addition, after controlling for covariates, no segregation measures confounded the association between the surgeon's percent of black patients and sub-optimal surgeon score.

For surgeon score defined as optimal (i.e., ≥9 vs. <9), after adjustment for covariates and confounders, statistically significant predictors were percent of black patients (low vs. high: aOR 2.83 (95% CI: 1.35-5.91), moderate vs. high: aOR 3.13 (95% CI: 1.41-6.95)) and census tract median racial dissimilarity index (moderate vs. high: aOR=2.40; 95% CI: 1.26-4.55). In addition, after controlling for covariates, no segregation measures confounded the association between the surgeon's percent of black patients and optimal surgeon score.

Discussion

Surgeon training and level of experience have been shown to predict patient outcomes such as mortality, post-surgery morbidity, re-hospitalization, cancer recurrence rates and delivery of quality treatment [7-12]. Most previous studies assessing the association between patient factors and surgeon quality focused on coronary artery bypass graft (CABG) procedures. [23-25]. To our knowledge, the current study is the first to examine the association of colon cancer patient factors with surgeon training and experience.

In our study, patient race was found to be associated with surgeon quality measures (expressed as a summary score), a result that is in agreement with the previously discussed cardiology literature [23-25]. The literature on rural-urban disparities in health care is sparse. It has been shown that rural patients tend to have less access to health care compared to their urban counterparts [10, 100]. Less access may indicate lower access to quality physicians among rural patients. Our study showed that surgeon quality did not differ by percent urban population. We also found that the census tract-level racial dissimilarity index was associated with surgeon training and experience; those residing in census tracts with lower racial dissimilarity were more

likely to have a higher trained or experienced surgeon than those residing in more racially segregated areas. No other studies to our knowledge have assessed this association.

A recent study suggested that provider characteristics may differ by geography and in fact it is the patient residential factors that may drive the racial differences in health care quality [157]. Our results indicate that patients' residential setting may explain only some of the racial differences in access to highly trained and experienced surgeons; however, race (particularly the percent of blacks in a given physician's patient population) is an independent predictor of surgeon quality. Other studies have indicated that surgeon quality is associated with hospital quality [130]. We accounted for one aspect of hospital quality (receipt of colon cancer surgery at a hospital in the top quartile of surgical volume among the study population) and found that it was associated with surgeon quality; surgeons with higher scores had a higher percentage of patients receiving surgery at high volume hospitals.

Studies have found patient residential characteristics to be associated with health care performance measures, such as cancer screening and diabetes management, access to specialists and to care in general [5, 6, 27]. Krieger previously recommended that census tract measures may be used as surrogates for individual level measures of socioeconomic factors [155]. Given this recommendation, our census tract level findings may suggest that individual and neighborhood level social and economic resources determine the quality of surgeons who care for the population. Our results may also suggest that personal and neighborhood measures of social and economic resources impact surgeon referral patterns and where and from whom patients seek medical care.

Our analyses revealed that surgeons were more likely to have optimal training and experience if their patients resided in census tracts with moderate (as opposed to high) racial dissimilarity. Auchincloss et al reported that elderly Medicare patients residing in communities

where at least 50% of the population shared a common ancestry had increased access to health care [158]. In support of this observation, Sampson showed that communities with populations who share ethnic heritage are characterized by greater social cohesion as evidenced in an increased density of community level friendships and acquaintanceships and reduced anonymity [159]. Given this, it is possible that the racial segregation gradient has a demarcation that separates socially cohesive communities from socially deteriorated communities. For instance, moderate segregation in the current study may indicate communities experiencing social cohesion and increased access to health care, whereas high segregation may mark communities with deteriorated social structures and decreased access to health care. This explanation would support our finding.

The major strength of this research project is the use of residential segregation measures to characterize surgeons' patient populations and assess the association with surgeon quality. The use of segregation measures provided additional insight over and above that of the traditional area-based factors (percent black population in area and percent population living below poverty). Political, social and economic factors drive community segregation and these processes influence the quality of community-level social resources, such as availability and quality of health care [83] [80, 82]. The use of segregation measures in this study allowed us to account in part for these political, social and economic processes.

Other strengths of this study are the use of contemporary data (study years 2001 to 2005) which provides an updated account of disparities in cancer care. In our analysis, we employed refined and detailed measures of neighborhood segregation and rural-urban residency that have been rarely used in either public health or health care research. Finally, multiple sources of data were combined to account for various relevant covariates.

The main limitation of this study is that the findings are based on surgeons and elderly colon cancer patients in the state of Georgia. It is possible that our results are not generalizable to other U.S. states or other patient age groups. In addition, since the analysis was performed at the surgeon level our results may not apply to individual patients.

Few studies have assessed the role of neighborhood characteristics in determining quality of care or sought to explain the rural-urban and racial disparities. We hope that this study will contribute to the understanding of the influence of non-clinical factors on the quality of surgeons who care for colon cancer patients receiving Medicare. Our findings should be considered in the development of focused social intervention strategies aimed at improving the quality of colon cancer care.

References:

1. Jemal, A., et al., *Cancer statistics, 2008.* CA: A Cancer Journal for Clinicians, 2008. **58**: p. 71-96.
2. Jessup, J.M., et al., *The National Cancer Data Base. Report on colon cancer.* Cancer, 1996. **78**(4): p. 918-26.
3. Cooper, G.S., et al., *Surgery for colorectal cancer: Race-related differences in rates and survival among Medicare beneficiaries.* Am J Public Health, 1996. **86**(4): p. 582-6.
4. Du, X.L., et al., *Racial disparities and socioeconomic status in association with survival in a large population-based cohort of elderly patients with colon cancer.* Cancer, 2007. **110**(3): p. 660-669.
5. Hayanga, A.J., et al., *Residential segregation and access to surgical care by minority populations in US counties.* Journal of the American College of Surgeons, 2009. **208**(6): p. 1017-22.

6. Hayanga, A.J., et al., *Racial clustering and access to colorectal surgeons, gastroenterologists, and radiation oncologists by African Americans and Asian Americans in the United States: a county-level data analysis.* Arch Surg, 2009. **144**(6): p. 532-5.

7. Hershman, D.L., et al., *Surgeon characteristics and use of breast conservation surgery in women with early stage breast cancer.* Annals of Surgery, 2009. **249**(5): p. 828-33.

8. Holm, T., et al., *Influence of hospital- and surgeon-related factors on outcome after treatment of rectal cancer with or without preoperative radiotherapy.* British Journal of Surgery, 1997. **84**(5): p. 657-63.

9. Porter, G.A., et al., *Surgeon-related factors and outcome in rectal cancer.* Annals of Surgery, 1998. **227**(2): p. 157-67.

10. Prystowsky, J.B., G. Bordage, and J.M. Feinglass, *Patient outcomes for segmental colon resection according to surgeon's training, certification, and experience.* Surgery, 2002. **132**(4): p. 663-672.

11. Schrag, D., et al., *Surgeon volume compared to hospital volume as a predictor of outcome following primary colon cancer resection.* J Surg Oncol, 2003. **83**(2): p. 68-78; discussion 78-9.

12. Hershman, D.L., et al., *Surgeon characteristics and receipt of adjuvant radiotherapy in women with breast cancer.* Journal of the National Cancer Institute, 2008. **100**(3): p. 199-206.

13. Dorrance, H.R., G.M. Docherty, and P.J. O'Dwyer, *Effect of surgeon specialty interest on patient outcome after potentially curative colorectal cancer surgery.* Dis Colon Rectum, 2000. **43**(4): p. 492-8.

14. Rodriguez, R.A., et al., *Geography matters: relationships among urban residential segregation, dialysis facilities, and patient outcomes.* Annals of Internal Medicine, 2007. **146**(7): p. 1746-1754.

15. *Medicare Physician Identifiers UPINs, PINs and NPI Numbers*, ResDAC, Editor. January 2003, Research Data Assistance, University of Minnesota: Minneapolis, MN.

16. Krieger, N., *Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology.* American Journal of Public Health, 1992. **82**(5): p. 703.

17. Frey, W. and D. Myers, *Neighborhood segregation in single-race and multirace America: a Census 2000 study of cities and metropolitan areas*. 2002, Citeseer.

18. Massey, D. and N. Denton, *The dimensions of residential segregation.* Social Forces, 1988. **67**(2): p. 281-315.

19. Lichter, D., et al., *National Estimates of Racial Segregation in Rural and Small-Town America.* Demography, 2007. **44**: p. 563-581.

20. Robinson, V., *Lieberson's Isolation Index; A Case Study Evaluation.* Area, 1980. **12**(4): p. 307-312.

21. Shihadeh, E. and N. Flynn, *Segregation and crime: The effect of black social isolation on the rates of black urban violence.* Social Forces, 1996. **74**(4): p. 1325-1352.

22. Kleinbaum, D.G. and M. Klein, *Additional Modeling Strategy Issues* *Logistic Regression*, in *Logistic Regression: A Self-Learning Text*. 2010, Springer New York. p. 241-299.

23. Campbell, N.C., et al., *Rural and urban differences in stage at diagnosis of colorectal and lung cancers.* Br J Cancer, 2001. **84**(7): p. 910-4.

24. Liff, J.M., W.-H. Chow, and R.S. Greenberg, *Rural-urban differences in stage at diagnosis. Possible relationship to cancer screening.* Cancer, 1991. **67**(5): p. 1454-1459.

25. Baicker, K., A. Chandra, and J.S. Skinner, *Geographic variation in health care and the problem of measuring racial disparities.* Perspect Biol Med, 2005. **48**(1 Suppl): p. S42-53.

26. Auchincloss, A.H., J.F. van Nostrand, and D. Ronsaville, *Access to Health Care for Older Persons in the United States.* Journal of Aging and Health, 2001. **13**(3): p. 329-354.

27. Sampson, R.J., *Linking the Micro- and Macrolevel Dimensions of Community Social Organization.* Social Forces, 1991. **70**(1): p. 43-65.

28. Fix, M., *Clear and convincing evidence: Measurement of discrimination in America.* 1993.

29. Ming Jr, W., *Racial Restrictions and the Fourteenth Amendment: The Restrictive Covenant Cases.* The University of Chicago Law Review, 1949: p. 203-238.

30. Gotham, K., *Urban space, restrictive covenants and the origins of racial residential segregation in a US city, 1900-50.* International Journal of Urban and Regional Research, 2000. **24**(3): p. 616-633.

31. Hynes, D.M., et al., *Surgery and adjuvant chemotherapy use among veterans with colon cancer: insights from a California study.* J Clin Oncol. **28**(15): p. 2571-6.

32. Cooper, G.S., et al., *Agreement of Medicare claims and tumor registry data for assessment of cancer-related treatment.* Med Care, 2000. **38**(4): p. 411-21.

33. Krieger, N., et al., *Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project.* American Journal of Epidemiology, 2002. **156**(5): p. 471.

34. Weinberg, D., *Measuring poverty in the United States: History and current issues.* Center for Economic Studies Research Paper, CES, 2006: p. 06-11.

Table 5-1. Descriptive Characteristics of Surgeons' Patient Populations#

Characteristics of Patient Populations:	Mean %* or Value**	SD	Range (min-max)	Median	IQR
Number of Patients/Surgeon	7.55	7.99	52.00	5.00	8.00
Patient Demographics					
Percent Black	25.00%	31.84%	100.00%	12.50%	37.50%
Percent Female	56.32%	29.38%	100.00%	57.14%	35.00%
Median Age	76.3	4.58	25.50	76.00	5.50
Percent Married	46.46%	29.65%	100.00%	50.00%	35.43%
Percent No Comorbidity: Based on Charlson Score	49.36%	29.16%	100.00%	50.00%	33.33%
Patient Tumor Characteristics					
Percent Stage III	34.87%	27.86%	100.00%	32.26%	33.33%
Percent Proximal tumors	62.10%	28.42%	100.00%	63.40%	30.00%
Percent High Grade: Poorly/Undifferentiated	16.15%	22.84%	100.00%	9.09%	25.00%
Patient's Residence (Area-based Measures)					
County Level					
Median Percent Black	30.13%	16.13%	59.77%	30.94%	27.19%
Median Percent Population Below Poverty	14.20%	5.34%	26.67%	14.76%	6.59%
Median Percent Population Age 65+ Below Poverty	13.49%	4.72%	26.32%	13.18%	5.87%
County Segregation Indices					
Median Racial Dissimilarity Index (x100)	44.8	18.73	76.72	39.56	26.86
Median Racial Isolation Index (x100)	43.86	23.63	79.21	43.51	39.60
Median Income Dissimilarity Index (x100)	25.97	10.89	44.16	26.63	15.50
Median Income Isolation Index (x100)	19.42	7.54	34.27	18.30	13.16
Census Tract Level					
Median Percent Black	28.09%	25.04%	97.91%	21.03%	29.69%
Median Percent Population Below Poverty	13.77%	7.95%	53.98%	12.32%	10.80%
Median Percent Population Age 65+ Below Poverty	13.17%	7.43%	64.46%	12.55%	10.08%
Census Tract Segregation Indices					
Median Racial Dissimilarity Index (x100)	24.49	11.82	74.61	23.36	14.5
Median Racial Isolation Index (x100)	31.94	25.77	97.70	25.57	36.23
Median Income Dissimilarity Index (x100)	18.73	8.57	78.89	17.91	9.28
Median Income Isolation Index (x100)	16.06	8.76	55.54	14.22	12.08
Rural Urban Commuting Area (RUCA)					
Percent with Urban Residence	69.44%	38.81%	100.00%	90.00%	60.00%
Percent of Patients Receiving Surgery at a Hospital in the Top Quartile for Volume (High Volume)	55.60%	46.64%	100.00%	82.76%	100.00%

#Values within table are surgeon level and not population level, e.g. mean % female patients in this table reflects the average % of female patients among the 525 surgeons in this study and is not equivalent to the % of female patients in the total study population

* Percent of categorical variable, e.g., black race, female gender, etc.,

** Value of continuous variable, e.g., age, segregation indices, etc.,

Table 5-2. Relation between Surgeon and Patient Characteristics (Unadjusted Odds Ratios and 95% Confidence Intervals)

	Surgeon Characteristics					
	Specialty	**Training**	**Patient Volume Tertile**		**Board Certifications**	
	Yes vs. No	U.S. vs. Foreign	3rd vs. 1st	2nd vs. 1st	1 vs. 0	2 vs. 0
Patient Demographics						
Percent Blacks						
0.0-14.9% vs. ≥30.0%			2.9 (1.7-4.9)		2.1 (1.1-4.0)	
15.0-29.9% vs. ≥30.0%	4.9 (1.9-12.5)	3.8 (1.3-11.2)				5.9 (1.8-19.7)
Median Age at Diagnosis						
66-<75 yrs vs ≥80 yrs						
75-<80 yrs vs ≥80 yrs			7.3 (3.8-14.3)			5.2 (1.3-20.9)
Percent Female Tertiles						
T1: 0.0-50.0% vs T3: ≥ 66.7%			2.2 (1.3-3.8)			
T2: >50.0-66.7% vs T3: ≥ 66.7%		2.4 (1.1-5.4)	9.4 (4.9-17.9)	2.5 (1.3-4.6)		4.3 (1.3-14.2)
Percent Married Tertiles						
T1: 0.0-37.5% vs T3: >58.5%		0.5 (0.2-0.9)	0.3 (0.2-0.6)			0.2 (0.1-0.7)
T2: >37.5-58.5% vs T3: >58.5%			5.1 (2.9-9.2)	3.5 (1.9-6.3)		
Charlson Score: % No Comorbidity Tertile						
T1: 0.0-38.9% vs T3: >58.3%						
T2: >38.9-58.3% vs T3: >58.3%			7.8 (4.3-14.1)	3.6 (2.0-6.3)		
Tumor Characteristics						
Percent Stage III Tertiles						
T1: 0.0-25.0% vs T3: >42.9%				1.8 (1.1-2.8)		
T2: >25.0-42.9% vs T3: >42.9%	3.2 (1.4-7.0)		7.8 (4.2-14.6)	4.0 (2.1-7.9)		6.1 (1.7-22.1)
Percent Proximal Colon Tumors Tertiles						
T1: 0.0-50.0% vs T3: >75.0%				2.0 (1.2-3.3)		
T2: >50.0-75.0% vs T3: >75.0%			18.3 (9.6-34.8)	7.7 (4.1-14.4)		
Percent High Grade Tumor						
0.0-<10.0% vs ≥10.0%			0.2 (0.1-0.3)	0.3 (0.2-0.4)		
Hospital Characteristic						
Percent with Surgery Received at Hospital in the Top Quartile for Volume 0.0-<55.6% vs ≥ 55.6%	0.3 (0.1-0.5)	0.5 (0.3-0.9)	0.3 (0.2-0.5)			0.3 (0.1-0.8)

Table 5-2. (continued)

	Surgeon Characteristics					
	Specialty	**Training**	**Patient Volume Tertile**		**Board Certifications**	
	Yes vs. No	U.S. vs. Foreign	3rd vs. 1st	2nd vs. 1st	1 vs. 0	2 vs. 0
Area-Based Measures						
County Level						
Segregation Indices						
Median Racial Dissimilarity Index						
0.0-<30.0% vs ≥60.0%	0.2 (0.1-0.6)					
30.0-<60.0% vs ≥60.0%	0.5 (0.2-0.9)		3.4 (1.9-5.9)	2.0 (1.2-3.4)		
Median Racial Isolation Index						
0.0-15.0% vs ≥30.0%						
15.0-<30.0% vs ≥30.0%	0.3 (0.1-0.9)					
Median Income Dissimilarity Index						
0.0-<15.0% vs ≥ 30.0%	0.3 (0.1-0.9)	2.7 (1.0-7.4)				
15.0-<30.0% vs ≥ 30.0%						
Median Income Isolation Index						
0.0-<10.0% vs ≥ 20.0%						
10.0-<20.0% vs ≥ 20.0%					2.1 (1.1-4.0)	
Median Percent Black						
0.0-<15.0% vs ≥30.0%	0.3 (0.1-0.8)					
15.0-<30.0% vs ≥30.0%	0.4 (0.2-1.0)					
Median Percent Population Living Below Poverty						
0-<10.0% vs ≥20.0%					3.5 (1.2-10.3)	
10.0-<20.0% vs ≥ 20.0%						
Median Percent Population Age 65+ Living Below Poverty						
0.0-<10.0% vs ≥20.0%			3.8 (1.2-11.9)		3.1 (1.1-8.9)	
10.0-<20.0% vs ≥ 20.0%			5.7 (1.9-17.1)			

Table 5-2. (continued)

	Surgeon Characteristics					
	Specialty	**Training**	**Patient Volume Tertile**		**Board Certifications**	
	Yes vs. No	U.S. vs. Foreign	3rd vs. 1st	2nd vs. 1st	1 vs. 0	2 vs. 0
Census Tract Level						
Segregation Indices						
Median Racial Dissimilarity Index						
0.0-<15.0% vs ≥ 30.0%						
15.0-<30.0% vs ≥ 30.0%	5.1 (1.8-14.5)		2.0 (1.2-3.4)		2.2 (1.1-4.4)	4.1 (1.4-11.7)
Median Racial Isolation Index						
0.0-<15.0% vs ≥30.0%					2.1 (1.0-4.3)	
15.0-<30.0% vs ≥30.0%			2.0 (1.2-3.5)			
Median Income Dissimilarity Index						
0.0-<10.0% vs ≥ 20.0%			0.2 (0.1-0.4)	0.5 (0.2-1.0)		
10.0-<20.0% vs ≥ 20.0%						
Median Income Isolation Index						
0.0-<10.0% vs ≥ 20.0%	2.3 (1.1-5.0)					
10.0-<20.0% vs ≥ 20.0%			2.0 (1.2-3.2)	1.7 (1.0-2.7)	2.2 (1.1-4.4)	
Median Percent Black						
0.0-<15.0% vs ≥30.0%		2.4 (1.2-4.6)	2.1 (1.3-3.5)		2.1 (1.1-4.3)	
15.0-<30.0% vs ≥30.0%			2.5 (1.4-4.3)			3.2 (1.1-9.3)
Median Percent Population Living Below Poverty						
0.0-<10.0% vs ≥20.0%	2.9 (1.2-7.3)		1.8 (1.0-3.3)			
10.0-<20.0% vs ≥20.0%			2.5 (1.3-4.4)			
Median Percent Population Age 65+ Living Below Poverty						
0.0-<10.0% vs ≥20.0%	4.0 (1.2-13.6)		3.3 (1.6-7.0)			
10.0-<20.0% vs ≥20.0%			3.5 (1.7-7.4)			
Percent Urban						
0.0-<10.0% vs ≥ 10.0%	0.3 (0.1-0.9)			0.5 (0.3-0.8)	0.4 (0.2-0.8)	

Table 5-3. Surgeon Score and Main Exposures (Crude and Adjusted Odds Ratios)

Main Exposures and Covariates of Interest	Surgeon Score ≤6 vs. >6		Surgeon Score ≥9 vs. <9	
	cOR (95% CI)	aOR (95% CI)	cOR (95% CI)	aOR (95% CI)
Patient Race: % Black Patients				
0-14.9%	0.42 (0.24-0.71)*	0.64 (0.32-1.28)	2.52 (1.56-4.09)*	2.83 (1.35-5.91)*
15.0-29.9%	0.09 (0.02-0.37)*	0.15 (0.03-0.71)*	5.07 (2.80-9.19)*	3.13 (1.41-6.95)*
≥30.0% (ref)	1	1	1	1
Rural Urban Commuting Area Categorization: % Urban				
0-<10.0 %	1.30 (0.70-2.43)		0.73 (0.44-1.21)	
>=10.0% (ref)	1		1	
County Level: Segregation Indices				
Median Racial Dissimilarity Index of Patients' Residence among Surgeons				
0-<30.0	0.79 (0.40-1.56)		0.65 (0.34-1.23)	
30.0-<60.0	0.44 (0.24-0.81)*		1.96 (1.20-3.22)*	
>=60.0 (ref)	1		1	
Median Racial Isolation Index				
0-<15.0	0.29 (0.09-0.95)*		0.92 (0.52-1.62)	
15.0-<30.0	1.00 (0.51-1.96)		0.79 (0.47-1.33)	
>= 30.0 (ref)	1		1	
Median Income Dissimilarity Index				
0-<15.0	1.22 (0.48-3.07)		0.52 (0.23-1.17)	
15.0-<30.0	0.86 (0.46-1.60)		0.76 (0.49-1.18)	
>=30.0 (ref)	1		1	
Median Income Isolation Index				
0-<10.0	0.59 (0.22-1.60)		0.76 (0.38-1.52)	
10.0-<20.0	0.70 (0.41-1.19)		1.08 (0.73-1.60)	
>=20.0 (ref)	1		1	

Table 5-3 (continued)

Main Exposures and Covariates of Interest	Surgeon Score ≤6 vs. >6		Surgeon Score ≥9 vs. <9	
	cOR (95% CI)	aOR (95% CI)	cOR (95% CI)	aOR (95% CI)
Census Tract Level: Segregation Indices				
Median Racial Dissimilarity Index of Patients' Residence among Surgeons				
0-<15.0	1.86 (0.93-3.74)		0.80 (0.42-1.51)	1.89 (0.81-4.39)
15.0-<30.0	0.82 (0.43-1.54)		2.24 (1.40-3.56)*	2.40 (1.26-4.55)*
>=30.0 (ref)	1		1	1
Median Racial Isolation Index				
0-<15.0	0.41 (0.21-0.80)*		1.29 (0.84-1.98)	
15.0-<30.0	0.90 (0.48-1.70)		1.67 (1.03-2.70)*	
>=30.0 (ref)	1		1	
Median Income Dissimilarity Index				
0-<10.0	1.34 (0.62-2.88)		0.36 (0.16-0.81)*	
10.0-<20.0	0.63 (0.36-1.10)		1.17 (0.79-1.73)	
>= 20.0 (ref)	1		1	
Median Income Isolation Index				
0-<10.0	0.82 (0.43-1.56)		1.31 (0.79-2.17)	
10.0-<20.0	0.56 (0.31-1.03)		1.52 (0.97-2.39)	
>=20.0 (ref)	1		1	

*= p<0.05

Multivariate Model (surgeon score <=6 vs >6) adjusted for: Patient: % black, % female, % married, % no comorbid illness, % stage III cancer, % tumor location in proximal colon, median age, Median County Level: % black living in county, % population living below poverty, % population age 65+ living below poverty ,Census Tract Level: % black living in census tract, % population living below poverty, % population age 65+ living below poverty, Hospital: % population receiving surgery at a top quartile volume hospital

Multivariate Model (surgeon score >=9 vs <9) adjusted for: Patient: % black, % female, % married, % no comorbid illness, % stage III cancer, % with high grade tumor, % tumor location in proximal colon, median age, County Level: % black living in county, % population living below poverty, % population age 65+ living below poverty, Census Tract Level: median racial dissimilarity index, % black living in census tract, % population living below poverty, % population age 65+ living below poverty, Hospital: % population receiving surgery at a top quartile volume hospital

