2016

Comparing The Quality Of End Of Life Cancer Care In The Medicare Population Prior To And After The Enactment Of The Medicare Prescription Drug, Improvement And Modernization Act Of 2003

Rene Jooste
University of Alabama at Birmingham

Recommended Citation

Jooste, Rene, "Comparing The Quality Of End Of Life Cancer Care In The Medicare Population Prior To And After The Enactment Of The Medicare Prescription Drug, Improvement And Modernization Act Of 2003" (2016). *All ETDs from UAB*. 2074.
https://digitalcommons.library.uab.edu/etd-collection/2074

COMPARING THE QUALITY OF END OF LIFE CANCER CARE IN THE MEDICARE POPULATION PRIOR TO AND AFTER THE ENACTMENT OF THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT AND MODERNIZATION ACT OF 2003

by

RENE JOOSTE

MEREDITH KILGORE, COMMITTEE CHAIR
MARIE BAKITAS
CARLA FALKSON
RODNEY TUCKER
ROBERT WEECH-MALDONADO

A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

2016

COMPARING THE QUALITY OF END OF LIFE CANCER CARE IN THE MEDICARE POPULATION PRIOR TO AND AFTER THE ENACTMENT OF THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT AND MODERNIZATION ACT OF 2003

RENE JOOSTE

PHD PROGRAM IN ADMINISTRATION-HEALTH SERVICES

ABSTRACT

Reimbursement for chemotherapy could account for two thirds of the income for oncologists in private practice. The Medicare prescription drug improvement and modernization act of 2003 (MMA) brought about a dramatic change in the way physicians were reimbursed for delivering chemotherapy in an attempt to slow the skyrocketing costs of drugs and Medicare costs for covering these drugs . The MMA reduced Medicare reimbursements for covered outpatient prescription drugs from 95% to 85% of the average wholesale price. In 2005, a new payment system was instituted that reimbursed fee-for-service providers for drugs at the national average sales price plus 6%. Aggressive treatment at end of life in the oncology population does not improve quality of life and during the 1990's a crisis was identified in end of life care in the U.S. Timely cessation of chemotherapy treatment and timely referral to hospice are two quality indicators which have been validated to be identified from insurance claims to measure quality end of life care. The study aims to study the quality of end of life care received by Medicare beneficiaries who died in the period 1999-2010 with a primary or secondary diagnosis of cancer, using the two abovementioned validated quality indicators.

Keywords: Medicare prescription drug improvement and modernization act of 2003 (MMA), end of life care, cancer, chemotherapy, hospice

ACKNOWLEDGEMENTS

.

My dissertation chair and mentor, Dr. Meredith Kilgore is a mentor with endless patience who always provides encouragement. He has been instrumental throughout this journey challenging me and keeping me focused. He was always available to provide assistance. I am also very grateful to my other dissertation committee members—Marie Bakitas, Carla Falkson, Robert Weech-Maldonado, and Rodney Tucker for sharing their knowledge and expertise during this process and for taking time to read this manuscript and provide valuable feedback.

My husband and children have always been supportive and without their love and support this would not have been possible. Thank you Theo, Ingrid, Cornelis, Christiaan and Wynand.

TABLE OF CONTENTS

CHAPTER

LIST OF TABLES

Table *Page*

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

The objective of this study is to compare the quality of end of life cancer care in the United States (U.S.) in the Medicare population using two quality indicators: timely cessation of chemotherapy and timely referral to hospice.

Background

Care at the end of life is a very sensitive and complicated area of medical decision making for health care providers as well as patients' and their families. Quality of life is a prominent topic in any discussion involving treatment of terminal diseases. When aggressive treatment options are chosen for cancer patients in the last weeks of their lives, quality of life is affected, often with no significant survival benefit.

Two important studies done in the 1990's, were the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT), and the Hospitalized Elderly Longitudinal Project (HELP). The studies highlighted the needs and preferences of dying patients. As a result of these studies, the Robert Wood Johnson Foundation (RWJF) identified a crisis in end of life care in the U.S. and launched a national program named "Promoting Excellence in End-of-Life Care". The study results showed that more than half of patients died while experiencing pain, between a third and a half of the caregivers were bankrupted in the process, and decisions about end of life care were either unknown or not carried out by the treating physicians according to the patients' wishes (Knaus et al., 1995). Decisions about care at the end of life ultimately resides with the patient with cancer, but many additional role players and other external factors may influence the outcome of the initial wishes of the patient.

In the last two decades there has been a movement to examine the quality of end of life care in oncology, and identify reasons for slow implementation or acceptance of the inclusion of palliative care in the continuum of oncology treatment.

The urgency for this research is heightened by the economics of cancer care, and escalating costs of treating, especially older patients, at the end of life with overly aggressive expensive treatments with no expectation of cure.

There is no easy answer to the complex question of when the exact time has come to stop potentially curative treatment and only provide palliation. The question arises, what would be indicators of a "good death", or "quality" end of life care for cancer patients. The published research on this subject could be categorized into two main groups, institution-based studies, where medical records could be accessed, and retrospective studies on deceased patients that could be either population or institution based.

The War on Cancer

The World Health Organization (WHO) has a definition of palliative care which includes the statement "Palliative care affirms life and regards dying as a normal process" (WHO, 2016). Cancer is a disease that enjoys a tremendous amount of media coverage in the U.S. When an incurable disease is involved, emotions can play heavily into decision making on the personal, professional and public health organizational levels. Television, radio, magazines and the internet abound with advertisements for specific cancer drugs and treatment centers.

When U.S. President Richard Nixon signed the National Cancer Act into law in 1971, he laid the foundation for the National Cancer Institute (NCI) to have special autonomy within the National Institutes of Health with a substantial budget (Sporn, 1996). This act ensured $100 million funding for the aggressive pursuit of finding a cure for cancer, and is often referred to as the “War on Cancer”. The culture of “fighting” the disease until the very end is strongly ingrained and enforced through the extensive media emphasis on treatments and drugs. This is in contrast to the abovementioned WHO palliative care definition which regards dying as a normal process. In this cultural environment, not opting for treatment may be seen as a failure to take the “fight” to the end.

Economic Implications

The annual report of the American Cancer Society estimated 595,690 cancer deaths for the year 2015 (American Cancer Society Cancer Facts and Figures, 2015). A large percentage of these deaths occur in the over 65 year age group. The incidence of a number of types of cancer tends to increase approximately exponentially with age and the mortality rates also increases with age. The Centers for Medicare and Medicaid Services (CMS) estimate that the U.S. will spend $4.3 trillion annually on healthcare by the year 2019, which would constitute 19.3% of the gross domestic product (Schnipper et al., 2012). Reducing costs is one of the top priorities of the Affordable Health Care Act, and evidence-based decision making in healthcare is essential for the sustainable future delivery of quality care.

Cancer treatments have evolved to levels of enormous sophistication and are today targeting specific cells which are modeled to be a fit for a very specific genetic profile identified in tumor cells. This kind of therapy is referred to as targeted therapy and is the basis for a vast number of both pre-clinical and clinical investigations in oncology today. As a consequence, these developments have dramatically escalated the cost of cancer treatments. The cost of treating especially older patients with cancer has risen steadily over the last decades. Previous published studies revealed a trend of increasing use of chemotherapy in older patients with cancer at the end of life (Earle et al., 2008). A recent study compared the costs of poor prognosis cancer patients enrolled in hospice to those not enrolled, and report significantly lower aggressive interventions at end of life which result in lower costs (Obermeyer et al., 2014).

With the looming retirement of increasingly large numbers of Baby Boomers who will be eligible for Medicare, the economic implications of aggressive end of life treatment are substantial, and the upward trend in escalating costs is unsustainable in the long term.

Medicare Reimbursement for Chemotherapy

For the last two decades, the costs of delivering care to beneficiaries in the last year of life remained stable at approximately 25% of total Medicare expenditures (Hogan, Lunney, Gabel, & Lynn, 2001). Since more than 80% of adults who die are Medicare beneficiaries, it is evident that financing end of life care is a significant component of the country’s Medicare budget.

Medicare’s financing of end of life care comprises a variety of mechanisms. Providers include hospitals, hospice, home health services, skilled nursing facilities and physician services. The provider type determines the fee for service payment system, e.g. hospitals are paid per diagnosis-related-group (DRG) system for inpatient services, hospice services are paid per diem, skilled nursing facilities and home health aides are on a prospective payment system and physicians are reimbursed on a prospective fee-for-service basis per visit. There are also managed care organizations contracted by Medicare to provide these services and they are paid a capitated monthly risk-adjusted fee (Buntin & Huskamp, 2002). These different options for payment, each with their unique administrative burden, complicate the coordination of end of life care. These payment systems influence end of life care in a number of significant ways.

In the study period, enrolling in hospice disqualified the enrollee for any additional treatment with curative intent. Hospice enrollment was also limited to patients with a certified life expectancy of less than six months. These limitations discouraged many patients from enrolling in hospice at the ideal time.

Medicare coverage for nursing homes and home health services are aimed towards patients with a potential for regaining their function, and therefore not available to patients who need terminal care in these settings. Approximately 38% of Medicare decedents will be in nursing homes for a part of the last year of their life. Medicare coverage for skilled nursing home stays is limited, and after twenty days significant co-payments are charged.

The types of payments may influence providers due to varying financial incentives. For inpatient services reimbursed by DRG, the expectation would be that a provider would strive for less treatment. The payment from Medicare would be the same for the same DRG, regardless of the services rendered. Physicians, who are paid per visit, could be incentivized to provide more services. Jacobson and colleagues investigated the influence of reimbursement on chemotherapy treatment and found that although reimbursement did not significantly influence the decision to give or not give treatment, higher reimbursed providers were more likely to prescribe more expensive therapy when the decision to give chemotherapy had been made (Jacobson et al, 2006).

During the period being studied, there was no financial incentive for physicians to spend time on end of life conversations or advance care planning meetings, since there was no code to bill for these services. This discouraged caregivers to provide these essential communication opportunities that could assist them in taking informative decisions at the end of life. In the population of people with cancer, effective communication with a patient who reached advanced disease stage could make a significant difference in health care costs in the final week of life as shown by Wright and Zhang & colleagues (Wright et al., 2008; Zhang et al., 2009). Zhang and colleagues (2009), reporting on the NCI’s Coping With Cancer study, show a 35.7% lower average cost for intensive care unit and hospital stays, hospice care and life sustaining procedures received in the last week of life, for those patients who reported having an end of life discussion at the time of the diagnosis of their advanced cancer.

Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA)

On December 8, 2003, U.S. President George W. Bush signed a new federal law, the MMA, to improve member benefits and introduce cost savings. A significant element of the MMA provided Medicare beneficiaries voluntary access to a prescription drug coverage plan, referred to as Medicare Part D. Chemotherapy drugs given intravenously are mostly covered under Part B of Medicare, while the oral drugs are covered under Part D. The decision to continue to include the expensive intravenous chemotherapy drugs in Part B was mostly for financial and political reasons- there was concern that the MMA with Part D would not be confirmed through the legislature if Part D included these expensive drugs (Downs, 2007). Before the enactment of MMA, these infusion drugs were covered under Medicare Part B, hence the argument not to change this to the new Medicare Part D outpatient prescription drug benefit. Presently, chemotherapy is increasingly administered in hospital outpatient clinics and physicians' offices and not in the inpatient setting.

Reimbursement for chemotherapy could account for two thirds of the income for oncologists in private practice. An important change in the way physicians received reimbursement for oncology drugs and the administration thereof in the outpatient setting was contained in the MMA and this caused a considerable reduction in the reimbursement to physicians providing these services (Downs, 2007; Friedman et al., 2007).

Before MMA, physicians could buy chemotherapy drugs from pharmaceutical companies at discounted prices and their reimbursement exceeded their costs. In some examples, the Medicare reimbursement was three times that of the acquisition costs of the drugs (Siegel, 2006). The MMA tried to address this imbalance by reducing payment for chemotherapy drugs and aligning reimbursement more closely to market prices.

There was concern at the time of the enactment of the law that the MMA would cause private oncology practices to close on a nationwide scale, forcing patients to travel longer distances to receive chemotherapy. Little evidence could be found in the literature that the MMA affected wait times or access to chemotherapy treatment (Friedman et al., 2007; Jacobson et al., 2006; Shea et al., 2008). Jacobson, Shea and colleagues investigated wait times for chemotherapy initiation and travel distances to treatment centers for the 2003-2006 period and found no major changes. Friedman and colleagues looked at the impact of reimbursement on costliness of drugs prescribed in 1995 and 1998 and found no support for the influence of reimbursement on prescribing patterns.

Guidelines on end of life care

During the 1990's, various organizations were involved in a national effort to provide guidelines and quality indicators for end of life care. A summary of the major efforts in the study period follows.

In 2001, five palliative care organizations met and discussed the development of guidelines or standards for palliative care with the objective to improve the quality of end of life care. The organizations were The American Academy of Hospice and Palliative Medicine (AAHPM – the physician membership association), The Center to Advance Palliative Care (CAPC – a palliative care advocacy and information organization), The Hospice and Palliative Nurses Association (HPNA – the nursing membership association), the National Hospice and Palliative Care Organization (NHPCO – the hospice membership organization), and the Last Acts Partnership (a consumer organization- now part of NHPCO). This resulted in the establishment of the National Consensus Project for Quality Palliative Care and the publishing in 2006 of a document titled Clinical Guidelines for Quality Palliative Care. Eight domains of care were identified that were considered essential for palliative care practice, one of them being the care of the patient at the end of life. The eight domains included in these guidelines are structure and processes of care, physical aspects of care, psychological and psychiatric aspects, social aspects of care, spiritual, religious, and existential aspects of care, cultural aspects of care, care of the patient at the end of life, and ethical and legal aspects of care. The guidelines were revised in 2009 and 2013 and more organizations joined in the collaboration (Ferrell et al., 2007). Another organization which published guidelines for end of life care in 2001 was the National Comprehensive Cancer Center Network.

In 2006, a national symposium organized by the Agency for Health Care Research and Quality (AHRQ) and the NCI focused on discussions about developing quality of life indicators for end-of-life care and identified eight key domains, two of which were communication about end-of-life treatment and care transitions. Ten evidence-based measures or indicator sets were identified, of which the following three included measures for end-of-life cancer treatment and hospice use: Dana-Farber, Cancer Care Nova Scotia (CCNS), and Georgia Cancer Coalition. The Dana Farber measure of “chemotherapy in the last 14 days of life,” defines more than 10% of a sample of patients receiving chemotherapy in the last 14 days of life as an indication of poor quality care. The measure “late referral to hospice” defines more than 8% of a sample of dying cancer patients referred less than three days before death as an indication of poor quality care (Lorenz et al., 2006).

In 2008, the AHRQ again collaborated with the NCI on a National Symposium involving multiple disciplines involved with end of life care to discuss the measurement of end of life quality, existing barriers and potential solutions. Evidence-based measures or indicator sets were identified, including timely cessation of aggressive therapy and timely referral to hospice (Seow et al., 2009). The symposium results highlighted the importance of patient-reported outcomes, which is an area vastly underrepresented in published end of life care research. Reporting of results of specific interventions to improve quality was also absent, and this would be imperative in measuring the effect of a specific intervention. The most challenging domains to measure are the ones involving psychosocial care, for which the conclusion was that both patient and family perspective would be essential.

Several academic cancer organizations issued guidelines to their members on appropriate end of life care. The American Society of Clinical Oncology (ASCO) includes chemotherapy cessation in the last two weeks of life and hospice referral more than three days before death as measures of the quality of end of life care in their Quality Oncology Practice Initiative (QOPI) (Kao, Shafiq, Vardy, & Adams, 2009). The QOPI initiative was launched in 2006 and membership has grown to include 1008 U.S. based and 30 international practices as of August 2014. The latest data analyses performed in the fall of 2010, showed a significant improvement in a number of end of life quality measures for those practices who had participated for a number of years compared to those reporting for the first time (Campion, Larson, Kadlubek, Earle, & Neuss, 2011).

The U.S. Advancing Medical Professionalism to Improve Health Care foundation partnered with nine medical specialties and in April 2012, a campaign was launched in the U.S. named “Choose Wisely” (Ferguson, 2012). There are more than 376,000 physicians represented in this campaign, including members of ASCO. The objective of this campaign is to encourage physicians to cut back on tests and treatments that have been shown to be of little value to their patients. One of the treatments listed as being overused is the treatment of very sick cancer patients with chemotherapy. Each medical society was requested to provide five treatments or tests that they thought could be questioned regarding their necessity. The active participation in this campaign by the physicians could be seen as a realization of the significance of overcoming the barriers to appropriate, cost- effective, evidence- based clinical care, including end of life care.

In February of 2012, the National Quality Forum (NQF) announced approval of endorsement of fourteen measures for palliative and end-of-life care. NQF is a standards-setting organization and contributions of quality measures for approval and endorsement are voluntary. Four of these measures were from the RAND corporation group and five from University of North Carolina, while twelve of the fourteen endorsed measures were newly submitted.

Quality Indicators

Measuring quality through validated quality indicators is the first step towards identifying areas of poor quality of end of life care. This would facilitate addressing areas where education and measures of intervention could be identified which could be focused on improving the quality of end of life care. Two validated quality indicators used to measure end of life care using administrative claims data are timely cessation of chemotherapy and referral to hospice. Research by Earle (2003, 2006, 2008) and Emanuel (2003) support that these indicators can be successfully extracted from administrative data such as Medicare claims. Earle and colleagues concluded that hospitalization and emergency room admissions in the last six months are not accurate indicators when using claims data, since the concomitant morbidities could not be ruled out as the main reason for the treatment received.

Reasons for Aggressive End of Life Care

Various explanations could be given for the incidence of aggressive overtreatment of older cancer patients. Some patients buy into the popular culture portrayed in the media and try to fight their disease until the very end. Family members could be insistent upon multiple regimens due to avoidance of facing the inevitable outcome of a terminal disease. Cultural and religious influences may dictate the choices made when approaching end of life.

Physicians are faced with demanding time constraints on their face time with patients, and the end of life discussion that should take place at the onset of cancer treatment is often absent from the treatment planning. Some physicians may be very optimistic about the possibility of exciting novel treatments and not base their decisions on the appropriate time to end treatment on evidence.

During the period under study, there was no Medicare reimbursement for spending time with patients to perform end-of-life discussions. Physicians were better compensated for delivering chemotherapy or ordering expensive radiologic examinations than for conducting a discussion on end of life care and referring the patient to other health care providers. Estimates of survival time could be very unrealistic from both the patient and the treating physician perspectives. All these factors and more could cause overtreatment of patients that have no proven value of cure or prolonged survival with quality of life.

In October of 2015, the Centers for Medicare and Medicaid Services (CMS) approved payment for physicians for end-of-life consultations. The expectation is that such a discussion would include advance care planning, hospice care and other end-of-life issues (Lowes, 2015). The initial proposal received strong resistance and a political uproar. Opponents of this proposal were of the opinion that reimbursing physicians for such a consultation could result in so called “death panels”, dictating the fate of sick elderly patients.

Palliative Care and Hospice

Palliative care programs and hospice are perceived as methods of reducing costs of medical care at the end of life. These end of life care options have different approaches that overlap in some aspects. Palliative care is a disease management approach where relief of physical suffering is augmented with psychosocial and spiritual support. Hospice care is palliative care directed at patients with a life expectancy of less than six months and is most often provided at home (Schulman-Green, Ercolano, Jeon, & Dixon, 2012).

End of life services have been covered by Medicare since 1983 and include nursing care, counseling, palliative medications and up to five days of respite care for family caregivers. To qualify for coverage under Medicare, a physician has to certify that the expected survival is no longer than six months. Coverage can be continued if survival exceeds six months by recertification of the eligibility for coverage. Hospice use increases with age and is higher amongst women and white beneficiaries (Riley & Lubitz, 2010).

Three important new developments announced in 2016 aim to improve the Medicare hospice benefit. The per diem reimbursement was changed to a two tier system where per diem payments are higher in the first sixty days and lower thereafter. The second change is the reimbursement for physicians for performing advanced care planning discussions. Lastly, there is the new Medicare Care Choices Model which allows patients to receive hospice benefits from specific hospice facilities while receiving potential curative treatments. There are 140 hospice facilities participating in this program. The hospice providers are reimbursed with a monthly fee for providing the supportive care. With these three changes, Medicare aims to improve the quality of end of life care for patients with terminal illnesses

Availability of palliative care units or professionals and hospice play an important role in the planning of end of life care. The hospice industry in the U.S. has undergone some substantial changes in the last twenty years. In a longitudinal study of hospices for the period from 1999-2009, Thompson and colleagues found that one fifth of the hospices active in 1999 had closed or withdrawn from the program by 2009 and more than 40% had undergone a change or changes in ownership. Most prominent was a shift from non-profit to for-profit status. There was also a shift to larger organizations in this period, and the proportion of hospices with 100 or more fulltime employees doubled to 5% in this period. The Medicare Payment Advisory Commission estimated that there were 3,555

Medicare-certified hospices in the U.S. in 2010 with proportionally more concentrated in the South and the West (Thompson, Carlson, & Bradley, 2012).

