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Examination of the Association of Receipt of Opioid Therapy and Lung Cancer Patient Survival Rates among South Carolina Medicaid Recipients

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Survival Rates among South Carolina Medicaid Recipients

by

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Submitted in Partial Fulfillment of the Requirements

For the Degree of Doctor of Philosophy in

Health Services Policy and Management

Norman J. Arnold School of Public Health

University of South Carolina

2015

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DEDICATION

This work is dedicated to my motivation, my sweet boy, Jaylen. Your existence in my life is indescribable. I thank God daily for the blessing of motherhood and choosing me to give life to someone so beautiful. As you continue to grow and mature, I hope that this work and my achievements serve as a means of encouragement and that you push yourself in everything you attempt. You are blessed and destined for greatness.

To my future husband, I am grateful for your love, constant words of encouragement, and support. Your understanding that this work sometimes needed to come first was crucial for its completion. We have evolved together through this process and this is only the beginning for us. What we are building together is unbreakable. It's you and I.

Last, but certainly not least, I express my sincere gratitude to my mother. You have been the support system and without you this achievement would have been beyond difficult. I thank God for a kind-hearted and loving figure to aspire to be like.

I share this accomplishment with each of you who are so vital in my life. We are finally finished!!

ABSTRACT

Introduction: Lung cancer is a high pain cancer that can require the attention of clinical specialists. Already vulnerable populations, like those that inhabit rural areas, when dealing with chronic diseases, like lung cancer, need and deserve adequate medical attention. However, rural communities often lack clinical specialists and are left without the needed care. It is necessary to investigate the current availability of treatment options (medications) available to cancer patients in rural communities. Gaining this knowledge can result in economic savings and improvement of the quality of life for rural populations.

Methods: Medicaid data from 1996-2010 was used to examine geographical disparities (urban and rural) in the state of South Carolina. Medicaid recipients identified as distant stage lung cancer patients were linked with data from the South Carolina Cancer Registry. All patients included in the sample were either prescribed an opioid or analgesic and were continuously enrolled in Medicaid for at least 9 months prior to diagnosis (N=1,334). Using the weighted data, logistic regression and Cox Proportional Hazard analyses were performed to assess the likelihood of disparate health care treatment and the survival rate of patients in the sample.

Results: Findings of the conducted logistic regression were not statistically significant. This indicates that none of the variables analyzed in the patient factor or structure and process of care components were directly associated with patient receipt of medications. For the Cox Proportional Hazard model, gender was the only statistically significant

variable that emerged from the model. Males (OR=1.31, CI: 1.03-1.65) were more likely than females to experience cancer-related death than females. Considering patient and provider geography, there was a greater presence of cancer specialists in the urban areas of South Carolina. The deficit of clinical resources referred to a lack of cancer specialists to treat and prescribe medications appropriately as well as pharmacies to fill prescriptions.   Each having the potential to impact the manner of health care treatment as well as influence the longevity of a patient's life.

Conclusion: The disparities in access to care in the urban and rural regions of South Carolina indicate the need for policy that improves the availability of specialty clinicians in rural areas as well as rural residents' access to pain medications. With proper regulatory stipulations in place, the concerns of substance diversion and dependence would decrease. The development of local and federal government policy is necessary to increase the degree of pain control among these populations.

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Lung cancer is the most frequently diagnosed cancer and pain is the most commonly experienced symptom (Simmons, MacLeod, Laird, 2014). Pain signifies a prominent medical, social and economic issue. It is estimated that the prevalence of chronic pain ranges from 8% to more than 60%, amongst the general population (Phillips, 2003). While medications available to relieve pain are innumerable, pain is the primary cause for individuals seeking medical attention (Berry, Dahl, 2000). Not only does this increase utilization of the health care system, it drastically impacts health care cost. The needed clinical attention of those affected by pain increases the significance of improving the manner in which pain is assessed and treated, specifically in cancer patients.

Pain management is considered to be adequate if there is resemblance between the patient's reported degree of pain and the appropriateness of analgesic therapy (Denadrea, Montari, Moja & Apolone, 2008). As a result of inadequate pain management, multiple studies document the frequency of uncontrolled pain ranging from 74% to 95% in the ill and declared hospice patients (Berry, Dahl, 2000). Pain is a chief concern for persons diagnosed with cancer (Herr, et al, 2012). Approximately 75% of cancer patients experience pain during the course of the disease, approximately 40% report inadequate analgesia, and 50%-80% of cancer patients report inadequate pain management that affects activities of daily living (ADLs) (Randall-David, Wright, Porterfield, Lesser, 2003; & Berry, Dahl, 2000). The impact of pain on the functional

status of patients is significant, especially as many diseases, specifically cancer, are managed on an outpatient basis, where individuals are cared for in the home by remote clinical and family caregivers (Ferrell, Ferrell, Ahn, & Tran K, 1994).

The control and alleviation of pain has become a main concern in oncology (Paice & Ferrell, 2011). Pain has been identified as a symptom of cancer disease as well as a side effect cancer treatment. It is estimated that 30-45% of cancer patients in the early to intermediate periods suffer with moderate to severe pain; 75% of cancer patients in the advanced stages suffer with moderate to severe pain; and 25-30% of cancer patients in the advanced phase experience severe pain (Pargeon & Hailey, 1999). However, experts state that approximately 90% of cancer patients could be relieved of pain through the use of appropriate pharmacological treatment (Pargeon & Hailey, 1999; Portenoy & Lesage, 1999). The successful management of cancer pain is necessary for the improvement of cancer survivorship, quality of life, and end-of-life care (Paice & Ferrell, 2011). Reasons for the ineffective relief of cancer pain range from improper utilization of opioids, institutional, geographical, and societal barriers (Deandrea, Montanari, Moja, & Apolone, 2008). Obstacles to cancer pain management were specifically identified in 1994 by the Agency for Health Care Policy and Research; this was the first nationwide clinical publication of its kind (Agency for Health Care Policy and Research, 1994). Additional identified barriers include inadequate pain assessment as a result of unqualified clinicians, the lack of patient-clinician communication, patient fears, and the absence of and access to pain medication- especially within minority neighborhoods and regions (Paice & Ferrell, 2011).

Pain assessments should be viewed as a basic component in routine cancer care. (Portenoy, 2011). A comprehensive assessment of pain in cancer patients to identify the relationship between the pain and the cancer is elemental in the treatment of cancer pain. The evaluation should be thorough enough to identify the need for additional assessments and a feasible strategy of care. (Portenoy, 2011). This assessment can offer clarity regarding the impact of pain on the pathogenesis of the disease and the patient's quality of life (Portenoy & Lesage, 1999). A complete and sufficient evaluation investigates the multi-dimensionality of the pain and the cancer (Portenoy & Lesage, 1999). However, because of the varying personal measurements of pain, the patient's report of pain is chief in the assessment (Portenoy & Lesage, 1999; Paice & Ferrell, 2011). Candid communication between the patient and clinician in combination with diagnostic results and laboratory and imaging reviews, enables an initial determination of the degree of pain and stage of the disease (Portenoy & Lesage, 1999). Diagnostic inferences are made from this relationship. The reluctance of cancer patients to accurately report pain to physicians is key in the inadequate treatment of cancer-related pain (Paice & Ferrell, 2011). Oncology patients are hesitant to report pain due to fear that pain equates to disease progression, the misunderstood perceptions about opioid usage, or the possibility of physicians being distracted from the ultimate goal—disease treatment and increased longevity (Herr, et al, 2012; Carlson, Morrison, Holford, & Bradley, 2007; & Ferrell, Ferrell, Ahn, 1994).

In the treatment process of cancer, it is recommended that pain is assessed frequently once treatment has begun (Pargeon, Hailey, 1999). This could present a challenge for cancer patients that reside in areas where access and quality issues are

constants. Cancer patients who live in rural areas have few options other than to seek medical care from "generalists", also of whom there are shortages to treat populations in these areas, who are untrained in pain assessment (Kelley, 2007). Insufficient pain management embodies a public health issue that plagues minority, rural and underserved populations who often suffer due to the healthcare disparities that plague this group— inadequate access to prescription opioid analgesia, usually prescribed for cancer patients to alleviate pain associated with the disease, the deficit of clinical specialists, and regulatory safeguards (Tollefson et al., 2011; Webster et al, 2007; Weisse, Sorum, Sanders, Syat, 2001).

Rural communities present unique challenges to cancer pain management (Baltic, 2002). Barriers to pain management in rural communities include attitudinal biases, fear and misconceptions of patients and families, and regulatory concerns (Baltic, 2002). In addition, the availability of opioids, used for pain management in cancer, are perceived to be in low demand and stocking opioids carries a high risk of safety concerns (Francouer, 2011; Baltic, 2002). The demographics, lower socioeconomic status and educational attainment and the higher number of uninsured population, of these communities impede the availability and access to such medications (Baltic, 2002). In addition it is difficult for rural communities to attract and retain specialists in pain or cancer care (Kelley, 2007). The limited and aged, nationally and state-specific, literature referencing cancer pain management in rural communities highlights the need for this focused and specific research agenda.

This study aims to examine medication treatment options for distant stage lung cancer patients in rural South Carolina and the impact of patient geography and ethnicity. **The primary aim of this study is to examine the association of the availability of medications that treat cancer pain, a primary side effect of distant stage lung cancer, with patient factors and geography.** The combined influence of these variables on the rate of patient survival was the primary outcome of interest. To date, no published studies were discovered that examined cancer pain management and its possible association to survival in a state-based insurance database in the state of South Carolina or other like geographical regions within the target population. This investigation explores the availability of pain medication based on race and ethnicity and geography as well as the impact of the receipt of medication on patient longevity and survivorship.

Rural residents face increased difficulty accessing health services and providers (Tollefson, et al, 2011). This lack of access is not only evident in the scope of access to health services and providers, but also in the lack of availability of prescription drugs to aid in pain management (Francoeur, 2011). Unfortunately, rural residents with chronic pain are often placed in an even more vulnerable state, as they are sometimes forced to forego the needed health services and adequate relief of pain. This is due to the limited availability of medications, trained clinicians, and decreased access to health care facilities.

It is because of rural community's inability to attract and retain health professionals and healthcare facilities that pain management care is usually provided by health care generalists, not pain management specialists (Kelley, 2007). In addition, pharmacists and pharmacies in rural, areas may not stock opioids, commonly used for

pain, because of safety and cost-effectiveness concerns (Francoeur). Rural areas often endure the brunt of economic strain without needed health care services due to pressure by health insurers to limit coverage on less cost-effective options, combined with health institutions and patients' out-of-pocket restrictions. (Francoeur; Morrsion et al, 2011) Health providers in rural areas also find it difficult to obtain medications because of higher costs and safe delivery concerns (Francoeur).

Each of these factors significantly affects the management of pain in patients in rural areas. Effective pain relief is significantly dependent upon a comprehensive assessment that highlights physical, psychological, social, and spiritual aspects for intervention (Paice, Ferrell, 2011). However, the limited availability of literature about the role the availability of prescribed pharmaceuticals plays in cancer pain management in rural areas only encourages the need to further examine (Kelley, 2007; Robinson, 2009). Effective pain management has a significant impact on the quality of life, health, and socioeconomic circumstances (Green, et al, 2003).

The Patient Protection Affordable Care Act highlights pain management with provisions extracted from the National Pain Care Policy Act. Proposed efforts include training for clinicians to improve care for pain, confronting barriers to care in underserved groups, and programs that specifically assess the impact of provider's knowledge on the practice of pain care (Affordable Care Act, 2010).

In the 2013 Progress Report Card, The American Cancer Society assigned the state of South Carolina a grade of "B+" for implementing pain management policies throughout the state (Pain & Policy Studies Group, 2013). This is an improvement over

the 2006 grade of "B", but there has been no improvement of the grade "B+" since 2007. It was hypothesized that distant stage lung cancer patients who lived in rural areas were at a greater risk for experiencing cancer-associated pain and would not receive adequate treatment for this pain (needed analgesic medications). In turn, it was also hypothesized that this inadequate treatment of patient's healthcare needs would decrease patient's survival rate.

BACKGROUND AND SIGNIFICANCE

RATES OF CANCER IN SOUTH CAROLINA

The American Cancer Society predicts an estimated incidence of 25,550 cases of cancer in South Carolina (2015). Of this, 4, 040 will be lung cancer cases. Advancements in the treatment of cancer have revealed an array of medications and drug combinations that focus on disease-specific treatments and symptomology, treating only a portion of the problem. These methodologies do not address the need for clinicians and healthcare systems to be prepared to provide the necessary care for the whole scope of treatment (Payne, 2000).

According to the South Carolina Cancer Registry, the 2009 incidence rate of cancer for the state of South Carolina was 442.7 per 100,000 (CDC, 2009) (Table 2.1). The cancer mortality rate was 178.6 per 100,000 (Table 2.2). Of the 4,723,723 people that live in South Carolina, 1,089,723 live in areas defined as rural (Rural Assistance Center, 2013). All of South Carolina's 46 counties are designated as whole or partial Health Professional Shortage Areas (HPSAs), highlighting the problem for rural South Carolina (South Carolina Office or Rural Health, 2013). Of the 46 counties, 35 are designated as wholly or partially rural areas according to the Economic Research Service Rural-Urban Commuting Areas (RUCA) ("USDA", 2010). The RUCA system uses census tracts to categorize applying the same concepts that the Office of Management and Budget uses; in addition, measures of population density, level of urbanization, and average daily

commute are used to make the distinction between micropolitan and metropolitan areas, adjacent tracts that are socially and economically incorporated, as well as rural tracts ("USDA", 2003).

CANCER CARE IN RURAL REGIONS

During the 2010 United States Census, approximately 19% of the United States population lived in an area designated as rural (US Census Bureau, 2010). In regions with access issues, proximity to specialized care can pose problems and influence both access and utilization. Specifically for cancer patients, extended travel times have been associated with advanced stages of the disease (Onega, et al., 2008). This can be attributed to the greater likelihood of lower socioeconomic status and decreased chances of survival among residents of rural areas. Patients with limited access presenting with advanced stages of the disease could also be associated with the greater likelihood of receipt of poorer treatment, generating poorer outcomes within regions designated as rural (Jong, Vale, & Armstrong, 2005).

In the advocacy for holistic, interdisciplinary cancer care, additional factors must be considered for rural populations. There is the constant question of who from the needed clinical disciplines is available to assist and meet the needs of cancer patients within rural areas? Generalists, alone, are primarily responsible for the delivery of clinical and psychological care for these patients; yet, generalists may not be adequately equipped for these responsibilities (Watanabe et al., 2013; Kelley, 2007). Such issues linger and manifest as medically unmet needs in rural regions.

Addressing the inequalities in cancer care and outcomes faced by rural residents, requires improvement in access and delivery of primary healthcare, access to clinical

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specialty services, and a coordinated continuum of clinical care. A major concern is the deficit of needed evidence to effectively guide and identify the placement of additional resources in the rural areas (Jong, Vale, & Armstrong, 2005). Current policies and legislation are fortified by the simple belief that patients should have access to quality health services that are as near to their homes as geographically possible. However, geographic variation is often unpredictable in rural areas, which impacts time and period of diagnosis, stage of disease, and outcome of the diagnosis and disease (Jong, Vale, & Armstrong, 2005). Efforts to increase the care being provided by specialists in rural areas include videoconferencing and telemedicine. Each has become integral components in the rural continuum of cancer care. A 2013 Canadian study indicated that these forms of care have demonstrated themselves to be both time- and cost-effective with both the patient and the provider reporting a high-degree of satisfaction (Watanabe).

Nevertheless, the establishment and implementation of an efficient and effective health care system that practices coordinated care with fidelity would require progressive information systems, actual collaboration between and within multidisciplinary teams, services, and regulatory bodies. Remoteness and scarcity of service providers may make this task increasingly difficult for rural areas (Jong, Vale, & Armstrong, 2005). Patients with diminished access to care are more likely to postpone treatment for pain (Francoeur, 2011). This could especially relate to persons who find themselves isolated from medical providers. For rural areas isolation is an evident barrier, and as a result many rural residents are often forced to endure the pain and suffering commonly associated with cancer.

INTERSECTION OF RACE AND GEOGRAPHY IN CANCER CARE AND CANCER PAIN MANAGEMENT

Pain is a measurable concept that can have varying perceptions based upon personal experiences and cultural expectations (Bonham, 2001). Cleeland et al's 1994 study of cancer treatment within multiple cancer centers found that cancer patients receiving outpatient therapy at clinics that had a greater service population of "ethnic and racial minority patients" were three times more likely to be under medicated with analgesics than were patients in other settings (1994). Patients indicating inadequate analgesic treatment were also more likely to be receiving their treatment in a community clinical oncology program, where the primary goal is to bring clinical trials to patients in their local communities. In addition, Cleeland discovered that regardless of the clinical setting, minority patients were still more likely to receive inadequate analgesia (1994).

Cleeland et al's 1997 follow-up study examined the degree of cancer-related pain experienced and the appropriateness of medication prescribed for pain relief. The follow-up study also found that patients who received treatment in a clinical setting that primarily services minority patients, either African American or Hispanic, were more likely to receive inadequate pain medication than those who received treatment in a community clinic setting that did not primarily see minority patients. In addition, the 1997 study found that minority patients were more likely to have the degree of their pain, as they reported to the clinician, underestimated by the physician (Bonham, 2001; Cleeland, 1997). Cleeland and colleagues discuss that potential causes for the stated disparities in pain assessment and determination may be the patient being intimidated by treatment and treatment alternatives; less economic and regulatory resources to provide minority patients with the needed pain medications; patients not being insistent about

their health care; lack of clinical expertise in assessment of patient conditions; and cultural and language barriers (Bonham, 2001; Cleeland, 1997; Cleeland, 1994). Cleeland's studies emphasize the significance of selecting the proper type of healthcare facility (Bonham, 2001); however, for rural patients who do not have the option to choose the type of health care facility suboptimal health care may be the only option.