Appendix

Surgery Claims Codes

Appendix Table 5-1: Surgery codes

Code	Label
ICD-9 colectomy procedure codes	
457	Open and other partial excision of large intestine
4571	Open and other multiple segment resection of large intestine
4572	Open and other cecectomy
4573	Open and other right hemicolectomy
4574	Open and other resection of transverse colon
4575	Open and other left hemicolectomy
4576	Open and other sigmoidectomy
4579	Other and unspecified partial excision of large intestine
458	Total intra-abdominal colectomy
4581	Laparoscopic total intra-abdominal colectomy
4582	Open total intra-abdominal colectomy
4583	Other and unspecified intra-abdominal colectomy
ICD-9 bypass procedure codes	
4601	Exteriorization of small intestine
4603	Exteriorization of large intestine
4610	Colostomy, not otherwise specified (NOS)
4611	Temporary colostomy
4613	Permanent colostomy
4614	Delayed opening of colostomy
4620	Ileostomy, NOS
4621	Temporary ileostomy
4622	Continent ileostomy
4623	Other permanent ileostomy
4624	Delayed opening of ileostomy
Additional codes	
4541	Excision of lesion or tissue of large intestine
4549	Other destruction of lesion or tissue of large intestine
173	Laparoscopic partial excision of large intestine
1731	Laparoscopic multiple segmental resection of large intestine
1732	Laparoscopic cecectomy
1733	Laparoscopic right hemicolectomy
1734	Laparoscopic resection of transverse colon
1735	Laparoscopic left hemicolectomy

1736 Laparoscopic sigmoidectomy
1739 Other laparoscopic partial excision of large intestine
484 Pull-through resection of rectum
4840 Pull-through resection of rectum, NOS
4841 Soave submucosal resection of rectum
4842 Laparoscopic pull-through resection of rectum
4843 Open pull-through resection of rectum
4849 Other pull-through resection of rectum
485 Abdominoperineal resection of rectum
4850 Abdominoperineal resection of rectum, NOS
4851 Laparoscopic abdominoperineal resection of rectum
4852 Open abdominoperineal resection of rectum
4859 Other abdominoperineal resection of rectum
486 Other resection of rectum
4861 Transsacral rectosigmoidectomy
4862 Anterior resection of rectum with synchronous colostomy
4863 Other anterior resection of rectum
4864 Posterior resection of rectum
4865 Duhamel resection of rectum
4869 Other (partial proctectomy, rectal resection, NOS)

HCPCS/CPT-4 colectomy surgery codes

44140 Colectomy, partial
44141 With skin level cecostomy or colostomy
44143 With end colostomy and closure of distal segment
44144 With resection, with colostomy or ileostomy and creation of mucofistula
44145 With coloproctostomy (low pelvic anastomosis)
44146 With coloproctostomy (low pelvic anastomosis), with colectomy
44147 Abdominal transanal approach
44150 Colectomy, total, abdominal, without proctectomy, with ileostomy or ileoproctostomy
44151 With continent ileostomy
44152 With rectal mucodectomy, ileoanal anastomosis, with or without loop ileostomy
44153 With rectal mucodectomy, ileoanal anastomosis, creation of ileal reservoir, with or without loop ileostomy
44155 Colectomy, total, abdominal, with proctectomy, with ileostomy
44156 With continent ileostomy
44157 Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, includes loop ileostomy, and rectal mucosectomy, when performed

44158 Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, creation of ileal reservoir (S or J), includes loop ileostomy, and rectal mucosectomy, when performed

44160 Colectomy with removal of terminal ileum and ileocolostomy

44200 Laparoscopy, surgical; enterolysis (freeing of intestinal adhesion) (separate procedure)

44201 Laparoscopy, surgical; jejunostomy (eg, for decompression or feeding)

44202 Laparoscopy, surgical-enterectomy, resection of small intestine, single resection and anastomosis

44203 Laparoscopy, surgical, each additional small intestine resection and anastomosis

44204 Laparoscopy, surgical-colectomy, partial, with anastomosis

44205 Laparoscopy, surgical-colectomy, partial, with removal terminal ileum with ileocolostomy

44206 Laparoscopy, surgical-colectomy, partial, with end colostomy and closure, distal segment

44207 Laparoscopy, surgical-colectomy, partial, with anastomosis, with coloproctostomy

44208 Laparoscopy, surgical-colectomy, partial, with anastomosis, with coloproctostomy, with colostomy

44209 Unlisted laparoscopy procedure, intestine (except rectum)

44210 Laparoscopy, surgical-colectomy, total, abdominal, without proctectomy, with ileostomy/ileoproctostomy

44211 Laparoscopy, surgical-colectomy, abdominal with proctectomy, with ileoanal anastomosis/ileal reservoir/loop ileostomy

44212 Laparoscopy, surgical-colectomy, total, abdominal, with proctectomy, with ileostomy

44213 Laparoscopy, surgical, mobilization (take-down) of splenic flexure performed in conjunction with partial colectomy

44227 Laparoscopy, surgical, closure of enterostomy, large or small intestine, with resection and anastomosis

HCPCS/CPT-4 bypass surgery codes

44310 Ileostomy or jejunostomy, non-tube (separate procedure)

44320 Colostomy or skin level cecostomy; (separate procedure)

SEER colectomy and surgery codes

30 Partial colectomy, segmental resection

31 30 plus resection of contiguous organ; example: small bowel, bladder

40 Subtotal colectomy/hemicolectomy (total right or left colon and a portion of transverse colon)

41	40 plus resection of contiguous organ; example: small bowel, bladder
50	Total colectomy (removal of colon from cecum to the rectosigmoid junction; may include a portion of the rectum)
51	50 plus resection of contiguous organ; example: small bowel, bladder
60	Total proctocolectomy (removal of colon from cecum to the rectosigmoid junction, including the entire rectum)
61	60 plus resection of contiguous organ; example: small bowel, bladder
70	Colectomy or coloproctotectomy with resection of contiguous organ(s), NOS
80	Colectomy, NOS
90	Surgery, NOS

Variable Categorization Descriptions

For each surgeon, the characteristics of their patient population were aggregated to provide analogous surgeon patient population profile variables. The definition of each patient characteristic and its associated surgeon patient population profile will be presented.

The main independent variables of interest in this study are calculated from patient race and patient residential area-based measures. Patient race is defined as Non-Hispanic black or white. The surgeon profile variable is percent (%) black patients, categorized on a priori consideration as: 0.0% - <15.0%, 15.0% - <30.0%, >=30.0% (reference group). The area based measures include patient rural-urban residence and patient residential county and census tract racial and income segregation indices. These variables were aggregated to the surgeon level as: percent urban patients, patients' median county racial segregation index, patients' median county income segregation index, patients' median census tract racial segregation index and patients' median census tract income segregation index.

The surgeon profile variables for the area based characteristics are % patients living in urban areas, categorized based on inspection of data distribution as: 0.0% -<10.0%, >=10.0% (reference group) and median residential racial and income segregation index of the surgeon's patient population. The categorizations of the segregation indices were based on both an inspection of the data (to allow for sufficient counts within each category) and the categorization scheme of previous studies [16, 21] as follows: Median county level racial dissimilarity index: 0.0% - <30.0%, 30.0%-<60.0%, >=60.0% (reference group); median county level racial isolation index: 0.0%-<15.0%, 15.0%-<30.0%, >=30.0% (reference group); median county level income dissimilarity index: 0.0%-<15.0%, 15.0%- <30.0%, >=30.0%; median county level income isolation index: 0.0%-<10.0%, 10.0%-<20.0%, >=20.0% (reference group). The median

segregation indices were also calculated and categorized at the census tract level. The categorization scheme is as follows: median census tract level racial dissimilarity index: 0.0% -<15.0%, 15.0%-<30.0%, >=30.0% (reference group); median census tract level racial isolation index: 0.0%-<15.0%, 15.0%-<30.0%, >=30.0% (reference group); median census tract level income dissimilarity index: 0.0%-<10.0%, 10.0%-<20.0%, >=20.0% (reference group); median census tract level income isolation index: 0.0%-10.0%, 10.0%-<20.0%, >=20.0% (reference group) .

Covariates/potential confounders:

The covariates include individual, facility and area-based variables. The surgeon's patient profile variables for these characteristics were categorized into tertiles of percentage: % female patients (T1:0-<=50.0%, T2:>50.0-<=66.7%, T3:>66.7% (reference)), % patients who are married (T1:0-<=37.5%, T2:>37.5-<=58.5%, T3:>58.5% (reference)), % patients with no co-morbid illness (T1:0-<=38.9%, T2:>38.9-<=58.3%, T3:>58.3% (reference)), % patients with cancer in the proximal colon site (T1:0-<=50.0%, T2:>50.0-<=75.0%, T3:>75.0% (reference)), % patients with stage III colon cancer (T1:0-<=25.0%, T2:>25.0-<=42.9%, T3:>42.9% (reference)), % patients with high grade tumors dichotomized based on inspection of the data distribution to ensure adequate counts within each category as (0-<10.0%, >=10.0% (reference)) and mean age of patients categorized based on inspection of the data distribution and a priori considerations as (66-<75 years, 75-<80 years, >=80 years of age (reference)).

The facility characteristic included in analysis, percent of surgeon's patients who received surgery at a hospital in the top quartile of colon cancer surgical volume among the study population , was dichotomized based on inspection of the data distribution to ensure adequate counts within each category using the mean value as the cut-point (0-<55.6%, >=55.6% (reference)).

Each patient was also assigned area-based measures of socioeconomic status (SES) at both the census tract and county level based on the percent of individuals in their census tract and the percent of individuals in their county living below the poverty line [155, 160]. These measures were used instead of median household income because it accounts for family size, age structure and relates to a family's ability to buy goods [161]. The census tract based measure has been found to be an effective substitute for individual level SES [155]. These variables were aggregated to the surgeon level as: median % population living below the poverty line in the residential areas ((1) county and (2) census tract) of the surgeon's patient population and median % population age 65 and older living below the poverty line in the residential areas ((3)county and (4) census tract) of the surgeon's patient population. All four variables were categorized as high, medium and low area based SES. High area-based SES was defined as a median % of less than 10% of population in the census tract or county living below the poverty line; medium SES was defined as a median % of 10.1-19.9% of the population living below poverty line and low SES was defined as a median % of ≥ 20% of the population living below poverty line.

Modeling Strategy

An initial model including all exposure variables, potential confounders and covariates yielded an unreliable model due the large number of variables being considered. Screening of the exposure variables as suggested by Kleinbaum and Klein was conducted to reduce the model [156]. All exposure variables were assessed individually for their association with the dependent variable, surgeon score. Only exposure variables found to be associated with the dependent variable at an $\alpha=0.10$ level were placed into the initial model. All other variables, potential confounders and covariates, were included in the model (no screening was performed on these variables to allow for adequate adjustment of confounding of the associations between the exposure variables and the dependent variable). No interaction terms (or effect modifiers) were

placed in the model. Collinearity of the initial model was assessed and no multicollinearity was found. In the initial model for surgeon sub-optimal score, the Condition Index=27.5163 and the largest Variance Decomposition Proportions were: Intercept 0.9007, County level percent of those age 65 and older living below the poverty line (category 1) 0.44670, County level percent of those age 65 and older living below the poverty line (category 2) 0.39525, indicating no multicollinearity in the model (see below for discussion of criteria for collinearity assessment). In the initial model for surgeon optimal score the Condition Index=39.7559 and the largest Variance Decomposition Proportions were: Intercept 0.9283, County level percent of those age 65 and older living below the poverty line (category 1) 0.49491, County level percent of those age 65 and older living below the poverty line (category 2) 0.52014, indicating no multicollinearity in the model.

Next backwards elimination of the exposure variables in the multivariate model was performed. Exposure variables found not to be statistically significant predictors of the dependent variable at an α=0.05 level were sequentially dropped. The final model included only exposure variables that were significantly associated with the dependent variable in the multivariate model. Lastly, collinearity diagnostics were assessed on the final model.

Assessment of Collinearity in Final Model and Hosmer-Lemeshow Goodness of Fit

Reduced Model, Surgeon Score <=6 vs >6 (Final Model):

Largest Condition Index= 21.225

Two Largest Variance Decomposition Proportions (VDP): intercept, VDP=0.8525 median county percent population age 65+ living below poverty (category 2), VDP=0.4880

Rule assessed- Collinearity between variables is present in a logistic regression model when both of the following conditions are satisfied: Condition Index > 30 and more than one

variable has a Variance Decomposition Proportion ≥ 0.5, not including the intercept. No collinearity was indicated in this model.

The p-value for the Hosmer-Lemeshow Goodness of Fit measure was 0.8764, which indicates that the model did not lack fit.

Reduced Model, Surgeon Score >=9 vs <9 (Final Model):

Largest Condition Index= 31.749

Largest Variance Decomposition Proportions (VDP): intercept, VDP=0.8622 median county percent population age 65+ living below poverty (category 1), VDP=0.5237 and median county percent population age 65+ living below poverty (category 2). VDP=0.5945

Rule assessed- Collinearity between variables is present in a logistic regression model when both of the following conditions are satisfied: Condition Index > 30 and more than one variable has a Variance Decomposition Proportion ≥ 0.5, not including the intercept.

:. No collinearity was indicated in this model.

The p-value for the Hosmer-Lemeshow Goodness of Fit measure was 0.1569, which indicates that the model did not lack fit.

Chapter 6: Receipt of Chemotherapy among Stage III Colon Cancer Patients: Race, Rural-Urban Residence and Residential Segregation

Abstract

Background: Adjuvant chemotherapy among stage III colon cancer patients is associated with improved prognosis; however, in the U.S. there are documented racial and rural-urban disparities in receipt of this treatment. Recent studies identified residential segregation measures as independent determinants of racial and geographic disparities in health care delivery. This association has not been assessed among elderly colon cancer patients.

Methods: Data from the Georgia Cancer Registry and Medicare on black and white stage III colon cancer patients aged 66 and older diagnosed during the years 2001-2005 were used to evaluate the receipt of chemotherapy. Logistic generalized estimating equation models were used in multivariate analysis to account for patient clustering of outcomes within hospital and residential areas.

Results: Overall, 680 patients (51.5%) received adjuvant chemotherapy. In multivariate analyses, patient race by rural-urban status was not associated with receipt of chemotherapy; however, census tract racial segregation was a significant predictor. Older patients, widowed and single patients, and those with comorbid illnesses were less likely to receive chemotherapy than their counterparts. In addition, county poverty and percent black population was associated with receipt of therapy.

Conclusion: The findings of this study suggest that receipt of colon cancer treatment is influenced by social factors, but it is particularly affected by factors that physicians may consider as contraindications to chemotherapy (advanced age and number of comorbid illnesses).

Introduction

The receipt of chemotherapy for cancer treatment is associated with improved survival, prognosis and outcomes [118, 162]. In the U.S., chemotherapy is not always delivered equitably [6, 12, 118, 163]. In general, marginalized populations are less likely to receive appropriate cancer therapy than their counterparts [15, 101, 120, 164]. Among colon cancer patients in the U.S., the receipt of adjuvant chemotherapy for stage III disease is the current most common measure of treatment quality [165 23, 24]. However, there are documented racial and rural-urban differences in the receipt of this treatment that persist after adjusting for patient demographics and tumor characteristics [101, 119, 120]. Few studies have sought to explain these differences [13].

Recent studies have assessed the role of area-based factors as determinants of access to and receipt of quality health care [8, 15, 16, 166]. There is indication that area-based measures such as residential segregation have an independent effect on the receipt of quality care and may explain part of the observed racial disparities as well [15, 166]. To our knowledge, the role of area based measures, such as residential segregation, in explaining rural-urban disparities in colon cancer treatment has not been assessed.

In the present study, we evaluated the independent association of race, rural-urban status and residential segregation with the receipt of adjuvant chemotherapy for stage III colon cancer. This association was assessed among Medicare patients in Georgia. We also investigated the role of residential segregation in explaining the effects of race and rural/urban residence on the receipt of adjuvant chemotherapy in our patient population.

Methods

Data Sources:

Three sources of information were used in this analysis: the linked Georgia Cancer Registry (GCR)-Medicare data, the U.S. Census Summary Files, and the Rural Urban Commuting

Area (RUCA) file from the United States Department of Agriculture (USDA) Economic Research Service (ERS). The GCR-Medicare database was used to identify a cohort of stage III colon cancer patients diagnosed between January 1, 2001 and December 31, 2005. Data from the linked GCR-Medicare file included patient demographics (including the census tract of the patient's residential address at the time of diagnosis), tumor characteristics, stage at diagnosis, and first course of treatment including surgery, chemotherapy and radiation therapy. The primary source of GCR data was hospital medical records with additional information obtained from pathologists, medical oncologists, and radiation oncologists. The Medicare claims included in the linked GCR-Medicare file reported diagnoses and procedures during hospitalization (MEDPAR-Medicare Provider Analysis and Review) along with physician and supplier bills for medical services and procedures (NCH-National Claims History).

The second data source was the 2000 U.S. Census Summary Files. For the census tracts corresponding to the cancer patients residential address at the time of diagnosis, these files were used to obtain tract-level information on community racial and income characteristics. This information was then used to calculate patient residential racial and income measures and segregation indices for each patient's residential neighborhood (county and census-tract). Lastly, Rural Urban Commuting Area (RUCA) codes from the United States Department of Agriculture (USDA) Economic Research Service (ERS) were used. These codes categorize patient residence (census tracts) into rural urban classifications.

Study Population

This study included all non-Hispanic white and black patients identified in the GCR-Medicare database who were over the age of 65 and were newly diagnosed as having primary stage III colon cancer (excluding lymphomas and sarcomas due to staging differences) during the years 2001-2005. Only patients with documented cancer directed surgery (defined as resection or bypass) were considered in these analyses because adjuvant chemotherapy by definition is the

chemotherapy delivered in addition to surgical treatment. Patients were excluded from analysis if they were not enrolled in Medicare Part B or were enrolled in a Medicare Health Maintenance Organization (HMO) because these patients are expected to have incomplete documentation regarding treatment.

For each eligible patient reported as having colon cancer surgery in the GCR, Medicare claims within 6 months after the date of diagnosis were searched to identify surgical interventions that would ordinarily be performed as part of curative colon cancer treatment. This time period was chosen to ensure the treatment documented in the claims data pertained to the cancer of interest and not a treatment for subsequent cancer. To account for discrepancies in the date of surgery between the cancer registry and the claims, any claim for colon cancer surgery reported up to three months prior to the reported date of colon cancer diagnosis in the registry was included if no post diagnosis colon cancer surgery claim was found and surgery was reported in the GCR.. We used International Classification of Diseases 9th Edition (ICD-9) procedure and Healthcare Common Procedure Coding System (HCPCS) codes indicating colectomy or bypass procedures (codes are listed in the Appendix) to identify curative treatment.

We excluded 63 patients for the following reasons: to ensure provider surgery claims pertained to the identified hospital surgery claims, all NCH and MEDPAR surgery claims that did not match for procedure and/ or date of surgery (i.e. claim date of surgery did not fall within 1 week of each other) were excluded; NCH claims with missing surgeon information were excluded because this missing information limits our ability to ensure that each patients' entire care experience was provided by licensed physicians in Georgia. Additionally, we excluded 42 patients who received care outside of Georgia, had missing census tract codes or comorbid illness information (to adjust for contraindication to chemotherapy). Among these patients, those receiving adjuvant chemotherapy within 3 months following the date of surgery were characterized as having received chemotherapy and those not receiving chemotherapy within this

period were characterized as not having received chemotherapy. Receipt of chemotherapy was assessed using ICD-9 procedure and supplementary classification chemotherapy codes, HCPCS and CPT (Current Procedural Terminology) codes, Revenue center codes and BETOS (Bereson-Eggers Type of Service) codes (see appendix). After applying the above criteria, a total of 1,321 colon cancer patients were included in analysis.

Dependent and Independent Variables of Primary Interest:

The dependent variable in this study was receipt of adjuvant chemotherapy within 3 months following surgery for colon cancer (yes or no) [167].

The main independent variables of interest were patient race by rural-urban status, and area-based racial and economic segregation measures at both the county and census tract level. County level measures serve as predictors of the quality of and access to community health care resources [5, 6] while census tract level measures serve as predictors of patient and neighborhood economic and social resources [155].

Four segregation indices were calculated for each patient's census tract and county (8 total indices): racial dissimilarity indices (tract and county) income dissimilarity indices (tract and county), racial isolation indices (tract and county) and income isolation indices (tract and county). The racial segregation measures assess black-white segregation. The income segregation measures assess segregation of those living below the federal poverty line from those living at or above the federal poverty line. These measures were calculated using data from the 2000 U.S. Census.

The dissimilarity index (D) measures the extent to which groups are segregated from each other [89, 90]. It represents the percent of group X members that would have to change their area of residence to achieve an even distribution of group X in relation to group Y residents within each sub-areal unit within the area being examined (e.g. sub-areal unit is census tract and area is county) [89]. This index ranges from 0 to 1, where D=1 indicates complete segregation (the

two groups live in completely different neighborhoods) and D=0 means complete integration (the two groups are distributed exactly the same way across the neighborhoods). When assessing black-white segregation of a given county, the D value of 0.66 indicates that 66 percent of blacks must move to a different census tract (sub-areal unit) so that the distribution of blacks in relation to whites will be equal across census tracts within the county. Values greater than 0.6 are considered a level of high segregation [21]. This index is invariant to relative size of groups.

Dissimilarity index calculation:

$$D = \left[\frac{1}{2}\sum_{i=1}^{N} \left|\frac{x_i}{X} - \frac{y_i}{Y}\right|\right] * 100$$

where,

x_i = the black population (when measuring black-white racial segregation) or those living below the federal poverty line (when measuring income segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total population living below the federal poverty line when measuring income segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

y_i = the white population (or those living at or above the federal poverty line, when measuring income segregation) of the i^{th} area

Y = the total white population (or the total population living at or above the federal poverty line when measuring income segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

The isolation index measures the extent by which group members are exposed to one another rather than to members of another group [89, 91]. It can be used to calculate the probability that a randomly selected member of Group X will come in contact with another member of Group X in the same residential area [90]. The isolation index may not only measure the isolation of the

disadvantaged populations (e.g., blacks or poor) from the more advantaged population (e.g., whites or non-poor), but may also measure the isolation of disadvantaged groups from social mobility and resources [17]. This index ranges from 0 to 1 and can be interpreted as the probability that a randomly selected member of Group X will come in contact with another member of Group X in the same residential area [90].

Isolation index calculation:

$$\mathrm{I_i} = xPx = \left[\sum_{i=1}^{N}\left(\frac{x_i}{X} * \frac{x_i}{T_i}\right)\right] * 100$$

where,

xPx is the usual notation of the Isolation index . It symbolizes that the index calculates the group x (e.g. black population) weighted average of the group x (e.g. black population) proportion in each areal unit (e.g. census tract).

x_i = the black population (when measuring black-white racial segregation) or those living below the federal poverty line (when measuring income segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total population living below the federal poverty line when measuring income segregation) of the large geographic entity for which the isolation index is being calculated.

T_i = the total population of the i^{th} area

Covariates/Potential Confounders:

The covariates included individual, facility and area-based variables. The individual-level covariates of interest were patient-related characteristics such as gender (male or female), age (categorized based on the distribution of the values within the study population to ensure adequate counts within each category), marital status (married, single, divorced/separated,

widowed or unknown), and number of co-morbid illnesses (0, 1, 2, or ≤ 3). In addition, cancer-related characteristics such as primary site and tumor grade were included.

Facility characteristics included Accreditation from the American College of Surgeons Oncology Group (Member, Non-Member: this recognition identifies facilities that provide excellence in care), medical school affiliation (affiliated or not affiliated), hospital ownership (Proprietary, Government or Non-profit) and colon cancer case volume (i.e. total number of claims for colon cancer surgery among study members) during the study period Jan 1 2001-Dec 31, 2005 (Quartile 1 – Quartile 4, low to high).

Area-based measures included the percent of black population within each census tract and county which were categorized into tertiles (T1-T3, low to high percent). Two different census tract and county level based measures of SES were used: the percent of the population living below the poverty level and the percent of the population age 65 and greater living below poverty. The percent of the population living below poverty may serve as a measure of overall economic status of a community while the percent of the population age 65 and greater living below poverty may indicate community economic status as well as familial ties and economic support for the elderly [168].

Statistical Analysis:

The data analyses began with descriptive statistics. Bivariate analyses were used to compare distributions of exposure variables and covariates among patients with and without receipt of adjuvant chemotherapy. Categorical variables were compared using χ^2 statistics or Fisher's exact tests depending on the number of observations under study. Stratified analyses were performed to test for interaction and assess confounding.

Multivariable analyses employed logistic generalized estimating equation (GEE) models to account for the correlation of the dependent variable, receipt of chemotherapy, among observations within the same hospital, census tract and/or county (i.e. clusters). The GEE model

accounts for these correlations by adjusting the variance estimates of the regression coefficients within each cluster. GEE models using a logit link, binomial distribution and working independent correlation structure (Miglioretti et al [169] method) were constructed using receipt of adjuvant chemotherapy as the dependent variable, and patient, facility and area-based characteristics as independent variables (see modeling appendix). The statistical methods used in our analyses were developed by Miglioretti and Heagerty to account for non-nested multilevel data in GEE models [169]. The data used in this analysis has a non-nested multilevel structure due to the observation that hospital clusters were not necessarily located (or nested) within either of the other two clusters, patient's residential census tract and/or county. However, observations sharing any or all of these clusters may have correlated outcomes, which require analyses to adjust for these correlations so that proper inferences can be made.