When investigating and comparing the availability of palliative care services in NCI and non-NCI cancer centers in the U.S. in 2009, Hui and colleagues found that NCI cancer centers were significantly more likely to have a palliative care program which includes at least one palliative care physician, an inpatient palliative care team and an outpatient palliative care program. Very few centers had dedicated palliative care beds or a hospice which was operated by the institution (Hui et al., 2010).

Several studies document lower Medicare expenditures at end of life for beneficiaries from all disease areas enrolled in hospice, but they are mostly non-randomized, retrospective and bias is problematic (Banaszak-Holl & Mor, 1996; Gray, MacAdam, & Boldy, 1987; Kidder, 1992). Kheirbek and colleagues reviewed 8032 Medicare beneficiaries who were hospitalized for heart failure in over a hundred hospitals in Alabama for the period 1998-2001. They report that a discharge to hospice referral was associated with lower re-admissions, but the majority of patients who died within six months of discharge did not receive a hospice referral (Kheirbek., et al, 2015).

The wish of a terminally ill patient is most often to die at home surrounded by family and loved ones, yet over a third of patients in the U.S. die in hospitals and intensive care units (McKinney, 2010). Overtreatment at end of life not only challenges the public health system but is also an ethical dilemma in the palliative care environment.

End of life care is one of the topics being reported on in the Dartmouth Atlas. Health policy experts and health services researchers recognize the Dartmouth Atlas as a primary source of information on variation in health services and use this extensively.

The Dartmouth researchers make use of a population based small area analysis to hone in on specific regions and patients using specific hospitals or physician services. In the latest report on end of life care based on Medicare cancer patient deaths between 2003 and 2007, it was noted that 29% of the patients died in a hospital (Mitchell, 2011).

Summary

The last two decades have been witness to a multitude of incentives to focus attention to end of life oncology care. The goal is to strive for minimal aggressive treatments towards the end of life with timely involvement of hospice care to ensure adequate palliation and the possibility of avoiding death in a hospital or intensive care unit.

More than half of annual cancer deaths in the U.S. occur in patients over 65, which renders the Medicare claims a suitable sample to analyze for the quality indicators of chemotherapy cessation and hospice involvement. Timely referral to hospice has been shown to be associated with less aggressive therapy at end of life. Analyzing the two quality indicators over a period including prior to and after the MMA, could provide useful insight into the difference, if any, between the delivery of end of life care before and after the MMA. This could confirm if legislation driven reimbursement changes influence the prescription patterns of physicians. Furthermore, it could help identify focus areas for additional initiatives to address overtreatment with no additional survival benefit and substantial cost implications.

CHAPTER 2

LITERATURE REVIEW AND CONCEPTUAL FRAMEWORK

Prognostication

Estimating when a patient with advanced cancer will die is one of the challenges facing the treating physician as well as the patients and their families. Contrary to the popular portrayal in the media of a physician communicating to a patient exactly how many weeks or months of life they have left, this is an area where most physicians prefer to avoid any such time frames during this conversation. The skill of predicting life expectancy is referred to as “prognostication”. Honest and open discussion, giving the patient accurate information regarding life expectancy and quality of life to be expected with various options of palliation, forms an integral part of the end of life care continuum.

Prognosis in oncology patients with advanced disease consists of two main methods: clinical prediction of survival (CPS) and actuarial estimation of survival (AES). CPS makes use of the treating physician’s clinical expertise using clinical indicators, whilst AES is based on the performing of indexes and scores which are then compared to evidence-based norms defining specific mortality data points. The two methods can be used in combination to determine prognosis. AES has become an important tool in the last decade, and the focus is shifting from mostly clinical tumor-related indicators to an assessment of the patient individually and as a whole. Several web-based prediction risk calculators are now available to physicians treating patients with advanced cancer, such as Prognostat and the Memorial Sloan Kettering Cancer Center nomograms. These tools typically include risk calculators, and survival tables.

A survey conducted in the 1990s examined more than 700 physicians' attitudes towards prognostication. More than 50% of the oncologists reported that they felt inadequately trained in the field of prognostication (Christakis & Iwashyna, 1998). The majority of the survey respondents stated that they typically avoid being specific when asked about expected survival and would tend to be optimistic, especially if the patient had a personal optimistic outlook. Reasons given for reluctance were fear of feeling intimidated or judged by colleagues and patients if their estimate was inaccurate, patients wanting information that was too specific, and difficulty in formulating and communicating a prognosis.

There are a number of validated scoring systems available which combine clinical and laboratory data, e.g. the Palliative Prognostic Score, the Palliative Prognostic Index and the Terminal Cancer Prognostic score (Finlay & Casarett, 2009). These tools could be used to develop prognostication skills which would assist in recognizing patients that are ready to be referred to hospice. The tools are, however, no substitute for communication skills, which are vital when the end of life treatment period is reached.

It is important to know what the needs of the patient with advanced cancer are when the request for information of prognosis is received. There is the same general desire for all available information about disease and possible cure in the newly diagnosed and the advanced disease populations (Gripp et al., 2007; Jenkins, Fallowfield, & Saul, 2001). Patients who receive an estimate of 40% or less for surviving two months are more likely to initiate discussion on advanced directives with their treating physicians (Knaus et al., 1995). Emotional distress, especially symptoms of anxiety and depression, is prevalent in a significant group of patients with advanced cancer (Gripp., et al, 2007). Self- reporting of emotional status and qualitative status of indicators such as pain by the patient should ideally be combined with the clinical prognostic factors used by clinicians when formulating an estimate of survival.

Maltoni and Amadori (2002) remind their readers that prognostic information has at best probabilistic value, and therefore should be used with caution. A patient with a terminal diagnosis should therefore be evaluated as a unique individual and not the median of any given population. Clinicians, including oncologists, are prone to be overly optimistic when asked the question: “How long do I have to live?”(Glare et al., 2003). When patient and oncologist estimates of survival were compared in a study of 50 patients with advanced cancer and a median age of 63.5 years, the oncologists were overly optimistic in their predictions in 42% of cases and accurate in 32% of cases (Kao, Butow, Bray, Clarke, & Vardy, 2011).

Studies published about accuracy of prognostication in the oncology population typically report accuracy of between 30-40% (Christakis & Lamont, 2000; Tanneberger, Malavasi, Mariano, Pannuti, & Strocchi, 2002). Results from the SUPPORT (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment) study provided valuable information regarding the use of prognostic information in the quest to improve quality of life in patients faced with terminal disease. (Freeborn, Lynn & Desbiens, 2000).

A study done in Italy in 2011-2012 studied the use of a “surprise” question used by physicians when treating patients with advanced cancer. The premise was that using the question “Would you be surprised if this patient died in the next year?“ would be useful to improve prognostication and identify patients in need of palliative care. The study was small (231 patients) but the results showed higher accuracy of predicting survival when using this question (Moroni., et al, 2014).

Advance care planning (ACP) is an essential component of the palliative care continuum, and a patient-initiated conversation about ACP signifies understanding of a prognosis. When the decision needs to be made about switching from cure to care, more than only prognostic data need to be considered. The patient’s desires should be fulfilled and special attention given to psychological and spiritual needs. Other factors for consideration should be costs, treatment with investigational drugs in a clinical trial setting and expected quality of life with the different options (Maltoni & Amadori, 2002).

Measuring the Quality of End of Life Care

The question: “what constitutes a good death?” in the context of terminally ill cancer patients has no definitive answer. How does one measure the quality of life at the end of life? Traditionally, physicians used changes in clinical status as supported by laboratory and radiology data as the main criteria for making treatment decisions. Survival or disease-free survival was the most common endpoint for all oncology clinical trials two decades ago.

The importance of health-related quality of life (HRQOL) is today recognized by the Federal Drug Administration, and investigators are encouraged to include assessment of HRQOL in the design of oncology clinical trials. HRQOL involves patient reported subjective perception of their physical, emotional, social, and cognitive functions. Patients report on their disease symptoms as well as treatment side effects.

Measuring HRQOL has inherent obstacles, mainly due to the subjective nature of the reporting. This is exacerbated at the end of life, when cognitive function is often impaired and poses a challenge to self-reporting. The reliability of a measure is dependent on the ability of the subjects who have to complete the quality of life questionnaire. Family members could be used as reliable proxies to report on symptoms at the end of life in only a limited number of domains (Bakitas et al., 2008). Collecting HRQOL in a target population in the terminal phase of a disease presents many challenges, but researchers recognize the importance of this field of study and a number of studies explore the ability to extract HRQOL data from medical records.

Researchers from the Southern California Evidence-based Practice Center contracted by AHRQ, conducted research to identify quality measures and the evidence supporting them. The project was named the Cancer Quality-ASSIST (Assessing Symptoms Side Effects and Indicators of Supportive Treatment) project. The result was the development of evidence-based quality indicators which could be used to evaluate supportive cancer care by extracting information from medical records.

Indicators addressed in the ASSIST project are pain, dyspnea, depression, nausea and vomiting, diarrhea, fatigue, and information and care planning, including symptoms related to cancer, common complications, and treatment-related toxicities. The project was multi-disciplinary and included input from experts in the fields of geriatrics, internal medicine, and oncology. The method used was a systematic literature review followed by the RAND/University of California Los Angeles modified Delphi process. The Delphi method was originally designed by the RAND Corporation in the 1950’s and involves a group of experts who complete questionnaires typically containing questions requiring an answer scaled from one to nine, and receive feedback in the form of a statistical representation of the "group response," after which the process is repeated. The goal is to reach expert consensus.

The result was a final set of 42 indicators out of the initial 92 evaluated, which were found to be sufficiently feasible, reliable, and valid to be used in advance cancer care. The main domains identified were pain, dyspnea, fatigue, anorexia, nausea and vomiting, depression, treatment related toxicities, and information and care planning (Dy et al., 2010). Dy and colleagues (2011) subsequently evaluated 21 of the indicators from the ASSIST project that they considered to be most relevant to end-of-life care and concluded that they were useful as measures and could be used in the area of quality improvement. Referral to a palliative unit or hospice before death and informing the patient about chemotherapy intent, palliative or curative, are amongst the quality indicators in the domain of information and care planning that met the validity and feasibility criteria (Dy et al., 2011).