CANCER PAIN MANAGEMENT: A GROWING PRIORITY IN ONCOLOGY CARE

The pathophysiology of cancer incorporates multiple diseases of multiple variations. Symptom distress significantly influences the manner and approach of care for cancer patients (Portenoy, 2011). Chronic pain is one of the most significant symptoms in cancer. Pain in cancer patients and cancer survivors receive subpar descriptions, and currently there are no standard procedures in place regarding the methodology of treatment and best practices in this population where the degree of disease and pain greatly varies (Portenoy, 2011). In advanced stages of the disease severe pain affects approximately 70-80% of patients (Pargeon & Hailey, 1999; Caraceni et al., 2012). As the focus placed on the degree of understanding and skill involved in the evaluation of and tending to cancer pain progresses to the notion of patients being entitled to effective pain management; the breakdown to provide efficient pain management demonstrates the inadequate delivery of medical care and the failure of the healthcare system in its responsibility to meet the needs of cancer patients (Ashburn, 2008).

Pain can be a direct result of the disease or the therapy associated with treatment of the disease. Pain has also been found to be the most anticipated and feared symptom of cancer (Nersesyan & Slavin, 2008). Conventional methods of pain control do not meet

the needs of a portion of the cancer patient population; however, an emerging continuum to include innovative, efficient practices is being executed as a result of the recognized need for alternative methods of pain control and the consistently increasing incidence of cancer (Gulati, Joshi, Baqai, 2012).

PREVALENCE OF CANCER PAIN AND THE UNDERTREATMENT OF CANCER PAIN

The American Cancer Society reports expected 1,665,540 new cancer cases in 2014 (American Cancer Society, 2013; Siegel, Ma, & Jemal, 2014). Among these cancer patients, their pain experiences will vary depending upon the stage of the disease and the type of cancer. For newly diagnosed patients the prevalence of pain is approximately 25%; 33% for patients undergoing active therapy; and the prevalence of pain exceeds 75% for cancer patients in the advanced stages of the disease (Paice & Ferrell, 2011). Chronic pain, referred to interchangeably with pain in this context, experienced by those diagnosed with cancer who have concluded treatment is approximated to be 33%. (Paice & Ferrell, 2011).

Because the occurrence and incidence of cancer is increasing, cancer pain should be expected and attended to as soon as possible instead of at later stages (Paice & Ferrell, 2011). Utilizing the pain management index, Cleeland's 1994 examination revealed that 42% of metastatic cancer patients were given insufficient anesthetics at an inadequate strength level (Cleeland, Gonin, Hatfield, Edmonson, Blum, 1994; de Wit, 1999). Additional studies that used a pain management index to assess the level of pain demonstrated that 27% to 74% of cancer patients received inferior cancer pain treatment. (de Wit; Bekkering et al., 201

Reasons for the under treatment of cancer pain vary. The under treatment of cancer pain can be related to inaccurate assessments of pain by clinicians, the manner in which the pain is reported by the patients and the misuse of opioids as a result of barriers—family, patient, provider, social, and organizational (Deandrea, Montanari, Moja, & Apolone, 2008; Kroenke, Theobald, Wu, & Krebs, 2012). Additional elements that complicate the management of cancer pain are patients who experience inconsistent pain, neuropathic pain, those who suffer from substance abuse issues, and those with limited intellectual or communication abilities (Thapa, Rastogi, & Ahuja, 2011).

Barriers highlighted in a 1995 report are barriers still encountered by both patients and physicians today (Thapa, Rastogi, & Ahuja, 2011). Attempts to emphasize the need for standardized approaches to cancer pain treatment highlight the necessity for the further evaluation of the efficacy of pain assessment tools and resources to establish benchmark pain evaluation techniques (de Wit et al., 1999).

PAIN MEDICATIONS AND CANCER SURVIVORSHIP

Opioids have been considered the "gold-standard" for the relief of chronic cancer pain for over 200 years (The Unviersity of Chicago-Medicine, 2012). Required opioid doses for pain alleviation does vary with circumstance, cannot be predicted, and is impacted by many influences (Brescia, Portenoy, Ryan, Krasnoff, & Gray, 1992). A 1992 study conducted by Brescia et al at Calvary Hospital inidcated that a lack of opioid dose escalation in patients with advanced cancer could be related to the immobility of this specific group of patients—also an indicator of quality of life. However, it is equally important to note that cancer patients who do use opioids as instructed will have

increased survival times and those who do not remain compliant could have decreased survival times (Wade, 2013).

Opioid Dosage and Impact of Opioid Usage for Advanced Cancer Suvivorship Studies

A study conducted in a palliative care setting examined the common concern of clinicians that the dosage of opioids used resulted in a quicker demise of the patients (Alsirafy, et al., 2013). Patients were categorized according to dosage: low dose (<120 mg in a 24-hour period), intermediate dose (120-<300 mg in a 24-hour period), and high dose (≥300 mg in a 24-hour period). The investigation examined the relationship between survival and the dosage of opioids advanced cancer patients received. Patients were receiving a mean dosage of 167 mg per day. The final result demonstrated that opioid dosage had no influence on survival in patients with advanced cancer, including lung cancer, in this setting (Alsirafy, et al., 2013). Patient insurance type and geography were not reported.

Published in 2001, Morita, examined the effects of opioid dosage in hospice inpatients. Over 80% of patients were prescribed opioids with a median dose of 80 milligrams per 48 hours. Dosages were categorized as low (< 240 mg in a 48-hour period), intermediate (240-599 mg in a 48-hour period), and high (≥ 600 in a 48-hour period). The final result demonstrated that opioid dosage had no influence on survival in patients with advanced cancer, including lung, in this setting (Morita, Tsunoda, Inoue, & Chihara, 2001). Patient insurance type, race/ethnicity, and geography were not reported.

The 1997 study lead by Bercovitch, Waller and Ansdunsky examined the medical records of 651 inpatients hospitals at their medical center. The mean daily morphine

given to patients was categorized by age and ranged from <60 mg to >599 mg. The final result demonstrated that morphine dosage had no influence on survival in patients with advanced cancer, including lung, in this setting (Bercovitch, Waller, Adunsky, 1999). Patient insurance type , race/ethnicity, and geography were not reported.

Thorn and Sykes (2000) examined 238 who dies in a palliative care unit. Within the last week of life in the 24-hour period, daily dosage of opiods were recorded. During the last week of life, the average daily dose increased rom 42 milligrams to 55.5 milligrams. The final result demonstrated that morphine dosage had no influence on survival in patients with advanced cancer in this setting (Thorn & Sykes, 2000). Patient insurance type , race/ethnicity, and geography were not reported.

Azoulay et al. reviewed hospice admissions from June through November 2006 (2008). Data regarding demographics, primary tumor site, presence of metastases on admission, opioid dose upon entry to the hospice and on the last day of life, and length of survival in the hospice were documented (Azoulay et al., 2008). From the 94 patients who entered hospice during this period, 63% received opioids and 56% required an increase in opioid dosage. There was a correlation between prolonged life and increased opioid dosage. Patient insurance type , race/ethnicity, and geography were not reported.

From February 2000 to December 2000, Good and colleagues (2005) conducted a review of medical records and medication charts for all deaths of patients admitted to hospice. The investigators examined survival in patients on opioids during the last 24 hours of life. There was no association found between opioids and decreased survival. However, inpatients that were administered a higher dosage, greater than or equal to 300 milligrams per day, as opposed to the lower (less than or equal to 120 milligrams) or mid-

range dosages 120 to 299 milligrams, experienced an increased survival period (Good, Ravenscroft, Cavenagh, 2005). One possible explanation the authors provide for this increased survival time was the potential relationship with better pain control as a result of opioid usage. Patient insurance type , race/ethnicity, and geography were not reported.

Two studies considered the relationship between opioid dosage and survival in the home health care setting. The 2004 published lead by Bercovitch and Ansdunsky examined the medical records of 661 patients enrolled in home healthcare hospice. In the study, 66% of patients were receiving morphine for pain relief. Dosages ranged from 5 milligrams to over 600 milligrams per day. The use of the increased dosage did not have an adverse impact on patient life expectancy (Bercovitch & Andunsky, 2004). The final result demonstrated that morphine dosage had no influence on survival in patients with advanced cancer, including lung, in this setting (Bercovitch & Adunsky, 2004). Patient insurance type , race/ethnicity, and geography were not reported.

The second home health care study was conducted by Bengoechea et al. from 2003 to 2007 (2010). This review of 223 oncology patients of the Hospital at Home unit found that the median survival time was longer for patients who received higher doses than lower doses of opioids. Regular doses were less than 120 milligrams and higher doses were defined as more than 120 milligrams. However, after adjusting for demographic and clincial variables, the differences dissolved. Patient insurance type, race/ethnicity, and geography were not reported (Bengoechea, Gutierrez, Vrotsou, Onaindia, Lopez, 2010).

Each of the previously delineated studies provides insight about the relationship between medication dosage and survival of cancer patients and the non-existent level of

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clarity that exists around this matter. However, the role of the physician remains key when examining the treatment of cancer patients.

PHYSICIAN ATTITUDE AND RATIONALE INFLUENCING CANCER PAIN MANAGEMENT

Generalists and oncologists have an overall insufficient breadth of knowledge of pain management and lack the skills to properly practice pain management therapy (Breivik et al., 2009; Gallagher, Hawley, & Yeomans, 2004; Okuyama, et al., 2004). Between 2007 and 2008, a 40-question questionnaire was distributed to 98 Finnish oncologists and a total of 2,055 generalists, specialists, and internists. The questionnaire revealed a significant difference between the pain management knowledge of oncologists and physicians (Silvoniemi, et al., 2012). Over 60% of the oncologists assumed their current knowledge of the WHO analgesic ladder was correct; however, only 46% of oncologists could remember the number of steps and the order of opioid application for the analgesic ladder as well as the WHO's suggestion of medication for ingestion primarily by mouth. In addition, 80% of oncologists replied pain therapy should only be provided as needed compared with 2% of physicians (Silvoniemi, et al., 2012). As expected of trained oncologists, the Finnish study showed that oncologists had a clearer understanding that increasing the quantities of opioids during the course of the disease does not increase the potential risk for efficacy of the medication (Silvoniemi, et al., 2012).

A 2009, 46-item questionnaire was disseminated nationally to 2,000 actively practicing oncologists, inclusive of palliative care and pain management specialists. The survey contained numeric rating scales to evaluate physician attitudes and behavior

regarding pain management and posed situational questions to examine the physician knowledge and attitudes towards prescribing opioids and opioid safety (Breuer, Fleishman, Cruciani, & Portenoy, 2011). Study results indicated that oncologists perceived the reports of pain provided by patients to be an accurate report of pain and that oncologists offered effective pain management, yet they were "less conservative" in their prescribing of opioids when compared to general physicians and other specialists (Breuer, Fleishman, Cruciani, & Portenoy, 2011). Most importantly, the surveyed oncologists believed that the greatest obstacles to effective pain management were: the assessment of pain, patients not wanting to take opioids, and patient hesitation to report pain (Breuer, Fleishman, Cruciani, & Portenoy, 2011). The oncologist's responses corresponded with the standard of clinical care when asked questions concerning common clinical practices. Surveyed oncologists were more likely to contend that opioid therapy is the primary line of treatment for patients with active cancer and that routine administration of opioid therapy is more effective than administration when chronic pain is present (Breuer, Fleishman, Cruciani, & Portenoy, 2011).

The results presented in this 2009 survey, mirrored those of a 1990 questionnaire distributed by Von Roenn et al. (1993). This is a clear indication of the lingering issues surrounding cancer pain management. The ratings of pain management have not evolved as one would assume, especially in an era of progressive technology and medication. Oncologists perceive that this lack of progress remains related to the previously mentioned barriers: inferior pain assessment, patients not reporting pain, and patients not wanting to take prescribed opioids (Breuer, Fleishman, Cruciani, & Portenoy, 2011). These barriers continue to reinforce the need for cancer pain therapy that is

tailored for each individual patient and addresses both the challenges and benefits when

the ultimate goals, improved quality of life and increased life expectancy, are considered.

UTILIZATION OF OPIOID ANALGESICS FOR PAIN CONTROL

The WHO estimates that approximately 80% of cancer patients do not have proper access

to opioids (Thapa, Rastogi, & Ahuja, 2011). The WHO established a platform to

improve cancer pain therapy in 1982. In 1986 the recommendations were printed, with

an update being made in 1996. These guidelines are founded on the principle of routine

administration of pain medication following a three-step ladder, for each individual

patient. (Wahlberg, Vuorinen, Clemens, & Salminen, 2012). The ladder serves as a

guide for the administration of opioid therapy relevant to the level of pain.

Opioid-centered therapy is the primary line of therapy for cancer pain. It should

be the goal of practitioners who prescribe opioids to offer cancer patients therapy that

optimizes the potential for positive outcomes and decreases the potential for possible side

effects and possible substance abuse. Successful opioid treatment depends greatly on the

drug selected for therapy, the selected dosage, and the manner in which the side effects of

the drugs are treated (Portenoy, 2011). In 1996, the WHO developed a visual aid to

complement the already developed analgesic ladder as a depiction of the recommended

guidelines to be adopted by clinicians and oncologists to aid in the relief of cancer pain

(Figure 2.1). The analgesic ladder is utilized internationally but has not been updated to

maintain compatibility with current clinical practices, recommendations and therapies

(Caraceni, 2012).

Optimal strategies with optimal benefits for pain relief entail analgesia with oral opioids, adjuvant analgesics, and progressive pain management practices. Nevertheless, the potential risks of these therapy regimens must be measured (Rana, et al., 2011). Improvements in the availability of oral opioid and interventional pain management techniques can serve as an aid in the breakdown of the barriers of treating cancer pain, while enhancing patient quality of life. Such improvements in cancer pain therapy, the increase in the availability and accessibility to opioids, nerve blocks, other non-invasive techniques relevant to palliative care which considers the whole being and those they surround themselves with, can result in adequate pain relief for most patients (Portenoy, 2011).
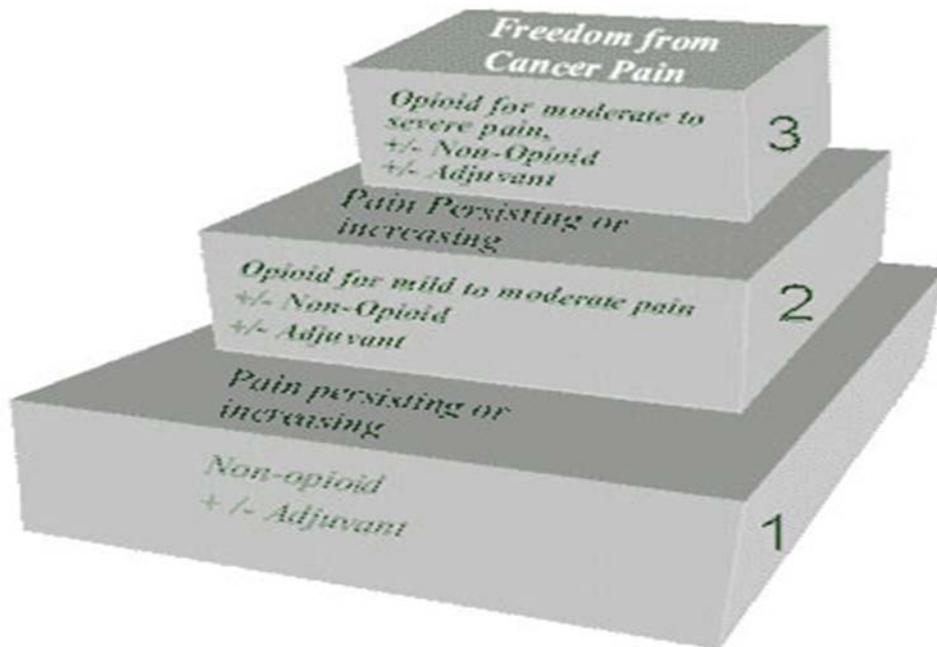
Figure 2.1 The World Health Organization's Analgesic Ladder (1996)

Adopting a consistent routine of opioid use in patients should effectively offer relief from chronic cancer pain with manageable side effects, overall improving patient quality of life (Portenoy, 2011). Opioids are agonists that become active by binding to opioid receptors which are found in the membrane of neurons located in the pain related areas of the brain. These receptors are called mu, kappa and delta receptors. The most essential is the mu-receptor (Schafer, 2010). The majority of all prescribed opioids stimulate as a result of activation of the mu-receptor and are most commonly selected for cancer pain (Portenoy, 2011; Schafer, 2010). While other options do exist, unadulterated mu-agonists, buprenorphine, tramadol, tapentadol, provide more dosing options (Portenoy, 2011; Schafer, 2010).

Opioids are categorized according to how they bind to receptors in the body: full-agonists (successful in increasing dosages with no plateau), partial agonists (plateau and are less effective than full agonists), or mixed agonists/antagonists (inhibit specific receptor activity while activating other opioid receptors) ((National Institutes of Health, National Cancer Institute, 2014). In cancer pain management the most commonly prescribed opioid is morphine, primarily because of clinical familiarity and availability. Although many clinicians are comfortable with the chemical structure of morphine and how it reacts to cancer pain, it is still important to have a knowledge of the various opioids used to treat cancer pain.

Opioids commonly prescribed to cancer patients are listed with a brief description of drug activity. Each of these opioids have been assigned to a step within the WHO ladder based on moderate or severe pain intensity.

Buprenorphine has been categorized as a mixed agonist/antagonist. This drug attaches to the mu- and k-opioid receptor with a delayed onset, postponed optimal effect (3 hours) and is long-lasting (8-10 hours).

Tramadol is a weak opioid assigned to step 2 of the WHO analgesic ladder. Tramadol attaches to norepinephrine and serotonin inhibitors, raising the levels of both norepinephrine and serotonin resulting in pain inhibition.

Hydromorphone is a mu-opioid agonist assigned to step 3 of the WHO analgesic ladder. Hydromorphone has an average of four and a half times the pain reducing strength of morphine. This drug can be administered orally and parenterally.

Morphine is a strong mu-opioid agonist that is grouped into step 3 of the WHO analgesic ladder. Morphine is primarily used as a reference drug for all other opioids and can be administered via all routes.