The initial model included all exposures, covariates and the interaction term, race× marital status which has been previously reported in similar models [170]. The GEE models assessed the independent effects of the exposures of interest (race, rural-urban residence and area residential segregation (racial and economic)) on the receipt of adjuvant chemotherapy after controlling for covariates. These models produced standard error estimates that account for the effect of outcome correlations among observations clustered within hospital, residential census tract and county (see Appendix).

Collinearity diagnostics were assessed for the initial and final model. The modeling results were expressed as adjusted odds ratios (OR) accompanied by the corresponding 95% confidence intervals (CI). Statistical significance of each term in the GEE models were assessed at a level of statistical significance of $\alpha=0.05$, two-tailed for all analyses. Analyses were performed using SAS statistical software system, version 9.2 for Windows (SAS Institute Inc., Cary, NC).

This study was approved by the Human Subject Review Committees, Institutional Review Board (IRB) of Emory University in Atlanta, Georgia.

Results

There were 1,321 patients included in this analysis. Of these patients, 80.5% were white, 19.5% were black, 68.4% were urban residents and 31.6% were rural. Overall, 680 of the stage III patients (51.5%) received adjuvant chemotherapy within 3 months following surgery for colon cancer. Among those less than 80 years of age, receipt of chemotherapy was higher than that of the overall population (594/902 = (65.9%)) within 3 months following surgery for colon cancer. In the unadjusted analyses (Tables 1 and 2), patient age, gender, marital status, number of co-morbid illnesses and percent of population in census tract and county living below poverty were statistically significant predictors of receipt of chemotherapy at $\alpha < 0.05$ level.

In multivariate analyses (Table 3), patient race/rural-urban status did not independently predict receipt of chemotherapy within 3 months of surgery. One census tract level segregation measure, racial isolation index was statistically significantly associated with receipt of chemotherapy. Those residing in moderately racially segregated census tracts were more likely than those residing in less racially segregated areas to receive chemotherapy within 3 months following surgery. Increased patient age was inversely associated with this outcome. Marital status and number of co-morbid illnesses were independent predictors of receipt of chemotherapy. Widowed and single patients were less likely to receive chemotherapy than married patients and receipt of chemotherapy decreased with increasing number of co-morbid illnesses. In addition, county level poverty and percent black population independently predicted receipt of therapy.

Discussion

An important finding of our study is that just about half (52%) of stage III colon cancer patients in our study received adjuvant chemotherapy. A similar frequency (54.9%) was found among all (not limited to Medicare) stage III colon and stages II/III rectal cancer cases reported to the GCR between 2000 and 2004 [171]. Our data also showed no disparities in the receipt of adjuvant chemotherapy by race/rural urban status or levels of residential segregation. These findings should be interpreted in the context of other similar studies, which are summarized below.

In the previously mentioned GCR-based study Hao et al found evidence of black-white disparity in receipt of adjuvant chemotherapy among urban colon and rectal cancer patients, but no racial disparity among rural populations [171]. The researchers did not assess separately disparities among colon cancer patients and rectal cancer patients. It is possible that the observed disparity in the Hao study was driven by the results among rectal cancer patients. Also, our study assessed disparities in a marginal effects model whereas Hao et al used a mixed effects model so the results cannot be directly compared. Similar to our findings, Hao showed that overall the unadjusted rates of chemotherapy were comparable among blacks (54.6%) and whites (55.5%) [171].

Studies using nationally representative linked data from the SEER registry and Medicare have typically found evidence supporting the existence of racial disparities in the receipt of adjuvant chemotherapy among Stage III colon cancer patients [12, 13, 19, 103]. The majority of these studies used data from the 1990s during the immediate years following the 1990 NIH consensus that recommended the use of adjuvant chemotherapy for stage III colon cancer. The chemotherapy rates and disparities found in these studies most likely do not reflect the rates for the current study's time period of 2001-2005. Rates of chemotherapy have increased following

the NIH consensus as evidenced in the study by Gross et al [19]. Gross et al also noted a persistent racial disparity in receipt of chemotherapy from 1992 to 2002 despite a steady increase in chemotherapy rates over this time period. However, it is possible that this persistent national disparity may not be generalized to our study population of Georgia residents over 65 years of age diagnosed with colon cancer between 2001 and 2005. The social and demographic characteristics of Georgia residents differ from those of the overall U.S. population and these differences may influence differential health care practices [147, 148].

A number of studies reported findings that were similar to ours. Roetzheim et al. used data from the state of Florida cancer registry to assess racial disparities in colorectal cancer (CRC) care among patients diagnosed in 1994 [5]. Investigators used hospital discharge abstract data and cancer registry data on first course of treatment to assess receipt of radiation and chemotherapy. No racial disparities in the receipt of adjuvant therapy were found in crude or adjusted analyses (controlling for health insurance type, census-derived measures of income and education, and rural/urban residence). In a more recent study, McGory et al assessed the association between race/ethnicity and the underuse of appropriate adjuvant therapy for CRC among patients in the California Cancer Registry who were diagnosed with stage III colon or stage II/III rectal cancer from 1994 to 2001 [93]. Investigators adjusted for patient demographic factors including type of insurance, year of diagnosis and census tract based SES measure (percentage of person living below the 200 percent poverty threshold in the patient's census tract). For stage III colon cancer, there was no statistically significant association between race and receipt of chemotherapy.

These studies are similar to the current study in the use of state based cancer registry data to obtain a population of colon cancer patients and assess treatment characteristics. They differ in their lack of use of outpatient claim data or medical record review to supplement the adjuvant

treatment data among their population. This lack of supplementation of outpatient medical information on treatment may have resulted in an underestimate of receipt of adjuvant chemotherapy in these two studies. These two studies also included non-Medicare age patients and the study years were predominantly in the 1990s, whereas the current study used a more contemporary cohort of Medicare patients diagnosed during years 2001-2005.

The literature on rural-urban disparities in colon cancer care is sparse. A study of colorectal and lung cancer patients in Scotland assessed the effect of deprivation and rural residence on treatment [11]. This study found that rural-urban residence (defined by distance to treatment center in kilometers) was associated with the receipt of radiotherapy among CRC patients. Patients living further away were less likely to receive treatment than those living closer to the treatment center. In a study conducted in France, Launoy et al, found that rural residence was associated with treatment at specialized centers, advanced stage at diagnosis and poor prognosis for CRC [9]. Investigators found that the observed rural-urban difference is primarily explained by the distance between patients' residence and treatment centers. Based on these previous findings, the lack of rural-urban differences in receipt of chemotherapy in the current study may indicate that travel distance does not play a large role in receipt of chemotherapy in this population.

Although relevant data for CRC are not available, other studies have examined the association between measures of segregation and treatment for other cancer sites. In an analysis similar to ours, Haas et al, found a statistically significant association between racial segregation and quality of breast cancer care [15]. They found that blacks were less likely than whites to receive adequate care [15]. After adjusting for racial segregation, the black-white disparity decreased. As black segregation increased, patients were less likely to receive adequate breast cancer care [15], which is the opposite of what we found among colon cancer patients. The differences in the

findings of the Haas et al study and the current study may suggest that receipt of quality care for breast and colon cancers may be influenced by different underlying factors.

Research on the relation of economic segregation to health and health care is scant. No studies to date have assessed the role of economic segregation on racial disparities in cancer care. To our knowledge, ours is the first study to evaluate the role of this segregation measure on quality of cancer care.

Our findings of age, marital status andnumber of co-morbid illnesses as determinants of adjuvant chemotherapy for stage III colon cancer patients have been substantiated elsewhere in the literature. Increasing age predicts a decreased likelihood of receipt of adjuvant therapy as reported in multiple studies [5, 6, 12, 93, 94, 101, 104, 108, 113, 115-120]. Increased number of comorbid conditions and the presence of medical contraindications to adjuvant therapy are also associated with a decreased likelihood of adjuvant care [5, 12, 93, 94, 104, 108, 113, 116-118, 120]. It has been consistently reported that married patients are more likely to receive chemotherapy than their single, widowed or divorced counterparts [5, 113, 116, 120].

The major strengths of this study are its ability to combine tools of social epidemiology and health care research, and its use of novel refined and detailed measures of neighborhood segregation to assess the social determinants of colon cancer care quality among Medicare patients. The contemporary data (study years range from 2001 to 2005) provide an updated account of disparities in colon cancer care. Lastly, multiple sources of data were combined to enhance the study's ability to ascertain the receipt of chemotherapy and to adjust for various relevant confounders of the association under examination.

In summary we found no evidence of race by rural-urban status associated with the receipt of adjuvant chemotherapy among stage III colon cancer patients with Medicare in the state of Georgia. On the other hand, strong independent predictors of adjuvant chemotherapy included

age, marital status, number of comorbid illnesses and area based factors, census tract racial isolation index and county level poverty and percent black population. The findings of this study suggest that receipt of colon cancer treatment is influenced by social factors but is most strongly affected by factors that physicians may consider as contraindications to chemotherapy (advanced age and number of comorbid illnesses). Studies have shown that advanced age is not a contraindication to adjuvant treatment [23, 172]. It is important that interventions aimed to improve the quality of cancer care focus efforts on educating physicians on the benefits of chemotherapy among elderly patients. Future studies, should assess the effect of race on receipt of chemotherapy within communities with differing levels of residential racial and economic segregation. These studies may help design community interventions aimed at increasing quality of cancer care.

References

1. Neugut, A.I., et al., *Use of adjuvant chemotherapy and radiation therapy for rectal cancer among the elderly: a population-based study.* Journal of Clinical Oncology, 2002. **20**(11): p. 2643-50.
2. Dobie, S.A., et al., *Survival benefits and trends in use of adjuvant therapy among elderly stage II and III rectal cancer patients in the general population.* Cancer, 2008. **112**(4): p. 789-99.
3. Earle, C.C., et al., *Who gets chemotherapy for metastatic lung cancer?* Chest, 2000. **117**(5): p. 1239-46.
4. Sundararajan, V., et al., *Variations in the use of adjuvant chemotherapy for node-positive colon cancer in the elderly: a population-based study.* Cancer J, 2001. **7**(3): p. 213-8.

5. VanEenwyk, J., J.S. Campo, and E.M. Ossiander, *Socioeconomic and demographic disparities in treatment for carcinomas of the colon and rectum.* Cancer, 2002. **95**(1): p. 39-46.

6. Berrios-Rivera, J.P., et al., *Variations in chemotherapy and radiation therapy in a large nationwide and community-based cohort of elderly patients with non-Hodgkin lymphoma.* American Journal of Clinical Oncology, 2007. **30**(2): p. 163-71.

7. Tropman, S.E., et al., *Colon cancer treatment in rural North and South Carolina.* Cancer Detect Prev, 1999. **23**(5): p. 428-34.

8. Ayanian, J.Z., et al., *Use of adjuvant chemotherapy and radiation therapy for colorectal cancer in a population-based cohort.* J Clin Oncol, 2003. **21**(7): p. 1293-300.

9. Haas, J.S., et al., *Racial segregation and disparities in breast cancer care and mortality.* Cancer, 2008. **113**(8): p. 2166-72.

10. American College of Surgeons. *CoC Quality of Care Measures*. Cancer Programs 2007; Revised March 2, 2011:[Available from: www.facs.org/cancer/qualitymeasures.html.

11. Sargent, D.J., et al., *A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients.* N Engl J Med, 2001. **345**(15): p. 1091-7.

12. Gill, S., et al., *Pooled Analysis of Fluorouracil-Based Adjuvant Therapy for Stage II and III Colon Cancer: Who Benefits and by How Much?* Journal of Clinical Oncology, 2004. **22**(10): p. 1797-1806.

13. Cronin, D.P., et al., *Patterns of care for adjuvant therapy in a random population-based sample of patients diagnosed with colorectal cancer.* American Journal of Gastroenterology, 2006. **101**(10): p. 2308-18.

14. Baldwin, L.M., et al., *Explaining black-white differences in receipt of recommended colon cancer treatment.* J Natl Cancer Inst, 2005. **97**(16): p. 1211-20.

15. Hayanga, A.J., et al., *Residential segregation and access to surgical care by minority populations in US counties.* Journal of the American College of Surgeons, 2009. **208**(6): p. 1017-22.

16. Hayanga, A.J., et al., *Racial clustering and access to colorectal surgeons, gastroenterologists, and radiation oncologists by African Americans and Asian Americans in the United States: a county-level data analysis.* Arch Surg, 2009. **144**(6): p. 532-5.

17. Haas, J.S., et al., *Association of area sociodemographic characteristics and capacity for treatment with disparities in colorectal cancer care and mortality.* Cancer, 2011. **117**(18): p. 4267-4276.

18. Schrag, D., et al., *Age and adjuvant chemotherapy use after surgery for stage III colon cancer.* Journal of the National Cancer Institute, 2001. **93**(11): p. 850-7.

19. Krieger, N., *Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology.* American Journal of Public Health, 1992. **82**(5): p. 703.

20. Frey, W. and D. Myers, *Neighborhood segregation in single-race and multirace America: a Census 2000 study of cities and metropolitan areas*. 2002, Citeseer.

21. Massey, D. and N. Denton, *The dimensions of residential segregation.* Social Forces, 1988. **67**(2): p. 281-315.

22. Lichter, D., et al., *National Estimates of Racial Segregation in Rural and Small-Town America.* Demography, 2007. **44**: p. 563-581.

23. Robinson, V., *Lieberson's Isolation Index; A Case Study Evaluation.* Area, 1980. **12**(4): p. 307-312.

24. Shihadeh, E. and N. Flynn, *Segregation and crime: The effect of black social isolation on the rates of black urban violence.* Social Forces, 1996. **74**(4): p. 1325-1352.

25. Rendall, M.S. and A.S. Jr, *Elderly Poverty Alleviation through Living with Family.* Journal of Population Economics, 1995. **8**(4): p. 383-405.

26. Miglioretti, D. and P. Heagerty, *Marginal modeling of nonnested multilevel data using standard software.* American Journal of Epidemiology, 2007. **165**(4): p. 453.

27. Hao, Y., et al., *Race, neighbourhood characteristics and disparities in chemotherapy for colorectal cancer.* Journal of Epidemiology and Community Health. **65**(3): p. 211-217.

28. Gross, C.P., et al., *Racial disparities in cancer therapy: did the gap narrow between 1992 and 2002?* Cancer, 2008. **112**(4): p. 900-8.

29. White, A., et al., *Racial disparities and treatment trends in a large cohort of elderly African Americans and Caucasians with colorectal cancer, 1991 to 2002.* Cancer, 2008. **113**(12): p. 3400-9.

30. The Kaiser Family Foundation statehealthfacts.org. *Georgia: Poverty Rate by Race/Ethnicity, states (2007-2008), U.S. (2008).* Data Source: 2008 and 2009 U.S. Census Bureau's Current Population Survey; Available from: http://www.statehealthfacts.org/.

31. U.S. Census Bureau: State and County QuickFacts. *Georgia*. Data Source: Population Estimates, Census of Population and Housing, Small Area Income and Poverty Estimates March 12, 2010]; Available from: quickfacts.census.gov.

32. Roetzheim, R.G., Pal N., Gonzalez E. C., Ferrante J. M., Van Durme D. J., Krischer J. P., *Effects of health insurance and race on colorectal cancer treatments and outcomes.* American Journal of Public Health, 2000. **90**(11): p. 1746-1754.

33. McGory, M.L., et al., *A patient's race/ethnicity does not explain the underuse of appropriate adjuvant therapy in colorectal cancer.* Dis Colon Rectum, 2006. **49**(3): p. 319-29.

34. Campbell, N.C., et al., *Impact of deprivation and rural residence on treatment of colorectal and lung cancer.* Br J Cancer, 2002. **87**(6): p. 585-90.

35. Launoy, G., et al., *Influence of rural environment on diagnosis, treatment, and prognosis of colorectal cancer.* J Epidemiol Community Health, 1992. **46**(4): p. 365-7.

36. Dominitz, J.A., et al., *Race, treatment, and survival among colorectal carcinoma patients in an equal-access medical system.* Cancer, 1998. **82**(12): p. 2312-20.

37. Wu, X., et al., *Treatment patterns for stage III colon cancer and factors related to receipt of postoperative chemotherapy in Louisiana.* Journal of the Louisiana State Medical Society, 2004. **156**(5): p. 255-61.

38. Bradley, C.J., et al., *Adjuvant chemotherapy after resection in elderly Medicare and Medicaid patients with colon cancer.* Arch Intern Med, 2008. **168**(5): p. 521-9.

39. Potosky, A.L., et al., *Age, sex, and racial differences in the use of standard adjuvant therapy for colorectal cancer.* J Clin Oncol, 2002. **20**(5): p. 1192-202.

40. Luo, R., et al., *Referral to medical oncology: a crucial step in the treatment of older patients with stage III colon cancer.* The Oncologist, 2006. **11**(9): p. 1025-33.

41. Schrag, D., et al., *Who gets adjuvant treatment for stage II and III rectal cancer? Insight from surveillance, epidemiology, and end results--Medicare.* Journal of Clinical Oncology, 2001. **19**(17): p. 3712-8.

42. Schrag, D., et al., *Age and adjuvant chemotherapy use after surgery for stage III colon cancer.* J Natl Cancer Inst, 2001. **93**(11): p. 850-7.

43. Schrag, D., et al., *Influence of hospital procedure volume on outcomes following surgery for colon cancer.* JAMA, 2000. **284**(23): p. 3028-35.

44. Popescu, R.A., et al., *Adjuvant or palliative chemotherapy for colorectal cancer in patients 70 years or older.* J Clin Oncol, 1999. **17**(8): p. 2412-8.

45. Hynes, D.M., et al., *Surgery and adjuvant chemotherapy use among veterans with colon cancer: insights from a California study.* J Clin Oncol. **28**(15): p. 2571-6.

46. Cooper, G.S., et al., *Agreement of Medicare claims and tumor registry data for assessment of cancer-related treatment.* Med Care, 2000. **38**(4): p. 411-21.

47. Institute, N.C. *National Cancer Institute. Health Services and Economics. Procedure Codes for SEER-Medicare Analysis*. [cited 2010 10/29/2010]; Available from: http://healthservices.cancer.gov/seermedicare/considerations/procedure_codes.html.

48. Liang, K.-Y. and S.L. Zeger, *Longitudinal data analysis using generalized linear models.* Biometrika, 1986. **73**(1): p. 13-22.

Table 6-1. Descriptive Characteristics and Receipt of Chemotherapy

Variables	Total N	Chemotherapy Received No. (%) n=680	Chemotherapy Not Received No. (%) n=641	P-Value
Patient Demographics				
Patient Race and RUCA code				0.7201
Black Urban	172	92 (53.5)	80 (46.5)	
Black Rural	85	41 (48.2)	44 (51.8)	
White Urban	732	370 (50.6)	362 (49.5)	
White Rural	332	177 (53.3)	155(46.7)	
Age, y				<0.0001
66-69	236	179 (75.9)	57 (24.2)	
70-74	323	221 (68.4)	102 (31.6)	
75-79	343	194 (56.6)	149 (43.4)	
80-84	223	74 (33.2)	149 (66.8)	
85+	196	12 (6.1)	184 (93.9)	
Gender				0.0006
Male	579	329 (56.8)	250 (43.2)	
Female	742	351 (47.3)	391 (52.7)	
Marital Status				<0.0001
Married	665	409 (61.5)	256 (38.5)	
Widowed	462	172 (37.2)	290 (62.8)	
Separated/Divorced	89	59 (66.3)	30 (33.7)	
Single	67	25 (37.3)	42 (62.7)	
Unknown	38	15 (39.5)	23 (60.5)	
Patient Clinical Characteristics				
Comorbid Illness				<0.0001
0	649	375 (57.8)	274 (42.2)	
1	366	189 (51.6)	177 (48.4)	
2	181	78 (43.1)	103 (56.9)	
3 or more	124	38 (30.7)	86 (69.4)	
Tumor Location				0.5871
Proximal Colon (Right)	847	441 (52.1)	406 (47.9)	
Distal Colon (Left)	431	220 (51.0)	211 (49.0)	
Overlap Lesion and NOS*	43	19 (44.2)	24 (55.8)	
Tumor Grade				0.6545
Low Grade	954	492 (51.6)	462 (48.4)	
High Grade	320	161 (50.3)	159 (46.7)	
Unknown	47	27 (57.5)	20 (42.6)	

Table 6.1. (continued)

Variables	Total	Chemotherapy Received	Chemotherapy Not Received	P-Value
	N	No. (%) n=680	No. (%) n=641	
Hospital Characteristics				
Hospital Volume (Quartile)				0.2092
Q1	21	9 (42.9)	12 (57.1)	
Q2	108	47 (43.5)	61 (56.5)	
Q3	291	159 (54.6)	132 (45.4)	
Q4	901	465 (51.6)	436 (48.4)	
Medical School Affiliation				0.8867
Affiliated	394	204 (51.8)	190 (48.2)	
Not Affiliated	927	476 (51.4)	451 (48.7)	
Hospital Ownership				0.785
Proprietary	184	93 (50.5)	91 (49.5)	
Government and Non-Profit	1137	587 (51.6)	550 (48.4)	
American College of Surgeons Oncology Group				0.3995
Member	209	102 (48.8)	107 (51.2)	
Non-Member	1112	578 (52.0)	534 (48.0)	

Table 6-2. Area Based Characteristics and Receipt of Chemotherapy

Area Based Residential Characteristics	Total N	Chemotherapy Received	Chemotherapy Not Received	P-value
		No. (%) n=680	No. (%) n=641	
Census Tract -level				
Racial Dissimilarity Index (Tertiles)				0.4776
T1 (Least Segregated)	310	161 (51.9)	148 (48.1)	
T2 (Moderately Segregated)	490	242 (49.4)	248 (50.6)	
T3 (Most Segregated)	521	277 (53.2)	244 (46.8)	
Income Dissimilarity Index (Tertiles)				0.673
T1	328	173 (52.7)	155 (47.3)	
T2	485	242 (49.9)	243 (50.1)	
T3	508	265 (52.2)	243 (47.8)	
Racial Isolation Index (Tertiles)				0.2988
T1	486	243 (50.0)	243 (50.0)	
T2	473	257 (54.3)	216 (45.7)	
T3	362	180 (49.7)	182 (50.3)	
Income Isolation Index (Tertiles)				0.0636
T1	437	232 (53.1)	205 (46.9)	
T2	473	256 (54.1)	217 (45.9)	
T3	411	192 (46.7)	219 (53.3)	
Percent Black Population (Tertiles)				0.8057
T1 (Lowest Percent)				
T2 (Moderate Percent)	498	256 (51.4)	242 (48.6)	
T3 (Highest Percent)	471	238 (50.5)	233 (49.5)	
	352	186 (52.8)	166 (47.2)	
Percent Population Age 65+ Living Below Poverty				0.0512
1 (0-≤10%: High SES)				
2 (>10-<20%: Moderate SES)	524	279 (53.2)	245 (46.8)	
3 (≥ 20%: Low SES)	513	273 (53.2)	240 (46.8)	
	284	128 (45.1)	156 (54.9)	
Percent Population Living Below Poverty				0.0086
1 (0-≤10%: High SES)	515	273 (53.0)	242 (47.0)	
2 (>10-<20%: Moderate SES)	466	256 (54.9)	210 (45.1)	
3 (≥ 20%: Low SES)	340	151 (44.4)	189 (55.6)	

Table 6.2. (continued)

Area Based Residential Characteristics	Total N	Chemotherapy Received No. (%) n=680	Chemotherapy Not Received No. (%) n=641	P-value
County-level				
Racial Dissimilarity Index (Tertiles)				0.6868
T1 (Least Segregated)	153	79 (51.6)	74 (48.4)	
T2 (Moderately Segregated)	285	153 (53.7)	132 (46.3)	
T3 (Most Segregated)	883	448 (50.7)	435 (49.3)	
Income Dissimilarity Index (Tertiles)				0.8023
T1	135	72 (53.3)	63 (46.7)	
T2	276	145 (52.5)	131 (47.5)	
T3	910	463 (50.9)	447 (49.1)	
Racial Isolation Index (Tertiles)				0.3127
T1	375	205 (54.7)	170 (45.3)	
T2	357	176 (49.3)	181 (50.7)	
T3	589	299 (50.8)	290 (49.2)	
Income Isolation Index (Tertiles)				0.8517
T1	466	242 (51.9)	224 (48.1)	
T2	352	184 (52.3)	168 (47.7)	
T3	503	254 (50.5)	249 (49.5)	
Percent Black Population (Tertiles)				0.0506
T1 (Lowest Percent)	416	232 (55.8)	184 (44.2)	
T2 (Moderate Percent)	388	183 (47.2)	205 (52.8)	
T3 (Highest Percent)	517	265 (51.3)	252 (48.7)	
Percent Population Age 65+ Living Below Poverty				0.0934
1 (0-≤10%: High SES)	318	150 (47.2)	168 (52.8)	
2 (>10-<20%: Moderate SES)	859	461 (53.7)	398 (46.3)	
3 (≥ 20%: Low SES)	144	69 (47.9)	75 (52.1)	
Percent Population Living Below Poverty				0.0387
1 (0-≤10%: High SES)	292	146 (50.0)	146 (50.0)	
2 (>10-<20%: Moderate SES)	827	445 (53.8)	382 (46.2)	
3 (≥ 20%: Low SES)	202	89 (44.1)	113 (55.9)	