Trends in end of life care in study period

Chemotherapy

The definition of the period comprising “end of life” in patients with advanced cancer is a problematic one and consensus has not been reached. For most studies that use retrospective measurement of indicators, the end of life period is defined, e.g. the last six months of life. As discussed in the prognostication section, potential bias exists since the date of death is most often not precisely predictable.

The Institute of Medicine published a report in 1997 titled “Approaching Death: Improving Care at the End of Life”, wherein they find evidence of overtreatment with potentially curative regimens and under treatment with regimens that could enhance quality of life, i.e. pain control (Field & Cassel, 2011).

Earlier studies on the trends in chemotherapy given at the end of life are dominated by two authors, Emanuel and Earle. Earle and colleagues studied a large sample of the Medicare population who died between 1993 and 1996 within one year of diagnosis of lung, breast, colorectal or gastro-intestinal cancer. They defined the end of life period as the last six months of life and their sample was extracted from patients included in the Surveillance, Epidemiology and End Results (SEER) Medicare database. This database is a linkage of the SEER Program of the NCI and Medicare claims data for covered health services for beneficiaries from the point of eligibility to death. SEER cancer registries collect clinical, demographic and cause of death information for cancer patients and their Medicare claims for covered health care services from the time of Medicare eligibility until death. SEER includes eleven tumor registries; San Francisco/Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle/Puget

Sound, Utah, Atlanta, San Jose/Monterey, and Los Angeles. Aggressive chemotherapy in this study is defined as chemotherapy given in the last two weeks of life. There was an increase in the percentage of patients receiving chemotherapy in the last two weeks before death from 13.8% in 1993 to 18.5% in 1996 ($p<0.001$) (Earle et al., 2004).

In a retrospective cohort analysis of patients who died in Massachusetts and California in 1996, chemotherapy was frequently used in the last three months of life, regardless of the sensitivity of the tumor type to the treatment given (Emanuel et al., 2003). The percentage of patients in this cohort receiving chemotherapy in the last six months of life was more than 25%. In 2008, Earle and colleagues again reviewed the literature. In a cohort of all patients 65 years and older with cancer who died between 1991 and 2000 in the eleven regions listed above, the trend towards more aggressive chemotherapy at the end of life is continuing. The percentage of patients who received chemotherapy within two weeks of death increased from 9.7 % in 1993 to 11.6% in 1999 (Earle et al., 2008).

A number of smaller studies reported increased use of chemotherapy at end of life. At one Veteran’s Administration hospital, there was a significant increase in chemotherapy received in the last 30 days of life in 2008 compared with 2002 (Gonsalves et al., 2011). A study compared incidence of aggressive chemotherapy at end of life in ovarian cancer patients from 2002 to 2006, and found a statistically significant increase with no survival benefit linked to the aggressive treatment (von Gruenigen, Daly, Gibbons, Hutchins, & Green, 2008).

In a comparison of end of life care in the U.S. and Canada for patients with lung cancer who died between 1999 and 2003, extensive end of life care was seen in both countries but the U.S. patients received statistically significant higher rates in every month preceding death. The U.S. cohort was from the SEER-Medicare database (Warren et al., 2011). Regional variations in expenditures for cancer patients' care delivered in the last year of life is well described (Barnato et al., 2007). Barnato and colleagues investigated whether patient preferences could be the reason for the regional variations and concluded that this was unlikely.

The Dartmouth Atlas report included data on comprehensive cancer centers and these also varied widely regionally with respect to their end of life care, e.g. patients receiving chemotherapy in the last two weeks of life varied from 2.9 % at the Cleveland Clinic in Ohio to 6.7 % at M.D. Anderson in Texas. Substantial regional variation is seen in the intensity of end of life care received by patients at academic institutions. Despite all the refocus on this topic, including guidelines from several oncology organizations on appropriate cessation of treatment and timely inclusion of hospice, some academic institutions still showed an upward trend in the intensity of treatment given to patients at end of life (Morden et al., 2012).

More recently, Colla and colleagues investigated the impact of payment reform in Medicare beneficiaries dying from poor prognosis cancer in the 2003-2007 time period. They found a significant reduction in the use of chemotherapy in physician offices after the reimbursement reduction and no similar reduction in the use of chemotherapy in hospital outpatient departments. They acknowledge that a cultural shift occurred in the year following the MMA towards more awareness of end-of-life care and the cost benefit relation. (Colla, Morden, Skinner, Hoverman,& Meara, 2012).

A conclusion from these studies is that aggressive care at the end of life needs to be studied in a more controlled and prospective fashion to allow for information to be valuable in developing models for shared decision making between medical personnel and patients and families.

Hospice and palliative care

In the period under study, there was growing evidence for the support of earlier introduction of palliative care for patients with cancer. The Balanced Budget Act of 1997 included legislation that was intended to encourage the use of hospice care. Kilgore and colleagues evaluated the effect of this act on hospice and home health costs and utility and report that hospice utilization increased in the period 1996-2002 (Kilgore, et al, 2009).

Just prior to the study period, in 1998, an important trial was activated which evaluated an in person palliative care intervention for patients with advanced cancer and their caregivers. The sessions with palliative care nurses were focused on problem-solving, empowerment, symptom management, support and communication, and advanced care planning. The pilot study was named ENABLE, an acronym for Educate, Nurture, Advise Before Life Ends and was funded by the RWJF. The pilot study was followed by ENABLE II where phone-based interventions were evaluated. Participants were randomized to phone session interventions immediately after diagnosis or 12 weeks after diagnosis. Results of ENABLE II showed that early palliative care improves quality of life and mood. ENABLE III followed where participants with advanced cancer were randomized to palliative care either 30-60 days after diagnosis or 12 weeks after diagnosis. Results published in 2015 showed an improved one year survival rate for the group that received earlier palliative care. Caregivers of the group receiving the earlier intervention reported lower rates of stress and depression, but the link between depression and survival in the dying patients needs further investigation (Bakitas et al, 2015).

Over the last two decades, there has been a substantial increase in both the number of hospice programs and the number of patients receiving hospice care. In 2001, 18,8% of Medicare patients were reported to have had hospice care for a minimum of three days. This figure increased to 30% by 2007. The majority of hospice services are delivered in the home. This includes private residences, nursing homes and residential facilities. In 2014, 58,9% of patients received care at home. (Teno, Freedman, Kasper, Gozalo & Mor, 2015).

When end of life treatment is planned, the inclusion of palliative care and hospice have been shown to result in more symptom-directed care (Mack, Weeks, Wright, Block, & Prigerson, 2010). Quality of life is dramatically decreased in over- treated patients who do not benefit from the team approach of palliative care alongside oncology care which would include timely involvement of hospice and
appropriately timed cessation of aggressive treatments with curative intent (Jenkins, Fallowfield & Saul, 2001).

In the period of 2000-2009, an upward trend was seen in patients discharged to hospice from the inpatient setting and a decrease in the number of deaths occurring in the inpatient setting (Lin, Levine, & Scanlon, 2012). In 2009, patients discharged from a hospital inpatient setting to hospice care with any diagnosis accounted for approximately

27% of the total number of Medicare hospice patients for that year. Their hospitalizations alone cost more than the total Medicare costs for hospice care in 2009. This study was the first to look specifically at the population of patients discharged to hospice from a hospital inpatient setting.

A large study examined the relationship between hospice referral and end of life care in the Medicare prostate cancer population with deaths recorded between 1992 and 2005. Patients with no hospice referral were more likely to receive aggressive care at the end of life. A trend was seen in overall increased hospice referral over this time, however the referral was not timely which caused an increase of number of patients dying within a week of hospice enrollment over the same time period (Bergman et al., 2011). Earle and colleagues report a similar trend of increased hospice referral for Medicare patients who died between 1991 to 2000, with a substantial percentage of patients being referred less than three days before death.

The Dartmouth Atlas report regarding hospice referral in the last three days of life, showed regional variation for comprehensive cancer centers that ranged from 4.9% at Duke in North Carolina to 11.5% at Fox Chase in Pennsylvania (Morden et al., 2012). Morden and colleagues, using data from the Dartmouth project, showed a direct relationship between the geography of patients with advanced cancer and the intensity of care they would receive at end of life. Another finding of this report was that regions or hospitals associated with higher hospice utilization had a much smaller likelihood of patients dying in hospital.

In their 2011 annual report on clinical cancer advances, ASCO reports that in at least fifty academic medical centers, less than half of the patients with advanced cancer had hospice referrals in their last month of life (Vogelzang et al., 2012).

The conclusion from these publications is that hospice utilization increased over the time period studies, and that there was growing evidence that including palliative and hospice care decreased costs at end of life for terminally ill patients.

Research questions

Although the MMA was officially signed into law in 2003, the law took effect in outpatient clinics in 2005. The research sample consists of predominantly outpatient claims, and for that reason the research questions distinguish between the periods before and after 2005.

Research Question 1

Did the MMA have any influence on the quality of end of life care of Medicare beneficiaries?

- Were Medicare patients more likely to have cessation of chemotherapy in the last two weeks before death before or after 2005?
- Were Medicare patients more likely to receive Hospice care earlier than three days of death before or after 2005?

Research Question 2

Did the treatment guidelines for end-of-life care published in the period just prior to and during 1999-2010 have any influence on the quality of end of life care of Medicare beneficiaries?

- Was there a trend towards less aggressive end-of-life care in the period 1999-2010 in the Medicare population?
- Was there a trend towards earlier Hospice referral in the period 1999-2010 in the Medicare population?

Conceptual Framework

A recognized quality improvement framework in health care settings was postulated by Donabedian and examines three components affecting quality: structure, process, and outcome (Donabedian, 2005). Structure involves the characteristics of the system, process includes the methods of treatment and protocols and outcome addresses the result of the interaction between process and structure.

Stewart and colleagues used a Donabedian structure-process-outcome framework to integrate quality indicators and quality of life at the end of life (Stewart, Teno, Patrick, & Lynn, 1999). Byock and colleagues built on the model proposed by Stewart and colleagues to offer a framework for research involving the community, with the goal of addressing the culture surrounding end of life and thus improving the quality of life for patients with terminal diagnoses and their families (Byock, Norris, Curtis, & Patrick, 2001).