Oxycodone is a powerful mu-opioid that is only administered orally. This agonist belongs to step 3 of the WHO analgesic ladder and is 8 times more potent than morphine.

Meperidine is a weak opioid mu-receptor that is grouped with step 2 of the WHO analgesic ladder. Meperidine has 0.13 the analgesic strength of morphine

Methadone has a moderately long half-life and is cost-efficient when compared to other opioids. Its effectiveness in the treatment of pain and the inexpensive nature of the medication has encouraged the increase in the use of methadone (Portenoy, 2011). In

addition, methadone is a drug that curves the appetite decreasing the possibility of substance abuse (Sandoval, 2005).

Fentanyl is a strong opioid mu-agonist that has been categorized into step 3 of the WHO analgesic ladder. Fentanyl possesses 80-100 times the analgesic strength of morphine. Fentanyl has a fast onset but does not have a long-lasting effect.

Sufentanil is an extremely aggressive mu-opioid agonist with 800-1000 times the analgesic strength of morphine. When compared to fentanyl, sufentanil has a decreased risk of accumulation (Schafer, 2010).

Opioids have been used for the past 200 years in various forms. The administration of opioids to alleviate cancer pain remains common practice, especially according to the guidelines outlined by the WHO (Portenoy, 2011). The pure mu-agonists medications, like morphine and oxycodone, can be administered in miniscule doses. Smaller doses allow for the safe and successful management of moderate pain. The most important standard in the treatment of pain can be introduced with the routinely used pure agonist opioid drugs. This characteristic of the opioid allows the clinician to isolate the drug that provides the optimal outcome for the patient (Portenoy, 2011; Schafer, 2010; Sandoval, 2005).

South Carolina Opioid Prescribing Guidelines

South Carolina requires that a physician and a patient have a valid relationship before a physician can prescribe a controlled substance to the patient. Valid encompasses the physician having adequate knowledge of the patient's medical history and the need and ability to confidently determine the potential risks and benefits that could befall the

patient while taking this medication (Bolen, 2008). In addition, South Carolina has a prescription monitoring plan that records the prescription fill and refill habits of patients prescribed these substances.

Access levels to opioid treatment vary due to government regulation for the purposes of prevention and reduction of substance dependence. However, because of its effectiveness for cancer patients, this should serve as a motivation for the clinical community to adamantly campaign for the increased regulation of the drug with increased, secured measures for access for the legitimate purposes (Portenoy, 2011; Okie, 2010; Baltic, 2002). Such an attempt will ensure that there are adequate supplies for those that require medication from this drug class, yet the increased regulatory process may reduce the prevalence of drug misuse.

HIGH-PAIN CANCER IN SOUTH CAROLINA: LUNG CANCER

Nationwide, South Carolina has the 14th highest incidence of cancer (Lung Cancer, 2010). In South Carolina lung cancer is the leading cause of death among cancer deaths and is the second most frequently diagnosed cancer (South Carolina Cancer Alliance, 2011). A national meta-analysis completed by the International Association for the Study of Pain determined that the occurrence of pain for those diagnosed with lung cancer was 47%, affecting 27% of outpatients and 76% of palliative care patients (IASP, 2009). A diagnosis of pain was associated with cancer (73%) and cancer treatment (11%) (IASP, 2009).

Considering gender, males are twice as likely to be diagnosed with lung cancer as well as to die of the disease in South Carolina. While Non-Hispanic Whites have a

15% higher diagnosis rate and a 10% higher death rate than other races and ethnicities (South Carolina Cancer Alliance, 2010). Lung cancers was selected because of its high pain prevalence in the later stages of the disease and its incidence and prevalence in the state of South Carolina.

BARRIERS TO PROVIDING ADEQUATE CANCER PAIN MANAGEMENT

The absence of a clear understanding and clinical knowledge of the complexity of cancer pain and the management of cancer pain among health care professionals, patients, and the public; lack of institutional commitment; lack of proper regulatory control; and limited access to and reimbursement for interdisciplinary care all present substantial obstacles to the successful control of pain (Gordon et al., 2005). Within health care systems, obstacles preventing adequate management of pain are clear evidence of the priority assigned to pain management. The absence of sustainable policies; pain education initiatives and disjointed, uncoordinated care are all indications of systematic barriers (Gunnarsdottir, Donovan, & Ward, 2003).

An additional challenge that presents an obstacle for healthcare systems and individuals, and specifically relevant to the issue of pain management, is the fact that pain is the most significant clinical symptom in regards to prevalence and outcomes, and application of evidence-based methodologies for the management of pain is essential (Portenoy, 2011). For some patients, cancer care has evolved into a complicated structure of disjointed medical care. Each interaction with a medical provider has a suited objective that is heavily influenced by psychosocial and mental components (Portenoy, 2011; Verhoef, Vanderheyden, & Fonnebo, 2005).

Communication is a necessary interaction between the patient, the patient's

family, and the medical providers. If this is restricted for any reason it can impact the

outcome of the patient's health care and the delivery of health care (Portenoy, 2011).

Cultural beliefs, language barriers, or an uncomfortable patient-provider relationship, can

lead to ambiguity about the goals of care, misconceptions and misunderstandings about

the care the patient is receiving and plans of future care; especially if the care is outside

of a clinical environment (Portenoy, 2011; M. Chang, Y. Chang, Chiou, Tsou, & Lin,

2002).

A less evident barrier is the nonexistence of randomized controlled trials to

provide support for suggested evidence-based practices (Caraceni, 2012). The majority

of randomized controlled trials focusing on pain control have low subject enrollment,

give little insight about pain characteristics and processes, and involve diverse

interventions and conclusions with expectations of generalizability (Carr et al., 2004).

Such instances force reliance on the specialists who provide care to cancer patients.

However, this also presents a dilemma as much of the medical attention sought is

provided by primary care practitioners (Caraceni, 2012; Tollefson et al., 2011).

Regulatory barriers are most relevant to opioids. These barriers that are

increasingly difficult to control because it is sometimes challenging to differentiate

between the need for pain relief and the need to satisfy an addiction (Gunnarsdottir,

Donovan, & Ward, 2003). Restrictions enforced by national and regional laws can be

strict and excessive, mainly because of the potential for abuse (Bosnjak, Maurer, Ryan,

Leon, Maiye, 2011). While the concern of becoming addicted to opioids may be

"exaggerated" and dated, there is ample evidence about the societal and economic impact of substance abuse (Bosnjak et al.).

SOCIAL AND ECONOMIC DISPARITIES IN THE PROVISION AND RECEIPT OF CANCER PAIN CONTROL

In addition to race and ethnicity, socioeconomic status, and other social demographics like education, insurance status, and geographic location are interlinked in the description of disparities in pain management (McNeill, Reynolds, & Ney, 2007). Patient characteristics can also be a likely predictor of who will not be provided adequate pain relief. While not a sole determinant, patient's race and ethnicity are critical factors of treatment received. The locality of the treatment facility has also been found to be an important factor (Gunnarsdottir, Donovan, Ward, 2003). An additional demographic determinant is the under treatment of pain according to gender.

Mounting evidence supports that populations of a lower socioeconomic status are not only at greater risk of being diagnosed with cancer but also being diagnosed at a later stage with inferior outcomes (McNeill, Reynolds, Ney, 2007). The poor are more likely to be the racial minority. Poor individuals that reside in rural areas are also more likely to be either uninsured or underinsured than inhabitants of urban areas. This lack of coverage limits access to healthcare and needed medications (McNeill, Reynolds, & Ney, 2007). More specifically pain medication is prescribed to suit the needs of the particular patient and costs can be excessive. Lacking the financial means to purchase the pain medication can result in poorer health outcomes (Freeman, 2004; McNeill, Reynolds, & Ney, 2007). In South Carolina, the 2012 rural poverty rate was 22.5% compared to

17.7% in the urban areas and the average per capita income rural regions was $30,304 —

$3,084 less than the urban comparison, (Rural Assistance Center, 2013). In addition, the

poor are more likely to have less than appropriate or the complete absence of pain

management plans in place. They may also be less educated about the pain management

process and what is defined as sufficient pain management. These circumstances are

exacerbated by the limited access to some medications and the unwillingness of providers

to prescribe opioids because of fears of abuse and pharmacies that restrict quantities and

types of certain medications (McNeill, Reynolds, & Ney, 2007).

Within minority communities approximately 25% of pharmacies have an

adequate stock of sufficient opioids for pain management, compared with 72% of non-

minority neighborhood pharmacies (Anderson, 2002). Morrison et al. conducted an

examination of pharmacies in an urban city, comparing the available stock of sufficient

opioids in minority and non-minority neighborhoods (2000). Morrison's study found that

51% of the responding pharmacies did not have a sufficient supply of opioids to meet

patient's needs; only 25% of those in "non-white neighborhoods" did have an adequate

supply of opioids to meet patient needs; while 72% of the pharmacies in majority white

communities had a sufficient supply of opioids (2000).

RECOMMENDATIONS FOR THE TREATMENT OF CANCER PAIN

While cancer is a terminal illness, this is no excuse to refuse patients the opportunity to

maintain a certain quality of life, free of pain (Nersesyan & Slavin, 2008). A valid and

daunting question is what is considered to be adequate pain control? Optimal pain

management is defined as effective if there is a similarity between what the patient

reports their level of pain to be and the recommended therapy regimen for the relief of the

pain. The WHO also supports the claim that the recommendations for the treatment of

cancer pain are vastly inadequate (1996).

During the course of treatment, clinicians should offer pain education, breakthrough

opioids for patients receiving long-acting formulations, bowel regimens in patients

receiving long-acting opioid formulations and confirmation of the coordination of care of

opioid doses across the health care continuum (Dy et al., 2008).

Recommendations from the American Pain Society for the improvement of the

quality of acute and cancer pain management stated that health care settings should

establish a strong foundation for a coordinated, multilevel systems methodology (Gordon

et al., 2005). The routine practices within the health care system should constantly keep

in mind patient sensitivity to pain, the population served, the type of pain and the

environment in which the care is provided (Gordon et al., 2005). This multidimensional

approach should warrant hasty acknowledgement and treatment of pain, participation of

patients and families in the pain management plan, improved treatment trends, frequent

reevaluation and modification of the pain control plan when and if necessary, and

measurement of processes and outcomes of pain management (Gordon et al., 2005).

CONCLUSIONS

The ultimate objective of pain control in any patient with a diagnosis of cancer should be

to optimize the patient's comfort and function. However, the remaining need for

improvements in the treatment of chronic cancer pain is evident in the literature and the

data. The presented literature highlights remnants of past issues of pain control that

currently plague the medical community. Despite advancements in technology and improvement in the quality of care initiatives, opportunities to improve the delivery of pain relief and related health outcomes and quality of life remain.

Overcoming these challenges can be increasingly difficult for individuals who are confronted with sociodemographic, geographic, and economic barriers. These obstacles are of great significance and impact the management of pain in patients in rural areas. Furthermore, the limited availability of literature specific to this geographic area and the role the availability of prescribed pharmaceuticals plays in pain management in rural areas only encourages the need to further examine (Kelley, 2007; Robinson, 2009).

Table 2.1 1996-2009 Lung Cancer Incidence Rate (per 100,000 persons) in South Carolina counties (South Carolina Department of Health and Environmental Control, SCANG, 1996-2009)

South Carolina County	Incidence of Lung Cancer
South Carolina (overall)	**32.0**
Abbeville*	30.0
Aiken*	26.7
Allendale*	26.4
Anderson	36.7
Bamberg*	39.6
Barnwell*	22.1
Beaufort*	24.7
Berkeley	33.9
Calhoun*	27.1
Charleston	28.6
Cherokee*	41.4
Chester*	39.8
Chesterfield*	33.2
Clarendon*	29.0
Colleton*	43.0
Darlington*	30.7
Dillon*	34.9
Dorchester*	34.5
Edgefield*	29.6
Fairfield*	35.5
Florence	29.5
Georgetown*	31.0
Greenville	32.0
Greenwood*	29.5
Hampton*	32.1
Horry	30.6
Jasper*	27.7
Kershaw*	41.3
Lancaster*	32.3
Laurens*	34.9
Lee*	30.6
Lexington	35.2
McCormick*	22.6
Marion*	32.5
Marlboro*	40.2
Newberry*	34.4
Oconee*	34.8
Orangeburg*	29.6
Pickens*	35.4
Richland	33.6
Saluda*	20.3
Spartanburg	34.7
Sumter*	30.0
Union*	41.2
Williamsburg*	21.8
York	28.5

* Indicates counties classified as wholly or partially rural by the Economic Research Service Rural-Urban Commuting Areas (RUCA, 2010)

Table 2.2 1996-2009 Lung Cancer Mortality Rate (per 100,000 persons) in South Carolina counties (South Carolina Department of Health and Environmental Control, SCANG, 2009)

South Carolina County	Mortality of Lung Cancer
South Carolina (overall)	**58.9**
Abbeville*	58.3
Aiken*	57.2
Allendale*	56.2
Anderson	63.3
Bamberg*	58.7
Barnwell*	54.5
Beaufort*	45.4
Berkeley	64.8
Calhoun*	47.3
Charleston	53.8
Cherokee*	71.2
Chester*	71.1
Chesterfield*	71.2
Clarendon*	60.1
Colleton*	70.6
Darlington*	69.2
Dillon*	71.3
Dorchester*	56.0
Edgefield*	57.7
Fairfield*	60.7
Florence	60.8
Georgetown*	59.0
Greenville	55.0
Greenwood*	56.7
Hampton*	58.8
Horry	59.3
Jasper*	50.6
Kershaw*	65.1
Lancaster*	61.3
Laurens*	61.0
Lee*	70.4
Lexington	58.9
McCormick*	55.4
Marion*	66.4
Marlboro*	78.1
Newberry*	60.4
Oconee*	54.4
Orangeburg*	51.9
Pickens*	58.1
Richland	59.3
Saluda*	54.1
Spartanburg	63.9
Sumter*	57.3
Union*	67.1
Williamsburg*	58.6
York	61.7

*Indicates counties classified as wholly or partially rural by the Economic Research Service Rural-Urban Commuting Areas (RUCA, 2010)

CHAPTER 3

RESEARCH DESIGN AND METHODS

To conduct this secondary data analysis, data was requested from the South Carolina Central Cancer Registry and the state's Medicaid program. Medicaid is a federal government eligibility program that provides health insurance coverage for health care and other medical services at no cost or at a reduced cost. Combined, both the Medicaid and the Children's Health Insurance Program (CHIP) enable approximately 60 million Americans, including children, pregnant women, parents, seniors and individuals with disabilities, to seek needed medical attention ("Medicaid", 2013). Medicaid is a health and long-term care coverage program that is jointly funded by individual states and the federal government. Each state establishes and administers its own Medicaid program. States are responsible for establishing eligibility criteria within the guidelines outlined by the federal government. However, there are groups that have "mandatory eligibility" ("Medicaid", 2013). South Carolina's state Medicaid data is housed at the South Carolina Department of Health and Environmental Control (SCDHEC).

The South Carolina Central Cancer Registry (SCCCR) is a population-based data system that assembles information over cancer incidence in the state of South Carolina. The compiled data was used to examine trends in prevalence and frequency of cancer in defined areas, changes in diagnosis and treatment patterns, and patients' survival rates (SCDHEC, 2013). Information on cancer mortality (deaths) is collected by the Division of Vital Records and published by the Division of Biostatistics and Division of Public

Health Informatics within DHEC. The SCCCR's dissemination efforts highlight cancer incidence and mortality in the state and nationally.

Demographic, disease stage, tumor size and grade, cancer therapy and prescription variables were requested from the South Carolina Cancer Registry as identified by the North American Central Cancer Registry (NACCR, 2010). This cross-sectional study examined the impact of geography on medications prescribed for cancer pain and its association with survival for South Carolina Medicaid lung cancer patients.

CONCEPTUAL FRAMEWORK

This research was based on Stewart and Teno's *Conceptual Model of Quality of Life of Dying Patients and their Families* (Figure 3.1). This model examines the factors that impact quality of life, which can be a direct indicator of the quality of care, of terminally-ill patients (Stewart, Teno, Patrick & Lynn, 1999). The model developed by Stewart et al. evaluates the quality and outcomes of care with three principal classes: Patient Factors Affecting Health Care and Outcomes of Care; Structure and Process of Care; and Outcomes of Care.

Patient factors affecting health care and outcomes of care include personal and social elements. These elements include the patient's financial ability to seek health care, patient race and ethnicity, location standing life situations, clinical diagnosis (severity and history), and external support that the patient has access to (marital status). This class also considers support, both clinical

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and external This could be viewed as a limitation in rural communities where the

healthcare system may not offer such support or residents may not be able to access such

provisions; as well as for those whose personal and social networks do not support health

needs (Stewart, Teno, Patrick & Lynn, 1999). These factors directly influence the

structure and process of care.

Structure and process of care

   Outcomes of Care are shaped by the structure and process of care. Both structure

and process are variables that can promote or hamper outcomes. The structure of the

health care system can determine access, and eligibility to access services, to the system's

organization—the level at which care is provided and support services are made

obtainable. These characteristics of the health care system determine health care

outcomes (receipt of medication, survival, vital status, etc.) on various levels. The

system's organization concentrates on the leadership and the tenets deemed to be

significant to support the system's practices (Stewart, Teno, Patrick & Lynn, 1999).

Access issues and the availability of services can vary depending upon economic

classifications and geographic limitations.

   Cancer patients who live in rural areas are forced to receive the majority of their

medical services from "generalists", of whom there are shortages of, to treat those with

such specific needs in these areas (Kelley, 2007). This is an infrastructural component

that incites concern. Operationally, the lack of a standard methodology of care that can

be individualized remains a limitation (Wagner, Austin, von Korff, 1996). The non-

compliance of clinicians to act in accordance with set recommendations can be attributed

to inadequate training. General clinicians are primarily trained to respond to acute

medical needs and diagnose and treat (Wagner, Austin, von Korff, 1996).Yet, clinical

practitioners in rural areas are forced to attempt to craft their clinical approach to assist

patients with chronic illnesses who may not have alternative options for medical

treatment (Wagner, Austin, von Korff, 1996).