Table 6-3. Multivariable Analyses of Associations with Receipt of Chemotherapy

Patient Variables	N	Adjusted OR	95% CI
Patient Demographics			
Patient Race and RUCA code			
Black Urban	172	1	Reference
Black Rural	85	1.35	0.71-2.56
White Urban	732	1.14	0.75-1.73
White Rural	332	1.41	0.88-2.56
Age, y			
66-69	236	1	Reference
70-74	323	0.70	0.52-0.96
75-79	343	0.42	0.30-0.60
80-84	223	0.16	0.13-0.21
85+	196	0.02	0.01-0.04
Gender			
Male	579	1	Reference
Female	742	0.99	0.75-1.31
Marital Status			
Married	665	1	Reference
Widowed	462	0.64	0.48-0.85
Separated/Divorced	89	1.11	0.71-1.72
Single	67	0.41	0.25-0.67
Unknown	38	0.51	0.22-1.20
Patient Clinical Characteristics			
Number of Comorbid Illnesses			
0	649	1	Reference
1	366	0.72	0.53-0.98
2	181	0.50	0.36-0.70
3 or more	124	0.25	0.15-0.41
Tumor Location			
Proximal Colon (Right)	847	1	Reference
Distal Colon (Left)	431	0.78	0.59-1.03
Overlap Lesion and NOS*	43	0.78	0.33-1.87
Tumor Grade			
Low Grade	954	1	Reference
High Grade	320	0.95	0.68-1.35
Unknown	47	1.14	0.62-2.11

Table 6-3 (continued)

Hospital Characteristics	N	Adjusted OR	95 % CI
Hospital Volume (Quartile)			
Q1 (Lowest Volume)	21	0.38	0.11-1.30
Q2	108	0.68	0.46-1.01
Q3	291	0.91	0.63-1.32
Q4 (Highest Volume)	901	1	Reference
Medical School Affiliation			
Affiliated	394	1	Reference
Not Affiliated	927	1.10	0.84-1.43
Hospital Ownership			
Proprietary	184	1	Reference
Government and Non-Profit	1137	1.15	0.77-1.72
American College of Surgeons Oncology Group			
Member	209	1	Reference
Non-Member	1112	1.19	0.85-1.66

Table 6-3. (continued)

Area Based Residential Characteristics	Total N	Adjusted OR	95% CI
Census Tract –level			
Racial Dissimilarity Index (Tertiles)			
T1 (Least Segregated)	310	1	Reference
T2 (Moderately Segregated)	490	0.95	0.67-1.34
T3 (Most Segregated)	521	1.00	0.65-1.53
Income Dissimilarity Index (Tertiles)			
T1	328	1	Reference
T2	485	0.79	0.59-1.06
T3	508	0.93	0.67-1.30
Racial Isolation Index (Tertiles)			
T1	486	1	Reference
T2	473	2.70	1.64-4.44
T3	362	1.47	0.69-3.13
Income Isolation Index (Tertiles)			
T1	437	1	Reference
T2	473	0.90	0.54-1.50
T3	411	1.41	0.69-2.91
Percent Black Population (Tertiles)			
T1 (Lowest Percent)	498	1	Reference
T2 (Moderate Percent)	471	0.60	0.35-1.03
T3 (Highest Percent)	352	1.55	0.69-3.48
Percent Population Age 65+ Living Below Poverty			
1 (0-≤10%: High SES)	524	1	Reference
2 (>10-<20%: Moderate SES)	513	0.99	0.68-1.43
3 (≥ 20%: Low SES)	284	0.68	0.43-1.09
Percent Population Living Below Poverty			
1 (0-≤10%: High SES)	515	1	Reference
2 (>10-<20%: Moderate SES)	466	0.88	0.48-1.60
3 (≥ 20%: Low SES)	340	0.39	0.15-1.00

Table 6-3. (continued)

Area Based Residential Characteristics	Total N	Adjusted OR	95% CI
County-level			
Racial Dissimilarity Index (Tertiles)			
T1 (Least Segregated)	153	1	Reference
T2 (Moderately Segregated)	285	1.25	0.71-2.19
T3 (Most Segregated)	883	0.94	0.54-1.63
Income Dissimilarity Index (Tertiles)			
T1	135	1	Reference
T2	276	0.75	0.46-1.24
T3	910	0.97	0.54-1.74
Racial Isolation Index (Tertiles)			
T1	375	1	Reference
T2	357	1.29	0.75-2.22
T3	589	0.88	0.40-1.94
Income Isolation Index (Tertiles)			
T1	466	1	Reference
T2	352	1.24	0.89-1.73
T3	503	1.59	0.91-2.79
Percent Black Population (Tertiles)			
T1 (Lowest Percent)	416	1	Reference
T2 (Moderate Percent)	388	0.50	0.30-0.85
T3 (Highest Percent)	517	0.70	0.33-1.49
Percent Population Age 65+ Living Below Poverty			
1 (0-≤10%: High SES)	318	1	Reference
2 (>10-<20%: Moderate SES)	859	1.55	0.99-2.42
3 (≥ 20%: Low SES)	144	2.47	1.23-4.94
Percent Population Living Below Poverty			
1 (0-≤10%: High SES)	292	1	Reference
2 (>10-<20%: Moderate SES)	827	0.95	0.69-1.30
3 (≥ 20%: Low SES)	202	0.53	0.32-0.86

Appendix

Chemotherapy Claims Codes

Appendix Table 6-1. Chemotherapy Claims Codes

Chemotherapy Claims Code[108, 173]	Label
HCPCS chemotherapy codes	
C9205	Injection, oxaliplatin, per 5 mg
C9418	Cisplatin, powder or solution, brand name, per 10 mg
J8520	Capecitabine, oral, 150 mg
J8521	Capecitabine, oral, 500 mg
J0640	Injection, leucovorin calcium, per 50 mg
J9060	Cisplatin powder/solution per 10 mg
J9062	Cisplatin 50 mg
J9190	Fluorouracil 500 mg
J9206	Irinotecan 20 mg
J9263	Injection, oxaliplatin, 0.5 mg
Q0083	Chemotherapy administration not infusion technique only visit
Q0084	Chemotherapy administration infusion technique only visit
Q0085	Chemotherapy administration infusion and other technique visit
S0177	Levamisole hydrochloride, oral, 50 mg
CPT-4 chemotherapy codes	
96400	Chemotherapy, subcutaneous/intramuscular
96401	Chemotherapy administration, nonhormonal antineoplastic
96402	Chemotherapy administration, hormonal antineoplastic
96405	Intralesional chemotherapy administration
96406	Intralesional chemotherapy administration
96408	Chemotherapy, push technique
96409	Chemotherapy administration; push technique, single or initial substance/drug
96410	Chemotherapy, infusion method
96411	Chemotherapy administration;

	intravenous, push technique
96412	Chemotherapy, infuse method add-on
96413	Chemotherapy administration, infusion technique; single or initial substance/drug (1 hour)
96414	Chemotherapy, infuse method add-on
96415	Chemotherapy administration, infusion technique; each additional hour
96416	Chemotherapy administration, infusion technique (> 8 hours)
96417	Chemotherapy administration, infusion technique (1 hour)
96420	Chemotherapy, push technique
96422	Chemotherapy, infusion method
96423	Chemotherapy, infuse method add-on
96425	Chemotherapy, infusion method
96440	Chemotherapy, intracavitary
96445	Chemotherapy, intracavitary
96450	Chemotherapy, into CNS
96520	Pump refilling, maintenance
96521	Refilling and maintenance of portable pump
96522	Refilling and maintenance of implantable pump or reservoir for drug delivery
96523	Irrigation of implanted venous access device for drug delivery systems
96530	Pump refilling, maintenance
96542	Chemotherapy injection
96545	Provide chemotherapy agent
96549	Chemotherapy, unspecified
96567	Photodynamic treatment, skin
96570	photodynamic treatment, 30 minutes
96571	Photodynamic treatment, additional 15 minutes
ICD-9 supplementary classification chemotherapy codes	
E0779	Ambulatory infusion pump, for infusion ≥ 8 hours
E0780	Ambulatory infusion pump, for infusion < 8 hours
E0781	Ambulatory infusion pump, single or multiple channels
E0782	Infusion pump, implantable, nonprogrammable
E0783	Infusion pump system, implantable, programmable
E0786	Implantable programmable infusion

	pump, replacement
E0791	Parenteral infusion pump, stationary, single or multichannel
E9331	Antineoplastic and immunosuppressive drug reactions
E9307	Antineoplastic antibiotics
V581	Encounter or admission for chemotherapy
V662	Convalescence following chemotherapy
V672	Cancer chemotherapy follow-up
ICD-9 procedure chemotherapy code	
9925	Injection or infusion of cancer chemotherapy substance
Medicare Noninstitutional Data BETOS code	
O1D	Chemotherapy
Revenue Center chemotherapy codes	
0331	Radiology therapeutic–chemotherapy injected
0332	Radiology therapeutic–chemotherapy oral
0335	Radiology therapeutic–chemotherapy intravenous
Claims diagnosis-related group code	
410	Chemotherapy
Additional codes used as suggested from the literature and/or National Cancer Institute[108, 174] : HCPCS codes J8530-J8999, J9000-J9999 **CPT-4 codes** 96550-96599 **HCPCS Level II Chemotherapy Administration codes**, including 2005 Medicare Oncology Demonstration Project HCPCS codes related to symptoms associated with chemotherapy use (in **boldface**): EA, C8953- C8955, G0292, G0355, G0359, G0361, G0362, G8371, G8372, G8373, G8374, G8377, **G9021-G9032**, J8510, J8520, J8521, J0640, Q0083-Q0085, Q0163-Q0181, S9329-S9331	

Modeling Strategy

For the initial model:

1. No covariate was dropped from the model to allow for adequate control of potential confounders for each of the 9 exposure variables; 1: race by rural-urban status, 2-5: census tract level segregation indices and 6-9: county level segregation indices.

2. The interaction term, race by marital status was included in the model based on findings from the literature noting this variable as a potential effect modifier in similar models using receipt of adjuvant chemotherapy as the dependent variable.

Multivariate GEE Logistic Models

Model specification

Fully adjusted model accounting for covariates, potential confounders and effect modifier

$$\text{Logit } P(\mathbf{X}) = \beta 0 + \sum_{i=1}^{2} \beta_i E_i + \sum_{i=1}^{p2} \gamma_i V_i + E_i\left(\sum_{i=1}^{p4} \delta_{1i} W_i\right) + E_i\left(\sum_{i=1}^{2} \delta_{2i} E\right) + \varepsilon$$

Where

P(**X**) = probability of receipt of adjuvant chemotherapy, given the collection of **X**s, (E, V, and Ws)

E_i=the primary exposures of interest (race and rural-urban residence, 8 residential segregation indices)

V_i=potential confounders and covariates

W_i=potential effect modifiers

β0 = baseline or background log odds, ignoring all other E, V, Ws

β =coefficient of the main exposure variables, represents the change in the log odds for 1 unit change in E, when all other variables are fixed

γ = coefficient of the control variables (potential confounders and covariates)

δ = coefficient of the effect modifiers

ε = random error

Model Specification:

1. For the first step in model specification, collinearity of the initial model was conducted.

Collinearity Diagnostic Results

Initial Model:

Largest Condition Index= 21.803.

The rule assessed- Collinearity between variables is present in a logistic regression model when both of the following conditions are satisfied: Condition Index > 30 and more than one Variance Decomposition Proportion, not including the intercept is ≥ 0.5. No collinearity was indicated in this initial model.

2. Backwards elimination for the multivariate model was performed on the effect modifier (interaction term). The p-value for the interaction term race by marital status was 0.6929, so this term was eliminated from the model. No interaction terms remained in the model.
3. All covariates including potential confounders were kept in the model (final model).
4. Collinearity of the final model was conducted.

Collinearity Diagnostic Results

Reduced Model (Final):

Largest Condition Index= 21.4338

No collinearity was indicated in this final model.

In this analysis, we presumed that the outcome, receipt of chemotherapy, was correlated among observations treated within the same hospital, and/or residing in the same census tract and /or county (clusters). To account for these within cluster correlation among observations, we employed a GEE model. The GEE model was built using the Miglioretti method [169] which uses a SAS macro program to calculate the variance of each regression coefficient (beta estimate) while accounting for correlation in outcome within each separate cluster (e.g. hospital, census tract and county). In order to calculate corrected standard errors adjusted for three levels of clustering (hospital, census tract and county), seven separate models must be fit: three clustering separately on each of the clustering factors; three clustering on each pair-wise combination of the cluster levels; and one clustering on the combination of all three cluster levels. Each of the seven models produce a covariance matrix based on the clustering unit (hospital, census tract, etc). The corrected covariance matrix accounting for the correlation of outcome within the three clusters is given by the addition of the first three covariance matrices minus each of the second three matrices plus the final matrix [169] .

The seven models and each covariance matrices are produced by running multiple iterations of the model (with the use of the macro) where each iteration calculates the variance of the regression coefficients for a single cluster or cluster combination. For example, iteration 1 fits a model accounting for the correlation of the outcome within hospital clusters, iteration 2 fits a model accounting for correlation of the outcome within census tract clusters and so on. In order for the regression coefficients to remain unmodified during each iteration of the macro (model fitting) an independent correlation structure was used. If another correlation structure was used, such as exchangeable, the regression coefficients may change during each model fit (iteration) which is undesired. To support the use of the independent correlation structure in this analysis,

Liang et al showed that the choice of the correlation structure is not critical for valid inference. They state that within a GEE model a "sandwich variance" estimator is empirically calculated from the data and accounts for arbitrary correlations among observations within a cluster [175]. Therefore, the use of the independent correlation structure produces a robust sandwich variance estimator which provides valid standard errors for the regression coefficients [175]. The sandwich variance is estimated by the sum of the weighted residual cross-product terms for all pairs of observations that are from the same cluster.

Below is the SAS macro used to create a corrected covariance matrix that adjusts for the correlation of outcomes among the non-nested clusters within our analysis.

SAS Code for Final GEE Model and Variance (Standard Error) Calculation

```
data models2;
set final.study2;
c1id=Hospital code;
c2id=Census tract code;
c3id=County code;
c1c2id=Hospital code|| '|' || Census tract code;
c1c3id=Hospital code|| '|' || County code;
c2c3id=Census tract code|| '|' || County code;
c1c2c3id=Hospital code|| '|' || Census tract code || '|' || County code;
run;
```

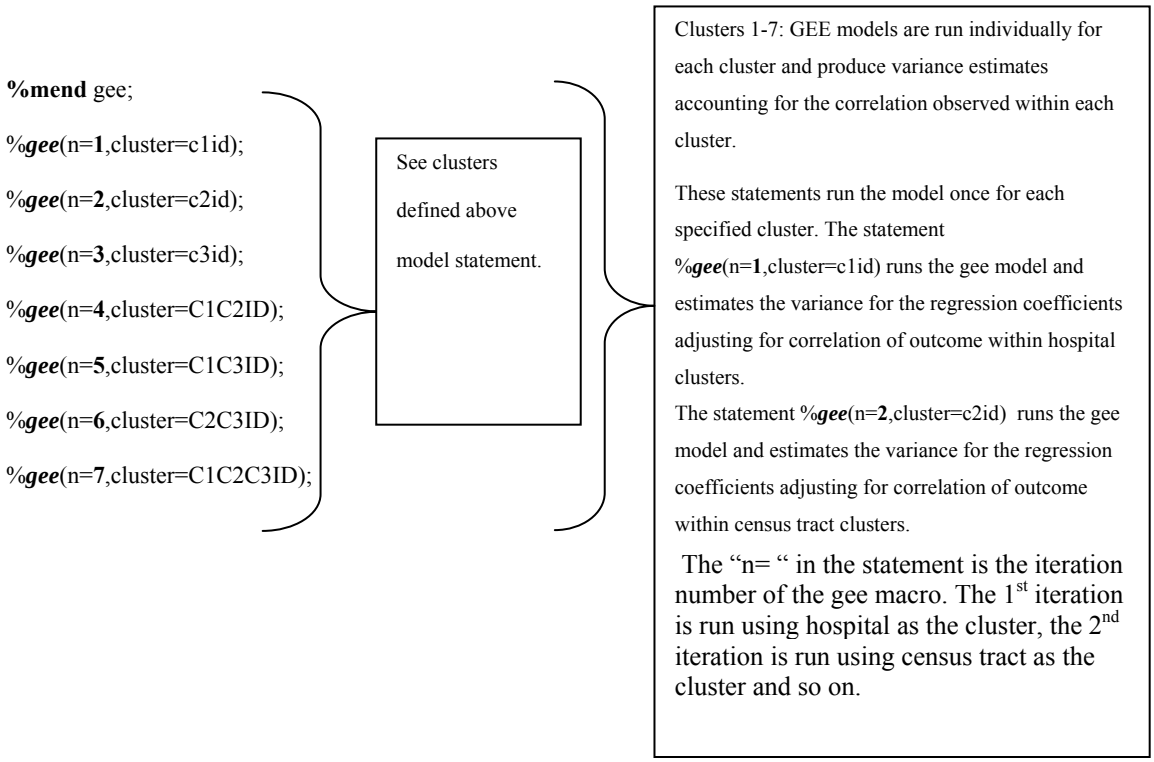
This data step creates cluster identifiers for the model. Let c1id identify observations belonging to the same cluster c1, c2id identify observations belonging to c2 and c1c2id identify observations belonging to both c1 and c2 and so on.

This macro is used to run a model for each cluster assigned below.

Initializing macro:

```
%macro gee(n=1,cluster=c1id);

 proc genmod data=models2 descending;

 class  race_ruca (ref='Black Urban' param=ref) age_cat1 (ref='1' param=ref)  sex_cat (ref='Male' param=ref)
      marital_cat2 (ref='married' param=ref) comorbid_trend (ref='0' param=ref) grade_cat2 (ref='Low Grade' param=ref)
      sitelabel (ref='Proximal Colon (Right)' param=ref) hospvol_quart (ref='4' param=ref)
      hosp_aff2lev (ref='1' param=ref) hosp_own2(ref='1' param=ref) acosog_02_2 (ref='Member' param=ref)
      new_cnty_diss_pov_cat (ref='1' param=ref) new_cnty_iso_pov_cat (ref='1' param=ref)
      new_cnty_diss_race_cat (ref='1' param=ref) new_cnty_iso_race_cat (ref='1' param=ref)
      new_ctbg_diss_race_cat (ref='1' param=ref) new_ctbg_iso_race_cat (ref='1' param=ref)
      new_ctbg_iso_pov_cat (ref='1' param=ref) new_ctbg_diss_pov_cat (ref='1' param=ref)
      new_cnty_perc_blk_cat (ref='1' param=ref) new_cnty_pov_pop_cat (ref='1' param=ref)
      new_cnty_pov_age65_cat(ref='1' param=ref) new_ctbg_perc_blk_cat (ref='1' param=ref)
      new_ctbg_pov_pop_cat (ref='1' param=ref) new_ctbg_pov_age65_cat (ref='1' param=ref)
      &cluster;Model  medicare_chemo = race_ruca age_cat1 sex_cat marital_cat2 comorbid_trend grade_cat2 sitelabel
          hospvol_quart hosp_aff2lev hosp_own2 acosog_02_2 new_cnty_diss_pov_cat new_cnty_iso_pov_cat
          new_cnty_diss_race_cat new_cnty_iso_race_cat new_ctbg_diss_race_cat new_ctbg_iso_race_cat
          new_ctbg_iso_pov_cat new_ctbg_diss_pov_cat new_cnty_perc_blk_cat new_cnty_pov_pop_cat new_cnty_pov_age65_cat
         new_ctbg_perc_blk_cat new_ctbg_pov_pop_cat new_ctbg_pov_age65_cat /dist=binomial;

 repeated subject=&cluster/type=indep ecovb;
 ods output GEEEmpPEst=beta GEERCov=V&n;

quit;
```

Variance estimates are produced from each model. These estimates are used below in a matrix using proc iml to calculate estimates of standard errors for each β adjusting for clustering of outcomes at hospital and


%mend gee;
%gee(n=1,cluster=c1id);
%gee(n=2,cluster=c2id);
%gee(n=3,cluster=c3id);
%gee(n=4,cluster=C1C2ID);
%gee(n=5,cluster=C1C3ID);
%gee(n=6,cluster=C2C3ID);
%gee(n=7,cluster=C1C2C3ID);
See clusters defined above model statement.
Clusters 1-7: GEE models are run individually for each cluster and produce variance estimates accounting for the correlation observed within each cluster.
These statements run the model once for each specified cluster. The statement %gee(n=1,cluster=c1id) runs the gee model and estimates the variance for the regression coefficients adjusting for correlation of outcome within hospital clusters.
The statement %gee(n=2,cluster=c2id) runs the gee model and estimates the variance for the regression coefficients adjusting for correlation of outcome within census tract clusters.
The "n= " in the statement is the iteration number of the gee macro. The 1st iteration is run using hospital as the cluster, the 2nd iteration is run using census tract as the cluster and so on.

The variance calculation for the beta estimates accounting for three clusters (i.e. hospital, census tract and county is the diagonal of the covariance matrix defined as the linear combination of seven covariance matrices as follows:

V(β)= V(hospital cluster) + V (census tract cluster) + V(county cluster)-V(hospital and census tract cluster) – V (hospital and county cluster) –V(census tract and county cluster) + V (hospital, census tract and county cluster)

V(x) is the estimated variance from a working independence correlation GEE clustering on cluster x. V(x,y) clusters on unique combinations of cluster x and cluster y. V(x,y,z) clusters on unique combinations of cluster x, cluster y and cluster z.

*The covariance matrices may be read into PROC IML to combine and to calculate the corrected standard errors for the regression coefficients;

```
proc iml;
use V1; read all var {rowname}; read all var(rowname) into V1; close V1;
use V2;  read all var(rowname) into V2; close V2;
use V3;  read all var(rowname) into V3; close V3;
use V4;  read all var(rowname) into V4; close V4;
use V5;  read all var(rowname) into V5; close V5;
use V6;  read all var(rowname) into V6; close V6;
use V7;  read all var(rowname) into V7; close V7;
V=V1+V2+V3-V4-V5-V6+V7; SE=sqrt(vecdiag(V)); print SE;
quit;
```

Variance and standard error estimates are calculated for the model, incorporating the variance estimates previously calculated from each cluster's respective model.

Chapter 7: Racial Differences in Receipt and Completion of Adjuvant Chemotherapy among Stage III Colon Cancer Patients in Southwest Georgia

Abstract

Background: The receipt and completion of adjuvant chemotherapy among stage III colon cancer patients is associated with improved prognosis. Racial differences in these measures have been documented in largely urban and suburban populations. No studies to our knowledge have evaluated these disparities and the roles of area-based segregation measures in these disparities among patients residing in the rural parts of the U.S. South.

Methods: Study data was abstracted from medical records of persons diagnosed with stage III colon cancer in Southwest Georgia (SWGA) during 2001-2003. Multivariable logistic models were used to assess the effect of race on the receipt and completion of chemotherapy and the results were expressed as adjusted odds ratios (ORs) accompanied by 95% confidence intervals (CIs).

Results: Overall, 81 patients (65%) received chemotherapy and of those who initiated or had a chemotherapy plan, 56 (65%) completed treatment. While race was not a significant predictor of chemotherapy receipt (aOR=0.60; 95% CI: 0.21-1.67), white SWGA patients were less likely to complete adjuvant chemotherapy compared to their Black counterparts (aOR=0.06, 95% CI: 0.01-0.37). Additionally, receipt of chemotherapy was higher among younger patients and those receiving therapy at an accredited cancer facility. Chemotherapy completion was more common among married patients and those with private insurance.

Conclusion: Our findings in SWGA are different from those reported in other parts of the US, and thus require confirmation. If confirmed, however, the observed racial disparities in the completion of therapy may be explained by differences in chemotherapy tolerance, toxicity and patient support.

Introduction

Among colon cancer patients in the U.S., the receipt of adjuvant chemotherapy for stage III disease is associated with improved survival, prognosis and outcomes [118, 162] and is the current most common measure of treatment quality [23, 24, 165]. Clinical trials among breast cancer patients have shown that survival and prognosis are further improved when chemotherapy is completed as planned [176, 177]. Studies showing the effect of the completion of therapy among colon cancer cases also suggest improved survival and prognosis but the literature is not as well-established [73, 178, 179]. The previous studies used data from clinical trials or medical claims, and to our knowledge no previous research relied on information directly abstracted from medical records as a means of determining receipt and completion of chemotherapy.

Of interest in this study is the extent of racial disparities in the receipt and completion of chemotherapy among predominantly rural stage III colon cancer patients. In the U.S., disparities in the receipt of chemotherapy have been observed [6, 12, 118, 163]. In general, marginalized populations are less likely to receive appropriate cancer therapy than their counterparts [15, 101, 120, 164]. For colon cancer, few studies have assessed disparities in the receipt and completion of adjuvant chemotherapy among patients residing in predominantly rural areas [180].