To adapt a Donabedian framework to end of life care for the purpose of this study, the recommended framework components are outlined in Figure 1.:

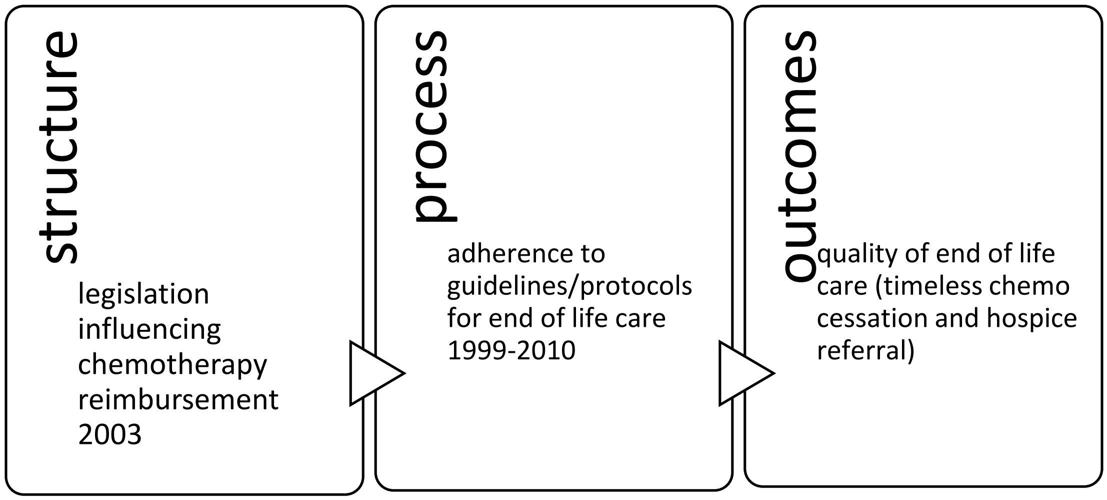


Fig 2.1 *Conceptual Framework*

Study Objective

To compare the quality of end of life cancer care before and after 2005 in the Medicare cancer population using two validated quality indicators: timely cessation of chemotherapy and timely referral to hospice.

Hypotheses

Hypothesis 1

1a.The impact of the MMA on cancer drug reimbursement resulted in a trend towards less aggressive chemotherapy treatment at the end of life

1b. The impact of the MMA on cancer drug reimbursement resulted in a trend towards more timely hospice referral at the end of life.

Hypothesis 2

2a. Treatment guidelines for end-of-life care published in the period just prior to and during 1999-2010 resulted in a trend towards less aggressive chemotherapy treatment at the end of life

2b. Treatment guidelines for end-of-life care published in the period just prior to and during 1999-2010 resulted in a trend towards timely hospice referral at the end of life

CHAPTER 3

METHODS

Data source

Medical records, patient and physician surveys and insurance claims are all sources of information on end of life care delivered and patient preferences. Extracting information from medical records and performing surveys are both time consuming methods, and could not compare with reviewing existing administrative data about the provision of results in a timely fashion for measuring indicators. Administrative date is a dependable and economical source of information on care delivered to patients in the end of life stage. Administrative data is available electronically and includes large samples of patients. A drawback when using administrative data is the retrospective nature, which does not allow for any measurement of the reasons why patients or physicians chose a specific intervention. Prediction of the date of death is also not a precise science. A number of studies have shown that death certificates often do not list cancer as an underlying cause of death, and this could lead to an underestimation of the number of deaths related to cancer (Hoel, Ron, Carter, & Mabuchi, 1993; Sington & Cottrell, 2002).

Berke and colleagues investigated the most appropriate means of identifying cohorts of patients for the purpose of studying care at the end of life using claims data. Their conclusion was that a combination of Part A and Part B Medicare claims using a

180-day window before death includes the largest number of patients and also overlap with hospice patients with a principal diagnosis of cancer (Berke, Smith, Song, Halpern, & Goodman, 2009). This method has an advantage over using death certificates to identify patients with cancer related deaths.

CMS is a federal agency that collects data for all Medicare beneficiaries and providers. Medicare is a federal insurance program that provides coverage for hospital and medical care for elderly and certain disabled Americans. The CMS Medicare database includes files for inpatient and outpatient care, physician services and hospice care.

Research identifiable files were used for this study and they include beneficiary level protected health information. The Office of the Institutional Review Board of the University of Alabama at Birmingham approved the project. A Data Use Agreement was approved by CMS's Privacy Board to use a 5% sample of the period 1999-2010. Inpatient and outpatient claims were combined and cases identified on the basis of a primary or secondary cancer definition.

Study Population

The study sample include Medicare beneficiaries who received services on a fee-for-service basis. The Medicare program consists of two main sections for hospital (Part A) and medical insurance (Part B). The study sample was extracted from a 5 percent longitudinal sample of all Medicare beneficiaries for the years 1999 through 2010, which included approximately 2.5 million beneficiaries in each year, including 150 million Medicare Parts A and B claims per year. Beneficiaries were included if their date of death was between 1999 and 2010 with a primary or secondary diagnosis of cancer using the International Classification of Diseases (ICD9) to identify a diagnosis of cancer. Beneficiaries included had at least one hospital claim or at least 2 clinician visits in the last seven months of life. For the purpose of this study, beneficiaries who did not have continuous Part A and Part B coverage in the last seven months of life and those enrolled in Medicare Advantage plans (MA) were excluded. MA plans receive capitated payments from Medicare and do not submit individual claims. Beneficiaries with end stage renal disease were excluded. Hematologic cancer types e.g. leukemia, lymphoma and multiple myeloma were also excluded, since these typically include high dose intensive treatment resulting in lengthy hospitalizations and co-morbidities. Basal cell and squamous cell skin cancers were excluded since the use of chemotherapy in these cancers is very limited.

Research identifiable files were obtained from the CMS Research Data Assistance Center (ResDAC). The files used were:

1. Beneficiary summary file (information on age, gender race)
2. Carrier file (also known as the Physician/Supplier Part B claims file) contains final action fee-for-service claims, mostly from non-institutional providers, such as physicians, physician assistants, clinical social workers, nurse practitioners and free-standing facilities. This file includes:
    - diagnosis and procedure (ICD-9 diagnosis, CMS Common Procedure Coding System (HCPCS) codes)
    - dates of service
    - beneficiary demographic information

3. Inpatient file contains final action fee-for-service claims data submitted by inpatient hospital providers for reimbursement of facility costs. This file includes:
   - diagnosis (ICD-9 diagnosis),
   - procedure (ICD-9 procedure codes
   - Medicare Severity Diagnosis Related Group (MS-DRG)
   - dates of service
   - beneficiary demographic information

4. Outpatient file contains final action, fee-for-service claims data submitted by institutional outpatient providers. Examples of institutional outpatient providers include hospital outpatient departments. This file includes:

- diagnosis (ICD-9 diagnosis)
- Healthcare Common Procedure Coding System (HCPCS) codes,
- dates of service,
- revenue center codes
- beneficiary demographic information

5. Hospice file contains final action claims submitted by Hospice providers. Once a beneficiary elects Hospice, all Hospice related claims will be found in this file, regardless if the beneficiary is in Medicare fee-for-service or in a Medicare managed care plan. This file includes:

- the level of hospice care received (e.g., routine home care, inpatient respite care) terminal diagnosis (ICD-9 diagnosis)
- the dates of service
- beneficiary demographic information

Variables and operationalization

Variables and measurement operationalization summarized in Table 3.1:

Table 3.1 *Variables and Operationalization*

Variable	Definition	Operationalized Measure
	Dependent variables	
EOL chemotherapy (chemo_2wks)	chemotherapy claim in the 14 days prior to death	[a] no EOL chemo = 1 EOL chemo = 0
EOL hospice (three_day_to_death)	claim associated with last hospice episode	[b]timely referral =1 not timely referral = 0
	Independent variables	
MMA (MMA2005_date)	EOL Hospice or Chemotherapy claim prior to or after 2005	after 2005 =1 before 2005 = 0
Race (race_white)	White ,non-white	White = 1 Non-white= 0
Age	Age at death	<65 65-69 (reference) 70-74 75-79 >= 80
Cancer type	Cancer types defined by diagnosis codes (ICD9)	Gastro-intestinal cancer (GI) Genito-urinary cancer (GU) Lung cancer Breast cancer Prostate cancer (reference) Other cancer
Sex (sex_male)	Male or female	male = 1 female = 0
Death date as continuous variable (time_trend1)	Year of death (1999-2010)	Time_trend1- 1-death date 2000, time_trend1-death date 2001 etc. (death date in 2000 = reference)

[a]No chemo in 14 days before death

[b]Timely referral is more than three days before death

Dependent variables

EOL chemotherapy-this variable was dichotomous (1= yes; 0= no) that indicates chemotherapy was discontinued at least 14 days prior to death. Chemotherapy administration was identified from claims in the inpatient, outpatient and carrier files. The identifying billing codes used were

- Healthcare Common Procedure Coding System (HCPCS) based on CPT codes 96401, 96402, 96405, 96406, 96409, 96411,96413,96415,96416,96417, 96420, 96422, 96423, 96425,96440,96446,96450,96542,96549, 99555. All codes are indicative of administration of chemotherapy
- International Classification of Diseases Ninth Revision (ICD-9) codes 99.25 - injection/infusion of chemotherapy
- ICD-9 codes V58.1, V67.2. (encounter for chemotherapy or post chemotherapy care)
- Revenue center codes: 0331 (chemo administration-injected) and 0335 (chemotherapy administration IV). This identifying metric was validated by Earle et al. (Earle et al, 2008).

EOL Hospice-this variable was dichotomous (1= yes; 0= no) that indicates if hospice care was initiated more than three days before death. All claims in the Hospice file were included if they had a diagnosis of cancer per the entry criteria for this study and met the entry criteria for continuous Part A and Part B coverage in the last seven months of life

Independent variables

MMA- The independent variable refers to the Medicare Prescription Drug, Improvement and Modernization Act of 2003, also referred to as the Medicare Modernization Act. The law became official at the end of 2003 but was only implemented in physician offices in 2005. This variable was dichotomous (1= yes; 0= no) that indicates if the chemotherapy or hospice claim was 2005 or later.

Race. This variable is dichotomous (1= yes; 0= no) that indicates if the patient was White.

Age-This variable is represented by four age groups: <65, 65-69, 70-74, 75-79, >=80, with the age group 65-69 used as the reference group.