The *Process of Care* considers who is delivering the care, the decisions that are

being made in regards to the patient's care, supportive services made available to the

patient and the patient's family, and the continuation and coordination of health care

services (Stewart, Teno, Patrick & Lynn, 1999). In both chronically and terminally ill

patients, symptom management is an essential part of decision-making. Medications

prescribed to assist in the alleviation and elimination of related systems are highly

significant in the quality of life and patient survival. Opioid therapy is necessary for the

provision of optimal care in cancer patients (Krishna, Poulose, Tan, & Goh, 2010;

Parsons et al., 2008).

Patient Factors Affecting Healthcare and Outcomes of Care	Structure and Process of Care	Outcomes of Care

- **Patient and family situation**
- **Clinical status, case-mix**
- Patient social support
- **Family social support**

- **Access to care within system**
- **Organization of care**
- Formal support services available
- **Physical environments of care**
- Process of care with physicians, nurses, and caregivers
- **Technical process with patient**
- Decision-making process
- Interpersonal and communication style

- Length of life (Patient & family)
- **Length of life**
- **Treatment (Therapy and prescribed medications)**

- Marital Status
- Race/ethnicity
- Regional location (urban/rural)
- Gender
- Primary diagnoses
- Diagnosis and stage of cancer type

- Date of diagnosis
- Drug indicator
- Vital status

- Provider location - Pharmacy and Physician (urban/rural)
- Outpatient care
- Type of clinical provider (primary care provider or cancer specialist

Figure 3.1 Conceptual model adapted from Stewart and Teno's *Model of Quality of Life of Dying Patients and Their Families* (1999)

*Bolded text in the conceptual model identifies variables analyzed in statistical models to address research questions. Patient length of life was built into the research design.

The South Carolina Medicaid sample is composed of women and those who are economically eligible for the public health insurance plan. Eligibility for the South Carolina public health insurance plan is determined by family size and annual income. To be eligible as a Medicaid enrollee with lung cancer, persons must qualify under the medically indigent program and the family's income must not exceed 200% of the Federal Poverty Level and personal assets are not allowed to exceed established thresholds. The Medicaid data has been linked with data from the South Carolina Central Cancer Registry (SCCCR) by the South Carolina Office of Research and Statistics. This linkage verifies all cancer types among the Medicaid patients in the sample by selected variables for linkage. Linkage variables included: patient's first, middle and last name, social security number. This information was not provided to the Investigator and only used by the South Carolina Office of Research and Statistics for data linkage purposes.

The 1996-2010 linked sample consists of non-Hispanic (NH) black and NH white advanced stage (at diagnosis) lung cancer patients (n~19,375) who were enrolled in Medicaid having a verified diagnosis in the SCCCR. Once coding for data analysis post-inclusion criteria, the analyzed sample was N=1,334. Criteria for being included in the analysis sample were:

1) patients had a prescription filled for either an opioid or analgesic through their SC Medicaid policy post-diagnosis;

2) patients had to have been enrolled in South Carolina Medicaid for at least 9 months prior to the lung cancer diagnosis; and

3) analyzed patients in the sample only had a primary diagnosis of lung cancer.

Clinically stages of cancer are determined by tumor size, quantity of lymph nodes impacted, and signs of metastasis. Evidence of metastasis can be found in the bones, surrounding organs or the brain. Stage 4, the most advanced stage of lung cancer, is confirmed by the metastasis of the cancer to both lungs, the fluid surrounding the lungs, and to other parts body (National Institutes of Health, U.S. National Library of Medicine, 2013). These cancers were selected because of their high pain prevalence in the later stages of the disease and their prevalence in the state of South Carolina (Yoon, 2013; Simmons, 2012;Centers for Disease Control and Prevention, National Cancer Institute, 2010).

MEASURES

South Carolina Medicaid provides health care coverage for approximately 40% of children, 58% of the health care for non-elderly women, and has contracts with 82% of the state's nursing homes. Medicaid pays for 70% of the people in those facilities and provides coverage for the treatment of female breast and cervical cancer according to federal screening and diagnosis guidelines and will cover an additional 2,600 cancer patients in 2014 as a result of this portion of the fully enacted Affordable Care Act (American Cancer Society Cancer Action Network, American Diabetes Association, American Lung Association, and Families USA, 2011; National Women's Law Center, 2010). In 2010, 22.5% of South Carolina's cancer patients were covered by Medicaid. It is also possible that some patients are dually enrolled in Medicare (Cancio, Bailey, & Mahan).

The most most recent data available is 2010—this was especially significant with the enactment of the Affordable Care Act and the impending expansion of Medicaid.

Sociodemographic, outcome, and health care infrastructure variables were all included in the analyses. In addition, variables reflecting the characteristics of Medicaid enrollees' social support system and socio economic status, the features of the health care system in which they receive their primary cancer treatment, and outcomes were included for demographic purposes.

Dependent variables

The primary outcomes of interest were the rate of patient survival in the rural regions of South Carolina for Medicaid recipients in the advanced stages for lung cancer and the receipt of medication. The relationship between patient survival and analgesic treatment, the dependent variables, have been examined in previous research but not outside of the palliative care setting and not with regard to specific racial/ethnic groups and geographies (Parsons, 2008) in the United States healthcare system in the southern state of South Carolina.

Independent variables

Characteristics and variables that impact the manner in which pain is managed was examined. Patient factors affecting health care and outcomes of care (i.e. marital status, race and ethnicity, and gender), the structure and process of care (provider county and declared specialty of the provider), and outcomes of care (i.e. date of diagnosis and vital status) characteristics and the impact of these social, environmental, and economic factors on the management of pain in rural, Medicaid-eligible lung cancer patients were included in the analysis, and controlled where needed. While the independent variables that considered patient stage of lung cancer and survival time in months were not listed in the conceptual model, they were built into the research design and were analyzed.

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Patient factors affecting health care and outcomes:

Family social support

o   Patient gender

o   Race/ethnicity - Non-Hispanic black and Non-Hispanic white

o   Marital status - married or single/divorced/separated. This variable was defined
    as the social and emotional support received from a patient's spouse.

Patient and family situation

o   South Carolina rural/urban residents – use of Urban Influence Codes and
    urban/rural continuum in non-metropolitan counties.

Clinical Status/ Case mix

o   Patients diagnosed with Stage 4 lung cancer- This can greatly impact the
    longevity of life as well as clinical treatment.

Structure and Process of Care:

*Access to and the process of care delivered by clinicians within the organization of
care*

o   Provider county – use of Urban Influence Codes and urban/rural continuum in
    non-metropolitan counties to identify the urbanicity or rurality of the managing
    provider's county

- Provider type/specialty – the managing provider who was the primary provider of oncologic care (i.e., cancer pain treatment)

Technical process with patient and formal support services available

- Primary diagnoses – patients having a primary diagnoses of cancer and available ICD-9 codes that indicate comorbidities
- Therapeutic class of drug – drug identified as being an opioid

Outcomes of care

- Cancer therapy – treatment being provided outside of prescribed opioids, chemotherapy and radiation
- Vital status – was the Medicaid recipient alive or dead

DATA COLLECTION PROCEDURES

South Carolina Medicaid's database is comprised of variables that provide demographics, economic circumstances, and claim and reimbursement codes for health care services provided to individuals enrolled in the program, diagnoses of diseases and laboratory services. This data was available upon request from the South Carolina Office of Research and Statistics.

The South Carolina Central Cancer Registry (SCCCR) is a population-based data system that assembles information over cancer incidence in the state of South Carolina. The compiled data was used to examine trends in prevalence and frequency of cancer in targeted areas, changes in diagnosis and treatment patterns, and patients' survival rates (SCDHEC, 2013). Information on cancer mortality (deaths) is collected by the Division of Vital Records and published by the Division of Biostatistics and Division of Public Health Informatics within DHEC. The SCCCR's dissemination efforts highlight cancer incidence and mortality in the state and nationally.

Upon receipt of Institutional Review Board approval from the University of South Carolina data applications were submitted to the Institutional Review Boards of the South Carolina Department of Health and Environmental Control, and the South Carolina Central Cancer Registry. Once data applications were approved, the South Carolina Office of Research and Statistics began to link the requested variables and the data was provided to the Principal Investigator in a password protected file. Data linkage occurred using unique identifiers: year of birth, last name, and social security number. Desired data was extracted from South Carolina Medicaid claims filed by enrolled late stage lung cancer patients. Rural/urban geography was assigned using rural/urban continuum codes. These codes distinguish non-metropolitan counties by level of urbanization and proximity to metropolitan areas.

The outlined study addressed two primary aims.

Aim #1 –To examine patient residence as a factor associated with the receipt of

prescribed opioid therapy among SC Medicaid lung cancer patients. .

Hypothesis: Rural patients will be less likely to receive opioid therapy.

Outcome: Receipt of opioid therapy

Covariates: Stewart and Teno's model components (Figure 3.1)

Analysis: Bivariate analysis and Logistic regression

Aim # 2 – To assess the association between patient residence and the survival

rate of distant stage lung cancer patients, considering the receipt of opioid

therapy.

Hypothesis: Rural patients will experience a decreased survival rate and will be

less likely to be prescribed opioid analgesics.

Outcome: Patient survival rate

Covariates: Stewart and Teno's model components (Figure 3.1)

Analysis: Bivariate analysis and Cox proportional hazard survival model

Using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) all of the following statistical analyses were conducted.

Aim 1 examined the relationship between the geographical association of the lung cancer patient and the receipt of a prescription for opioids. The outcome of interest was the receipt of opioid therapy for lung cancer patients among rural non-Hispanic white Medicaid recipients and rural non-Hispanic African-American Medicaid recipients after controlling for other demographics and type of cancer therapy. Because the two groups of recipients were being compared on a ratio outcome, univariate and bivariate analyses were conducted to obtain the descriptive properties of the sample. The bivariate analysis allowed cross tabulations to examine the trends and differences in patient factors affecting health care and outcomes of care, structure and process of care, and outcomes of care the prescribing of opioids and analgesics. In addition, the bivariate analysis was performed using chi-square to ascertain significance among the outcome variable and stated covariates.

Logistic regression analysis was conducted to assess associations between receipt of opioid analgesics and race/ethnicity, marital status, gender, patient county and the presence of cancer specialists. The outcome of the logistic analysis was a dichotomous measure of whether or not the patient was prescribed an opioid analgesic or received no medication.

Aim 2 assessed the association of patient geographical residence on the survival rate for distant stage lung cancer patients among SC Medicaid enrollees. The primary outcome of

interest was patient survival. Patient deaths were identified as cancer-related deaths or non-cancer related deaths. A descriptive, bivariate analysis was performed to determine the associations between patient factors affecting healthcare outcomes of care, the structure and process of care, and the outcomes of care for late stage lung cancer patients enrolled in South Carolina Medicaid. A survival analysis using Cox's proportional hazard model was used to calculate the survival rate, in months, from the primary cancer diagnosis to death, the event of interest.

The primary objective of the planned research was to investigate the association between geography and patient survival in relation to prescribed opioid medications for lung cancer patients. The impact of prescribed medications, opioids, on the longevity of patient life meeting and exceeding the average survival rate, while controlling for cancer therapy and other demographics, was the primary outcome of interest. In the principal analyses, adequate receipt of patient survival was measured according to prescribed opioid medication and dosage of prescribed opioid medication, after controlling for demographics and cancer therapy.

Descriptive data and results for the analyses is presented in two prepared manuscripts that constitute Chapter 4. These manuscripts will be composed and formatted for submission to two peer-reviewed journals (*The Journal of Rural Health* and *Journal of Pain*). Chapter 3 has presented the research design for the study, along with an outline of the methodology and statistical analyses.

CHAPTER 4

RESULTS

Chapter 4 presents findings of the conducted data analysis plan as designed in Chapter 3 in the form of two manuscripts. Manuscript #1 examines the relationship between urban and rural patient geography and prescription medications intended to alleviate pain among late stage lung cancer patients in South Carolina who are enrolled in Medicaid. Manuscript #2 investigates the influence of receipt of pain medication on the patient survival rate of late stage lung cancer patients of South Carolina who are enrolled in Medicaid.

MANUSCRIPT #1

RACE AND GEOGRAPHICAL BARRIERS TO PAIN MEDICATION IN LATE

STAGE LUNG CANCER PATIENTS[1]

Abstract:

Purpose: The barriers that prevent rural populations from receiving appropriate medication treatment are greater than geography. Obstacles range from a lack of availability of needed medications and providers to increasingly strict prescription regulatory policy   However, the existence of these barriers is especially true for rural residents with chronic conditions like lung cancer, a high-pain disease, who may not be able to access specialty care. Pain that results from lung cancer needs to be treated with medications meant for reduction and alleviation—opioids and analgesics. This study examined the prescribing practices of physicians and late stage lung cancer patient's level of accessibility to medications commonly prescribed for pain among residents of rural and urban geographies.

Methods: Data for the analysis was requested from the South Carolina Central Cancer Registry and linked with South Carolina Medicaid data. A bivariate and logistic analysis was conducted using SAS 9.4 to examine patients who received a single or combination prescription for opioids or analgesics and those who were not prescribed either.

Findings: In the sample of 1,334 late stage lung cancer patients, there was no statistically significant evidence that our target race and ethnicities or residents of particular geographies were more or less likely to be prescribed pain medications. When the patient factors and the structure and process factors impacting health care were examined, all variables and relationships were statistically similar.

Conclusions: Presented barriers only sustain the existence of health disparities, geographically and racially and potentially impact the method of treatment for patients as well as the type and frequency at which pain medications are prescribed. Demands for changes in local and national policy that monitor the accessibility to pain medication in rural communities is necessary, even if to simply insure the availability of an adequate amount of medication.

Introduction Population health is defined as "an approach [that] focuses on interrelated conditions and factors that influence the health of populations over the life course, identifies systematic variations in their patterns of occurrence, and applies the resulting knowledge to develop and implement policies and actions to improve the health and well-being of those populations."[1,2] The levels of variation that exist in health care accessibility for urban and rural populations are greatly dependent upon many determinants that heavily impact health care outcomes. Beyond adequate accessibility, existing policies and regulations can also be a hindrance. These are obstacles that some healthcare systems, specifically rural, may not have the means to overcome.

Descriptions of rural populations and regions entail increased elderly and children, flailing employment rates, financially disadvantaged, and uninsured and underinsured residents.[3,4] Providers practicing in these environments often bear the brunt of these circumstances. Moreover, rural providers must have the ability to adapt when the clinical workforce is lacking, specifically specialists.[3-5] This needed adaptation is equally true for the pharmacies located in rural areas. Rural demographics have an increased need for pharmacy services.[6] Pharmaceutical care is a critical part of the healthcare continuum. In rural areas, pharmacists are health care providers who take on a

larger role as one of few accessible health care providers. This adds to the challenges that rural pharmacies encounter and poses a threat to the health outcomes of the community.

These are the types of challenges that influence late stage lung cancer patients residing in rural areas—they are greater than medication affordability. Seventy-five percent of advanced stage cancer patients suffer with moderate to severe pain; and 25-30% of cancer patients in the advanced phases experience severe pain.[7] Opioids and analgesics are the principal medications prescribed for pain relief in cancer patients.[8,9] However, the possibility of limited access to pharmacists, primary care providers and cancer specialists, may prevent late stage lung cancer patients who need pain management medications, opioids and analgesics, from receiving them. It is necessary to understand who is receiving pain medications and where patients are seeking care. For this study's purpose, greater accessibility of patients to providers and medications were defined according to the quantity of clinical providers (cancer specialists) in the defined geographical areas, urban or rural, as well as the specific medications prescribed. Patient Factors Affecting Health Care and Outcomes of Care; Structure and Process of Care; and Outcomes of Care influences were examined to determine impact on patient receipt of medication. The research question this study sought to answer was whether patient geography influenced the type of pain medications late stage cancer patients were prescribed.

Methods

Expedited approval from the University of South Carolina Institutional Review Board was received to examine data from the South Carolina Central Cancer Registry

and South Carolina Medicaid for this cohort study. Patient data was requested from the South Carolina Cancer Registry for South Carolina Medicaid recipients who had been diagnosed with late stage lung cancer (stage 4) from 1996-2010. Data was then transferred to the South Carolina Office of Research and Statistics to be linked with South Carolina Medicaid data. Requested variables for the total population included demographic variables on patients and providers, rural-urban commuting area (RUCA) codes, and patient claims information.

Study Population The study sample was composed of 1,334 South Carolina Medicaid recipients who were diagnosed with late-stage lung cancer. Patients included in the sample had to have filled a prescription for either an opioid or an analgesic. These specific drug classes were selected because of their primary use for the alleviation of pain with high pain diseases, like lung cancer, and other ailments. Ethnicities and races included in the analysis were Non-Hispanic Whites and Non-Hispanic Blacks identified as residents of urban and rural regions of South Carolina.

Dependent Variables The primary outcome variable examined was receipt of either an opioid or analgesic for patients with late stage lung cancer. The receipt of medication variable was dichotomized: 1) patients who were prescribed either an opioid or analgesic, and 2) patients who were prescribed neither and opioid or analgesic.

Independent variables Main independent variables were: race/ethnicity of patients (Non-Hispanic White, Non-Hispanic Black), residence of patients (rural or urban), physicians serving the patient (cancer specialists), and pharmacists. Geography of each exposure variable was defined using rural and urban continuum codes assigned by the United States Department of Agriculture's Economic Research Service (USDA).

USDA uses these classification codes to distinguish metropolitan and non-metropolitan counties.[8] For the purpose of the study, urban was defined as central and neighboring counties of metropolitan regions where the population is 1,000,000 or more and counties in metropolitan regions made up of less than 250,000 to 1,000,000 residents. Criteria for rural regions were: 1) an urban population of 20,000 or more bordering or not bordering a metropolitan area, 2) an urban populace of 2,500-19,999, bordering or not bordering a metropolitan area, or 3) wholly rural (not having a population of 2,500 or more) bordering or not bordering to a metropolitan area.