Recent studies have assessed the role of area-based factors as determinants of access to and receipt of quality health care [8, 15, 16, 166]. There is indication that area-based measures such as residential segregation have an independent affect on quality of care and may also explain, at least in part the observed racial disparities [15, 166]. To our knowledge, the role of area-based measures, such as residential segregation, in explaining racial disparities in treatment among rural colon cancer patients has not been assessed.

This study presents the first focused evaluation of both the receipt and the completion of adjuvant chemotherapy for colon cancer in Southwest Georgia (SWGA) a largely rural area with population of approximately 700,000. In the current analyses we evaluate the independent

association of race with both the receipt and the completion of adjuvant chemotherapy for stage III colon cancer among SWGA residents and investigate to what extent (if any) the racial differences in this patient population can be explained by residential segregation and other area-based factors.

Methods

The study population included all women and men residing in SWGA who were diagnosed with stage III colon cancer between January 1, 2001 and December 31, 2003, and who received at least their first 12 months of therapy post diagnosis entirely within the region. Incident colon cancer cases were identified through the Georgia Cancer Registry. Only patients with documented cancer directed surgery (defined as resection or bypass) were considered in these analyses because adjuvant chemotherapy by definition is the chemotherapy delivered in addition to surgical treatment.

SWGA is comprised of 33 counties in which approximately 82% of the residents live in non-metropolitan areas [170]. The majority of cancer patients in this region receive care at one or more of the four SWGA cancer centers accredited by the American College of Surgeons' (ACoS) Commission on Cancer [170, 181]. The population of SWGA differs from the rest of the state and the U.S. as a whole in several respects including having a larger proportion of African Americans, lower median household income and lower levels of education [181]. A detailed discussion of the SWGA region, cancer care centers and study data collection methodologies can be found in previously published articles [170, 181].

The study was approved by the institutional review boards at Emory University, the Centers for Disease Control and Prevention, and the Georgia Department of Community Health and by research review committees at the four main cancer centers in SWGA.

<u>Data Collection</u>

Trained onsite abstractors used a customized electronic data collection instrument to abstract detailed information from medical records. The electronic instrument guided the abstractor through a sequence of study-relevant inquiries on treatments planned, delivered and discontinued. Data abstraction was conducted at each of the four cancer centers in SWGA and at free-standing clinics across the area. A more detailed account of the data abstraction has been previously published [170].

Variables of Interest:

The main independent variable of interest was patient race (black and white non-Hispanic). The dependent variables in this study were receipt of adjuvant chemotherapy following surgery for colon cancer (yes or no) and completion of adjuvant chemotherapy among those who started or had a plan for adjuvant chemotherapy. For the completion of chemotherapy analysis, patients whose reason for discontinuing chemotherapy was death (N=3) were coded as having completed therapy since discontinuation of chemotherapy in this instance was regarded as a necessary change in treatment rather than a discretionary decision.

County level segregation measures, which serve as predictors of the quality of and access to community health care resources [5, 6], were examined as potential confounders and effect modifiers. Four segregation indices were calculated for each patient's county: racial dissimilarity index, income dissimilarity index, racial isolation index and income isolation index. The racial segregation measures assess black-white segregation. The income segregation measures assess the segregation of those living below the federal poverty line from those living at or above the federal poverty line. These measures were calculated using data from the 2000 U.S. Census. The detailed description of the calculations required for obtaining these segregation indices is included in Appendix.

Additional covariates used in these analyses included individual, facility and area-based variables. The individual-level covariates of interest were patient-related characteristics such as

gender (male or female), age (categorized as <50, 50-64, 65-74 and 75+), marital status (married, not married), and number of co-morbid illnesses (0, 1 or more). Cancer-related characteristics considered in the analyses included primary site and tumor grade. Health insurance status (Private, Government and Uninsured) was also assessed. Private insurance included Private Fee for Service, HMO, Medicare with supplemental benefits, and VA/CHAMPUS. Government insurance included Medicare only (without supplement), Medicaid and Medicaid pending. The category "uninsured" included those with no insurance, self-pay or charity.

Facilities where care was received were categorized as either "SWGA cancer center" or "Other". The rural-Urban residence variable was based on the Rural Urban Commuting Area (RUCA) code and was categorized as "metro/urban," "large rural town," or "small rural town" [98, 146]. Other area-based variables included the percent of black population within each county of residence, which was divided into tertiles and the percent of the county population living below the poverty level dichotomized as high versus medium/low using the cutoff of 20%, which defines the "poverty areas" [155] .

Statistical Analysis:

The data analyses began with descriptive statistics. Unadjusted analyses were used to compare distributions of exposure variables and covariates among patients with and without receipt of adjuvant chemotherapy. A separate analysis limited to patients who received or had a plan for adjuvant chemotherapy compared those with and without therapy completion. Categorical variables were compared using χ^2 statistics or Fisher's exact tests depending on the number of observations under study. Stratified analyses were performed to test for interaction and assess confounding.

Multivariable logistic regression models were used to assess the independent effects of the exposure of interest (race) on the dependent variables (treatment receipt in model 1 and treatment completion in model 2) after controlling for potential confounders and effect modifiers. Because the study population was relatively small, the final models were limited to only those variables that served as confounders or effect modifiers of the main association between race and the dependent variable. Prior to model building, a variable screening process was performed as described by Kleinbaum and Klein [156]. The screening determined potential interactions and confounders of the association between race and each dependent variable. Interaction was evaluated by assessing the p-value associated with the cross-product term in the screening logistic models that contained the main exposure variable race, the covariate of interest (variable being assessed for interaction) and the cross-product of that covariate with race. Cross-product terms with p-values ≤ 0.10 were considered as possible interaction factors. Following the assessment of interaction, each covariate was then screened for confounding. Confounding was considered present when the crude odds ratio (cOR) of the association between race and the dependent variable differed by 10% or more from the adjusted odds ratio (aOR) after controlling for the covariate under evaluation.

The covariates and their cross-products that met the criteria for confounding or interactions were then included in the initial multivariable model. Backwards elimination was then conducted on the initial models to produce the parsimonious final models. Backwards elimination was accomplished by first removing all non-significant interaction terms, and then by excluding non-confounders (i.e., variables, which, once eliminated from the model, changed the aOR for race by less than 10%).

Collinearity diagnostics were performed for both the initial and the final models. The modeling results were expressed as aORs accompanied by the corresponding 95% confidence intervals (CI). Statistical significance of each term in the multivariable models was assessed at a level of $\alpha=0.05$, two-tailed for all analyses. Analyses were performed using SAS statistical software system, version 9.2 for Windows (SAS Institute Inc., Cary, NC). For more details of the modeling strategy see Appendix.

Results

The study population included 125 eligible stage III colon cancer cases, and of those 81 (65%) received adjuvant chemotherapy. Of those who began chemotherapy or had a plan for chemotherapy (n=86), 56 SWGA patients (65%) completed chemotherapy treatment.

Receipt of Adjuvant Chemotherapy

The percent of whites receiving adjuvant chemotherapy (63.7%) was slightly lower than that among blacks (66.7%) although the difference was not statistically significant (Table 1a). Those living in large rural towns were less likely to receive adjuvant chemotherapy than those living in metro/urban areas or small rural areas and this result was statistically significant. As shown in Tables 1a and 1b, receipt of adjuvant chemotherapy was statistically significantly associated with younger age, health insurance status (more likely for persons with private insurance), treatment site (more likely in facilities designated as a cancer center) and county

income dissimilarity index (those living in counties with a moderate level of income segregation were less likely to receive treatment than those living in counties with low or high level income segregation). The associations between receipt of adjuvant chemotherapy and county-level variables such as percent of blacks in the population, racial dissimilarity index and racial and income isolation indices, did not quite reach statistical significance with p-values less than 0.10 but greater than 0.05 (Table 1b).

In the multivariable analysis (Table 2) after controlling for potential confounders, white colon cancer patients were not statistically significantly different from their black counterparts with respect to receipt of adjuvant therapy (aOR of 0.60; 95% CI: 0.21-1.67), although the point estimate suggests a lower likelihood among white patients . Older age (75 years and older) patients were less likely to receive chemotherapy than younger patients (64 years and younger) and those treated at a SWGA cancer center were significantly more likely to receive chemotherapy than those who received care at other SWGA facilities. Insurance status did not demonstrate a statistically significant association with chemotherapy receipt.

Completion of Adjuvant Chemotherapy

Figure 1, shows the distribution of the reasons for early termination (non-completion) of chemotherapy among colon cancer patients in this study. Among the 30 patients who did not complete chemotherapy, the top reasons for early termination were toxicity (30%), disease progression (27%) and failing to start planned chemotherapy (17%).

In the unadjusted analyses (Tables 3a and 3b), 57.4% of whites (N=31) and 78.1% of blacks (N=25) completed chemotherapy but the difference was not statistically significant (p-value=0.05). The only factor showing a statistically significant association with treatment completion in the crude analyses was patient's marital status. Seventy-six percent (N=39) of

married patients completed chemotherapy compared to 48.6% percent (N=17) of non-married patients (p=0.0077).

In the multivariable analyses (Table 4), completion of chemotherapy was significantly less common among whites than among blacks (aOR=0.06, 95% CI: 0.01-0.37), among non-married than among married patients (aOR=0.26, 95% CI: 0.09-0.81), and among those without private insurance than among those with private insurance (aOR=0.13. 95% CI: 0.03-0.68).

Discussion

This study of stage III colon cancer patients in predominantly rural Southwest Georgia found that about two-thirds received (or initiated) chemotherapy and of those who initiated or had a plan for chemotherapy 65% completed their treatment. Contrary to expectations we found that white patients were significantly less likely to complete adjuvant chemotherapy compared to their black counterparts, although race was not a significant predictor of adjuvant chemotherapy receipt. These findings were incongruent with other population studies based on mostly urban and suburban populations.

Nation-wide studies linking data from the Surveillance Epidemiology and End Results (SEER) program and Medicare have typically reported that black stage III colon cancer patients were less likely to receive adjuvant chemotherapy compared to whites [12, 13, 19, 103]. These studies were conducted on predominantly urban and suburban populations and used data from the 1990s immediately following the NIH consensus that recommended the use of adjuvant chemotherapy for stage III colon cancer [114]. By contrast our study was based on 2001-2003 data that were limited to patients that received their treatment in SWGA, a type of geographic area that was likely under-represented in the previous research. Rates of chemotherapy have increased following the NIH consensus as demonstrated by Gross et al [19]. Although Gross et al noted a persistent racial disparity in receipt of chemotherapy from 1992 to 2002; it is also possible that

this persistent national disparity may not be generalized to our study population and to our study period. The social and demographic characteristics of SWGA residents differ from those of the overall U.S. population and these differences may influence differential health care practices [150]. Tropman et al assessed receipt of guideline recommended chemotherapy among rural North and South Carolina colon cancer patients and found treatment to be higher among white patients [101]. This finding along with ours suggests that rural health care is complex and differs by state and region.

Our study is not the only one to report absence of racial disparity in receipt of chemotherapy. Roetzheim et al. used data from the state of Florida cancer registry to assess racial disparities in colorectal cancer (CRC) care among patients diagnosed in 1994 [5]. Investigators used hospital discharge abstract data and cancer registry data on first course of treatment to assess receipt of radiation and chemotherapy. No racial disparities in the receipt of adjuvant therapy were found in crude or adjusted analyses (controlling for health insurance type, census-derived measures of income and education, and rural/urban residence). In a more recent study, McGory et al assessed the association between race/ethnicity and the underuse of appropriate adjuvant therapy for stage III colon or stage II/III rectal cancer patients reported to the California Cancer Registry from 1994 to 2001 [93]. Investigators adjusted for patient demographic factors including type of insurance, year of diagnosis and census tract based SES measure (percentage of person living below the poverty threshold). As in our study, there was no statistically significant association between race and receipt of chemotherapy for stage III colon cancer.

While Roetzheim et al and McGory et al. studies are similar to ours in the use of a single state population that included both non-Medicare and Medicare patients; they differ from our study with respect to the data collection methods. Only our study used a detailed medical record review to assess the receipt and completion of adjuvant treatment. In addition, only ours of the

three studies focused specifically on the rural population and used only the post-2000 information (others included data from the 1990s).

In another recent study also conducted in SWGA, Lipscomb et al observed that compared to black patients white women with early stage breast cancer had a lower rate of adjuvant chemotherapy receipt in unadjusted analyses, but the association was no longer statistically significant in the multivariable models [170]. When assessing the effect of race on completion of chemotherapy, Lipscomb and colleagues also found that white SWGA breast cancer patients were less likely to complete adjuvant chemotherapy than their black counterparts, but the difference was only detectable among the non-married women [170]. By contrast among married women there was no evidence of a racial disparity in adjuvant chemotherapy completion. In general, these findings mirror ours and suggest that race may play a different role in rural southwest Georgia than in other parts of the country.

To our knowledge only one other study (besides ours) evaluated both receipt and completion of adjuvant therapy among colon cancer patients [180]. This was an analysis of SEER-Medicare linked data, in which black colon cancer patients had lower rates of chemotherapy initiation than white patients in unadjusted analyses; a multivariable assessment of this outcome was not performed. In both unadjusted and adjusted analyses, there were no racial differences in chemotherapy completion rates. Although compared to ours this study controlled for a larger number of variables, their use of claim-based methods to assess chemotherapy receipt and completion rates may have led to incomplete ascertainment of treatment.

To our knowledge, our study is the first to evaluate racial differences in adjuvant chemotherapy completion rates among predominantly rural colon cancer patients. The finding that black patients were more likely than white patients to complete chemotherapy has not been reported previously. Lipscomb et al point to at least one potential explanation for this finding [170]. According to their discussions with providers and administrators at the four cancer centers in

SWGA, each center provided free transportation to patients petitioning for help [170]. It is possible that this service attenuated racial differences in care and may have led to increased chemotherapy completion rates among black patients.

The main limitation of the current study is its relatively small size, which limited our ability to simultaneously control for multiple variables; however, with the use of covariate screening techniques we were able to adjust for the most pertinent confounders. Our study was made possible by the active and established cancer research partnership involving eight institutions: Emory University in Atlanta, the Centers for Disease Control and Prevention (CDC), the Georgia Comprehensive Center Registry, the Southwest Georgia Cancer Coalition, and the four SWGA cancer centers [150]. The Coalition serves as the link between research institutions and local community cancer providers, and it is the key organizational force for cancer prevention, education, care and research in the region. The presence of an active patient support and advocacy organization such as the SWGA Cancer Coalition undoubtedly facilitates research efforts. However, it is also possible that the Coalition's success makes it difficult to generalize the findings in SWGA to other rural parts of Georgia and the rest of the country.

Our study is also notable for its methodological strengths. The use of detailed medical record abstraction to determine receipt and completion of chemotherapy allows for a thorough data collection that is presumed to be more compete than use of claims-based information. The study drew from a complete census (rather than a sample) of the SWGA colon cancer population during the years 2001-2003 and thus represents true population-based research that was unaffected by selection or non-response bias. The majority of the patients in our data received care at four of the cancer centers in the area that are partners in the SWGA Cancer Coalition. Medical record keeping and coding typically vary by institution and region, but this appears to be less of an issue across the SWGA health care facilities. The likely similarity in medical records is expected to lead to greater consistency of data in our study.

Future analyses of colon cancer patients in rural areas should extend to more recent years and include greater geographic diversity. Additional measures such as patient receipt of free transportation for treatment at the cancer centers should be included in analyses to evaluate the role of this service on rates of adjuvant chemotherapy receipt and completion. The finding that failure to complete therapy seems to disproportionately affect white colon cancer patients points to possible issues that may include racial differences in chemotherapy tolerance, toxicity and simply the provision of consistent transportation to rural cancer care centers. Further evaluation of racial disparities in rural Georgia and in similar areas is undoubtedly warranted.

References

1. Neugut, A.I., et al., *Use of adjuvant chemotherapy and radiation therapy for rectal cancer among the elderly: a population-based study.* Journal of Clinical Oncology, 2002. 20(11): p. 2643-50.
2. Dobie, S.A., et al., *Survival benefits and trends in use of adjuvant therapy among elderly stage II and III rectal cancer patients in the general population.* Cancer, 2008. 112(4): p. 789-99.
3. American College of Surgeons. *CoC Quality of Care Measures*. Cancer Programs 2007; Revised March 2, 2011:[Available from: www.facs.org/cancer/qualitymeasures.html.
4. Sargent, D.J., et al., *A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients.* N Engl J Med, 2001. 345(15): p. 1091-7.
5. Gill, S., et al., *Pooled Analysis of Fluorouracil-Based Adjuvant Therapy for Stage II and III Colon Cancer: Who Benefits and by How Much?* Journal of Clinical Oncology, 2004. 22(10): p. 1797-1806.
6. Bonadonna, G. and P. Valagussa, *Dose-response effect of adjuvant chemotherapy in breast cancer.* N Engl J Med, 1981. 304(1): p. 10-5.
7. *Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials.* Lancet, 2005. 365(9472): p. 1687-717.
8. Gill, S., et al., *Pooled analysis of fluorouracil-based adjuvant therapy for stage II and III colon cancer: who benefits and by how much?* J Clin Oncol, 2004. 22(10): p. 1797-806.
9. Moertel, C.G., et al., *Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report.* Ann Intern Med, 1995. 122(5): p. 321-6.
10. Haller, D.G., et al., *Phase III study of fluorouracil, leucovorin, and levamisole in high-risk stage II and III colon cancer: final report of Intergroup 0089.* J Clin Oncol, 2005. 23(34): p. 8671-8.
11. Earle, C.C., et al., *Who gets chemotherapy for metastatic lung cancer?* Chest, 2000. 117(5): p. 1239-46.
12. Sundararajan, V., et al., *Variations in the use of adjuvant chemotherapy for node-positive colon cancer in the elderly: a population-based study.* Cancer J, 2001. 7(3): p. 213-8.

13. VanEenwyk, J., J.S. Campo, and E.M. Ossiander, *Socioeconomic and demographic disparities in treatment for carcinomas of the colon and rectum.* Cancer, 2002. 95(1): p. 39-46.
14. Berrios-Rivera, J.P., et al., *Variations in chemotherapy and radiation therapy in a large nationwide and community-based cohort of elderly patients with non-Hodgkin lymphoma.* American Journal of Clinical Oncology, 2007. 30(2): p. 163-71.
15. Tropman, S.E., et al., *Colon cancer treatment in rural North and South Carolina.* Cancer Detect Prev, 1999. 23(5): p. 428-34.
16. Ayanian, J.Z., et al., *Use of adjuvant chemotherapy and radiation therapy for colorectal cancer in a population-based cohort.* J Clin Oncol, 2003. 21(7): p. 1293-300.
17. Haas, J.S., et al., *Racial segregation and disparities in breast cancer care and mortality.* Cancer, 2008. 113(8): p. 2166-72.
18. Dobie, S.A., et al., *Completion of therapy by Medicare patients with stage III colon cancer.* J Natl Cancer Inst, 2006. 98(9): p. 610-9.
19. Hayanga, A.J., et al., *Residential segregation and access to surgical care by minority populations in US counties.* Journal of the American College of Surgeons, 2009. 208(6): p. 1017-22.
20. Hayanga, A.J., et al., *Racial clustering and access to colorectal surgeons, gastroenterologists, and radiation oncologists by African Americans and Asian Americans in the United States: a county-level data analysis.* Arch Surg, 2009. 144(6): p. 532-5.
21. Haas, J.S., et al., *Association of area sociodemographic characteristics and capacity for treatment with disparities in colorectal cancer care and mortality.* Cancer, 2011. 117(18): p. 4267-4276.
22. Lipscomb, J., et al., *Black-white differences in receipt and completion of adjuvant chemotherapy among breast cancer patients in a rural region of the US.* Breast Cancer Res Treat. 133(1): p. 285-96.
23. Goodman, M., et al., *Cancer outcomes research in a rural area: a multi-institution partnership model.* J Community Health, 2009. 34(1): p. 23-32.
24. U.S. Department of Agriculture Economic Research Service. *ERS/USDA Briefing Room: Measuring Rurality: Rural-Urban Commuting Area Codes.* September 23, 2009]; Available from: http://www.ers.usda.gov/briefing/Rurality/RuralUrbanCommutingAreas/.
25. Cromartie, J. and S. Bucholtz. *ERS/USDA Data - Rural Definitions: State-Level Maps*. March 12, 2010]; Available from: www.ers.usda.gov/Data/Ruraldefinitions/GA.pdf.
26. Krieger, N., *Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology.* American Journal of Public Health, 1992. 82(5): p. 703.
27. Kleinbaum, D.G. and M. Klein, *Additional Modeling Strategy Issues Logistic Regression*, in *Logistic Regression: A Self-Learning Text*. 2010, Springer New York. p. 241-299.
28. Gross, C.P., et al., *Racial disparities in cancer therapy: did the gap narrow between 1992 and 2002?* Cancer, 2008. 112(4): p. 900-8.
29. Baldwin, L.M., et al., *Explaining black-white differences in receipt of recommended colon cancer treatment.* J Natl Cancer Inst, 2005. 97(16): p. 1211-20.
30. White, A., et al., *Racial disparities and treatment trends in a large cohort of elderly African Americans and Caucasians with colorectal cancer, 1991 to 2002.* Cancer, 2008. 113(12): p. 3400-9.

31. *NIH consensus conference. Adjuvant therapy for patients with colon and rectal cancer.* Jama, 1990. 264(11): p. 1444-50.
32. Goodman, M., et al., *Cancer outcomes research in a rural area: a multi-institution partnership model.* Journal of Community Health, 2009. 34(1): p. 23-32.
33. Roetzheim, R.G., Pal N., Gonzalez E. C., Ferrante J. M., Van Durme D. J., Krischer J. P., *Effects of health insurance and race on colorectal cancer treatments and outcomes.* American Journal of Public Health, 2000. 90(11): p. 1746-1754.
34. McGory, M.L., et al., *A patient's race/ethnicity does not explain the underuse of appropriate adjuvant therapy in colorectal cancer.* Dis Colon Rectum, 2006. 49(3): p. 319-29.
35. Frey, W. and D. Myers, *Neighborhood segregation in single-race and multirace America: a Census 2000 study of cities and metropolitan areas*. 2002, Citeseer.
36. Massey, D. and N. Denton, *The dimensions of residential segregation.* Social Forces, 1988. 67(2): p. 281-315.
37. Lichter, D., et al., *National Estimates of Racial Segregation in Rural and Small-Town America.* Demography, 2007. 44: p. 563-581.