Cancer type-this variable was represented by six groups: pancreas cancer, lung cancer, breast cancer, prostate cancer, gastro-intestinal cancer, genito-urinary cancer, other cancer, with prostate cancer used as reference. Prostate cancer was chosen as reference due to the high probability of hospice involvement. The cancer types were chosen to correspond with similar studies in the most recent literature (Colla et al, 2012).

Sex-this variable is dichotomous (1= yes; 0= no) that indicates if the patient was male.

Death date –continuous variable-this variable is continuous that indicates the date of death in a specific calendar year.

Statistical Methods

The dependent variables in this cross-sectional retrospective study are dichotomous, and indicate whether or not a patient received chemotherapy in the last two weeks of their life or timely referral to hospice, defined as more than three days before death. Multiple logistic regression analysis is the most appropriate analysis for a model containing multiple indicator variables and a dichotomous dependent variable. Logistic regression calculates the probability or success over the probability of failure, and the results are in the form of an odds ratio. Logistic regression analyses were conducted with the odds ratio (OR) and its 95% confidence interval (CI) as the measure of association. Statistical significance was assessed at the alpha level of 0.05.

Regression models:

1. EOL chemo = MMA + time trend +cancer type + race +age + sex
2. Hospice referral = MMA + time trend +cancer type + race + age + sex

CHAPTER 4

RESULTS

Sample demographics

There are 318,801 beneficiaries that met the inclusion criteria. The cohort is predominantly Caucasian (87%) and 52% are older than eighty. The cancer types predominating in the sample are genito-urinary, gastro-intestinal and lung cancer. More than half of the sample (55%) died in the period 2005-2010. The mean age at death was 79.6 years

The cohort demographics are listed in Table 4.1.

Table 4.1 *Cohort demographics*

Variable	Characteristic	N	%
Death date			
	Before 2005	142,324	45
	After 2005	176,477	55
Sex			
	Male	149,750	47
	Female	169,051	53
Race			
	White	276,913	87
	Non-white	41,888	13
Cancer type			
	Genito-urinary	70,673	22
	Gastro-intestinal	66,217	21
	Lung	54,534	17
	Other	51,964	16
	Prostate	42,630	14
	Breast	32,783	10
Age[a]			
	< 65	16,021	5
	65-69	31,430	9
	70-74	46,328	15
	75-79	60,555	19
	>= 80	164,467	52

[a] Mean age = 79.64

Regression results

Question 1-Chemotherapy

This question is answered by testing hypothesis 1- whether the MMA influenced the quality of end of life care in the Medicare oncology patient population as measured by two validated quality indicators

- Were Medicare patients more likely to have cessation of chemotherapy in the last two weeks before death before or after 2005?
- Were Medicare patients more likely to receive hospice care earlier than three days of death before or after 2005?

The chemotherapy cohort include 21,299 beneficiaries and 98% of them received chemotherapy in the outpatient setting. A chi-square test was used to determine whether there was a relationship between the dependent variable (timely chemo cessation) and the independent variable (before or after 2005). Before 2005, 90 % of beneficiaries did not receive chemotherapy in the 14 days before death and after 2005 this percentage went up to 91%. This difference is statistically significant with X^2 (1) 4.68, p = 0.03, which indicates a strong relationship between the dependent variable) and the independent variable. Table 4.2 includes the result of the contingency table for timely chemotherapy cessation and chemotherapy claim date.

Table 4.2 *Timely chemo cessation by EOL claim date*

	[b] MMA2005_date	
[a] chemo-2wks	0	1
1	7,950 (90.3%)	11,398 (91.2%)
0	851 (9.7%)	1,100 (8.8%)
[c] Total	8,801	12,498

[a] chemo_2wks = 1- no EOL chemo claim in 14 days before death

[b] MMA2005_date = 1 -EOL chemo claim > = 01/01/2005 [c] N= 21,299

On the basis of the significant association found in the x^2 analysis, a logistic regression was used to examine the simultaneous influence of more predictors.

Table 4.3 includes results of the logistic regression of factors associated with end of life cancer care with dependent variable no chemotherapy in the 14 days prior to death.

Table 4.3 *No chemotherapy in 14 days before death*

	OR	SE [a]	95 % CI [b]	
MMA	0.79**	0.09	0.66	0.95
Time trend	1.06***	0.01***	1.03	1.09
White race	0.84**	0.07	0.73	0.97
Male sex	0.93	0.05	0.84	1.02
Cancer type [c]				
Gastro-intestinal	0.75**	0.08	0.65	0.88
Genito-urinary	0.91	0.09	0.77	1.09
Lung	0.64***	0.07	0.56	0.74
Breast	0.68**	0.11	0.55	0.84
Other	0.80**	0.08	0.69	0.94
Age[d]				
<65	1.12	0.09	0.94	1.33
70-74	1.00	0.07	0.88	1.15
75-79	1.14	0.07	0.99	1.31
>= 80	1.28**	0.07	1.12	1.46

Overall Wald-chi-square test 94.55 ***

*p<0.1 **p<0.05 ***p<0.0001

[a] Standard Error [b] Confidence interval [c] Reference Prostate cancer [d] Reference 65-69

The time trend variable represents the date of death and the reference year of death is 2000. The year of death is significantly associated with timely chemo cessation (OR= 1.03, 95% CI 1.01, 1.05). This suggests that a trend existed in this period under study in this population towards timely chemo cessation. Another factor associated with timely chemotherapy cessation is age 80 and older vs 65-69 (OR= 1.28, 95% CI 1.12, 1.46).

Different factors are negatively associated with having timely chemo cessation and these include the MMA2005 or date of the claim being after January 1st 2005 (OR= 1.1, 95% CI 1.00, 1.21) being Caucasian (OR = 0.84, 95% CI: 0.73, 0.97); having gastro-intestinal cancer vs prostate cancer (OR =0.76, 95% CI 0.66, 0.88); having lung cancer vs prostate cancer (OR= 0.65, 95% CI 0.56,0.75); having breast cancer vs prostate cancer (OR= 0.70, 95% CI 0.57, 0.86); and having other cancer vs prostate cancer (OR= 0.83 95% CI 0.70, 0.97).

Question 1-Hospice

The hospice cohort includes 114,794 beneficiaries and 35% of them died in a hospice facility. Hospice episodes for the last year of life were reviewed and the first claim in the hospice episode closest to date of death was included for review for the three days to death variable.

A chi-square test was used to determine whether there was a significant association between the dependent variable (timely hospice referral) and the independent variable (before or after 2005). Before 2005, 59 % of beneficiaries had hospice services more than three days before death and after 2005 this percentage went down to 56 %. This difference is statistically significant with X^2 (1) 143.8,

p <.0001 which indicates a strong relationship between the dependent variable) and the independent variable.

Table 4.4 includes the result of the contingency table for timely hospice referral and hospice claim date.

Table 4.4

Timely hospice by EOL hospice claim date

	[b] MMA2005_date	
[a]Three_day_to_death	0	1
1	31,613 (59 %)	34,431 (56%)
0	21,954 (41%)	27,156 (44%)
[c] Total	53,567	61,587

[a] Three_days_to_death = 1- EOL hospice claim > 3 days before death
[b] MMA2005_date = 1 -EOL hospice claim > = 01/01/2005 [c] N= 114,794

On the basis of the significant association found in the x^2 analysis, a logistic regression was used to examine the simultaneous influence of more predictors.

Table 4.5 includes results of the logistic regression of factors associated with end of life cancer care with dependent variable hospice more than three days before death.

Table 4.5

Hospice > 3days before death

	Odds Ratio	SE [a]	95% CI [b]	
MMA2005	0.65***	0.02	0.62	0.68
Time trend	1.06***	0.00	1.05	1.07
White race	0.93**	0.02	0.90	0.97
Male sex	0.81***	0.01	0.79	0.83
Cancer type [c]				
Gastro-intestinal	0.75***	0.03	0.71	0.79
Genito-urinary	0.72***	0.03	0.67	0.76
Lung	0.73***	0.03	0.69	0.77
Breast	0.77***	0.04	0.72	0.83
Other	0.65***	0.03	0.61	0.69
Age [d]				
<65	1.31***	0.03	1.23	1.39
70-74	0.99	0.02	0.95	1.03
75-79	1.08**	0.02	1.04	1.12
>80	1.19***	0.02	1.16	1.23
Overall Wald-chi-square test 1048.14 ***				

*p<0.1 **p<0.05 *** p<0.0001 [a] Standard Error [b] Confidence Interval

[c] Reference Prostate cancer [d] Reference 65-69

The time trend variable represents the date of death and the reference year of death is 2000. The year of death is significantly associated with timely hospice referral (OR= 0.10, 95% CI 0.99, 1.00). This suggests that a trend did exist in this period under study in this population to move towards timely referral to hospice.

Other factors associated with timely hospice referral include age younger than 65 vs 65-69 (OR= 1.30, 95% CI 1.22, 1.37); age 75-79 vs 65-69 (OR= 1.08, 95% CI 1.04, 1.12); age 80 and older vs 65-69 (OR= 1.28, 95% CI 1.12, 1.46).

Different factors are negatively associated with timely hospice referral including the MMA2005 or date of the claim being after January 1st 2005 (OR= 0.871, 95% CI 0.85, 0.90);being Caucasian vs non Caucasian (OR = 0.93, 95% CI: 0.90, 0.97); being male sex vs female sex (OR = 0.81, 95% CI 0.79, 0.83); having gastro-intestinal cancer vs prostate cancer (OR =0.75, 95% CI 0.71, 0.79); having genito-urinary cancer vs prostate cancer (OR =0.72, 95% CI 0.67, 0.77); having lung cancer vs prostate cancer (OR= 0.73, 95% CI 0.69,0.77); having breast cancer vs prostate cancer (OR= 0.78, 95% CI 0.72, 0.83); having other cancer vs prostate cancer (OR= 0.68 95% CI 0.65, 0.72).

Question 2- Chemotherapy

This question is answered by testing hypothesis 2- whether the treatment guidelines for end-of-life care published in the period just prior to and during 1999-2010 had any influence on the quality of end of life care of Medicare beneficiaries?