Covariates Patient factors affecting health care and outcomes of care include gender and marital status of patients (single, separated or divorced or married); structure and process of care (presence of cancer specialists and primary care providers); and Outcomes of Care (patient vital status, receipt of medication (frequency) influences were assessed for the possibility of confounding.

The structure and process of care component of the analysis measured the presence and location of cancer specialists and other primary care providers. The presence and location of each type of provider was assessed to examine the potential influence of provider type on patient access to care and receipt of pain medication. Cancer specialists were grouped as providers who specialized in: pulmonary medicine, oncology, radiology (diagnostic and therapeutic), internal medicine, and thoracic surgery; clinical disciplines which commonly provide medical treatment to lung cancer patients.

Statistical Analyses Univariate (Table 4.1) and bivariate analysis were performed to obtain the descriptive properties of the sample population. The bivariate analysis allowed cross tabulations to examine the trends and differences in patient factors

affecting health care and outcomes of care, structure and process of care, and outcomes of

care the prescribing of opioids and analgesics. In addition, the bivariate analysis was

performed using chi-square to ascertain significance among the outcome variable and

stated covariates.

Logistic regression analysis was conducted to assess associations between receipt

of opioids or analgesics and race/ethnicity, marital status, gender, rural/urban county and

the presence of cancer specialists. The outcome of the logistic analysis was a

dichotomous measure of whether or not the patient was prescribed an opioid analgesic or

neither.

Results

From a sample of 1,334 patients, 561 were prescribed an opioid analgesic while

773 were not. Of the 1,334 sample patients, 679 were Non-Hispanic Black and 636 were

Non-Hispanic White. Patients identified as "Other" (n=19) were excluded from the

analysis because of the potential of the small sample size to influence accuracy of the

data. A larger proportion of sample patients resided in the urban region of South

Carolina (n=899) than the rural areas (n=435). Considering gender, males composed

58.5% of the sample, while there were a lesser percentage of females, 41.5%. In

addition, patients who were single, separated, separated, or divorced represented 39.8%

of the variable considering marital status, while 25.4% of this sample was married.

Sample characteristics from the study period when both race and ethnicity and geography

are considered are described in Table 4.1.

The only statistically significant variable when medication receipt was analyzed

was the location of the primary care provider patient location combination (p=0.02). The

rural patient, rural provider combination was present for 28.8% of persons studied, while

the urban patient, urban provider encounter combination was present for 51.4% of persons examined. Rural patient encounters with primary care providers in urban regions accounted for 1.8% of patient-provider encounters with primary care physicians. Within the sample, there were a total of 374 cancer specialists (Table 4.2). Cancer specialists had a greater presence in the urban geography. Also in the urban geography, the urban pharmacy, urban patient combination resulted in a greater amount of filled prescriptions.

The logistic regression examining receipt of analgesics and opioids is shown in Table 4.3. All analyzed associations were not statistically significant, demonstrating that none of the analyzed factors were direct factors related to patients' receipt of pain medication. Logistic results were statistically similar for all patient factor variables— patient county, race and ethnicity, and patient gender. Examining Structure and Process of Care also showed no statistically significant difference among considered variables.

Discussion

The results of the analysis reflected that none of the analyzed factors were statistically significant in showing the likelihood of pain medications being prescribed to either urban or rural populations as well as the different races and ethnicities considered. Within the data, rural persons prescribed pain medications composed less than half of those prescribed medications. Though not as extreme, this disparity was also present among the two races. Non-Hispanic Whites received more prescriptions than the Non-Hispanic Blacks. The disparity in the quantity of and to whom medications are dispensed among late stage lung cancer patients is supported by literature that speaks to the disparity in cancer pain management, especially among the minority race and rural geographical regions.[11,12]

Among the population of persons receiving medication, less married persons were prescribed pain medications than those who were single, separated, or divorced persons.

This could be a reflection of the emotional and support system that is readily available to married persons. Published research makes the connection between emotional and instrumental support.[13] This support system is related to increased mental health and quality of life.[13] Similar research also provides evidence that the psychological support from spouses result in improved outcomes for cancer patients.[14] In addition, because the number of persons whose marital status was not reported was high in comparison to the sample size of those prescribed medications, a "not reported" variable was created to ensure that this data was captured. Creating this variable was key because of the potential for this missing data to skew the results during analysis.

For the rural patient, primary care provider combination variable, the increased quantity of patient's receiving medication from primary care providers could be related to patient distance and greater accessibility to primary care providers. This could be associated to providers' awareness of patient's limited accessibility to healthcare which encourages them to more readily prescribe to rural patients. A second reason for this could be patient's sole access to healthcare is to seek care from this type of provider.

Lastly, the current data also showed a lack of cancer specialists in the rural region of South Carolina. Approximately 72% of the patient sample did not have an interaction with a cancer specialist, a clear issue of inadequate access to healthcare services (Table 4.3).

Limitations An encountered limitation of this study was the level of missing and unavailable data. This is often common with secondary data analyses in which investigators rely upon data compiled by agencies and organizations. A second limitation was the selected sample of patients who commonly experience less than adequate healthcare could have possibly impacted data outcomes, those who makeup vulnerable and disparate populations already pre-existed. A third limitation was the use of a homogenous Medicaid sample of patients. However, this was also viewed as a strength because of the reliability of data accuracy and a defined population who were covered under target public health services.

Conclusion

In 2014 there was an estimated 26, 390 new cancer cases in the South Carolina; 4,130 of those new cases were lung cancer cases.[18] Patients who do not receive appropriate medications that assist in the relief of pain must endure a diminished quality of life.[15,16] Previously published literature and provided data showed that decreased percentages of the minority race and geographic location of patients are barriers that disproportionately affect the percentage of rural patients who receive medication. Such barriers only sustain the existence of health disparities, geographically and racially. Demands for changes in local and national policy that monitor the availability of pain medications in rural communities are necessary, simply to ensure availability of adequate amounts. Increasing pain medication accessibility for certain populations raises concerns for patient abuse or the diversion of medications. One manner to combat this is the appropriate use of prescription monitoring programs. Not only should the use of these prescription monitoring programs be mandated, but also

requiring the utilization of systems that have the ability to communicate with one another is imperative. Lastly, incentivizing pharmacies to establish themselves in rural and minority communities is essential to the provision of quality healthcare and the healthcare continuum.[17]

Table 4.1. Factors associated with receipt of opioid analgesic pain medications

	Total N (%)	Opioid/Analgesic receipt N (%)	No pain medication N (%)	p (opioid receipt)
Total	1334 (100.0)	561 (100.0)	773 (100.0)	
Patient Factors				
Residence				
Rural	435 (32.6)	171 (30.5)	264 (34.2)	0.33
Urban	899 (67.4)	390 (69.5)	509 (65.8)	
Sex				
Male	780 (58.5)	313 (56.8)	467 (61.4)	0.29
Female	554 (41.5)	248 (44.2)	306 (39.6)	
Race[1]				
Non-Hispanic Black	679 (50.1)	268 (47.7)	411 (53.2)	0.13
Non-Hispanic White	636 (47.7)	288 (51.3)	348 (45.0)	
Marital status[2]				
Single/Separated/Divorced	531 (39.8)	223 (39.8)	299 (38.7)	0.82
Married	339 (25.4)	144 (25.7)	187 (24.2)	
Missing	464 (34.8)	191 (34.0)	273 (35.2)	
Structure and Process of Care				
Cancer specialist location				
Rural patient, rural MD	63 (4.7)	21 (3.7)	42 (5.4)	
Rural patient, urban MD	24 (1.8)	11 (2.0)	13 (1.7)	0.57
Urban patient, rural MD	20 (1.5)	9 (1.6)	11 (1.4)	
Urban patient, urban MD	267 (20.0)	123 (22.0)	144 (18.6)	
Primary care provider location				
Rural patient, rural MD	384 (28.8)	149 (26.6)	235 (37.8)	
Rural patient, urban MD	46 (3.4)	21 (3.7)	25 (3.2)	0.02
Urban patient, rural MD	195 (14.6)	94 (16.8)	101 (13.1)	
Urban patient, urban MD	685 (51.4)	291 (52.1)	394 (51.0)	
Pharmacy location[4]				
Rural patient, rural pharmacy	392 (29.4)	158 (28.2)	234 (30.3)	
Rural patient, urban pharmacy	36 (2.7)	11 (2.0)	25 (3.2)	0.34
Urban patient, rural pharmacy	76 (5.7)	38 (6.8)	38 (4.9)	
Urban patient, urban pharmacy	799 (59.9)	336 (59.9)	463 (59.9)	

[1] 19 patients removed from the Race variable to the "Other" race and ethnicity
[2] 191 marital status missing from patients prescribed medications. 273 marital status missing from patients not prescribed medications.
[3] 4 patients missing from Primary care physician/patient variable
[4] 31 total patients missing from pharmacy location, 18 from those prescribed and 13 from those not prescribed pain medication

Table 4.2. Quantity of South Carolina cancer specialist by geographical region

	Urban	Rural
Cancer Specialists	291	83

Table 4.3. Adjusted Odds for receipt of opioid pain medications for distant stage lung cancer patients (N=1334)

	Adjusted OR (95% CI)	Unadjusted OR (95%CI)	p-value[1]
Intercept	0.25 (-3.48, 0.76)		0.66
Patient Factors			
Residence			
Rural	0.83 (0.29-2.38)	1.46 (0.89-2.40)	0.73
Urban (ref)	1.00	1.00	
Sex			
Male (ref)	1.00	1.00	
Female	1.23 (0.79-1.91)	1.13 (0.75-1.73)	0.36
Race			
Non-Hispanic Black	0.86 (0.55-1.33)	0.75 (0.50-1.15)	0.49
Non-Hispanic White (ref)	1.00	1.00	
Marital status			
Single/Separated/Divorced	1.29 (0.46-3.65)	0.89 (0.54-1.48)	
Married (ref)	1.00	1.00	0.63
Missing	0.73 (0.41-1.30)	0.77 (0.45-1.32)	
Structure and Process of Care:			
Cancer specialist location			
Rural	-	0.66 (0.40-1.10)	
Urban (ref)	-	1.00	0.99
PCP location[2]			
Rural	0.74 (0.29-1.87)	0.62 (0.39-1.01)	
Urban (ref)	1.00	1.00	0.52
Pharmacy location			
Rural	1.73 (0.44-6.78)	0.61 (0.36-1.01)	
Urban (ref)	1.00	1.00	0.43

[1]p-value of Adjusted Odds Ratio [2]Primary care provider location

References

1. Hartley D. Rural health disparities, population health, and rural culture. Am J Public Health. 2004; 94: 1675–1678.

2. Kindig D, Stoddart G. What is population health? Am J Public Health. 2003; 93:380–383.

3. Ricketts TC, Johnson-Webb K D Randolph RK. Populations and places in rural America. In: Ricketts TC, eds, Rural Health US. New York Oxford University Press; 1999: 7-24.

4. Hart LG, Salsberg E, Phillips DM, Lishner DM. Rural health care providers in the United States. J Rural Health. 2002; 18(5): 211-232.

5. Kelley ML. Developing rural communities' capacity for palliative care: a conceptual model. J of Palliative Care. 2007; 23(3)L 143-153.

6. Rural Assistance Center (RAC). Rural pharmacy and prescription drugs. http://www.raconline.org/topics/pharmacy-and-prescription-drugs. Updated December 12, 2013. Accessed December 17, 2014.

7. Pargeon KL, Hailey BJ. (1999). Barriers to effective cancer pain management: A review of the literature. J Pain Symptom Manage. 1999; *18*(5): 358-368.

8. National Institutes of Health, National Cancer Institute. Pain: Pharmacologic management. http://www.cancer.gov/cancertopics/pdq/supportivecare/pain/HealthProfessional/page 3. Updated September 13, 2014. Accessed January 7, 2015.

9. Levy MH. Pharmacologic treatment of cancer pain. New Eng J Med. 1996; 335: 1124-1132.

10. United States Department of Agriculture (USDA), Economic Research Service. Rural-urban commuting area codes. Retrieved from http://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx. Updated May 10, 2013. Accessed December 19, 2014.

11. McNeill, J.A., Reynolds J., Ney, M.L. Unequal quality of cancer pain management: disparity in perceived control and proposed solutions. Oncol Nurs Forum. 2007; 34(6):1121–1128.

12. Reschovsky JD, Staiti AB. Access and quality: does rural America lag behind? Health Aff (Millwood). 2005 Jul-Aug; 24(4):1128-39.

13. Bloom JR, Stewart, SL, Johnston M, Banks P, Fobair P. Sources of support and the physical and mental well-being of young women with breast cancer. Soc Science Med. 2001; 63(11): 1613-1624

14. Haason-Ohayon I, Goldaweig G, Braun M, Galinsky D. Women with advanced breast cancer and their spouses: diversity of support and psychological distress. 2010; 19(11): 1195-1204.

15. Caraceni A., Hanks G. Kaasa S, Bennett MI, Brunelli C, Cherny N, & Zeppetella G. Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet oncol. 2012; 13(2) e58-e68.

16. Goudas LC, Bloch R, Gialeli-Goudas M, Lau J, Carr DB. The epidemiology of cancer pain. Cancer investigation. 2005; 23(2): 182-190.

17. Qato DM, Martha L. Daviglus ML, Jocelyn Wilder J, Lee T, Qato D, Lambert B. Pharmacy deserts' are prevalent in Chicago's predominantly minority communities, raising medication access concerns, Health Affairs. 2014; 33(11):1958-1965.

MANUSCRIPT #2

PATIENT SURVIVAL AND THE INFLUENCE OF PAIN MEDICATIONS AMONG
ADVANCED STAGE LUNG CANCER PATIENTS

Abstract:

Health care inequities faced by rural residents of South Carolina span the breadth of all clinical diagnoses. Inequalities in cancer care and outcomes, in particular those encountered by rural residents, include the shortage of qualified clinicians to treat cancer patients, a fragmented continuum of care, and a lack of evidence to effectively guide and identify the placement of administrative and clinical resources in South Carolina's rural regions. The deficit of clinical resources refers to a lack of cancer specialists to treat and prescribe medications appropriately as well as pharmacies to fill prescriptions. Each of the highlighted inequalities has the potential to not only impact the manner of health care treatment but also has the potential to influence the longevity of a patient's life. The conducted survival analysis to determine the impact of these factors on the rate of patient survival for those with distant stage lung cancer found that gender was statistically significant in the survival of patients (AHR=1.31, CI:1.03-1.65). This study sought to determine the geographical disparities in the prescribing of pain medications for Non-Hispanic Whites and Non-Hispanic Blacks and the impact of observed patient factors on patient's survival rate among late stage lung cancer patients enrolled in Medicaid.

Introduction

The geography and demography of South Carolina's rural regions create difficulties for residents who require health care. For these exact reasons, it is also difficult to attract health care providers, having a direct impact on health care outcomes and the increasing prevalence of health disparities.[1,2] The inability of rural areas to recruit and retain both primary care physicians and specialists greatly influences the level of care received by patients with chronic conditions, like lung cancer. Exacerbating circumstances for advanced stage lung cancer patients experiencing pain is the decreased likelihood of a rural pharmacy's inventory to contain an adequate supply of medications commonly prescribed to address cancer pain. [3-5]

Nationally, lung cancer is the most frequently diagnosed cancer and is the leading cause of cancer death. The American Cancer Society predicted, by the end of the year 2014, approximately 1,665,540 incidences of lung cancer.[6] Cancer related deaths, lung cancer included, are directly associated with time of diagnosis and stage of disease at diagnosis. For residents of rural areas this can pose specific barriers. Mounting evidence confirms that the demographic of South Carolina's rural communities are more likely to be composed of racial minorities and persons of a lower socioeconomic status—variables that not only increase the risk of being diagnosed with cancer but also being diagnosed at a later stage with inferior outcomes.[3]

Poor individuals that reside in rural areas are also more likely to be either uninsured or underinsured than inhabitants of urban areas. This lack of coverage limits access to healthcare and needed medications.[3] In addition to patients not being able to afford medications, pharmacists and pharmacies in rural areas may not stock opioids and analgesics, medications commonly used for pain, because of safety and cost concerns.[7]

66

More specifically, within minority communities approximately 25% of pharmacies have an adequate stock of sufficient opioids for pain management, compared with 72% of non-minority neighborhood pharmacies.[8]   Morrison et al. examined pharmacies in an urban city, comparing the available stock of sufficient opioids in minority versus non-minority neighborhoods.[9] Study results indicated that 51% of the area's pharmacies did not have a sufficient supply of opioids to meet patient's needs; only 25% of those in "non-white neighborhoods" had an adequate supply of opioids to meet patient needs; while 72% of the pharmacies in majority white communities had a sufficient supply of opioids.[9] The absence of needed medications to address cancer pain worsens the scenario for rural populations.

Pain is the symptom most commonly associated with lung cancer as it is experienced by 70-80% of advanced stage cancer patients at varying levels.[3-5,10] Cancer-related pain has been directly associated with reduced patient survival.[11,12] Because the occurrence and incidence of cancer is increasing, cancer pain should be expected and attended to as soon as possible instead of at later stages of the disease.[13] However, constant barriers continue to present themselves for rural regions and prevent immediate attention to the disease and its symptoms, impacting patient survival, the potential intensity of pain, as well as overall patient health outcomes.