Table 7-1a. Patient Based Characteristics by Chemotherapy Receipt

Characteristic	No. Patients (N=125)	% of Sample	% Received Adjuvant Chemotherapy (N=81)	X^2 p-value
Patient Based				
Race				
Black	45	36.0	66.7	0.7431
White	80	64.0	63.8	
Age at diagnosis (years)				
<50	15	12.0	80.0	<0.0001
50-64	40	32.0	80.0	
65-74	38	30.4	71.0	
75+	32	25.6	31.0	
Gender				
Male	59	47.2	62.7	0.6440
Female	66	52.8	66.7	
Marital Status				
Married	70	56.0	67.1	0.5361
Not Married	55	44.0	61.8	
Comorbid Conditions				
None	52	41.6	71.1	0.2093
1 or more	73	58.4	60.3	
Tumor Grade				
Low Grade	91	72.8	68.1	0.2019
High Grade or Unknown	34	27.2	55.9	
Primary Tumor Site				
Proximal Colon (Right)	69	55.2	63.8	0.7886
Distal Colon or Overlap Lesion and NOS	56	44.8	66.1	
Insurance Status				
Private	70	56.0	75.7	0.0061
Government	41	32.8	56.1	
Uninsured	14	11.2	35.7	

Table 7-1b. Area Based Characteristics by Chemotherapy Receipt

Characteristic	No. Patients (N=125)	% of Sample	% Received Adjuvant Chemotherapy (N=81)	X^2 p-value
Area Based				
Treatment Site				
A			83.0	<0.0001
B			78.9	
C			61.5	
D			65.0	
Other			23.1	
Care Received at a SWGA Cancer Center				
Yes	99	79.2	75.8	<0.0001
No	26	20.8	23.1	
Rural Residential Status				
Urban	40	32.0	70.0	0.0407
Large Rural Town	50	40.0	52.0	
Small or Small and Isolated Rural Town	35	28.0	77.1	
County				
Percent of Black Population				
Low (Tertile 1)	34	27.2	52.9	0.0913
Moderate (Tertile 2)	55	44.0	63.6	
High (Tertile 3)	36	28.8	77.8	
Percent Population Living Below Poverty Level				
Low to Moderate (≤20%)	55	44.0	60.0	0.3192
High (>20%)	70	56.0	68.6	
Racial Dissimilarity Index				
Low (Tertile 1)	18	14.4	77.8	0.0808
Moderate (Tertile 2)	34	27.2	50.0	
High (Tertile 3)	73	58.4	68.5	
Income Dissimilarity Index				
Low (Tertile 1)	17	13.6	76.5	0.0361
Moderate (Tertile 2)	44	35.2	50.0	
High (Tertile 3)	64	51.2	71.9	
Racial Isolation Index				
Low (Tertile 1)	34	27.2	50.0	0.0891
Moderate (Tertile 2)	46	36.8	67.4	
High (Tertile 3)	45	36.0	73.3	
Income Isolation Index				
Low (Tertile 1)	42	33.6	52.4	0.0870
Moderate (Tertile 2)	29	23.2	65.5	
High (Tertile 3)	54	43.2	74.1	

Table 7-2. Multivariable Associations for Race and Chemotherapy Receipt

Characteristic	Odds Ratio	95% CI	P-value
Race			
Black	1 (Referent)		
White	0.60	0.21-1.67	0.3274
Age at diagnosis (years)			
<64	1 (Referent)		
65-74	0.62	0.20-1.92	0.4070
75+	0.10	0.03-0.32	<0.0001
Insurance Status			
Private	1 (Referent)		
Not Private	0.37	0.14-1.01	0.0517
Care Received at a SWGA Cancer Center			
Yes	1 (Referent)		
No	0.08	0.03-0.27	<0.0001
Model Adjusted for: Race, Age, Insurance Status, Cancer Center			
Model Fit: Hosmer Lemeshow GOF, p=0.5349: c statistic=0.847			

Figure 7-1. Reasons for early termination of adjuvant chemotherapy (N=30)

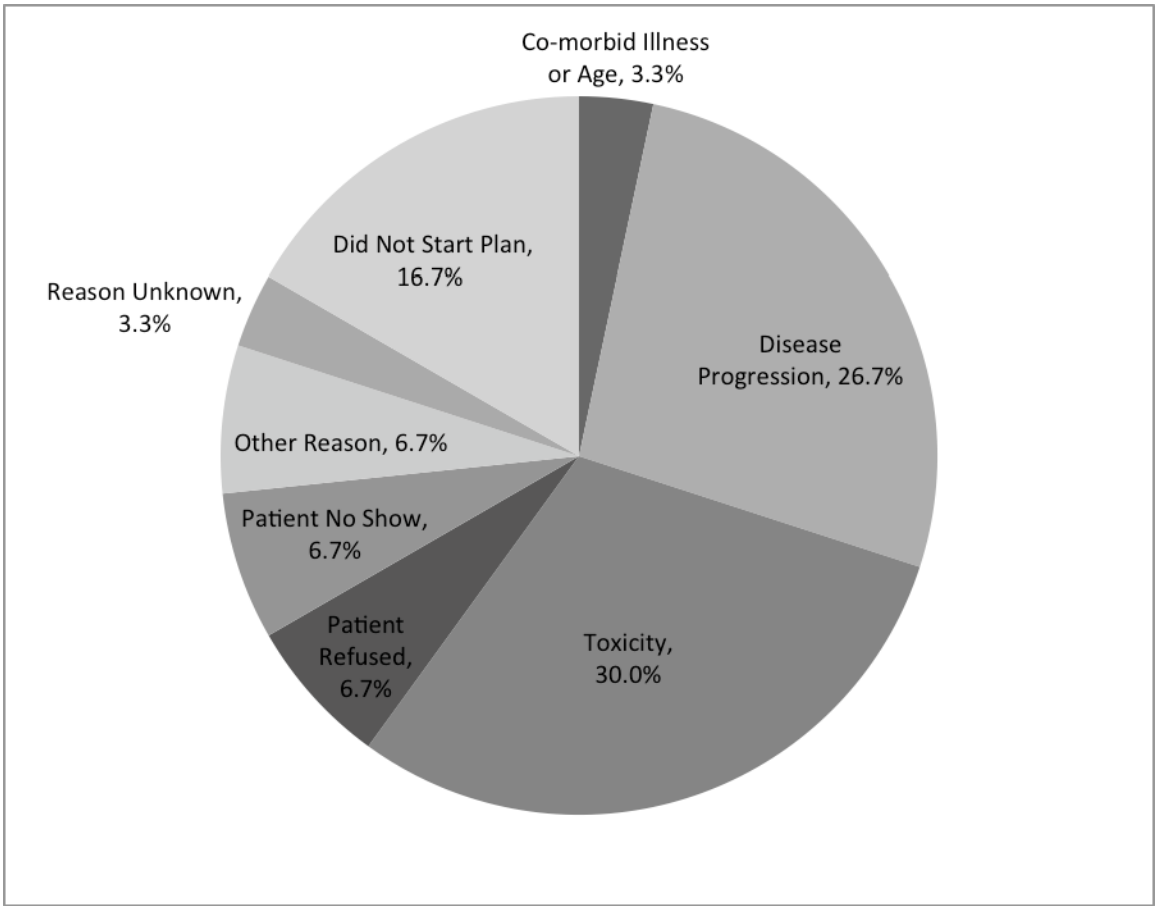


Table 7-3a. Patient Based Characteristics by Chemotherapy Completion

Characteristic	No. Patients who Began or Had Planned Chemotherapy (N=86)	No. (%) of Patients who Completed Chemotherapy (N=56)	X^2 p-value
Patient Based			
Race			
Black	32	25 (78.1)	0.0514
White	54	31 (57.4)	
Age at diagnosis (years)			
≤64	46	31 (67.4)	0.5648
65-74	30	20 (66.7)	
75+	10	5 (50.0)	
Gender			
Male	41	29 (70.7)	0.2970
Female	45	27 (60.0)	
Marital Status			
Married	51	39 (76.5)	0.0077
Not Married	35	17 (48.6)	
Comorbid Conditions			
None	39	30(76.9)	0.0364
1 or more	47	26 (55.3)	
Tumor Grade			
Low Grade	65	44 (67.7)	0.3779
High Grade or Unknown	21	12 (57.1)	
Primary Tumor Site			
Proximal Colon (Right)	48	29 (60.4)	0.3041
Distal Colon or Overlap Lesion and NOS	38	27 (71.1)	
Insurance Status			
Private	54	39 (72.2)	0.0725
Non-Private	32	17 (53.1)	

Table 7-3b. Area Based Characteristics by Chemotherapy Completion

Characteristic	Patients who Began or Planned Chemotherapy or (N=86)	No. (%) of Patients who Completed Chemotherapy (N=56)	X^2 p-value
Area Based			
Care Received at a SWGA Cancer Center			
Yes	80	51 (63.8)	0.6602
No	6	5 (83.3)	
Rural Residential Status			
Urban	32	22 (68.8)	0.7326
Large Rural Town	27	16 (59.3)	
Small or Small and Isolated Rural Town	27	18 (66.7)	
County			
Percent of Black Population			
Low (Tertile 1)	18	11 (61.1)	0.6919
Moderate (Tertile 2)	37	23 (62.2)	
High (Tertile 3)	31	22 (71.0)	
Percent Population Living Below Poverty Level			
Low to Moderate (≤20%)	34	21 (61.8)	0.5980
High (>20%)	52	35 (67.3)	
Racial Dissimilarity Index			
Low (Tertile 1)	14	11 (78.6)	0.5084
Moderate (Tertile 2)	18	11 (61.1)	
High (Tertile 3)	54	34 (63.0)	
Income Dissimilarity Index			
Low (Tertile 1)	13	10 (76.9)	0.5261
Moderate (Tertile 2)	24	14 (58.3)	
High (Tertile 3)	49	32 (65.3)	
Racial Isolation Index			
Low (Tertile 1)	18	11 (61.1)	0.6840
Moderate (Tertile 2)	31	19 (61.3)	
High (Tertile 3)	37	26 (70.3)	
Income Isolation Index			
Low (Tertile 1)	23	13 (56.5)	0.4475
Moderate (Tertile 2)	20	15 (75.0)	
High (Tertile 3)	43	28 (65.1)	

Table 7-4. Multivariable Association for Race and Chemotherapy Completion

Characteristic	Odds Ratio	95% CI	P-value
Race			
Black	1 (Referent)		
White	0.06	0.01-0.37	0.0022
Marital Status			
Married	1 (Referent)		
Not Married	0.26	0.09-0.81	0.0194
Insurance			
Private	1 (Referent)		
Not Private	0.13	0.03-0.68	0.0152
Model Adjusted for: Race, Marital Status, Insurance Status			
Model Fit: Hosmer Lemeshow GOF, p=0.7546: c statistic=0.774			

Appendix

Definitions and calculations of segregation indices

The dissimilarity index (D) measures the extent to which groups are segregated from each other [89, 90]. This index ranges from 0 to 1, where D=1 indicates complete segregation (the two groups live in completely different neighborhoods) and D=0 means complete integration (the two groups are distributed exactly the same way across the neighborhoods). Values greater than 0.6 are considered a level of high segregation [21]. This index is invariant to relative size of groups.

Dissimilarity index calculation:

$$D = \left[\frac{1}{2}\sum_{i=1}^{n}\left|\frac{x_i}{X} - \frac{y_i}{Y}\right|\right] * 100$$

where,

x_i = the black population (when measuring black-white racial segregation) or those living below the federal poverty line (when measuring income segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total population living below the federal poverty line when measuring income segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

y_i = the white population (or those living at or above the federal poverty line, when measuring income segregation) of the i^{th} area

Y = the total white population (or the total population living at or above the federal poverty line when measuring income segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

The isolation index measures the extent by which group members are exposed to one another rather than to members of another group This index ranges from 0 to 1 and can be interpreted as the probability that a randomly selected member of Group X will come in contact with another member of Group X in the same residential area [90].

Isolation index calculation:

$$I_i = xPx = \left[\sum_{i=1}^{n}\left(\frac{x_i}{X} \times \frac{x_i}{T_i}\right)\right] * 100$$

where,

xPx is the usual notation of the Isolation index . It symbolizes that the index calculates the group x (e.g. black population) weighted average of the group x (e.g. black population) proportion in each areal unit (e.g. census tract).

x_i = the black population (when measuring black-white racial segregation) or those living below the federal poverty line (when measuring income segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total population living below the federal poverty line when measuring income segregation) of the large geographic entity for which the isolation index is being calculated.

T_i = the total population of the i^{th} area

Modeling Strategy

Pre-Multivariable Modeling Assessment of Interaction and Confounding

Interaction

Interaction was evaluated by assessing the p-value associated with the cross-product terms in logistic models as follows:

(1) Logit $P(Y)=B0 + B(race) + B(Variable\ X) + B(race*Variable\ X) + \varepsilon$;

Cross product terms with p-values ≤ 0.10 were considered possible interaction factors and were placed in the initial multivariable model.

Statistically significant interaction terms were found between race and county level income isolation index for Y=Receipt of Chemotherapy. No statistically significant interaction terms were found between race and any other variable for Y=Completion of Chemotherapy.

Confounding

Confounding was assessed by comparing the crude odds ratios of the association between the exposure, patient race and outcomes of interest (receipt of chemotherapy and completion of chemotherapy, respectively) with the adjusted odds ratios, adjusting for only the potential confounder. If the crude and adjusted odds ratios differed by 10% or more, it was determined that the adjusting variable was a confounder of the association between the exposure variable (race) and the outcome of interest. Confounders of patient race and receipt of chemotherapy were insurance status, cancer center, county level income dissimilarity index, racial isolation index, income isolation index and percent black population. Confounders of patient race and completion of chemotherapy were marital status and insurance status.

Although not found to be confounders, variables: age and gender were included in the initial model as covariates for the model with outcome Y=Receipt of Chemotherapy, since these

variables are traditionally controlled for in cancer treatment analyses. For the initial model with outcome Y=Completion of Chemotherapy, this model contained only confounders since no significant interaction terms were found and no traditional covariates in order to avoid model over-specification due to the small size (N=88) of the analytical population for this outcome.

Multivariable Logistic Models

Model specification

The general form of the fully adjusted model accounting for potential confounders, effect modifiers and covariates

$$\text{Logit}\,P(\mathbf{X}) = \beta 0 + \sum_{i=1}^{2} \beta_i E_i + \sum_{i=1}^{p2} \gamma_i V_i + E_1\left(\sum_{i=1}^{p4} \delta_{1i} W_i\right) + E_1\left(\sum_{i=1}^{2} \delta_{2i} E\right) + \varepsilon$$

Where

P(**X**) = probability of receipt of adjuvant chemotherapy (or completion of therapy), given the collection of **X**s, (E, V, and Ws)

E_i=the primary exposure of interest (patient race)

V_i=potential confounders and covariates

W_i=potential effect modifiers

$\beta 0$ = baseline or background log odds, ignoring all other E, V, Ws

β =coefficient of the main exposure variables, represents the change in the log odds for 1

unit change in E, when all other variables are fixed

γ = coefficient of the control variables (potential confounders and covariates)

δ = coefficient of the effect modifiers

ε = random error

Model Specification:

1. For the first step in model specification, collinearity assessment of the initial model was conducted.

Collinearity Diagnostic Results

Initial Model:

Outcome 1: Receipt of Chemotherapy

Model, Outcome Y=Receipt of Chemotherapy: Largest Condition Index= 23.4760. The two largest Variance Decomposition Proportions (VDP): intercept 0.5275 and county racial isolation index 0.6545.

The rule assessed: Collinearity between variables is present in a logistic regression model when both of the following conditions are satisfied: Condition Index > 30 and more than one Variance Decomposition Proportion, not including the intercept is ≥ 0.5. No collinearity was indicated in this initial model.

Outcome 2: Completion of Chemotherapy

Model, Outcome Y=Completion of Chemotherapy: Largest Condition Index= 6.5869. The two largest Variance Decomposition Proportions (VDP): intercept 0.9756 and patient race 0.88109.

:. No collinearity was indicated in this initial model.

2. Backwards elimination for the multivariable model was performed on the effect modifiers (interaction terms). After removing the terms with the largest p-value (if greater than 0.05) sequentially from the model, no interaction terms remained in the model.

3. Backwards elimination was performed on all potential confounders and covariates. With the removal of each variable from the initial model, an assessment of confounding was conducted to ensure the removed variable was not a confounder of the association between the exposure of interest and the outcome. If the removal of a variable resulted in a ≥ 10% change in the odds ratio for the exposure of interest in the model after the removal of the variable compared to the model prior to the removal of the variable then the variable was returned to the model. Otherwise, the variable was dropped from the model. After either case, backwards elimination continued for the remaining variables until a final parsimonious model was reached.
4. Collinearity assessment of the final model was conducted.

Collinearity Diagnostic Results

Final Model:

Model Outcome Y=Receipt of Chemotherapy

Reduced Model (Final):

Largest Condition Index= 5.7481, Two Largest Variance Decomposition Proportions (VDP): intercept, 0.9815 and patient race VDP=0.5158

Rule assessed: Collinearity between variables is present in a logistic regression model when both of the following conditions are satisfied: Condition Index > 30 and more than one Variance Decomposition Proportion is, not including the intercept is ≥ 0.5. No collinearity was indicated in this final model.

Model, Outcome Y=Completion of Chemotherapy:

Initial Model =Final Model

Largest Condition Index= 6.5869. The two largest Variance Decomposition Proportions (VDP): intercept 0.9756 and patient race 0.88109. No collinearity was indicated in final model.

Chapter 8: Dissertation in Context, Limitations, Strengths and Recommendations for Future Studies

Racial and rural–urban differences in healthcare quality represent political and social challenges that are complex and difficult to meet [182]. Area-based measures such as residential segregation may be a socio-political structure that perpetuates disparities in healthcare [84]. This dissertation was designed to address the issue of racial and rural-urban health care inequities by assessing the influence of race, rural/urban residence and residential segregation on measures of health care quality regarding the medical treatment of colon cancer patients in the State of Georgia. Quality health care is reflected in the qualifications of physicians and in the adequacy of delivered treatment [120, 126, 130, 183]. We chose to evaluate the following quality measures among colon cancer patients: surgeon training and experience, receipt of chemotherapy among stage III patients (for whom this type of treatment is particularly important), and receipt and completion of chemotherapy among stage III patients in the largely rural Southwest Georgia (SWGA). The findings of these studies provide updated information about the presence or absence of treatment disparities among colon cancer patients in Georgia.

This dissertation evaluates the role of area-based socially constructed measures on the delivery of health care among a colon cancer patient population. The use of segregation indices along with traditional area-based racial and income measures, such as county and census tract percent black population and percent population living below the poverty line, further clarifies the influence of residential factors on health care delivery and receipt. The analyses included the

assessment of the independent effects of segregation measures on the dependent variable (surgeon qualifications, receipt of chemotherapy, completion of chemotherapy) while adjusting for the effects of traditional area-based variables.

Health Care Quality and Patient Race

Racial disparities in health care quality and delivery is a long-standing and consistent topic of population-based research [105, 184-190]. The majority of studies evaluated the existence of disparities rather than sought out explanation for these disparities. In a novel assessment of the relation between the characteristics of surgeons' patient populations and surgeon quality, we found that surgeons with higher percentages of black patients were more likely to be under-trained and inexperienced compared to those with lower percentages of black patients. We also found that percentage of blacks differed in the patient populations of the surgeons with the highest and the lowest levels of training and experience represented by quality scores of ≥9 and ≤6, respectively. Notably, area-based measures did not explain these associations.

The delivery of chemotherapy among colon cancer patients and its association with patient race has been assessed in the literature, but with varied findings [13, 93, 171]. We sought to provide an updated assessment of racial disparities in colon cancer care through the use of electronic medical record abstraction in SWGA and through a linkage of Medicare claims to Georgia Cancer Registry statewide data. Analyses produced mixed findings. Within both our Medicare and SWGA patient populations we found that black patients were as likely as white patients to receive adjuvant chemotherapy. Somewhat contrary to expectation, we found that in SWGA black patients were more likely to complete adjuvant chemotherapy than their white counterparts. Again, area-based measures did not explain these findings.

Health Care Quality and Rural/Urban Residence

Research on rural and urban disparities in colon cancer care is scant and few U.S. studies have focused on the direct influence of rural versus urban residence on health care quality [150, 191-193]. In this dissertation project we found that rural/urban residence was associated with several surgeon training and experience characteristics, which have not been previously reported in the literature. Surgeons serving predominant rural patents were less likely than surgeons with more urban patient populations to have specialized training, have a higher patient volume and have a board certification. Nevertheless, after adjusting for covariates and confounders, percent of urban patients was not associated with suboptimal surgeon score (≤6 vs. >6) nor optimal surgeon score (i.e., ≥9 vs. <9) in the population assessed.

A focused assessment of the role of rural-urban residence on the receipt of colon cancer therapy is also lacking in the healthcare literature [115]. We sought to bring light to this area of research in two of our studies. We found that rural versus urban residence did not affect the receipt of adjuvant chemotherapy in Georgia. In both unadjusted and multivariate analyses, rural colon cancer patients had the same likelihood of chemotherapy receipt as those residing in urban areas. This association was also assessed in our predominantly rural SWGA population. Level of urbanization in SWGA was associated with receipt of adjuvant chemotherapy in unadjusted analyses but it was not retained in the multivariable models. Additionally, urbanization did not significantly predict completion of adjuvant chemotherapy in unadjusted models nor did it serve as a confounder of the association between race and completion of treatment in the multivariate analysis.

Health Care Quality and Segregation (Racial and Income)

Research on the role of residential segregation in health care delivery and quality is fairly new [15, 16, 84, 92, 171, 194]. Our objective for this dissertation was to assess the impact of segregation

on colon cancer care and to assess its significance while taking into consideration traditionally assessed area-based measures. In two of our analyses, we showed that segregation measures predicted colon cancer care independently of traditional area-based measures. Interestingly, we found that surgeons who cared for patients residing in less racially segregated counties were less likely to be specialists than those caring for patients residing in more racially segregated counties; however, the opposite was true for the census tract level segregation. In multivariate models, census tract level racial segregation was significantly associated with optimal surgeon score. No segregation measures served as confounders of the association between surgeon's percent of black patients and suboptimal or optimal surgeon score.

Another objective of this dissertation was to highlight the role, if any, of residential segregation on the receipt and completion of adjuvant chemotherapy among colon cancer patients. We found that segregation measures as well as other area-based measures were not associated with receipt of chemotherapy among our larger population of Medicare patients. By contrast, in SWGA the income dissimilarity index was significantly associated with receipt of chemotherapy in the unadjusted analysis. Its independent effect was not assessed in multivariate models; however we did assess its role as a covariate and found that none of the segregation measures served as confounders or significant effect modifiers of the association between race and receipt of chemotherapy. Furthermore, no segregation measure was associated with completion of adjuvant chemotherapy in unadjusted analysis and none served as a confounders or effect modifiers of the association between race and completion of adjuvant chemotherapy in the multivariate model.

Limitations

One limitation of this dissertation is that the findings of its first two studies are based on Medicare data pertaining only to elderly colon cancer patients and to black and white non-

Hispanic residents of Georgia. Thus, it is possible that our results for these two studies are not generalizable to other U.S. states, other patient ages or racial/ethnic groups and uninsured or under-insured populations. Additionally, the two Medicare linkage studies were based on medical claims data which are subject to under-ascertainment of medical treatment.

The main limitation in the third study is the size of the population included in analysis. The small study size reduced our ability to control for a large number of covariates in multivariate models and thus limited our assessment to the independent effects of confounders and effect modifiers.

Strengths

The major strength of this research project is the use of residential segregation measures to characterize patient populations and assess its association with surgeon quality and the provision of chemotherapy. The use of segregation measures provided additional insight that allowed us to take into account political, social and economic factors that may influence the quality of community-level social resources, such as availability and quality of health care [83] [80, 82]. In addition, an important strength of these studies is the use of economic segregation indices. The use of these measures in health care research is rare, and the relevant data are scant. To our knowledge, ours is the first study to evaluate the role of these segregation measures on quality of cancer care.

In summary, this research is the first to show that patient race and racial residential segregation is associated with colon cancer surgeon's qualifications and that patient race predicts completion of adjuvant chemotherapy among a predominantly rural population of colon cancer patients. It is also the first to show an unexpected racial disparity among colon cancer patients indicating that black patients in rural SWGA may be more likely to complete adjuvant

chemotherapy than white patients. It is also one of the few studies to report a lack of racial disparity in the receipt of cancer care in a contemporary population of colon cancer patients.

The additional findings that factors such as age, co-morbid illnesses, marital status and site of care have a stronger impact on receipt and completion of chemotherapy than social factors suggests that our healthcare system may be more equitable (or perhaps equally inadequate) in some parts of the country. If confirmed by independent studies this dissertation will add a new dimension to the past and current social health research that tends to show persistent racial and income based differences in the receipt of quality health care.

Recommendations for Future Studies

To build on this research, it is necessary to broaden its scope to include a larger and more diverse population. There is a need to assess whether our findings are replicable in other parts of the U.S with particular focus on rural regions within SEER (Iowa, Kentucky, parts of California and Louisiana). While social factors were not significant predictors of health care delivery in black and white Georgia patients, it is possible that these factors will play a significant role in other populations (e.g. Hispanics, other states). Continued research on the role of social factors on health care delivery and receipt is vital in order to ensure steady movement in our health care system towards the provision of equitable care among all patients.

References

1. Baldwin, D.M., *Disparities in health and health care: focusing efforts to eliminate unequal burdens.* Online J Issues Nurs, 2003. **8**(1): p. 2.
2. Williams, D.R. and C. Collins, *Racial residential segregation: a fundamental cause of racial disparities in health.* Public Health Rep, 2001. **116**(5): p. 404-16.

3. Schrag, D., et al., *Surgeon volume compared to hospital volume as a predictor of outcome following primary colon cancer resection.* J Surg Oncol, 2003. **83**(2): p. 68-78; discussion 78-9.

4. Hershman, D.L., et al., *Surgeon characteristics and use of breast conservation surgery in women with early stage breast cancer.* Annals of Surgery, 2009. **249**(5): p. 828-33.

5. Hodgson, D.C., C.S. Fuchs, and J.Z. Ayanian, *Impact of patient and provider characteristics on the treatment and outcomes of colorectal cancer.* J Natl Cancer Inst, 2001. **93**(7): p. 501-15.

6. Ayanian, J.Z., et al., *Use of adjuvant chemotherapy and radiation therapy for colorectal cancer in a population-based cohort.* J Clin Oncol, 2003. **21**(7): p. 1293-300.

7. Egbert, L.D. and I.L. Rothman, *Relation between the Race and Economic Status of Patients and Who Performs Their Surgery.* New England Journal of Medicine, 1977. **297**(2): p. 90-91.

8. Jerant, A.F., J.J. Fenton, and P. Franks, *Determinants of racial/ethnic colorectal cancer screening disparities.* Archives of Internal Medicine, 2008. **168**(12): p. 1317-24.

9. McAlearney, A.S., et al., *Racial differences in colorectal cancer screening practices and knowledge within a low-income population.* Cancer, 2008. **112**(2): p. 391-8.

10. Hassan, M.O., et al., *Race does not impact colorectal cancer treatment or outcomes with equal access.* American Journal of Surgery, 2009. **197**(4): p. 485-90.

11. Gornick, M.E., et al., *Effects of race and income on mortality and use of services among Medicare beneficiaries.* N Engl J Med, 1996. **335**(11): p. 791-9.

12. McMahon, L.F., Jr., et al., *Racial and gender variation in use of diagnostic colonic procedures in the Michigan Medicare population.* Medical Care, 1999. **37**(7): p. 712-7.

13. Ayanian, J.Z., et al., *Quality of care by race and gender for congestive heart failure and pneumonia.* Med Care, 1999. **37**(12): p. 1260-9.