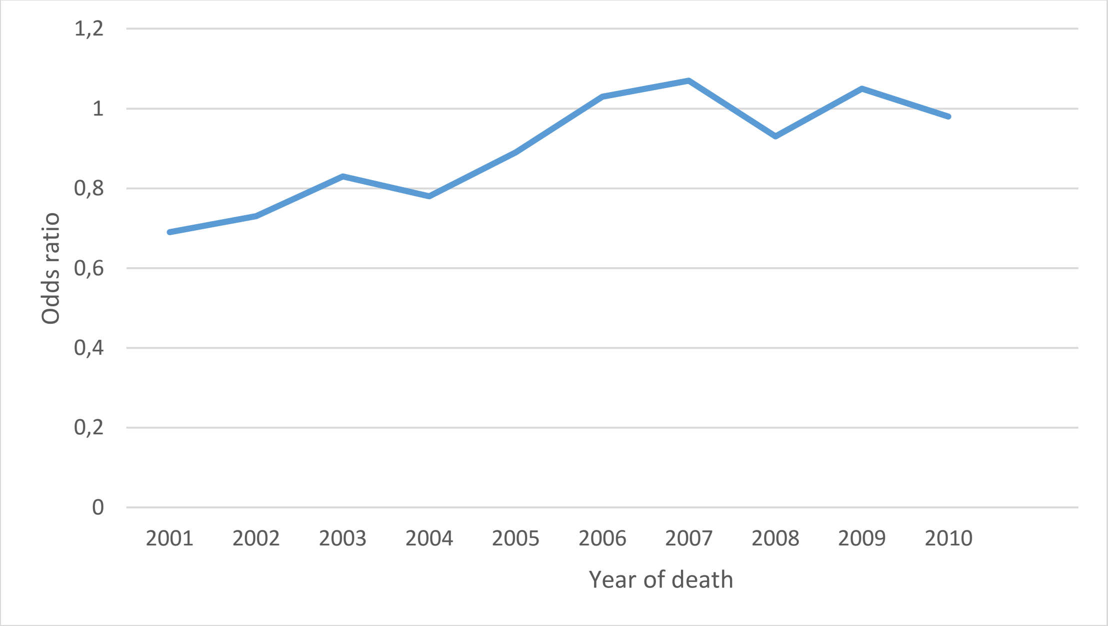
- Was there a trend towards less aggressive end-of-life care in the period 1999-2010 in the Medicare population?
- Was there a trend towards earlier Hospice referral in the period 1999-2010 in the Medicare population?

The percentage of beneficiaries who did not receive chemo in the last two weeks of life increased from 6.7% in 2000 to 9.1% in 2010. The year of death had a statistically significant positive relation to timely chemo cessation (OR= 1.03, 95% CI 1.02, 1.05).

This suggests that an overall trend did exist in this period under study in this population to move towards timely chemo cessation. Cancer patients in this population were 3% more likely to have timely chemo cessation in 2010 than in 2000.

Fig 4.1 plots the probability (odds ratio) for timely cessation of chemotherapy over this period. The year 2000 was used as the reference year for this analysis.
The period 2004-2007 shows the largest trend towards an increase in timely chemo cessation, with a return to the 2006 level in 2010.

Fig. 4.1. *Probability of not receiving chemotherapy in the 14 days before death for the period 2001-2010.*



Question 2 -Hospice

The time trend variable represents the date of death and the reference year of death is 2000. The year of death had a statistically significant association with timely hospice referral (OR= 0.994, 95% CI 0.990, 0.998). This suggests that an overall trend did exist in this period under study in this population to more timely referral to hospice. The period 2009-2010 shows the largest trend towards an increase in timely hospice referral. Fig 4.2 plots the probability (odds ratio) of timely hospice over this period.

Fig 4.2 *Probability of hospice referral earlier than 3 days before death for the period 2001-2010*

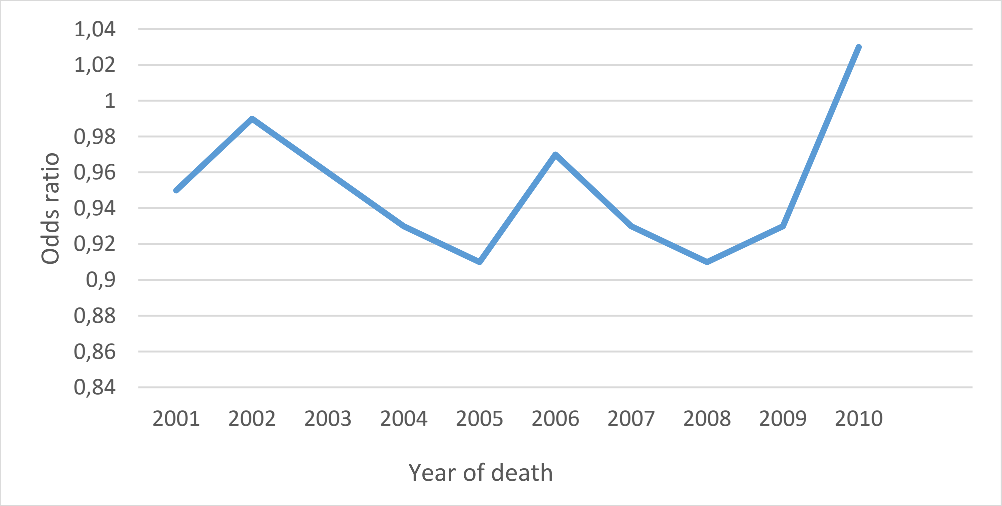


Table 4.6 summarizes the results of hypothesis testing.

Table 4.6
Summary of Findings from Hypotheses Testing

Hypothesis	Statement	Findings
1a	The MMA influenced the quality of end of life care in the Medicare oncology patient population as measured by chemotherapy cessation more than 14 days before death.	Not supported
1b	The MMA influenced the quality of end of life care in the Medicare oncology patient population as measured by hospice referral more than 3 days before death.	Not supported
2a	Treatment guidelines for end-of-life care published in the period just prior to and during 1999-2010 influenced the quality of end of life care in the Medicare oncology patient population as measured by chemotherapy cessation more than 14 days before death.	Supported
2b	Treatment guidelines for end-of-life care published in the period just prior to and during 1999-2010 influenced the quality of end of life care in the Medicare oncology patient population as measured by hospice referral more than 3 days before death.	Supported

CHAPTER 5

DISCUSSION

In this chapter the objective is to discuss the findings and results presented in the previous chapter and compare with findings from published studies. The study strengths, limitations and implications for policy will also be discussed.

Discussion of Findings from Research Question 1

Chemotherapy

***MMA*-**the question is whether the MMA influenced the probability of receiving chemotherapy in the last 14 days of life .The result was a statistically significant negative association with timeley cessation of chemotherapy. Patients were more likely to have chemotherapy in the last 14 days of life in the period 2005-2010 compared with 1999-2004 . The results from this study corresponds with findings by Wang et al (2016) and Hornbrook et al (2014).

In contrast, Colla and colleagues (2012) reviewed the two time periods 2003-2004 and 2006-2007 and report a decrease in the incidence of aggressive chemotherapy in the 2006-2007 period, which is the period directly following the MMA implementation. Their cohort included hematologic cancers and cancers considered to be of poor prognosis.

The drugs used in the periods before and after the MMA would provide more granular information on the influence of reimbursement. New drugs are developed every year and the treatment options in the two time periods are not identical. Hornbrook and colleagues reviewed chemotherapy prescribing patterns in lung and colorectal cancer in the period 2003- 2006 and found that the probabilty of receiving a drug affected by the MMA was lower in the period post the MMA, with variations by type of cancer (Hornbrook, et al, 2014).

Race- The 2015 report on racial distribution of Medicare beneficiaries reported the sample to be 76% white. This includes those covered by Medicare, Medicare Advantage and those who may be dual eligible and also covered by Medicaid. This study cohort consisted of 87% white beneficiaries and excluded Medicare Advantage.

White patients have a negative association with timely cessation of chemotherapy in this study. Other studies reporting white patients to be more likely to receive end-of-life chemotherapy include Wang et al (2016), Earle et al (2008) and Colla et al, (2012).

Studies reporting on the influence of race on aggressive end of life care have conflicting results. Comparison between published studies is complicated by the variation in sample cohorts e.g. restricted to one or two cancer types, excluding the comprehensive cancer centers when using Surveillance, Epidemiology and End Results (SEER) data, using only one specific calendar year versus a number of years , having different definitions of the end of life period and small sample size

The CanCors project was launched by the NCI in 2001 with the objective of better understanding the reasons for variations in treatments and outcomes of cancer. Newly diagnosed patients with lung and colorectal cancer completed surveys and the results showed that black patients were more likely than non-black patients to drain all personal financial resources to attempt to extend life (Martin, et al, 2011). Using the CanCORS cohort, Weeks and colleagues (2012) reported that non-white patients had a significantly higher risk of reporting inaccurate beliefs about the curative value of chemotherapy. Other studies which reported that black patients were more likely than white patients to receive intensive end of life care include Loggers et al (2009) and Hanchate, Kronman, Young-Xu, Ash & Emanuel, (2009).

Sex and age- the study cohort for this dissertation had a fairly equal distribution of males and females and results do not show a difference in males and females for predicting chemotherapy in the last 14 days of life. Age 80 and older was associated with timely chemotherapy cessation when compared with age group 65-69.

Studies reporting older age and female sex to be predictors for less aggressive care include Earle et al (2008) and Emanuel et al (2003). Tumor type, stage of disease and number of previous treatments play a major role in the decision for chemotherapy. Male to female distribution for each specific cancer type may be a factor in the result in this study.

Higher age is a predictor of advanced directives completion prior to a cancer diagnosis (Mc Donald, du Manoir, Kevork, Le & Zimmermann, 2016). The age group older than 70 and younger than 65 in this study were less likely than the reference group of 65-69 to receive chemotherapy in the last 14 days of life. Completion of advanced care directives involve discussions about preferences for end of life care which would explain the reported less aggressive end of life care.

Cancer type-the results from this analyses show a negative association between timely chemo cessation and the cancer types genito-urinary, other, gastro-intestinal, breast and lung when compared to prostate cancer. These cancer types tend to be more responsive to chemotherapy. Prostate cancer was used as reference due to its disease pattern which typically includes a period of observation post initial surgery , multiple treatment options and the high likelihood of treatment and hospice involvement in the last six months of life.

Hospice

MMA-the question in this study is whether the MMA influenced the probability of receiving hospice referral prior to three days before death. The result was a statistically significant higher probability of timely hospice referral in the 1999-2004 period when compared with the 2005-2010 period after MMA implementation .

A possible explanation for this result could be that more aggressive and longer periods of end of life chemotherapy was given after 2005 to compensate for lost evenue from chemotherapy drugs affected by the reimbursement change. Hospices were penalized if hospice stays were inappropriately long, which was a disincentive to early hospice referrals (Huskamp, Buntin, Wang & Newhouse, 2001). The requirement for patients to formally decline any curative care prior to hospice enrollment was another limiting factor to early referral.