To address whether or not opioids and analgesics influence the rate of patient survival and whether or not rural populations experience a reduced survival rate as a result of medication receipt, this study explores the relationship between rural residence, patient survival, and the receipt of medication to manage pain in a population of advanced stage lung cancer patients enrolled in South Carolina Medicaid

METHODS

Data: Study data was requested from the South Carolina Central Cancer Registry (SCCCR). Data from SCCCR was linked by the South Carolina Office of Research and Statistics (ORS) with South Carolina Medicaid claims data using patient identifiers assigned by the ORS (Office of Research and Statistics). Data is provided to SCCCR by South Carolina hospitals (registry and non-registry), pathology laboratories, treatment centers, and physician offices. SCCCR's database is not only representative of cancer incidence in South Carolina but also contains patient demographics and clinical data pertaining to each specific cancer case, changing trends in diagnosis and treatment, and patient survival rates.[14]

Cohort description: The study sample was composed only of South Carolina Medicaid beneficiaries who were diagnosed with lung cancer between the years 1996-2010. From this sample of lung cancer patients, only late stage lung cancer patients who were continuously enrolled in Medicaid for at least 9 months prior to diagnosis were included in the sample. For all patients, lung cancer was the first primary cancer diagnosis. Patients with a secondary malignancy were excluded from the analysis. Patient data was right-censored (those not experiencing the event of interest (death) for the study duration were not analyzed), to avoid bias in the survival analysis. For inclusion in the post-diagnosis population, patients had to have 1) had a prescription filled for either an opioid, analgesic, or both through their SC Medicaid policy post-diagnosis; 2) been enrolled in South Carolina Medicaid for at least 9 months prior to the lung cancer diagnosis; and lung cancer was the primary malignancy.

Patient geographic information was assigned using rural-urban commuting area (RUCA) codes. RUCA codes classify United States census tracts using measures of population density, urbanization, and daily commuting. These classification codes allowed for the identification of the geography of patient's location , urban or rural, according to assignments made by the United States Food and Drug Administration Economic Research Service.[15] To learn more about prescribing practices in rural areas, physician location and pharmacy location were also described as urban or rural using the RUCA codes. Each pharmacy and medical claim was linked with the patient's assigned ORS identifier to provide geographic data.

Measures

Conceptual framework: Stewart and Teno's *Conceptual Model of Quality of Life of Dying Patients and their Families* (Figure 4.1) was adapted to assess the variables that impact quality of healthcare received by terminally-ill patients, which is directly correlated to patient healthcare and healthcare outcomes.[16] The model evaluates the quality and outcomes of care with three principal classifications: patient factors affecting health care and outcomes of care; structure and process of care; and outcomes of care. The selected model conceptualizes health service utilization, the quality of patient care, and healthcare outcomes. The model is used as a measure of assessing patient quality of care and end-of life care.
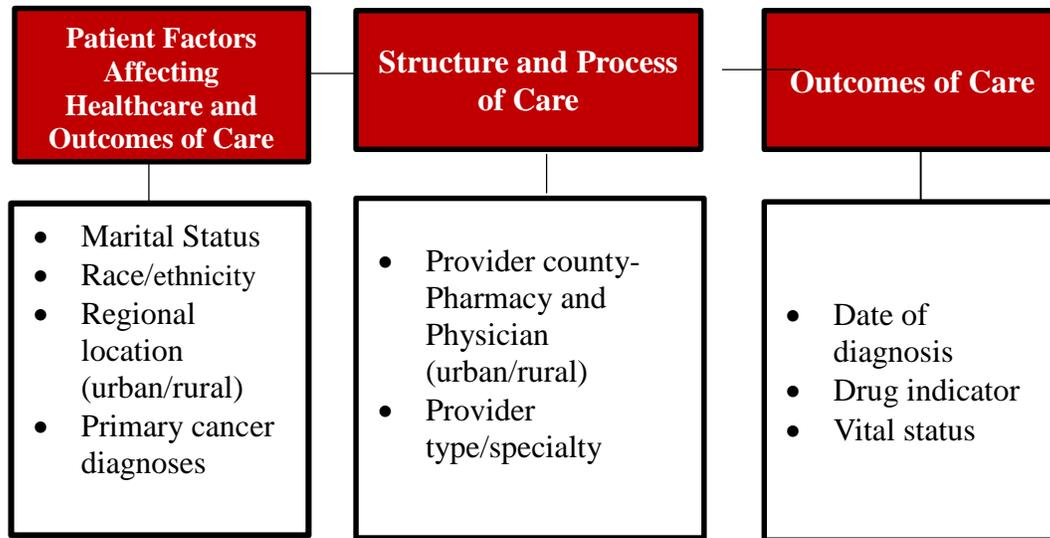
Patient Factors Affecting Healthcare and Outcomes of Care	**Structure and Process of Care**	**Outcomes of Care**
• Marital Status • Race/ethnicity • Regional location (urban/rural) • Primary cancer diagnoses	• Provider county-Pharmacy and Physician (urban/rural) • Provider type/specialty	• Date of diagnosis • Drug indicator • Vital status

Figure 4.1. Conceptual model adapted from Stewart and Teno's '*Model of Quality of Life of Dying Patients and Their Families* (1999)

Patient Factors Affecting Healthcare and Outcomes of Care The personal and social environments of patients impact health care utilization and outcomes. Examined personal and social environments included patient race/ethnicity (Non-Hispanic Black, Non-Hispanic White, and other), gender, marital status (single, married, separated or divorced), and patient geographical residence (urban/rural). Race/ethnicity, patient geographical residence, and gender influence the manner in which patients receive healthcare and are determinants in the availability and utilization of health care.[7-9, 17] The support system offered by marriage has also been shown to impact patient outcomes.[18] Marital status was operationalized as single, married, or separated/divorced. Patients at a specific stage of lung cancer was built into the data request; therefore a part of the research design.

Structure and Process of Care Patients within the dataset were all Medicaid patients. Patient enrollment in the same insurance program with the same eligibility

requirements, indicates similar levels of affordability and accessibility to health care, presumably. Establishing inclusion criteria that all patients were continuously enrolled in Medicaid for at least 9 months prior to diagnosis insured that there was not a break in health insurance coverage and that a lack of health insurance was not the patient's primary reason for not receiving medical care sooner.

Geographic location (urban/rural) was coded using rural urban commuting codes for all physicians (cancer specialists and all other physicians in the sample) and pharmacists by whom Medicaid claims were filed. The geography of providers (physicians and pharmacists) have an effect on patient access to healthcare.   Patient diagnosis is also impacted by access to care. For all patients, lung cancer was the first cancer diagnosis. Considering only the first cancer diagnosis reduced the influence of previous or post diagnoses in patient care, cancer staging in the current diagnosis and prognosis, and cancer progression.

Outcomes of Care The patient sample considered only patients who received pain medications commonly prescribed for cancer patients, opioids and analgesics. The patient survival rate was assessed from the point of the patient's primary diagnosis. Survival rate was assessed for cancer related deaths. Patients not experiencing the event of interest, death, were censored post December 2010. Patient survival time in months was calculated from the date of diagnosis to the point of death for all patients experiencing death. This was examined in the Cox Proportional Hazard survival model.

Statistical Analysis A descriptive, bivariate analysis was performed to determine the associations between patient factors affecting healthcare outcomes of care and the structure and process of care. A survival analysis using Cox's proportional hazard model was used to calculate the period from the primary cancer diagnosis to death. Cox proportional hazard model is defined as follows:

$$H_i(t) = \lambda_0(t) \exp\{\beta_1 x_{i1} + \ldots + \beta_k x_{ik}\}.$$

As modeled, the hazard of death for individual (i) at time (t) is the result of baseline hazard function ($\lambda_0(t)$) and linear function of a set of defined covariates(k) making up the components of the described conceptual model: patient factors affecting healthcare outcomes of care, the structure and process of care, and the outcomes of care previously described.[19] These covariates of the conceptual model are expressed through the x_{ik} function of the Cox model.

Results

Within the sample of 1,334 of late stage lung cancer patients, 561 were prescribed either an opioid or analgesic, while 773 patients did not receive opioid analgesic medications. In the sample 32.6 % (n=435) resided in rural South Carolina and 67.4% (n=899) resided in urban areas of South Carolina. More than half of the study sample was male (58.5), while exactly half of the study sample were Non-Hispanic Blacks (50.1). Results from the descriptive analysis are reported in Table 4.4.

To begin examining patient survival and death, a bivariate analysis of patient factors and health care system process factors was performed. There was a total of 1, 293 cancer-related patient deaths. Of these cancer deaths, 561 were persons that had received

prescriptions for opioids or analgesics, which was not statistically significant (Table 4.5).

Of those who were prescribed opioids or analgesics, 97.3% experienced death while

96.5% of those who were not prescribed opioid analgesics died a cancer-related death.

Presented data also shows a greater percentage of cancer deaths were within the urban

population (65.8). Also in the sample a greater number of males died, while a greater

number of females survived. Similarly, more Non-Hispanic Whites survived than Non-

Hispanic Blacks. Race and ethnicity were statistically significant in the bivariate analysis

of cancer related deaths. Though patient marital status was not statistically significant,

more single, separated, and divorced persons experienced cancer-related deaths than

married persons.

Considering the process and structure of patient care, the location of primary

care providers was a statistically significant factor. The rural primary care provider, rural

patient combination variable composed 97.4% of the deaths of among primary care

provider patient encounters. The urban patients, urban primary care provider combination

variable made up over half (7.3) of the sample of cancer deaths for this group as well.

This result was also true for the urban pharmacy, urban patient combination variable

(96.5). This data is shown in Table 4.5.

Table 4.6 exhibits patient survival rates specific to cancer deaths among late

stage lung cancer patients. After controlling for the patient factors affecting healthcare

outcomes of care, the structure and process of care and the outcomes of care variables,

patient receipt of pain medication there was only a single variable that resulted in

statistical significance for experiencing the event of interest, death, for those prescribed

or not prescribed medication, patient gender. Males were more likely to experience death

(OR=1.31) than the females studied in the sample. The likelihood of death for patients in urban and rural geographies was similar. This was also true for marital status in the sample. Although there were a greater number of males as well as persons who were single, separated or divorced this made no statistical difference. Examining the structure and process of healthcare also resulted in statistical similarities for primary care and cancer specialist provider locations, as well as pharmacy location.

Table 4.4 Descriptive characteristics of observed lung cancer patients

| | Total N (%) | Opioid Receipt | | p |
		Yes[1] N (%)	No N (%)	
Sample Total	1334 (100%)	561 (42.0)	773 (58.0)	
Residence				
Rural	435 (32.6)	171 (30.5)	264 (34.3)	0.33
Urban	899 (67.4)	390 (69.5)	509 (65.6)	
Gender				
Male	780 (58.5)	313 (56.8)	467 (61.4)	0.29
Female	554 (41.5)	248 (44.2)	306 (39.6)	
Marital status[2]				
Single/Separated/Divorced	531 (39.8)	227 (40.5)	304 (39.3)	0.80
Married	339 (25.4)	146 (26.0)	193 (25.0)	
Missing	276 (20.7)	193 (34.4)	276 (37.0)	
Race[3]				
Non-Hispanic White	636 (47.7)	288 (51.3)	348 (45.0)	0.13
Non-Hispanic Black	679 (50.1)	268 (47.7)	411 (53.2)	

[1]Includes single and combination prescription of opioids and analgesics
[2] 191 marital status missing from patients prescribed medications. 497 marital status missing from patients not prescribed medications.
[3]19 patients removed from the Race variable to the "Other" race and ethnicity

Table 4.5 Factors associated with patient cancer-related death within the observation period

	Total N (%)	Cancer death N (%)	Survived N (%)	*p*
Total	1334 (100.0)[1]	1293 (96.2)	41 (3.8)	0.11
Patient factors				
Medications				
Opioid received	561 (42.0)	547 (97.3)	14 (2.7)	0.63
No opioids	773 (58.0)	746 (96.5)	27 (3.5)	
Patient Residence				
Rural	456 (34.5)	425 (92.2)	31 (6.8)	0.51
Urban	878 (65.8)	868 (96.5)	10 (3.5)	
Gender				
Male	780 (58.5)	761 (97.6)	19 (2.4)	0.46
Female	554 (41.5)	532 (96.1)	22 (3.9)	
Race[1]				
Non-Hispanic Black	616 (46.2)	601 (97.6)	15 (2.4)	0.11
Non-Hispanic White	699 (52.5)	675 (96.6)	24 (3.4)	
Marital status				
Single/Separated/Divorced	521 (39.1)	512 (96.4)	19 (3.6)	0.73
Married	345 (25.9)	331 (95.9)	14 (4.1)	
Missing	458 (34.3)	450 (98.3)	8 (1.7)	
Structure and Process of Care				
Cancer specialist location[2]				
Rural patient, rural MD	54 (1.6)	54 (100.0)	0 (0.0)	
Rural patient, urban MD	20 (1.6)	18 (90.0)	2 (10.0)	0.81
Urban patient, rural MD	19 (1.6)	18 (90.0)	1 (5.3)	
Urban patient, urban MD	251 (20.6)	240 (95.6)	11 (4.4)	
Primary care provider location[3]				
Rural patient, rural MD	388 (29.1)	379 (97.4)	9 (2.3)	
Rural patient, urban MD	46 (3.4)	45 (9.7)	1 (0.2)	0.01
Urban patient, rural MD	195 (14.6)	193 (99.0)	2 (1.0)	
Urban patient, urban MD	690 (51.7)	671 (97.3)	29 (4.2)	
Pharmacy location[4]				
Rural patient, rural pharmacy	392 (2.8)	385 (98.2)	7 (1.8)	
Rural patient, urban pharmacy	36 (28.9)	35 (97.2)	1 (0.8)	
Urban patient, rural pharmacy	76 (5.8)	74 (97.4)	2 (2.6)	0.81
Urban patient, urban pharmacy	799 (60.3)	771 (96.5)	28 (3.5)	

[1]Other race excluded due to the ability of the small sample size to influence the data. [2]The absolute total of cancer specialists is 373. 64 missing.[3]15 primary care providers missing from the sample. [4]31 pharmacies missing from the sample.

Table 4.6 Hazard Model for factors associated with distant stage patient death (N=1334)

	Adjusted Hazard Ratio (95% CI)	Unadjusted Hazard Ratio (95% CI)	P^1
Outcomes of Care			
Opioids prescribed (ref)	1.00	1.00	0.41
Opioids not prescribed	1.14 (0.84, 1.54)	1.09 (0.89, 1.35)	
Patient Factors			
Residence			0.82
Rural	1.06 (0.62, 1.84)	0.93 (0.73-1.19)	
Urban (ref)	1.00	1.00	
Gender			
Male	1.31 (1.03, 1.65)	1.22 (0.98, 1.50)	0.02
Female (ref)	1.00	1.00	
Race			
Non-Hispanic Black	1.01 (0.81, 1.28)	1.01 (0.81, 1.24)	0.93
Non-Hispanic White (ref)	1.00	1.00	
Marital status			
Single/Separated/Divorced	0.96 (0.73, 1.28)	0.97 (0.75, 1.25)	0.79
Married (ref)	1.00	1.00	
Missing	1.26 (0.84, 1.88)	1.24 (0.95, 1.63)	
Process/Structure			
Physician Location			
Rural	1.26 (0.77, 2.06)	1.01 (0.80, 1.28)	0.36
Urban (ref)	1.00	1.00	
Cancer specialist location[2]			
Rural	-	1.08 (0.84, 1.38)	0.56
Urban (ref)	-	1.00	
Pharmacy location			
Rural	0.62 (0.35, 1.09)	0.84 (0.66, 1.08)	0.09
Urban (ref)	1.00	1.00	

[1]P-value for adjusted hazard ratio [2]N for cancer specialist =374. P-value shown is only for the unadjusted model.

Discussion

Study results indicate that with the exception of gender, prescribing pain medications does not significantly contribute to the survival rate of patients for all observed variables. These findings sustain the findings of multiple international studies reporting that the receipt of opioid therapy does not have a significant impact on the rate at which patients survive.[22-29] While some of the international studies did not consider geography or race and ethnicity in their analyses they did report the lack of influence of pain between patient geography and cancer survival.[29-31]

Research has shown males are twice as likely to be diagnosed with lung cancer as well as to die of the disease in South Carolina.[32] This is true in the current sample of patients where there is a greater representation of males who have been diagnosed with the disease, and the lung cancer mortality rate for males is 31% greater than the lung cancer mortality rate for females. The bivariate analysis demonstrated that a greater proportion of females survived than males.

Study Limitations

Primary limitations include: 1) the use of secondary data which restricts available data to only what is collected; 2) South Carolina has been declared a Health Professional Shortage Area for primary medical care, dental care and mental care; 3) 40% of South Carolina's population inhabit rural areas; and 4) the use of a Medicaid sample could possibly skew demographics and results. Limiting the sample to a population of lower socioeconomic status persons who are transients only further complicates the circumstance of working with claims data.

Additionally, there is limited literature depicting the United States and the US health care system that consistently reports the association between geographic variation and the prevalence and incidence of disease, treatment, and survival and lung cancer. Moreover, in the state of South Carolina the depiction that the literature provides is not dedicated to lung cancer; yet, is either broadly focused on all types of cancers, primarily including:, breast cancer, colon cancer or prostate cancer.

Conclusion

Lung cancer is a persistent condition in which patients require long-term care. In many instances, once patients are diagnosed with lung cancer the looming issue becomes the care or the treatment plan. This is an especially relevant circumstance for lung cancer patients who reside in rural areas. Normally when diagnosed, lung cancer has already dissipated to the regional lymph nodes or other areas of the body.[33] Presented evidence continues to be representative of the disparities presented by distance as well as circumstances that prevent access to care (finances, presence of specialists, etc.).[34] Presented data does not support an explicit relationship between race and ethnicity as direct factors in patient survival. However, the influence of variables that commonly have a greater prevalence in specific racial and ethnic groups is evident from presented data.

While there is existing policy that incentivizes clinicians who practice in remote areas, these benefits are only temporary. A 2011 study conducted by Merritt-Hawkins found that only 4% of final-year medical residents desired to practice medicine in a community with less than 25,000 persons.[35] Policy change encouraging permanent residency or a greater commitment to practice medicine in remote areas is required. Research is needed to examine how this cultural change needs to be established in rural

areas, not only considering the provider but also the possibility of a provider's family. Additional policy and research needs to focus on care management plans of late stage cancer patients that increases patient contact (incentivizing traveling Physician Assistants or Nurse Practitioners, additional funding of telemedicine, etc.) with specialists. In addition, the education of providers on direct patient care for this specific population as well cultural and social influences are essential. Lastly, the increased development of interventional practices, like smoking cessation courses, has proven to be beneficial in the reduction of smoking, a linked cause of lung cancer. Increasing the availability of such interventions has proved behavior change and could result in the reduction of lung cancer diagnoses overall.