14. Bach, P.B., et al., *Racial differences in the treatment of early-stage lung cancer.* N Engl J Med, 1999. **341**(16): p. 1198-205.

15. Hao, Y., et al., *Race, neighbourhood characteristics and disparities in chemotherapy for colorectal cancer.* Journal of Epidemiology and Community Health. **65**(3): p. 211-217.

16. Baldwin, L.M., et al., *Explaining black-white differences in receipt of recommended colon cancer treatment.* J Natl Cancer Inst, 2005. **97**(16): p. 1211-20.

17. McGory, M.L., et al., *A patient's race/ethnicity does not explain the underuse of appropriate adjuvant therapy in colorectal cancer.* Dis Colon Rectum, 2006. **49**(3): p. 319-29.

18. Elliott, T.E., et al., *Rural-urban differences in cancer care: results from the Lake Superior Rural Cancer Care Project.* Minn Med, 2004. **87**(9): p. 44-50.

19. Robertson, R., et al., *Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas.* Br J Cancer, 2004. **90**(8): p. 1479-85.

20. Esnaola, N.F., et al., *Urban/rural residence moderates effect of race on receipt of surgery in patients with nonmetastatic breast cancer: a report from the South Carolina central cancer registry.* Annals of Surgical Oncology, 2008. **15**(7): p. 1828-36.

21. Goodman, M., et al., *Cancer outcomes research in a rural area: a multi-institution partnership model.* Journal of Community Health, 2009. **34**(1): p. 23-32.

22. Wu, X., et al., *Treatment patterns for stage III colon cancer and factors related to receipt of postoperative chemotherapy in Louisiana.* Journal of the Louisiana State Medical Society, 2004. **156**(5): p. 255-61.

23. Smith, D.B., *The racial segregation of hospital care revisited: Medicare discharge patterns and their implications.* Am J Public Health, 1998. **88**(3): p. 461-3.

24. Rodriguez, R.A., et al., *Geography matters: relationships among urban residential segregation, dialysis facilities, and patient outcomes.* Annals of Internal Medicine, 2007. **146**(7): p. 1746-1754.

25. Haas, J.S., et al., *Racial segregation and disparities in breast cancer care and mortality.* Cancer, 2008. **113**(8): p. 2166-72.

26. Hayanga, A.J., et al., *Residential segregation and access to surgical care by minority populations in US counties.* Journal of the American College of Surgeons, 2009. **208**(6): p. 1017-22.

27. Fix, M., *Clear and convincing evidence: Measurement of discrimination in America.* 1993.

28. Ming Jr, W., *Racial Restrictions and the Fourteenth Amendment: The Restrictive Covenant Cases.* The University of Chicago Law Review, 1949: p. 203-238.

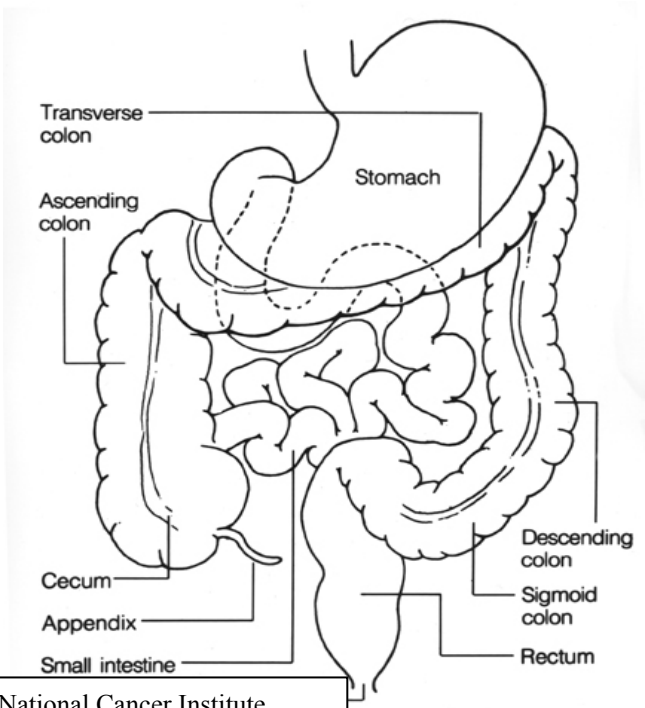
29. Gotham, K., *Urban space, restrictive covenants and the origins of racial residential segregation in a US city, 1900-50.* International Journal of Urban and Regional Research, 2000. **24**(3): p. 616-633.

30. Georgia Comprehensive Cancer Registry, *Policy and Procedure Manual for Reporting Facilities*, Division of Public Health: Georgia Department of Human Resources, Editor. March 2003.

Appendices

A: Anatomy of the Large Intestine

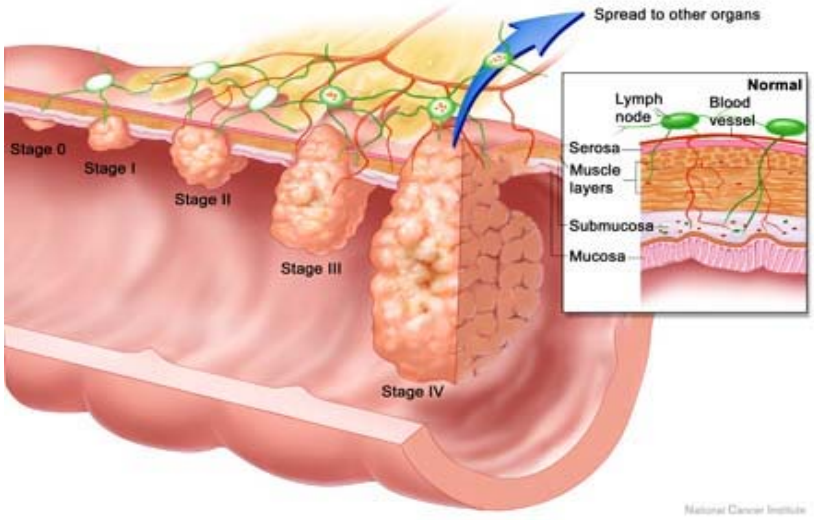
Appendix Figure 1. Anatomy of the Large Intestine



Source: National Cancer Institute

B. Colon Cancer Stages

Appendix Figure 2: Depiction of Colon Cancer Stages



Source: National Cancer Institute

C: Colorectal Cancer TNM Stages

Appendix Table 1. TNM Colorectal Cancer Staging System

The T category describes the original (primary) tumor.

TX	Primary tumor cannot be evaluated
T0	No evidence of primary tumor
Tis	Carcinoma in situ (early cancer that has not spread to neighboring tissue)
T1–T4	Size and/or extent of the primary tumor T1: Tumor invades submucosa T2: Tumor invades muscularis propria T3: Tumor invades through the muscularis propria into the subserosa, or into non-peritonealized pericolic or perirectal tissues T4: Tumor directly invades other organs or structures, and/or perforates visceral peritoneum

The N category describes whether or not the cancer has reached nearby lymph nodes.

NX	Regional lymph nodes cannot be evaluated
NO	No regional lymph node involvement (no cancer found in the lymph nodes)
N1-N2	Involvement of regional lymph nodes (number and/or extent of spread) N1: Metastasis in 1 to 3 regional lymph nodes N2: Metastasis in 4 or more regional lymph nodes

The M category tells whether there are distant metastases (spread of cancer to other parts of the body).

MX	Distant metastasis cannot be evaluated
MO	No distant metastasis (cancer has not spread to other parts of the body)
M1	Distant metastasis (cancer has spread to distant parts of the body)

D: Colon Cancer Treatment by Stage

Appendix Table 2: Colon Cancer Stage and Treatment

Cancer Stage	Treatment
Stage 0: Tis, N0, M0: The cancer is in the earliest stage. It has not grown beyond the inner layer (mucosa) of the colon or rectum. This stage is also known as carcinoma in situ or intramucosal carcinoma[62, 71].	Polypectomy or local excision of small lesions with clear margins. Colon resection for larger lesions when local excision is inappropriate [2].
Stage I: T1, N0, M0, or T2, N0, M0: The cancer has grown through the mucosa into the submucosa (T1) *or* it may also have grown into the muscularis propria (T2), but it has not spread into nearby lymph nodes (N0) or distant sites[62, 71].	Surgical procedures, wide surgical resection and anastomosis, are the standard treatment. The affected colon is surgically removed (resected) and the healthy remaining colon is attached (anastomosis) [2, 195]
Stage IIA: T3, N0, M0: The cancer has grown through the wall of the colon or rectum, into the outermost layers (T3). It has not yet spread to the nearby lymph nodes (N0) or distant sites [62, 71]. **Stage IIB: T4, N0, M0:** The cancer has grown through the walls of the colon or rectum into other nearby tissues or organs (T4). It has not yet spread to the nearby	Treatment is not well-established, wide surgical resection and anastomosis is the standard recommendation; however, clinical trials are underway to assess the added benefit of adjuvant chemotherapy on the treatment of these patients [2].

lymph nodes (N0) or distant sites [62, 71].	
Stage IIIA: T1-2, N1, M0: The cancer has grown through the mucosa into the submucosa (T1) *or* it may also have grown into the muscularis propria (T2), and it has spread to 1 to 3 nearby lymph nodes (N1) but not distant sites [62, 71]. **Stage IIIB: T3-4, N1, M0:** The cancer has grown through the wall of the colon or rectum (T3) *or* into other nearby tissues or organs (T4) and has spread to 1 to 3 nearby lymph nodes (N1) but not distant sites [62, 71]. **Stage IIIC: Any T, N2, M0:** The cancer can be any T but has spread to 4 or more nearby lymph nodes but not distant sites [62, 71].	Wide surgical resection and anastomosis along with adjuvant (treatment postoperative) chemotherapy with fluorouracil (5-FU)-leucovorin for 6 months [2, 195].
Stage IV: Any T, Any N, M1: The cancer can be any T, any N, but has spread to distant sites such as the liver, lung, peritoneum (the membrane lining the abdominal cavity), or ovary (M1) [62, 71].	Wide surgical resection and anastomosis of primary lesion, resection of other organ metastases, palliative radiation therapy and palliative chemotherapy [2].

E: Formulas for Residential Segregation Indices

Appendix Formula 1: Dissimilarity Index

$$D = \left[\frac{1}{2}\sum_{i=1}^{n}\left|\frac{x_i}{X} - \frac{y_i}{Y}\right|\right] * 100$$

where,

x_i = the black population (when measuring black-white racial segregation) or the poor population, those below the federal poverty line (when measuring economic segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total poor population when measuring economic segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

y_i = the white population (or the non-poor population, when measuring economic segregation) of the i^{th} area

Y = the total white population (or the total non-poor population when measuring economic segregation) of the large geographic entity for which the index of dissimilarity is being calculated.

Appendix Formula 2: Isolation Index

$$I_i = xPx = \left[\sum_{i=1}^{n}\left(\frac{x_i}{X} \times \frac{x_i}{T_i}\right)\right] * 100$$

where,

x_i = the black population (when measuring black-white racial segregation) or the poor population, those below the federal poverty line (when measuring economic segregation) of the i^{th} area, e.g. census tract

X = the total black population (or the total poor population when measuring economic segregation) of the large geographic entity for which the isolation index is being calculated.

T_i = the total population of the i^{th} area

F: Rural Urban Commuting Area (RUCA) Codes and Categorization Schemes

Appendix Table 3: Rural–Urban Commuting Area Codes for 2000 U.S. Census Tracts

1 Metropolitan area core: primary flow within an urbanized area (UA)
- 1.0 No additional code
- 1.1 Secondary flow 30 to 50% to a larger UA

2 Metropolitan area high commuting: primary flow 30% or more to a UA
- 2.0 No additional code
- 2.1 Secondary flow 30 to 50% to a larger UA

3 Metropolitan area low commuting: primary flow 5 to 30% to a UA
- 3.0 No additional code

4 Micropolitan area core: primary flow within an Urban Cluster of 10,000 to 49,999 (large UC)
- 4.0 No additional code
- 4.1 Secondary flow 30 to 50% to a UA
- 4.2 Secondary flow 10 to 30% to a UA

5 Micropolitan high commuting: primary flow 30% or more to a large UC
- 5.0 No additional code
- 5.1 Secondary flow 30 to 50% to a UA
- 5.2 Secondary flow 10 to 30% to a UA

6 Micropolitan low commuting: primary flow 10 to 30% to a large UC
- 6.0 No additional code
- 6.1 Secondary flow 10 to 30% to a UA

7 Small town core: primary flow within an Urban Cluster of 2,500 to 9,999 (small UC)
- 7.0 No additional code
- 7.1 Secondary flow 30 to 50% to a UA
- 7.2 Secondary flow 30 to 50% to a large UC
- 7.3 Secondary flow 10 to 30% to a UA
- 7.4 Secondary flow 10 to 30% to a large UC

8 Small town high commuting: primary flow 30% or more to a small UC
- 8.0 No additional code
- 8.1 Secondary flow 30 to 50% to a UA
- 8.2 Secondary flow 30 to 50% to a large UC
- 8.3 Secondary flow 10 to 30% to a UA
- 8.4 Secondary flow 10 to 30% to a large UC

9 Small town low commuting: primary flow 10 to 30% to a small UC
- 9.0 No additional code
- 9.1 Secondary flow 10 to 30% to a UA
- 9.2 Secondary flow 10 to 30% to a large UC

10 Rural areas: primary flow to a tract outside a UA or UC

- 10.0 No additional code
- 10.1 Secondary flow 30 to 50% to a UA
- 10.2 Secondary flow 30 to 50% to a large UC
- 10.3 Secondary flow 30 to 50% to a small UC
- 10.4 Secondary flow 10 to 30% to a UA
- 10.5 Secondary flow 10 to 30% to a large UC
- 10.6 Secondary flow 10 to 30% to a small UC

Source: Economic Research Service, United States Department of Agriculture.

Appendix Table 4: RUCA Code Categorization Schemes

Categorization A.

Urban focused RUCA codes: 1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 7.1, 8.1, and 10.1.
Large Rural City/Town (micropolitan) focused RUCA codes: 4.0, 4.2, 5.0, 5.2, 6.0, and 6.1
Small Rural Town focused RUCA codes: 7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2
Isolated Small Rural Town focused RUCA codes: 10.0, 10.2, 10.3, 10.4, 10.5, and 10.6

Categorization B.

Urban: 1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 7.1, 8.1, and 10.1
Large Rural City/Town: 4.0, 4.2, 5.0, 5.2, 6.0, and 6.1
Small and Isolated Small Rural Town: 7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2, 10.0, 10.2, 10.3, 10.4, 10.5, and 10.6

Categorization C.

Urban: 1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 7.1, 8.1, and 10.1
Rural: 4.0, 4.2, 5.0, 5.2, 6.0, 6.1, 7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2, 10.0, 10.2, 10.3, 10.4, 10.5, and 10.6

Source: University of Washington, Rural Health Research Center

There are many other categorization schemes; however these are the most frequently used schemes as reported by the Washington Wyoming Alaska Montana Idaho (WWAMI) Rural Health Research Center based at the University of Washington School of Medicine [99]

References

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA: A Cancer Journal for Clinicians 2008;58:71-96.

2. National Cancer Institute. PDQ database: Colon cancer treatment. In. 2008 ed. Bethesda, MD: Bethesda, MD; 2008.

3. Neugut AI, Timony D, Murray T. Colorectal cancer: differences between community and geographically distant patients seen at an urban medical center. Dis Colon Rectum 1991;34:64-8.

4. Mahoney T, Kuo YH, Topilow A, Davis JM. Stage III colon cancers: why adjuvant chemotherapy is not offered to elderly patients. Arch Surg 2000;135:182-5.

5. Roetzheim RG, Pal N., Gonzalez E. C., Ferrante J. M., Van Durme D. J., Krischer J. P. Effects of health insurance and race on colorectal cancer treatments and outcomes. Am J Public Health 2000;90:1746-54.

6. VanEenwyk J, Campo JS, Ossiander EM. Socioeconomic and demographic disparities in treatment for carcinomas of the colon and rectum. Cancer 2002;95:39-46.

7. Krzyzanowska MK, Regan MM, Powell M, Earle CC, Weeks JC. Impact of patient age and comorbidity on surgeon versus oncologist preferences for adjuvant chemotherapy for stage III colon cancer. J Am Coll Surg 2009;208:202-9.

8. Hayanga AJ, Waljee AK, Kaiser HE, Chang DC, Morris AM. Racial clustering and access to colorectal surgeons, gastroenterologists, and radiation oncologists by African Americans and Asian Americans in the United States: a county-level data analysis. Arch Surg 2009;144:532-5.

9. Launoy G, Le Coutour X, Gignoux M, Pottier D, Dugleux G. Influence of rural environment on diagnosis, treatment, and prognosis of colorectal cancer. J Epidemiol Community Health 1992;46:365-7.

10. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Rural and urban differences in stage at diagnosis of colorectal and lung cancers. Br J Cancer 2001;84:910-4.

11. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Impact of deprivation and rural residence on treatment of colorectal and lung cancer. Br J Cancer 2002;87:585-90.

12. Sundararajan V, Grann VR, Jacobson JS, Ahsan H, Neugut AI. Variations in the use of adjuvant chemotherapy for node-positive colon cancer in the elderly: a population-based study. Cancer J 2001;7:213-8.

13. Baldwin LM, Dobie SA, Billingsley K, et al. Explaining black-white differences in receipt of recommended colon cancer treatment. J Natl Cancer Inst 2005;97:1211-20.

14. Haas JS, Earle CC, Orav JE, Brawarsky P, Neville BA, Williams DR. Racial segregation and disparities in cancer stage for seniors. J Gen Intern Med 2008;23:699-705.

15. Haas JS, Earle CC, Orav JE, et al. Racial segregation and disparities in breast cancer care and mortality. Cancer 2008;113:2166-72.

16. Hayanga AJ, Kaiser HE, Sinha R, Berenholtz SM, Makary M, Chang D. Residential segregation and access to surgical care by minority populations in US counties. J Am Coll Surg 2009;208:1017-22.

17. Shihadeh E, Flynn N. Segregation and crime: The effect of black social isolation on the rates of black urban violence. Soc Forces 1996;74:1325-52.

18. Cutler D, Glaeser E, Vigdor J. The rise and decline of the American ghetto. Journal of Political Economy 1999;107:455-506.

19. Gross CP, Smith BD, Wolf E, Andersen M. Racial disparities in cancer therapy: did the gap narrow between 1992 and 2002? Cancer 2008;112:900-8.

20. Jargowsky P. Take the money and run: economic segregation in US metropolitan areas. Am Sociol Rev 1996;61:984-98.

21. Lichter D, Parisi D, Grice S, Taquino M. National Estimates of Racial Segregation in Rural and Small-Town America. Demography 2007;44:563-81.

22. Massey D. American apartheid: Segregation and the making of the underclass. The American Journal of Sociology 1990;96:329-57.

23. Sargent DJ, Goldberg RM, Jacobson SD, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Engl J Med 2001;345:1091-7.

24. Gill S, Loprinzi CL, Sargent DJ, et al. Pooled Analysis of Fluorouracil-Based Adjuvant Therapy for Stage II and III Colon Cancer: Who Benefits and by How Much? J Clin Oncol 2004;22:1797-806.

25. Luo R, Giordano SH, Zhang DD, Freeman J, Goodwin JS. The role of the surgeon in whether patients with lymph node-positive colon cancer see a medical oncologist. Cancer 2007;109:975-82.

26. Gilligan MA, Neuner J, Sparapani R, Laud PW, Nattinger AB. Surgeon characteristics and variations in treatment for early-stage breast cancer. Arch Surg 2007;142:17-22.

27. Hershman DL, Buono D, McBride RB, et al. Surgeon characteristics and receipt of adjuvant radiotherapy in women with breast cancer. J Natl Cancer Inst 2008;100:199-206.

28. McClish DK, Penberthy L, Whittemore M, et al. Ability of Medicare claims data and cancer registries to identify cancer cases and treatment. Am J Epidemiol 1997;145:227-33.

29. Cress RD, Zaslavsky AM, West DW, Wolf RE, Felter MC, Ayanian JZ. Completeness of information on adjuvant therapies for colorectal cancer in population-based cancer registries. Med Care 2003;41:1006-12.

30. Warren JL, Harlan LC, Fahey A, et al. Utility of the SEER-Medicare data to identify chemotherapy use. Med Care 2002;40:IV-55-61.

31. Garcia M, Jemal A, Ward EM, et al. Global Cancer Facts and Figures 2007. Atlanta, GA: American Cancer Society; 2007.

32. Stewart BW, Kleihues P, eds. World Cancer Report. Lyon: IARCPress; 2003.

33. Troisi R, Freedman A, Devesa S. Incidence of colorectal carcinoma in the U.S.: An update of trends by gender, race, age, subsite, and stage, 1975-1994. Cancer 1999;85:1670-6.

34. Singh S BA, McNamara C, Redding K. Colorectal Cancer in Georgia, 1999-2003. In: Georgia Department of Human Resources DoPH, Chronic Disease, Injury, and Environmental Epidemiology Section, ed.: Publication number DPH06/165W; December, 2006.

35. Vogelstein B, Fearon E, Hamilton S, et al. Genetic alterations during colorectal-tumor development. N Engl J Med 1988;319:525-32.

36. Cho KR, Vogelstein B. Genetic alterations in the adenoma-carcinoma sequence. Cancer 1992;70:1727-31.

37. Potter JD. Colorectal Cancer: Molecules and Populations. J Natl Cancer Inst 1999;91:916-32.

38. Ilyas M, Straub J, Tomlinson IP, Bodmer WF. Genetic pathways in colorectal and other cancers. Eur J Cancer 1999;35:1986-2002.

39. Rowan AJ, Lamlum H, Ilyas M, et al. APC mutations in sporadic colorectal tumors: A mutational "hotspot" and interdependence of the "two hits". Proc Natl Acad Sci U S A 2000;97:3352-7.

40. Bansal P, Sonnenberg A. Risk factors of colorectal cancer in inflammatory bowel disease. Am J Gastroenterol 1996;91:44-8.

41. Mayer R, Wong WD, Rothenberger DA, Goldberg SM, Madoff RD. Colorectal cancer in inflammatory bowel disease: a continuing problem. Dis Colon Rectum 1999;42:343-7.

42. Zisman TL, Rubin DT. Colorectal cancer and dysplasia in inflammatory bowel disease. World J Gastroenterol 2008;14:2662-9.

43. Chung YW, Han DS, Park YK, et al. Association of obesity, serum glucose and lipids with the risk of advanced colorectal adenoma and cancer: a case-control study in Korea. Dig Liver Dis 2006;38:668-72.

44. Dai Z, Xu YC, Niu L. Obesity and colorectal cancer risk: a meta-analysis of cohort studies. World J Gastroenterol 2007;13:4199-206.

45. Le Marchand L, Wilkens LR, Kolonel LN, Hankin JH, Lyu LC. Associations of sedentary lifestyle, obesity, smoking, alcohol use, and diabetes with the risk of colorectal cancer. Cancer Res 1997;57:4787-94.

46. Moghaddam AA, Woodward M, Huxley R. Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. Cancer Epidemiol Biomarkers Prev 2007;16:2533-47.

47. Giovannucci E, Rimm EB, Stampfer MJ, Colditz GA, Ascherio A, Willett WC. Intake of fat, meat, and fiber in relation to risk of colon cancer in men. Cancer Res 1994;54:2390-7.

48. Luchtenborg M, Weijenberg MP, de Goeij AF, et al. Meat and fish consumption, APC gene mutations and hMLH1 expression in colon and rectal cancer: a prospective cohort study (The Netherlands). Cancer Causes Control 2005;16:1041-54.

49. Oba S, Shimizu N, Nagata C, et al. The relationship between the consumption of meat, fat, and coffee and the risk of colon cancer: a prospective study in Japan. Cancer Lett 2006;244:260-7.

50. Akhter M, Kuriyama S, Nakaya N, et al. Alcohol consumption is associated with an increased risk of distal colon and rectal cancer in Japanese men: the Miyagi Cohort Study. Eur J Cancer 2007;43:383-90.

51. Ferrari P, Jenab M, Norat T, et al. Lifetime and baseline alcohol intake and risk of colon and rectal cancers in the European prospective investigation into cancer and nutrition (EPIC). Int J Cancer 2007;121:2065-72.

52. Samowitz WS, Albertsen H, Sweeney C, et al. Association of smoking, CpG island methylator phenotype, and V600E BRAF mutations in colon cancer. J Natl Cancer Inst 2006;98:1731-8.

53. Chan AT, Giovannucci EL, Meyerhardt JA, Schernhammer ES, Curhan GC, Fuchs CS. Long-term use of aspirin and nonsteroidal anti-inflammatory drugs and risk of colorectal cancer. JAMA 2005;294:914-23.

54. Chan AT, Giovannucci EL, Meyerhardt JA, Schernhammer ES, Wu K, Fuchs CS. Aspirin dose and duration of use and risk of colorectal cancer in men. Gastroenterology 2008;134:21-8.