References

1. Farley DO, Shugarman LR, Taylor P, et al: Trends in Special Medicare Payments and Service Utilization for Rural Areas in the 1990s. Santa Monica, Calif: Rand. 2002; MR-1595-CMS.

2. Shugarman LR, Farley DO: Shortcomings in Medicare bonus payments for physicians in under-served areas. Health Aff. 2003; 22:173–178

3. McNeill JA, Reynolds J, Ney ML. Unequal quality of cancer pain management: disparity in perceived control and proposed solutions. Oncol Nurs Forum. 2007; 34(6):1121–1128.

4. Pargeon, KL, & Hailey BJ. Barriers to effective cancer pain management: A review of the literature. J Pain and Symptom Management 1999; 18(5), 358-368.

5. Caraceni AH, Hanks G, Kaasa S, Bennett MI, Brunell, C, Cherny N, et al. European Palliative Care Research Collaborative (EPCRC); European Association for Palliative Care (EAPC). Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol. 2012; 13(2), e58-68.

6. American Cancer Society. Cancer Facts & Figures 2013. Atlanta. http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-036845.pdf. Accessed December 5, 2014.

7. Francoeur, R. Ensuring safe access to medication for palliative care while preventing prescription drug abuse: innovations for American inner cities, rural areas, and communities overwhelmed by addiction. Risk Manag Healthc Policy. 2011; 4: 97-105.

8. Anderson KO, Richman SP, Hurley J, Palos G, Valero V, et al. Cancer pain management among underserved minority outpatients. Cancer. 2002; 94(8): 2295-2304.

9. Morrison R, Wallenstein S, Natale DK, Senzel RS, Huang LL. "We don't carry that"-Failure of pharmacies in predominantly nonwhite neighborhoods to stock opioid analgesics. New England Journal of Medicine. 2000; *342*(14): 1023-1026.:

10. Simmons CPL, MacLeod N, Laird BJA. Clinical Management of Pain in Advanced Lung Cancer. Clin Med Insights Oncol. 2012; 6: 331–346.

11. Mantyh, P. (2006). Cancer pain and its impact on diagnosis, survival and quality of life. Nature Reviews Neuroscience. 2006; 7, 797-809. doi:10.1038/nrn1914

12. Zylla D, Kuskowski MA, Gupta K, Gupta P. Association of opioid requirement and cancer pain with survival in advanced non-small cell lung cancer. Br J Anaesth. 2014; doi: 10.1093/bja/aeu351.

13. Paice JA & Ferrell B. The management of cancer pain. CA Cancer J Clin. 2011; 61: 157-182.

14. South Carolina Department of Health and Human Services. South Carolina Central Cancer Registry. Overview http://www.dhec.sc.gov/Health/DiseasesandConditions/Cancer/CancerStatisticsReports/CancerRegistry/. Accessed December 8, 2014.

15. United States Department of Agriculture Economic Research Service. Urban Influence Codes. http://www.ers.usda.gov/data-products/urban-influence-codes.aspx. Accessed December 8, 2014.

16. Stewart AL, Teno J, Patrick DL, Lynn J. The concept of quality of life of dying persons in the context of health care. J Pain Symptom Manage 1999 Feb; 17 (2):93-108.

17. Healthcare quality and disparities in women: Selected findings from the 2010 National Healthcare Quality and Disparities Reports. Agency for Healthcare Research and Quality, Rockville, MD. Pub. No. 11-0005-1-EF. http://www.ahrq.gov/research/womenqrdrfs2010.htm.

18. Wang L, Wilson SE, Stewart DB, Hollenbeak CS. Marital status and colon cancer outcomes in US Surveillance, Epidemiology and End Results registries: Does marriage affect cancer survival by gender and stage?." Cancer Epid. 2011; 35(5): 417-422.

19. Allison PD. Survival analysis using the SAS system: A practical guide. Cary, NC: SAS Institute Inc; 1995.

20. Reschovsky JD, Staiti AB. Access and quality: Does rural America lag behind? Health Affairs; 24(4): 1128-1151.

21. Borders TF, Rohrer JE, Hilsenrath PE, Ward MM. Why rural residents migrate for family physician care. J Rural Health. 2000; 16(4): 337-348.

22. Alsirafy, SA., Khaled MG, Enas NA, Noha YI, Dina EF, Ahmed MH. The use of opioids at the end-of-life and the survival of Egyptian palliative care patients with advanced cancer." Ann of Palliat Med. 2013; 2(4): 173-177.

23. Azoulay D, Hammerman-Rozenberg R, Cialic R, Ein Mor E, Jacobs JM Stessman, J. Increasing opioid therapy and survival in a hospice. Journal of the American Geriatrics Society, 2008; 56(2): 360-361.

24. Bercovitch MW, Adunsky A. Patterns of high dose morphine use in a home-care hospice service: should we be afraid of it? Cancer, 2004; 1001: 1473-1477.

25. Bercovitch MW, Waller A, Adunsky A. High dose morphine use in the hospice setting: A database survey of patient characteristics and effect on life expectancy. Cancer. *1999; 86:* 871-877.

26. Good PR, Ravenscroft, PJ, Cavenagh, J. Effects of opioids and sedatives on survival in an Australian inpatient palliative care population. Internal Medicine Journal. 2005; 35: 512-517.

27. Morita T, Tsunoda J, Inoue S, Chihara S. (2001). Effects of high dose opioids and sedatives on survival in terminally ill cancer patients. J Pain Symptom Management. 2001; *21*(4): 282-289.

28. Thorns A, Sykes N. Opioid use in last week of life and implications for end-of-life decision-making. The Lancet. 2000; *356*(9227): 398-399.

29. Bengoechea I, Gutiérrez SG, Vrotsou K, Onaindia MJ, Lopez JM. Opioid use at the end of life and survival in a hospital at home unit. J Palliative Med. 2010; *13*(9): 1079-1083.

30. 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;84:910–914.

31. 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;87:585–590.

32. Park ER, Japuntich SJ, Traeger L, Cannon S, Pajolek H. Disparities Between Blacks and Whites in Tobacco and Lung Cancer Treatment. The Oncologist. 2011; 16(10): 1428-1434. doi:10.1634/theoncologist.2011-0114.

33. Hébert JR, Daguise VG, Hurley DM, et al. Mapping Cancer Mortality-to-Incidence Ratios to Illustrate Racial and Sex Disparities in a High-risk Population. Cancer. 2009; 115(11):2539-2552. doi:10.1002/cncr.24270.

34. Shugarman LR, Sorbero MES, Tian H, Jain AK, Ashwood JS. An exploration of urban and rural differences in lung cancer survival among Medicare beneficiaries. Amer J Public Health. 2008; 98(7): 1280-1287.

35. Merrittt-Hawkins. 2011 Survey of final-year medical residents. http://www.merritthawkins.com/pdf/mha2011residentsurvpdf.pdf. Accessed February 5, 2015.

CHAPTER 5

CONCLUSION

An estimated 221,200 persons in the United States are expected to be diagnosed with lung cancer in 2015 (American Lung Association, 2015). Of those Americans newly diagnosed and those living with the pre-existing condition, an estimated 158,040 deaths are expected from lung cancer in 2015 alone. These deaths comprise nearly 27 percent of overall cancer mortality (American Lung Association, 2015). Even more, the number of deaths resulting from lung cancer has risen approximately 3.5 percent between 1999 and 2012, inclusive of our study years. Patient mortality and quality of survival were examined in this descriptive research study with two primary goals that consider the influence of patient demographics and geography. The first aim of the study was to determine associations between patient residence (urban and rural) and the receipt of prescribed opioid analgesic therapy among late stage lung cancer patients. The second aim was to assess the association between patient residence and the patient survival rate of distant stage lung cancer patients, considering the receipt of opioid therapy. This chapter discusses the main findings of the study, strengths and limitations, policy implications and recommendations for future research

5.1 Research Aim 1

Research aim 1 addressed the urban and rural geography of patient residence and its association with receipt of prescribed opioid therapy among SC Medicaid lung cancer patients with a diagnosis. Selected variables used to determine access to health care and the likelihood of patients being prescribed medications are commonly applied and supported in social research to contribute to both the social and health determinants of patients and communities. Variables assessed in the receipt of either or both an opioid and analgesic were race and ethnicity (Non-Hispanic Blacks), the residential geography of the patient, marital status, gender, and the availability of primary care physicians and cancer specialists.

These data suggest that while the mixed relationships of variables is complex, there are no evident trends that support the receipt of an opioid analgesics, the outcome measure, is associated with where patients reside as well as the race and ethnicity of patients. Paper 1 of the dissertation further explored the possible relationships that have the potential to influence patient access to needed medications. All statistical findings from the regression were not statistically significant. However, bivariate analysis results demonstrated the statistical significance of the location of primary care providers and patient's locations. These results correlate with published data stating that the disparities in the treatment of cancer patients can be linked to the provider from whom they receive treatment (Kelley, 2007).

Rural South Carolina is affected by healthcare access issues and there are prominent disparities and persistent health care challenges among minority populations. The Centers for Disease Control and Prevention reports the prevalence of and contributors to chronic diseases are increased in rural regions when compared to urban

regions (Downey, 2013). Exacerbating risks at the person-level are communal characteristics that include the significant deficit of health care professionals, the lack of availability of specialty care, and decreased reimbursement from insurers. The disparate care available to rural populations is not specific to lung cancer but it can be broadly applied. The availability of and access to healthcare professionals (doctors and pharmacists) to provide adequate treatment, the underinsuring of patients, and transportation are only a few factors that rural populations have to contend with to get needed, and deserved, healthcare. Challenges incurred by rural environments are unique.

The existing circumstances of healthcare access for lung cancer patients in the rural environment have been investigated by an innumerable amount of researchers (Shugarman, 2008; Jong, Vale, & Armstrong, 2005); however, we were not able to identify any published studies to date that examined healthcare access by geography and its relationship to late stage lung cancer patient's receipt of pain medication in South Carolina.

5.2 Research Aim 2

Research aim 2 explored the association between patient geographical residence and the rate of survival of distant stage lung cancer patients, considering the receipt of opioid therapy, either drug or both drugs. The goal of the second research aim was to assess patient and social factors that influenced the rate at which patients with this chronic condition survived. The applied bivariate analysis allowed us to study the availability of primary care and specialty providers in each geographic region as well as

each type of providers prescribing behavior in relation to identified covariates (gender, marital status, and patient race/ethnicity).

Resulting data of the bivariate analysis indicated an association between cancer deaths and patient race and ethnicity, as well as cancer deaths and the location of the primary care provider and patient residence combination variable. The included Cox proportional survival analysis was unique in its examining both cancer-related deaths as well as non-cancer related deaths among distant stage lung cancer patients prescribed medication for pain. In addition to the survival analysis of each group, this was a unique examination of data involving provider prescribing practices among distant stage lung cancer Medicaid patients of South Carolina. The only significant variable resulting from the survival analysis was patient gender. Males were more likely to experience a higher rate of death than females in the studied sample.

There has been no prior research found that has assessed patient access to pain medication in a population likely to require it in the identified geographical region (South Carolina), and healthcare system (Medicaid in the United States), while adjusting for a necessary and significant treatment variables, like the presence of cancer specialists, which greatly affects cancer outcomes. This current research fills this gap.

Research Applications Overall, this study contributes to the current knowledge and literature on the disparities in healthcare access and treatment and its influence on patient healthcare and healthcare outcomes in the United States, but specifically creates a needed niche for healthcare research in South Carolina. Utilizing state-level datasets assists in establishing a foundation that will propel future work examining the prescribing of pain

medications and influencing environmental factors and social relationships that allow or hinder patient access and physician prescribing behaviors in South Carolina.

Study Limitations There were several limitations to this study. First, the manner in which availability of physicians (primary or cancer specialists) was defined did not capture other obstacles to patient accessibility, like transportation and distance from the patient, that could have prevented patient access. Secondly, the use of a secondary dataset restricts investigators to only what is collected or reported by hospitals, coroner's offices, and providers' offices. A third limitation of the study is the use of a Medicaid sample which could possibly skew demographics and results. Limiting the sample to a population of lower socioeconomic status persons who are commonly transient only further complicates the circumstance of working with claims data. A fourth and final limitation to the study is the declaration of South Carolina as a Health Professional Shortage Area for primary medical care. This HPSA declaration is a statewide shortage yet will have a significantly greater impact on the rural communities of the state.

Policy Implications and Future Research While there is existing policy that incentivizes clinicians who practice in remote areas, these benefits are only temporary. A 2011 study conducted by Merritt-Hawkins found that only 4% of final-year medical residents desired to practice medicine in a community with less than 25,000 persons. Policy change encouraging permanent residency or a greater commitment to practice medicine in remote areas is required. Research is needed to examine methods to strategically building the infrastructure of rural areas, not only considering the provider

but also the possibility of a provider's family. Building such an infrastructure will require an investment. Most importantly additional policy and research needs to focus on care management plans of late stage cancer patients that increases patient contact (creating and incentivizing clinical specialty tracks for Physician Assistants or Nurse Practitioners who will be willing to relocate or travel, additional funding of telemedicine, etc.) with specialists.

Additionally, demands for changes in local and national policy that monitor the availability of pain medications in rural communities are necessary, simply to ensure availability of adequate amounts of medications to meet the needs of the population. Increasing accessibility to highly addictive pain medications for certain populations raises concerns of patient abuse or the diversion of medications. One manner to combat this is the appropriate and mandated use of prescription monitoring programs. Not only should the use of these prescription monitoring programs be mandated, but also requiring the utilization of systems that have the ability to communicate with one another. The overprescribing opioids is a public health issue that puts an economic strain on financial and health resources. In addition, it is necessary to increase provider's awareness of the direct care needs for this specific population as well as cultural and social influences through education. Lastly, the increased development of interventional practices, like smoking cessation courses, have proven to be beneficial in the reduction of smoking, a cause of lung cancer. Increasing the availability of such interventions has resulted in significant behavior change and could result in the reduction of lung cancer diagnoses overall.

REFERENCES

Agency for Health care Policy and Research. (1994). *Management of cancer pain: Clinical practice guideline.* Rockville: AHCPR.

American Cancer Society. (2013). Cancer Facts & Figures 2013. Atlanta. Retrieved from http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-036845.pdf

American Cancer Society Cancer Action Network. (2013, June 4). *Media Center.* Retrieved from Movement Grows in States to Address Effective Pain Management for Cancer and Other Chronic Diseases: movement-grows-in-states-to-address-effective-pain-management-for-cancer-and-other-chronic-diseases

American Cancer Society, C. A. (2010). *Affordable Care Act: Pain managemnt.* Retrieved from American Cancer Society Cancer Action Network: http://www.acscan.org/pdf/healthcare/implementation/factsheets/hcr-pain-management.pdf

Anderson KO, Richman SP, Hurley J, Palos G, Valero V, et al. Cancer pain management among underserved minority outpatients. Cancer. 2002; 94(8) : 2295-2304.

American Society of Pain. (1992). *Principles of analgesic use in the treatment of acute pain and chronic cancer pain: A concise guide to medical practice.* Skokie: American Pain Society.

Azevedo, S.K.., Kimura, M., & Texiera, M.J. (2006). The WHO analgesic ladder for cancer pain control, twenty years of use. How much pain relief does one get from using it. *Support Care Cancer, 14*, 1086-1093.

Azoulay, D., Hammerman-Rozenberg, R., Cialic, R., Ein Mor, E., Jacobs, J.M., & Stessman, J. (2008). Increasing opioid therapy and survival in a hospice. *Journal of the American Geriatrics Society, 56*(2), 360-361.

Baltic TE, Wheldon, M.B., Ahles, T.A., & Fanicullo, G. (2002). Improving relief in a rural cancer center. *Cancer Practice, 10*(1), S39-S44.

Bercovitch, M.W., &. Adunsky, A. (2004). Patterns of high dose morphine use in a home-care hopsice srvice: should we be afraid of it? *Cancer, 1001*, 1473-1477.

Bercovitch, M. W., Waller, A., & Adunsky, A. (1999). High dose morphine use in the hospice setting: A database survey of patient characteristics and effect on life expectancy. *Cancer, 86*, 871-877.

Berry P.H., &. Dahl, J.H. (2000). The new JCAHO pain standards: Implications for pain management nurses. *Pain Management Nursing, 1*(1), 3-12.

Bolen, J. (2008). *State Prescribing Policies: South Carolina.* Retrieved from A Guide to State Opioid Prescribing Policies: http://www.medscape.com/resource/opioid/opioid-southcarolina

Bonham, V. L. (2001). Race, Ethnicity, and Pain Treatment:Striving to understand causes and solutions to the disparities in pain treatment. *Journal of Law, Medicine & Ethics, 29*, 52-68.

Breivik, H. C., Cherny,N., Collett, B., de Conno, F., Fibet, M., Foubert, A.J., Cohen, R., & Dow, L. (2009). Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. *Annals of Oncology, 20*(8), 1420-1433. doi:10.1093/annonc/mdp001. Epub 2009 Feb 24.

Brescia, F. P., Portenoy, R.K., Ryan, M., Krasnott, L., & Gray G. (1992). Pain, opioid use, and survival in hospitalized patients with advanced cancer. *Journal of Clinical Oncology, 10*, 149-155.

Breuer, B. F., Fleishman, S.B., Cruciani, R.A., & Portenoy, R.K. (2011). Medical oncologists' attitudes and practice in cancer pain management: a national survey. *Journal of Clinical Oncology, 29*(36), 4769-4775.

Caraceni, A. H., Hanks, G., Kaasa, S., Bennett, M.I., Brunelli, C., Cherny, N., Dale, O., De Conno, F., Fallon, M., Hanna, M., Haugen, D.F., Juhl, G., King, S., Klepstad, P., Laugsand, E.A., Maltoni, M., Mercadante, S., Nabal, M., Pigni, A., Radbruch, L., Reid, C., Sjogren, P., Stone, P.C., Tassinari, D., Zeppetella, G.; European Palliative Care Research Collaborative (EPCRC); European Association for Palliative Care (EAPC). (2012). Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. *Lancet Oncology, 13*(2), e58-68.