55. Chan AT, Giovannucci EL, Schernhammer ES, et al. A prospective study of aspirin use and the risk for colorectal adenoma. Ann Intern Med 2004;140:157-66.
56. Grodstein F, Martinez ME, Platz EA, et al. Postmenopausal hormone use and risk for colorectal cancer and adenoma. Ann Intern Med 1998;128:705-12.
57. Borgelt L, Umland E. Benefits and challenges of hormone replacement therapy. J Am Pharm Assoc (Wash) 2000;40:S30-1.
58. Libutti SK, Saltz LB, Tepper JE. Chapter 39-Cancers of the Gastrointestinal Tract, Section 12: Colon Cancer. In: Devita, Hellman and Rosenberg's Cancer: Principle and Practice of Oncology, 8th Edition. 8 ed: Lippincott Williams & Wilkins; 2008:1233-85.
59. Abeloff MD, Armitage, James O., Niederhuber, John E., Kastan, Michael B., McKenna, W. Colon Cancer In: Abeloff MD, ed. Abeloff's Clinical Oncology 4th Edition Expert Consult Premium Edition Churchill Livingstone; 2008.
60. Chapter 26. Regulation of Gastrointestinal Function. In: Ganong W, ed. Review of Medical Physiology, 22nd Edition: The McGraw-Hill Companies; 2005.
61. Ehrenpreis E. Chapter 81. Gut and Hepatobiliary Dysfunction. In: Hall J, Schmidt G, Wood L, eds. Principles of Critical Care, 3rd Edition: The McGraw-Hill Companies; 2005.
62. Greene F, Page D, Fleming I, et al. AJCC Cancer Staging Manual. New York: Springer-Verlag; 2002.
63. Vogelstein B, Fearon ER, Hamilton SR, et al. Genetic alterations during colorectal-tumor development. N Engl J Med 1988;319:525-32.
64. Yashiro M, Carethers JM, Laghi L, et al. Genetic pathways in the evolution of morphologically distinct colorectal neoplasms. Cancer Res 2001;61:2676-83.
65. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. N Engl J Med 1993;329:1977-81.
66. Rex DK, Johnson DA, Lieberman DA, Burt RW, Sonnenberg A. Colorectal cancer prevention 2000: screening recommendations of the American College of Gastroenterology. In conjunction with ACG Consumer Brochure: "ACG

Recommendations on Colorectal Cancer Screening for Average and Higher Risk Patients in Clinical Practice". The American Journal of Gastroenterology 2000;95:868-77.

67. Faivre J, Dancourt V, Lejeune C, et al. Reduction in colorectal cancer mortality by fecal occult blood screening in a French controlled study. Gastroenterology 2004;126:1674-80.

68. Saito H, Soma Y, Koeda J, et al. Reduction in risk of mortality from colorectal cancer by fecal occult blood screening with immunochemical hemagglutination test. A case-control study. Int J Cancer 1995;61:465-9.

69. Vogelaar I, van Ballegooijen M, Schrag D, et al. How much can current interventions reduce colorectal cancer mortality in the U.S.? Mortality projections for scenarios of risk-factor modification, screening, and treatment. Cancer 2006;107:1624-33.

70. Rex DK. Colonoscopy: A Review of Its Yield for Cancers and Adenomas by Indication. Am J Gastroenterol 1995;90:353-65.

71. Colon and Rectal Cancer Stages. (Accessed May 2008, at http://www.nccn.org/patients/patient_gls/_english/_colon/3_stages.asp.)

72. Eden J, Simone JV. Assessing the quality of cancer care: an approach to measurement in Georgia. Washington, D.C.: National Academies Press; 2005.

73. Moertel CG, Fleming TR, Macdonald JS, et al. Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report. Ann Intern Med 1995;122:321-6.

74. O'Connell MJ, Mailliard JA, Kahn MJ, et al. Controlled trial of fluorouracil and low-dose leucovorin given for 6 months as postoperative adjuvant therapy for colon cancer. J Clin Oncol 1997;15:246-50.

75. Taal B, Van Tinteren H, Zoetmulder F. Adjuvant 5FU plus levamisole in colonic or rectal cancer: improved survival in stage II and III. Br J Cancer 2001;85:1437.

76. Benson AB, III, Schrag D, Somerfield MR, et al. American Society of Clinical Oncology Recommendations on Adjuvant Chemotherapy for Stage II Colon Cancer. J Clin Oncol 2004;22:3408-19.

77. Institute of Medicine (U.S.). Division of Health Care Services., Lohr KN, Institute of Medicine (U.S.). Committee to Design a Strategy for Quality Review and Assurance in Medicare., United States. Health Care Financing Administration. Medicare : a strategy for quality assurance. Washington, D.C.: National Academy Press; 1990.

78. Donabedian A. Evaluating the quality of medical care. Milbank Mem Fund Q 1966;44:Suppl:166-206.

79. Schuster MA, McGlynn EA, Brook RH. How good is the quality of health care in the United States? 1998. Milbank Q 2005;83:843-95.

80. Gotham K. Urban space, restrictive covenants and the origins of racial residential segregation in a US city, 1900-50. International Journal of Urban and Regional Research 2000;24:616-33.

81. Kenn D. Institutionalized, Legal Racism: Housing Segregation and Beyond. Boston University Public Interest Law Journal 2001;11:35.

82. Ming Jr W. Racial Restrictions and the Fourteenth Amendment: The Restrictive Covenant Cases. The University of Chicago Law Review 1949:203-38.

83. Fix M. Clear and convincing evidence: Measurement of discrimination in America. 1993.

84. Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. Public Health Rep 2001;116:404-16.

85. Charles C. The Dynamics of Racial Residential Segregation. Annual Review of Sociology 2003;29:167-207.

86. Sampson R, Wilson W. Toward a theory of race, crime, and urban inequality. Race, Crime, and Justice: A Reader 2005:177.

87. Kawachi I, Kennedy BP, Lochner K, Prothrow-Stith D. Social capital, income inequality, and mortality. Am J Public Health 1997;87:1491-8.

88. Kaplan G, Pamuk E, Lynch J, Cohen R, Balfour J. Inequality in income and mortality in the United States: analysis of mortality and potential pathways. Br Med J 1996;312:999.

89. Massey D, Denton N. The dimensions of residential segregation. Soc Forces 1988;67:281-315.

90. Frey W, Myers D. Neighborhood segregation in single-race and multirace America: a Census 2000 study of cities and metropolitan areas: Citeseer; 2002.

91. Robinson V. Lieberson's Isolation Index; A Case Study Evaluation. Area 1980;12:307-12.

92. Rodriguez RA, Sen S, Mehta K, Moody-Ayers S, Bacchetti P, O'Hare AM. Geography matters: relationships among urban residential segregation, dialysis facilities, and patient outcomes. Ann Intern Med 2007;146:1746-54.

93. McGory ML, Zingmond DS, Sekeris E, Bastani R, Ko CY. A patient's race/ethnicity does not explain the underuse of appropriate adjuvant therapy in colorectal cancer. Dis Colon Rectum 2006;49:319-29.

94. Schrag D, Cramer LD, Bach PB, Begg CB. Age and adjuvant chemotherapy use after surgery for stage III colon cancer. J Natl Cancer Inst 2001;93:850-7.

95. Hall SA, Kaufman JS, Ricketts TC. Defining urban and rural areas in U.S. epidemiologic studies. J Urban Health 2006;83:162-75.

96. Hawley ST, Chang S, Risser D, Zhang Q. Colorectal Cancer Incidence and Mortality in Texas 1990–1992: A Comparison of Rural Classifications. The Journal of Rural Health 2002;18:536-45.

97. Hawley ST, Foxhall L, Vernon SW, Levin B, Young JE. Colorectal cancer screening by primary care physicians in Texas: a rural-urban comparison. J Cancer Educ 2001;16:199-204.

98. ERS/USDA Briefing Room: Measuring Rurality: Rural-Urban Commuting Area Codes. (Accessed September 23, 2009, at http://www.ers.usda.gov/briefing/Rurality/RuralUrbanCommutingAreas/.)

99. RUCA Data: Using RUCA Data. (Accessed September 23 2009, at http://depts.washington.edu/uwruca/ruca-uses.php.)

100. Liff JM, Chow W-H, Greenberg RS. Rural-urban differences in stage at diagnosis. Possible relationship to cancer screening. Cancer 1991;67:1454-9.

101. Tropman SE, Hatzell T, Paskett E, Ricketts T, Cooper MR, Aldrich T. Colon cancer treatment in rural North and South Carolina. Cancer Detect Prev 1999;23:428-34.

102. Smedley BD, Stith AY, Nelson AR, Institute of Medicine (U.S.). Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care. Unequal treatment : confronting racial and ethnic disparities in health care. Washington, D.C.: National Academies Press; 2003.

103. White A, Liu CC, Xia R, et al. Racial disparities and treatment trends in a large cohort of elderly African Americans and Caucasians with colorectal cancer, 1991 to 2002. Cancer 2008;113:3400-9.

104. Dominitz JA, Samsa GP, Landsman P, Provenzale D. Race, treatment, and survival among colorectal carcinoma patients in an equal-access medical system. Cancer 1998;82:2312-20.

105. Hassan MO, Arthurs Z, Sohn VY, Steele SR. Race does not impact colorectal cancer treatment or outcomes with equal access. Am J Surg 2009;197:485-90.

106. Morris AM, Billingsley KG, Hayanga AJ, Matthews B, Baldwin LM, Birkmeyer JD. Residual Treatment Disparities After Oncology Referral for Rectal Cancer. J Natl Cancer Inst 2008.

107. Hardiman KM, Cone M, Sheppard BC, Herzig DO. Disparities in the treatment of colon cancer in octogenarians. Am J Surg 2009;197:624-8.

108. Bradley CJ, Given CW, Dahman B, Fitzgerald TL. Adjuvant chemotherapy after resection in elderly Medicare and Medicaid patients with colon cancer. Arch Intern Med 2008;168:521-9.

109. Demissie K, Oluwole OO, Balasubramanian BA, Osinubi OO, August D, Rhoads GG. Racial differences in the treatment of colorectal cancer: a comparison of surgical and radiation therapy between Whites and Blacks. Ann Epidemiol 2004;14:215-21.

110. Folprecht G, Cunningham D, Ross P, et al. Efficacy of 5-fluorouracil-based chemotherapy in elderly patients with metastatic colorectal cancer: a pooled analysis of clinical trials. Ann Oncol 2004;15:1330-8.

111. Jessup JM, Stewart A, Greene FL, Minsky BD. Adjuvant chemotherapy for stage III colon cancer: implications of race/ethnicity, age, and differentiation. JAMA 2005;294:2703-11.

112. Sundararajan V, Mitra N, Jacobson JS, Grann VR, Heitjan DF, Neugut AI. Survival associated with 5-fluorouracil-based adjuvant chemotherapy among elderly patients with node-positive colon cancer. Ann Intern Med 2002;136:349-57.

113. Potosky AL, Harlan LC, Kaplan RS, Johnson KA, Lynch CF. Age, sex, and racial differences in the use of standard adjuvant therapy for colorectal cancer. J Clin Oncol 2002;20:1192-202.

114. NIH consensus conference. Adjuvant therapy for patients with colon and rectal cancer. JAMA 1990;264:1444-50.

115. Wu X, Chen VW, Andrews PA, Chen L, Hsieh M, Fontham ET. Treatment patterns for stage III colon cancer and factors related to receipt of postoperative chemotherapy in Louisiana. J La State Med Soc 2004;156:255-61.

116. Luo R, Giordano SH, Freeman JL, Zhang D, Goodwin JS. Referral to medical oncology: a crucial step in the treatment of older patients with stage III colon cancer. Oncologist 2006;11:1025-33.

117. Schrag D, Gelfand SE, Bach PB, Guillem J, Minsky BD, Begg CB. Who gets adjuvant treatment for stage II and III rectal cancer? Insight from surveillance, epidemiology, and end results--Medicare. J Clin Oncol 2001;19:3712-8.

118. Neugut AI, Fleischauer AT, Sundararajan V, et al. Use of adjuvant chemotherapy and radiation therapy for rectal cancer among the elderly: a population-based study. J Clin Oncol 2002;20:2643-50.

119. Cronin DP, Harlan LC, Potosky AL, Clegg LX, Stevens JL, Mooney MM. Patterns of care for adjuvant therapy in a random population-based sample of patients diagnosed with colorectal cancer. Am J Gastroenterol 2006;101:2308-18.

120. Ayanian JZ, Zaslavsky AM, Fuchs CS, et al. Use of adjuvant chemotherapy and radiation therapy for colorectal cancer in a population-based cohort. J Clin Oncol 2003;21:1293-300.

121. Gorin SS, Ashford AR, Lantigua R, et al. Intraurban influences on physician colorectal cancer screening practices. J Natl Med Assoc 2007;99:1371-80.

122. Nattinger AB, Laud PW, Sparapani RA, Zhang X, Neuner JM, Gilligan MA. Exploring the surgeon volume outcome relationship among women with breast cancer. Arch Intern Med 2007;167:1958-63.
123. Thompson MJ, Lynge DC, Larson EH, Tachawachira P, Hart LG. Characterizing the General Surgery Workforce in Rural America. Arch Surg 2005;140:74-9.
124. Diehr P, Yergan J, Chu J, et al. Treatment modality and quality differences for black and white breast-cancer patients treated in community hospitals. Med Care 1989;27:942-58.
125. Hershman DL, Buono D, McBride RB, Tsai WY, Neugut AI. Influence of private practice setting and physician characteristics on the use of breast cancer adjuvant chemotherapy for elderly women. Cancer 2009;115:3848-57.
126. Hershman DL, Buono D, Jacobson JS, et al. Surgeon characteristics and use of breast conservation surgery in women with early stage breast cancer. Ann Surg 2009;249:828-33.
127. Prystowsky JB, Bordage G, Feinglass JM. Patient outcomes for segmental colon resection according to surgeon's training, certification, and experience. Surgery 2002;132:663-72.
128. Porter GA, Soskolne CL, Yakimets WW, Newman SC. Surgeon-related factors and outcome in rectal cancer. Ann Surg 1998;227:157-67.
129. Schrag D, Panageas KS, Riedel E, et al. Hospital and surgeon procedure volume as predictors of outcome following rectal cancer resection. Ann Surg 2002;236:583-92.
130. Schrag D, Panageas KS, Riedel E, et al. Surgeon volume compared to hospital volume as a predictor of outcome following primary colon cancer resection. J Surg Oncol 2003;83:68-78; discussion -9.
131. Silvestri G, Handy J, Lackland D, Corley E, Reed C. Specialists achieve better outcomes than generalists for lung cancer surgery. Chest 1998;114:675.
132. Goodney P, Lucas F, Stukel T, Birkmeyer J. Surgeon specialty and operative mortality with lung resection. Ann Surg 2005;241:179.
133. Zhang W, Ayanian JZ, Zaslavsky AM. Patient characteristics and hospital quality for colorectal cancer surgery. Int J Qual Health Care 2007;19:11-20.

134. Holm T, Johansson H, Cedermark B, Ekelund G, Rutqvist LE. Influence of hospital- and surgeon-related factors on outcome after treatment of rectal cancer with or without preoperative radiotherapy. Br J Surg 1997;84:657-63.

135. Cress RD, O'Malley CD, Leiserowitz GS, Campleman SL. Patterns of chemotherapy use for women with ovarian cancer: a population-based study. J Clin Oncol 2003;21:1530-5.

136. Simons AJ, Ker R, Groshen S, et al. Variations in treatment of rectal cancer: the influence of hospital type and caseload. Dis Colon Rectum 1997;40:641-6.

137. Birkmeyer N, Goodney P, Stukel T, Hillner B, Birkmeyer J. Do cancer centers designated by the National Cancer Institute have better surgical outcomes? Cancer 2005;103:435-41.

138. Landis J, Koch G. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.

139. Du XL, Key CR, Dickie L, Darling R, Geraci JM, Zhang D. External validation of medicare claims for breast cancer chemotherapy compared with medical chart reviews. Med Care 2006;44:124-31.

140. Du XL, Key CR, Dickie L, et al. Information on chemotherapy and hormone therapy from tumor registry had moderate agreement with chart reviews. J Clin Epidemiol 2006;59:53-60.

141. Bickell NA, Chassin MR. Determining the quality of breast cancer care: do tumor registries measure up? Ann Intern Med 2000;132:705-10.

142. Malin JL, Kahn KL, Adams J, Kwan L, Laouri M, Ganz PA. Validity of cancer registry data for measuring the quality of breast cancer care. J Natl Cancer Inst 2002;94:835-44.

143. Edwards BK, Brown ML, Wingo PA, et al. Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. J Natl Cancer Inst 2005;97:1407-27.

144. Renouf D, Kennecke H, Gill S. Trends in chemotherapy utilization for colorectal cancer. Clin Colorectal Cancer 2008;7:386-9.

145. Klarman M. From Jim Crow to civil rights: The Supreme Court and the struggle for racial equality: Oxford University Press, USA; 2004.

146. ERS/USDA Data - Rural Definitions: State-Level Maps. (Accessed March 12, 2010, at www.ers.usda.gov/Data/Ruraldefinitions/GA.pdf.)

147. Georgia. (Accessed March 12, 2010, at quickfacts.census.gov.)

148. Georgia: Poverty Rate by Race/Ethnicity, states (2007-2008), U.S. (2008). (Accessed at http://www.statehealthfacts.org/.)

149. Medicare Physician Identifiers UPINs, PINs and NPI Numbers. In: ResDAC, ed. Minneapolis, MN: Research Data Assistance, University of Minnesota; January 2003.

150. Goodman M, Almon L, Bayakly R, et al. Cancer outcomes research in a rural area: a multi-institution partnership model. J Community Health 2009;34:23-32.

151. Jessup JM, McGinnis LS, Steele GD, Jr., Menck HR, Winchester DP. The National Cancer Data Base. Report on colon cancer. Cancer 1996;78:918-26.

152. Cooper GS, Yuan Z, Landefeld CS, Rimm AA. Surgery for colorectal cancer: Race-related differences in rates and survival among Medicare beneficiaries. Am J Public Health 1996;86:582-6.

153. Du XL, Fang S, Vernon SW, et al. Racial disparities and socioeconomic status in association with survival in a large population-based cohort of elderly patients with colon cancer. Cancer 2007;110:660-9.

154. Dorrance HR, Docherty GM, O'Dwyer PJ. Effect of surgeon specialty interest on patient outcome after potentially curative colorectal cancer surgery. Dis Colon Rectum 2000;43:492-8.

155. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health 1992;82:703.

156. Kleinbaum DG, Klein M. Additional Modeling Strategy Issues Logistic Regression. In: Logistic Regression: A Self-Learning Text. 3rd ed: Springer New York; 2010:241-99.

157. Baicker K, Chandra A, Skinner JS. Geographic variation in health care and the problem of measuring racial disparities. Perspect Biol Med 2005;48:S42-53.

158. Auchincloss AH, van Nostrand JF, Ronsaville D. Access to Health Care for Older Persons in the United States. J Aging Health 2001;13:329-54.

159. Sampson RJ. Linking the Micro- and Macrolevel Dimensions of Community Social Organization. Soc Forces 1991;70:43-65.

160. Krieger N, Chen J, Waterman P, Soobader M, Subramanian S, Carson R. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. Am J Epidemiol 2002;156:471.

161. Weinberg D. Measuring poverty in the United States: History and current issues. Center for Economic Studies Research Paper, CES 2006:06-11.

162. Dobie SA, Warren JL, Matthews B, Schwartz D, Baldwin LM, Billingsley K. Survival benefits and trends in use of adjuvant therapy among elderly stage II and III rectal cancer patients in the general population. Cancer 2008;112:789-99.

163. Earle CC, Venditti LN, Neumann PJ, et al. Who gets chemotherapy for metastatic lung cancer? Chest 2000;117:1239-46.

164. Berrios-Rivera JP, Fang S, Cabanillas ME, Cabanillas F, Lu H, Du XL. Variations in chemotherapy and radiation therapy in a large nationwide and community-based cohort of elderly patients with non-Hodgkin lymphoma. Am J Clin Oncol 2007;30:163-71.

165. CoC Quality of Care Measures. 2007. (Accessed at www.facs.org/cancer/qualitymeasures.html.)

166. Haas JS, Brawarsky P, Iyer A, Fitzmaurice GM, Neville BA, Earle C. Association of area sociodemographic characteristics and capacity for treatment with disparities in colorectal cancer care and mortality. Cancer 2011;117:4267-76.

167. Schrag D, Cramer LD, Bach PB, Begg CB. Age and adjuvant chemotherapy use after surgery for stage III colon cancer. Journal of the National Cancer Institute 2001;93:850-7.

168. Rendall MS, Jr AS. Elderly Poverty Alleviation through Living with Family. Journal of Population Economics 1995;8:383-405.

169. Miglioretti D, Heagerty P. Marginal modeling of nonnested multilevel data using standard software. Am J Epidemiol 2007;165:453.

170. Lipscomb J, Gillespie TW, Goodman M, et al. Black-white differences in receipt and completion of adjuvant chemotherapy among breast cancer patients in a rural region of the US. Breast Cancer Res Treat;133:285-96.

171. Hao Y, Landrine H, Jemal A, et al. Race, neighbourhood characteristics and disparities in chemotherapy for colorectal cancer. J Epidemiol Community Health;65:211-7.

172. Popescu RA, Norman A, Ross PJ, Parikh B, Cunningham D. Adjuvant or palliative chemotherapy for colorectal cancer in patients 70 years or older. J Clin Oncol 1999;17:2412-8.

173. Hynes DM, Tarlov E, Durazo-Arvizu R, et al. Surgery and adjuvant chemotherapy use among veterans with colon cancer: insights from a California study. J Clin Oncol;28:2571-6.

174. National Cancer Institute. Health Services and Economics. Procedure Codes for SEER-Medicare Analysis. (Accessed 10/29/2010, 2010, at http://healthservices.cancer.gov/seermedicare/considerations/procedure_codes.html.)

175. Liang K-Y, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13-22.

176. Bonadonna G, Valagussa P. Dose-response effect of adjuvant chemotherapy in breast cancer. N Engl J Med 1981;304:10-5.

177. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687-717.

178. Gill S, Loprinzi CL, Sargent DJ, et al. Pooled analysis of fluorouracil-based adjuvant therapy for stage II and III colon cancer: who benefits and by how much? J Clin Oncol 2004;22:1797-806.

179. Haller DG, Catalano PJ, Macdonald JS, et al. Phase III study of fluorouracil, leucovorin, and levamisole in high-risk stage II and III colon cancer: final report of Intergroup 0089. J Clin Oncol 2005;23:8671-8.

180. Dobie SA, Baldwin LM, Dominitz JA, Matthews B, Billingsley K, Barlow W. Completion of therapy by Medicare patients with stage III colon cancer. J Natl Cancer Inst 2006;98:610-9.
181. Goodman M, Almon L, Bayakly R, et al. Cancer outcomes research in a rural area: a multi-institution partnership model. J Community Health 2009;34:23-32.
182. Baldwin DM. Disparities in health and health care: focusing efforts to eliminate unequal burdens. Online J Issues Nurs 2003;8:2.
183. Hodgson DC, Fuchs CS, Ayanian JZ. Impact of patient and provider characteristics on the treatment and outcomes of colorectal cancer. J Natl Cancer Inst 2001;93:501-15.
184. Egbert LD, Rothman IL. Relation between the Race and Economic Status of Patients and Who Performs Their Surgery. N Engl J Med 1977;297:90-1.
185. Jerant AF, Fenton JJ, Franks P. Determinants of racial/ethnic colorectal cancer screening disparities. Arch Intern Med 2008;168:1317-24.
186. McAlearney AS, Reeves KW, Dickinson SL, et al. Racial differences in colorectal cancer screening practices and knowledge within a low-income population. Cancer 2008;112:391-8.
187. Gornick ME, Eggers PW, Reilly TW, et al. Effects of race and income on mortality and use of services among Medicare beneficiaries. N Engl J Med 1996;335:791-9.
188. McMahon LF, Jr., Wolfe RA, Huang S, Tedeschi P, Manning W, Jr., Edlund MJ. Racial and gender variation in use of diagnostic colonic procedures in the Michigan Medicare population. Med Care 1999;37:712-7.
189. Ayanian JZ, Weissman JS, Chasan-Taber S, Epstein AM. Quality of care by race and gender for congestive heart failure and pneumonia. Med Care 1999;37:1260-9.
190. Bach PB, Cramer LD, Warren JL, Begg CB. Racial differences in the treatment of early-stage lung cancer. N Engl J Med 1999;341:1198-205.
191. Elliott TE, Elliott BA, Renier CM, Haller IV. Rural-urban differences in cancer care: results from the Lake Superior Rural Cancer Care Project. Minn Med 2004;87:44-50.

192. Robertson R, Campbell NC, Smith S, et al. Factors influencing time from presentation to treatment of colorectal and breast cancer in urban and rural areas. Br J Cancer 2004;90:1479-85.

193. Esnaola NF, Knott K, Finney C, Gebregziabher M, Ford ME. Urban/rural residence moderates effect of race on receipt of surgery in patients with nonmetastatic breast cancer: a report from the South Carolina central cancer registry. Ann Surg Oncol 2008;15:1828-36.

194. Smith DB. The racial segregation of hospital care revisited: Medicare discharge patterns and their implications. Am J Public Health 1998;88:461-3.

195. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Colon Cancer; 2008.