Carlson, M. D., Morrison, R.S., Holford, T.R., & Bradley, E.H. (2007). Hospice care: what services do patients and their families receive? *Health Services Research, 42*(4), 1672-1690.

Centers for Disease Control and Prevention, National Cancer Institute. (2010). *State Cancer Profiles*. Retrieved from Quick Profliles: http://statecancerprofiles.cancer.gov/cgi-bin/quickprofiles/profile.pl?45&055

Chang, M. C., Chang, Y.C., Chiuo, J.F., Tsou, t.S., & Lin, C.C. (2002). Overcoming patient-related barriers to cancer pain management for home care patients. *Cancer Nursing, 25*(6), 470-476.

Cleeland, C. G., Gonin, R., Hatfield, A.K., Edmonson, J.H., Blum, R.H., Stewart, J.A., & Pandya K.J. (1994). Pain and its treatment in outpatients with metastatic cancer. *New England Journal of Medicine, 330*(9), 592-596.

Cromartie, J. &. Bucholtz, S. (n.d.). *United States Department of Agriculture*. Retrieved from Economic Research Service: http://www.ers.usda.gov/datafiles/Rural_Definitions/StateLevel_Maps/SC.pdf

de Wit R., van Dam F., Abu-Saad, H.H., Loonstra, S., Zandbelt, L., van Buuren, A., van der Heijden K., Leenhouts, G.. (1999). Empirical comparison of commonly used measures to evaluate pain treatment in cancer patients with chronic pain. *Journal of Clinical Oncology, 17*(4), 1280-1287.

Denadrea, S., Montanari, M., Moja, L., & Apolone, G.. (2008). Prevalence of undertreatment in cancer pain. A reveiw of published literature. *Annals of Oncology, 19*(12), 1985-1991.

Dy, S.M., Asch, S.M., Naeim, A., Sanati, H., Walling, A., Lorenz, K.A. (2008). Evidence-Based Standards for Cancer Pain Management. *Journal of Clinical Oncology, 26*(23), 3879-3885.

Ferrell, B. R., Ferrell, B.A., Ahn, C., & Tran, K.. (1994). Pain management for elderly patients with cancer at home. *Cancer Supplement, 74*(7), 2139-2146.

Francoeur, R. (2011). Ensuring safe access to medication for palliative care while preventing prescription drug abuse: innovations for American inner cities, rural areas, and communities overwhelmed by addiction. *Risk Management and Healthcare Policy*, 4: 97-105.

Gallagher, R., Hawley, P., Yeomans, W. (2004). A survey of cancer pain management knowledge and attitudes of British Columbian physicians. *Pain Research Management, 9*(4), 188-194.

Good, P. R., Ravenscroft, P.J., & Cavenagh, J. (2005). Effects of opioids and sedatives on survival in an Australian inpatient palliative care population. *Internal Medicine Journal, 35*, 512-517.

Gordon, D.B., Dahl, J.L., Miaskowski, C., McCarberg, B., Todd, K.H., Paice, J.A., Lipman, A.G., Bookbinder, M., Sanders, S.H., Turk, D.C., Carr, D.B. (2005). American pain society recommendations for improving the quality of acute and cancer pain management: American Pain Society Quality of Care Task Force. *Archives of Internal Medicine, 165*(14). doi:doi:10.1001/archinte.165.14.1574.

Green, C.R., Anderson, K.O., Baker, T.A., Campbell, L.C., Decker, S., Fillingim, R.B., Kalauokalani, D.A., Lasch, K.E., Myers, C., Tait, R.C., Todd, K.H., & Vallerand, A.H. (2003). The unequal burden of pain: Confronting racial and ethnic disparities in pain. *American Academy of Pain Medicine, 4*(3), 277-294.

Gulati, A., Joshi, J., & Bagai, A. (2012). An overview of treatment strategies for cancer pain with a focus on interventional strategies and techniques. *Pain Management, 2*(6), 569-580.

Gunnarsdottir, S., Donovan, H.S., Ward, S. (2003). Interventions to overcome clinician- and patient-related barriers to pain management. *The Nursing Clinics of North America*, 419-434.

Hernandez-Cancio, S. Bailey, K., & Mahan, D. (2010). Medicaid: A lifeline for blacks and latinos with serious health care needs. Retrieved from American Cancer Society: www.lung.org/assets/documents/publications/medicaid

Herr, K., Titler, M., Fine, P.G., Sanders, S., Cavanaugh, J.E., Swegle, J., Tang, X., & Forcucci, C. (2012). The effect of a Translating Research into Practice (TRIP)-Cancer intervention on cancer pain management in older adults in hospice. *Pain Medicine, 13*(8), 1672-1690.

Higginson, I. M. (2010). Cancer pain epidemiology. In E. P. Bruera, *eds), Cancer Pain: Assessment and Management.* (pp. 37–52). Cambridge University Press.

International Association for the Study of Pain. (2009). *Global Year Against Cancer Pain.* Retrieved from Lung cancer and pain: http://www.iasp-pain.org/AM/Template.cfm?Section=Fact_Sheets1&Template=/CM/ContentDisplay.cfm&ContentID=8936

Jadad, A. R.., & Browman G.P. (1995). The WHO analgesic ladder for cancer pain management: Stepping up the quality of its evaluation. *Journal of the American Medical Association, 274*, 1870-1873.

Jong, K., Vale, P.J., & Armstrong, B.K. (2005). Rural inequalities in cancer care and outcome. *The Medical Journal of Australia, 182*(1), 13-14.

Juarez, G. F., Ferrell, B. & Bornemna, T. (1999). Cultural considerations in education for cancer pain management. *Journal of Cancer Education, 14*(3), 168-173.

Kelley, M. L. (2007). Developing rural communities' capacity for palliative care: a conceptual model. *Journal of Palliative Care, 23*(3), 143-153.

Krishna, R. P., Poulose, J.V., Tan, B.S., & Goh, C. (2010). Opioid use amongst cancer patients at the end of life. *Annals of Academic Medicine of Singapore, 39*(10), 790-797.

Kroenke, K., Theobald, D., Wu, J. tu, W., & Krebs, E.E. (2012). Comparative responsiveness of pain measures inn cancer pain. *The Journal of Pain, 13*(8), 764-772.

Larue, F., Colleau, S.M., Brasseur, L., & Cleeland, C.S. (1995). Multicentre study of cancer pain and its treatment in France. *BMJ, 310*, 1034-1037.

Mantyh, P. (2006). Cancer pain and its impact on diagnosis, survival and quality of life. *Nature Reviews Neuroscience, 7*, 797-809. doi:10.1038/nrn1914

Maxwell, K. (2012). The challenges of cancer pain assessment and management. *Ulster Medical Journal, 81*(2), 100-101.

McNeill J.A., Reynolds J., & Ney, M.L. (2007). Unequal quality of cancer pain management: disparity in perceived control and proposed solutions. *Oncology Nursing Forum,* 34(6):1121–1128.

Morita, T., Tsunoda, J., Inoue, S., & Chihara, S. (2001). Effects of high dose opioids and sedatives on survival in terminally ill cancer patients. *Journal of Pain Symptom Management, 21*(4), 282-289.

Morrison, R., Wallenstein, S., Natale, D.K., Senzel, R.S., & Huang, L.L. (2000). "We don't carry that"-Failure of pharmacies in predominantly nonwhite neighborhoods to stock opioid analgesics. *New England Journal of Medicine, 342*(14), 1023-1026.

Myers, J. & Shetty, N. (2008). Going beyond efficacy: Strategies for cancer pain management. *Current Oncology, 15*, S41-S49.

National Breast Cancer Foundation, I. (2012). *National Breast Cancer Foundation*. Retrieved from Breast Pain: http://www.nationalbreastcancer.org/breast-pain

National Institutes of Health, National Cancer Institute. (2014, January 30). *Pain (PDQ)*. Retrieved from Pharmacologic Management: http://www.cancer.gov/cancertopics/pdq/supportivecare/pain/HealthProfessional/page3

National Institutes of Health, U.S. National Library of Medicine. (2013, September 20). *Lung-cancer non-small cell*. Retrieved from MedLine Plus: http://www.nlm.nih.gov/medlineplus/ency/article/007194.htm

Nersesyan, H. &. Slavin, K.V. (2007). Current aproach to cancer pain management: Availability and implications of different treatment options. *Therapeutics and Clinical Risk Management, 3*(3), 381-400.

Okie, S. (2010). A flood of opioids, a rising tide of deaths. *New England Journal of Medicine, 363*, 1981-1985. doi:10.1056/NEJMp1011512

Okuyama, T. W. (2004). Adequacy of cancer pain management in a Japanese Cancer Hospital. *Japanese Journal of Clinical Oncology, 34*(1), 37-42.

Onega, T., Duell, E.J., Shi, X., Wang, D., Demidenko, E., & Goodman, D. (2008). Geographic Access to Cancer Care in the U.S. *Cancer, 112*(4), 909-918.

Paice, J. A., & Ferrell, B. (2011). The management of cancer pain. *Cancer Journal for Clinicians, 61*, 157-182.

Pain & Policy Studies Group, University of Wisconsin School of Medicine and Public Health, Carbone Cancer Center. (2013, June 3). *Achieving balance in state pain policy: A progress report card.* Madison. Retrieved from States are addressing pain management for cancer patients better than ever: http://www.acscan.org/content/states-are-addressing-pain-management-for-cancer-patients-better-than-ever/

Pargeon, K.L., & Hailey, B.J. (1999). Barriers to effective cancer pain management: A review of the literature. *Journal of Pain and Symptom Management, 18*(5), 358-368.

Parsons, H.A., Shukkoor, A., Quan, H., Delgado-Guay, M.O., Palmer, J.L., Fainsinger, R., Bruera, E. (2008). Intermittent subcutaneous opioids for the management of cancer pain. *Journal of Palliative Medicine, 11*(10), 1319-1324.

Payne, R. (2000). Chronic Pain: Challenges in the Assessment and Management of Cancer Pain. *Journal of Pain and Symptom Management, 19*, S12-S15.

Phillips, C.J. (2003). Pain management: health economics and quality of life considerations. *Drugs, 63*(2), 47-50.

Portenoy, R. & Lesage, P. (1999). Management of cancer pain. *The Lancet, 353*, 1695-1700.

Portenoy, R. (2011). Treatment of cancer pain. *Lancet, 377*, 2236-2247.

Rana, S., Gupta, R., Chaudhary, P., Khurana, D., Mishra, S., Bhatnagar, S. (2011). Cancer pain management: basic information for the young pain physicians. *Indian Journal of Palliative Care, 17*(2), 127-130. doi:10.4103/0973-1075.84533.

Randall-David, E., Wright, J., Porterfield, D.S., & Lesser, G. (2003). Barriers to cancer pain management: home-health and hospice nurses and patients. *Support Care Cancer, 11*, 660-665.

Research and Markets. (July 2013). *Pain Management Therapeutics Market to 2019 -
Impact of Patent Expiries Offset by Demand for Neuropathic and Rheumatoid
Pain Medications and Strong Pipeline.*

Ripamonti, C. S., Santini, D., Maranzano, E., Berti, M., Roila, F., & ESMO Guidelines
Working Group (2012). Management of cancer pain: ESMO Clinical Practice
Guidelines. *Annals of Oncology, 23*(7), 139-154.

Robinson, C. A., Pesut, B., Bottorff, J.L., Mowry, A., Broughton, S., & Fyles, G. (2009).
Rural palliative care: A comprehensive review. *Journal of Palliative Care, 12*(3),
253-258.

Rural Assistance Center. (2013). *South Carolina*. Retrieved from
http://www.raconline.org/states/south-carolina/

Sandoval, J., Furlan, A.D., Mailis-Gagnon, A. (2005). Oral methadone for chronic
noncancer pain: a systematic literature review of reasons for adminsitration,
prescription patterns, effectiveness and side effects. *Clinical Journal of Pain, 21*,
503-512.

Schafer, M. (2010). Opioids in pain management. In I. A. Pain, & A. P. Kopf (Ed.),
Guide to pain management in low-resource settings (pp. 39-45). Seattle.

Serlin, R., Mendoza, T.R., Nakamura, Y., Edwards, K.R., & Cleeland, C.S. (1995). When
is cancer pain mild, moderate or severe? Grading pain severity by its interference
with function. *Pain, 61*(2), 277-284.

Siegel, R., Ma, J., Zou, Z., & Jemal, A. (2014). Cancer statistics, 2014. *Cancer Journal
for Clinicians, 64*(1): 9-29.

Simmons, C.P., Macleod, N., & Laird, B.J. (2012). Clinical Management of Pain
Advanced Lung Cancer. *Clinical Medicine Insights: Oncology*(6), 331-346.

Society of Obstetricians and Gynecologists in Canada. (2011). Substance use in
pregnancy. *Journal of Obstetrics and Gynaecology Canada, 33*(4), 367-384.

South Carolina Cancer Alliance (2010). *Lung Cancer in South Carolina.* Retrieved from
South Carolina Cancer Alliance:
http://www.sccanceralliance.org/UserFiles/2010%20Cancer%20Report%20Card9
%20Lung%20Cancer.pdf

South Carolina Cancer Alliance (2011). South Carolina cancer control plan: 2011-2015.
Retrieved from South Carolina Department of Health and Environmental Control:
http://wwwprod.dhec.sc.gov/Health/docs/scca_cancerplan.pdf

South Carolina Department of Health and Environmental Control(SCDHEC), S. C. (2009). *SCANG*. Retrieved from Cancer Mortality: http://scangis.dhec.sc.gov/scan/cancer2/mortinput.aspx

South Carolina Department of Health and Environemntal Control. (2009). *SCANG*. Retrieved from Cancer incidence: http://scangis.dhec.sc.gov/scan/cancer2/incinput.aspx

South Carolina Office of Rural Health. (2013, September). *South Carolina Office of Rural Health*. Retrieved from www.scorh.net

Rana, S., Gupta, R., Chaudhary, P., Khurana, D., Mishra, S., & Bhatnagar, S. (2011). Cancer Pain Management: Basic Information for the Young Pain Physicians. *Indian Journal of Palliative Care, 17*(2), 127-130.

Sun, V., Borneman, T., Piper, B., Koczywas, M., & Ferrell, B. (2008). Barriers to pain assessment and management in cancer survivorship. *Journal of Cancer Survivorship, 2*, 65-71.

Susan G. Komen Foundation. (2014). *Metastatic Breast Cancer (Stage IV or Advanced Breast Cancer) Introduction*. Retrieved from Understanding Breast Cancer: http://ww5.komen.org/Content.aspx?id=19327354391

Syrjala, K. C. (1984). Measurement of clinical pain: A review and integration of research findings. In B. C. (ed):, *Advances in Pain Research and Therapy.* New York: Raven Press.

Thapa, D., Rastogi, V., & Ahuja, V. (2011). Cancer pain management-current status. *Journal of Anaesthesiology & Clinical Pharmacology, 27*(2), 162-168.

The Unviersity of Chicago-Medicine. (2012). *Univeristy of Chicago Medicine Press Release*. Retrieved from Evidence mounts for the link between opioids and cancer growth: http://www.uchospitals.edu/news/2012/20120321-opioid.html

Tollefson, J., Usher, K., & Foster, K. (2011). Relationships in pain: The experience of relationships to people living with chronic pain in rural areas. *International Journal Nursing Practice, 17*, 478–485.

Trescot, A.M. (2010). Review of the role of opioids in cancer pain. *Journal of the National Comprehensive Cancer Network, 8*, 1087-1094.

United States Census Burerau. (2010). 2010 census urban and rural classification and urban area criteria. Retrieved from http://www.census.gov/geo/reference/ua/urban-rural-2010.html.

United States Department of Agriculture (USDA), Economic Research Service (2013). *Rural-urban commuting area codes.* Retrieved from http://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx

United States Department of Health and Human Services. (n.d.). *Centers for Disease Control and Prevention*. Retrieved from Cancer Prevention and Control, State Cancer Facts: http://apps.nccd.cdc.gov/statecancerfacts/state.aspx?state=South Carolina

US Department of Health and Human Services, A. f. (1994). *Clincal practice guideline for cancer pain management.* Rockville, MD.

Verhoef, M.J., Vanderheyden, L.C., & Fonnebo, V. (2006). A whole systems research approach to cancer care: Why do we need it and how do we get started? *Integrative Cancer Therapies, 5*, 287-292.

Von Roenn, J. H., Cleeland, C.S., Gonin, R., Hatfield, A.K., Pandya, K.J. (1993). Physician attitudes and practice in cancer pain management. A survey from the Eastern Cooperative Oncology Group. *Annals of Internal Medicine, 119*(2), 121-126.

Wade, M. (2013). Opioid rotation can improve pain control and reduce neurotoxicity for cancer patients. *OncoLog, 58*(9).

Ware, J. E., Snyder, M.K., Wright, W.R., & Davies, A.R. (1983). Defining and measuring patient satisfaction with medical care. *Evaluation & Program Planning, 6*(3-4), 247-263.

Watanabe, S. M., Fairchild, A., Pitusking, E., Borgersen, P., Hanson, J., & Fassbender, K. (2013). Improving access to specialist multidisciplinary palliative care consultation for rural cancer patients by videoconferencing: Report of a pilot project. *Support Cancer Care, 21*, 1201-1207. doi:10.1007/s00520-012-1649-7

Weisse, C. S., Sorum, P.C., Sanders, K.N., & Syat, B.L. (2001). Do gender and race affect decisions about pain management? *Journal of General Internal Medicine, 16*, 211-217.

WHO. (1996). *Cancer pain relief.* Geneva, Switzerland: World Health Organization.

Yoong, J., Traeger, L.N., Gallagher, E.R., Pirl, W.F., Greer J.A., & Temel, J.S. (2013). A pilot study to investigate adherence to long-acting opioids among patients with advanced lung cancer. *Journal of Palliative Medicine, 16*(4), 391-397.