A time trend variable was inserted to control for a possible existing pre-MMA trend towards more timely hospice referral and this was statistically significant. In 2010, the likelihood of hospice referral prior to three days before death was statistically significant higher than in 1999.This could be attributed to the effect of multiple guidelines published by various organizations in the same time period, which was hypothesized to support a move toward more timely hospicreferral.

Race-non-white beneficiaries were significantly more likely when compared with white beneficiaries to have hospice referral earlier than three days before death in this study. There are very few studies reporting on hospice referral patterns for this time period. The result from this study conflicts with results from studies which reported a cultural difference regarding the value of aggressive treatment in the final stages of life, and the greater willingness of non-white patients to spend all available financial resources to extend life (Martin et al 2011,Weeks et al 2012, Loggers et al, 2009). The cancer type, cultural and economic profiles, and region play significant roles in the decision to decline potential aggressive curative treatment at end of life The influence of race on aggressive end of life treatment leaves this question to be studied further in more racially balanced cohorts.

Sex and age-the higher likelihood of advanced directives and willingness to have end of life discussions in advanced age groups would explain the higher likelihood of hospice referral prior to three days before death for the older than 75 age group in the study cohort. Males were found to be less likely to have timely hospice referral. The higher probability of males to have aggressive end of life treatment can be the reason for late hospice referral.

Cancer type-the results from this analysis reported a negative association between timely hospice referral and the cancer types genito-urinary, other, gastro-intestinal, breast and lung when compared to prostate cancer. These cancer types tend to be more responsive to chemotherapy. The variations in the cancer types included in study cohorts in the literature does not allow for comparison with published literature.

Discussion of Findings from Research Question 2

Chemotherapy

The results for a trend over this time period was a positive trend towards timely chemotherapy cessation and timely hospice referral.

The guidelines on end of life published in this time could have contributed to the trend towards timely chemotherapy cessation, but many other variables have to be considered. The guidelines could have contributed to a growing awareness and cultural shift in the patient and medical communities towards more consideration for quality of life at the end of life.

The trend towards more timely chemotherapy cessation was most prominent in the period directly after 2005, which would suggest that the reduced financial incentives for prescribing drugs could have been a factor for this year. However, in the period 2006-2010, the effect was stable with very little change which corresponds with the literature (Wang, et al, 2016). The drugs used in this cohort were not identified, and the time period was long enough (11 years) to have seen significant changes in drug combinations used. Targeted therapy was becoming more prominent in this period and would have made a substantial impact on the drug regimes used. The identification of chemotherapy in this cohort did not include oral chemotherapy drugs, which is a limitation.

Hospice

The guidelines on end of life published in this time could have contributed to the trend towards timely hospice referral, but many other variables should be considered. The guidelines could have contributed to a growing awareness and cultural shift in the patient and medical communities towards less aggressive treatment and earlier involvement of palliative care and hospice in the treatment continuum.

Teno and colleagues reported that the overall proportion of beneficiaries receiving hospice care increased over the time period 2000-2009. The number of patients in their study that had a transition in care in the last three days of life as well as the number of intensive care unit stays also significantly increased over this time. A possible explanation for the late hospice referral in this study could be a significant component of hospitalizations which included admission to an intensive care unit (Teno, et al, 2013).

Limitations of the Study

The study has a number of limitations. Claims data important data elements which will influence the analyses. The cause of death is not known, neither is the information of the patient's preference for end of life care. The identification of cancer is dependent on coding, which inherently contains a margin of human error. Missing data are also prevalent and the reason for the collection of the data is not reseach focused. When chemotherapy administration is identified, it is not known if the reason for prescribing was therapeutic or palliative or if the drugs prescribed were affected by the reimbursement change. There is no clinical information on stage of disease, reason for chemotherapy cessation, or date of relapse. The data do not include any non-covered services or services provided by managed care providers and long-term care facilities. Lastly, the retrospective nature of the study may lead to bias. Prospective studies in the dying population are complicated, but should be attempted to confirm results from retrospective reviews.

Directions for Future Research

The published literature on end of life care in the United States vary widely with regards to disease areas , time periods and data elements studied. Few studies published in recent years update information published on this topic in the 1990's. Prospective research would contribute greatly to the understanding of the trends in this discipline . The question of whether reimbursement incentive changes brought about by legislation could drive prescribing patterns and treatment decisions remains unanswered.

The inclusion of more clinical detail, e.g. identification of all prescription drugs now available in Part D data, tumor and disease stage information and services provided by managed care providers would improve our understanding of the issues needing management through policy. Linking the Medicare claims data to other national or regional data sources e.g. cancer registires and data from large NCI clinical trials could provide additional elements and the possibility to follow patients over a longer time.

Regional variations have been widely reported and this could direct future research and possible policy intervention. Regions with improvement in incidence of aggressive care and timely hospice referrals could provide valuable information about processes that could be tested and impleneted in regions with increasing aggressive care. Cultural beliefs, level of education and income have been shown to play a role in decisionmaking about end of life and this should be a focus of ongoing family directed research and education. One aspect of study that is largely under represented, is the influence on quality of end of life of short hospice stays. It would be interesting to see if the mix of drugs prescribed changed significantly after the reimbursement change.

Conclusion

The reimbursement change for outpatient prescription drugs brought about by the MMA did not significantly influence the quality of end of life care as measured by two quality indicators when comparing five year periods before and after the implementation.

There is evidence of an overall trend towards timely chemo cessation and hospice referral in the 1999-2010 period and multiple guidelines on quality indicators for end of life care published in this time may have been a factor. However, many additional factors influence end of life decisions and care.

The reasons for receiving aggressive end of life care and late or no hospice referral are many and varied. Healthcare advances in the period under study was remarkable, but there is sparse and conflicting information in the published literature on the quality of end of life care as measured by quality indicators such as chemotherapy cessation in the 14 days before death and referral to hospice more than three days before death.

The challenge is to continue rigorous examination of end of life care to seek for ways to improve on the current models of care so as to be closer aligned with the dying patients' wish and at the same time provide optimal cost effective quality care at the end of life.

LIST OF REFERENCES

American Cancer Society Cancer Facts and Figures 2015 –Retrieved from http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2015/ -Cited 07.17.16

Bakitas, M., Ahles, T. A., Skalla, K., Brokaw, F. C., Byock, I., Hanscom, B., .ENABLE project team (2008). Proxy perspectives regarding end-of-life care for persons with cancer. *Cancer,* 112(8), 1854-1861.

Bakitas, M.A., Tosteson, T.D., Li, Z., Lyons, K.D., Hull, J.G., Dionne-Odom, J.N., Frost, J., Dragnev, K.H., Hegel, M.T., Azuero, A., & Ahles, T.A.(2015). Early versus delayed Initiation of Concirrent Palliative Oncology Care :Patient Outcomes in the ENABLE III Randomized Controlled Trial. Journal of Clinical Oncology, 33(13), 1438-1445

Banaszak-Holl, J., & Mor, V. (1996). Differences in patient demographics and expenditures among Medicare hospice providers. *The Hospice Journal* 11(3), 1-19.

Barnato, A. E., Herndon, M. B., Anthony, D. L., Gallagher, P. M., Skinner, J. S., Bynum, J. P., & Fisher, E. S. (2007). Are regional variations in end-of-life care intensity explained by patient preferences?: A Study of the US Medicare Population. *Medical Care,* 45(5), 386-393.

Bergman, J., Saigal, C. S., Lorenz, K. A., Hanley, J., Miller, D. C., Gore, J. L., Urologic Diseases in America project (2011). Hospice use and high-intensity care in men dying of prostate cancer. A*rchives of Internal Medicine* 171(3), 204-210.

Berke, E. M., Smith, T., Song, Y., Halpern, M. T., & Goodman, D. C. (2009). Cancer care in the United States: identifying end-of-life cohorts. *Journal of Palliative Medicine* 12(2), 128-132.

Buntin, M. B., & Huskamp, H. (2002). What is known about the economics of end-of-life care for medicare beneficiaries? *Gerontologist,* 42 Spec No 3, *4*0-48.

Byock, I., Norris, K., Curtis, J. R., & Patrick, D. L. (2001). Improving end-of-life experience and care in the community: a conceptual framework. J*ournal of Pain and Symptom Management,* 22(3), 759-72.

Campion, F. X., Larson, L. R., Kadlubek, P. J., Earle, C. C., & Neuss, M. N. (2011). Advancing performance measurement in oncology: quality oncology practice initiative participation and quality outcomes. *Journal of Oncology Practice,* 7(3 Suppl), 31s-35s.

Christakis, N. A., & Iwashyna, T. J. (1998). Attitude and self-reported practice regarding prognostication in a national sample of internists. *Archives of Internal Medicine,* 158(21), 2389-2395.

Christakis, N. A., & Lamont, E. B. (2000). Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. *British Medical Journal,* 320(7233), 469-472.

Colla, CH.C., Morden, N.E., Skinner, J.S., Hovermann, J.R., & Meara, E (2012). Impact of Payment reform on Chemotherapy at the End of Life.. *American Journal of Managed Care,* 18(5), e200-e208.

Donabedian, A. (2005). Evaluating the Quality of Medical Care. *Milbank Memorial Fund Quarterly* , 83(4), 691-729.

Downs, C. (2007). The Medicare Prescription Drug Improvement and Modernization Act and the delivery of cancer chemotherapy. *American Journal of Health- systems Pharmacy,* 64(15 Suppl 10), S13-15.

Dy, S. M., Asch, S. M., Lorenz, K. A., Weeks, K., Sharma, R. K., Wolff, A. C., & Malin, J. L. (2011). Quality of end-of-life care for patients with advanced cancer in an academic medical center. *Journal of Palliative Medicine,* 14(4), 451-457.

Dy, S. M., Lorenz, K. A., O'Neill, S. M., Asch, S. M., Walling, A. M., Tisnado, D., . . . Malin, J. L. (2010). Cancer Quality-ASSIST supportive oncology quality indicator set: feasibility, reliability, and validity testing. *Cancer,* 116(13), 3267-3275.

Earle, C. C., & Ayanian, J. Z. (2006). Looking back from death: the value of retrospective studies of end-of-life care. *Journal of Clinical Oncology,* 24(6), 838-840.

Earle, C. C., Landrum, M. B., Souza, J. M., Neville, B. A., Weeks, J. C., & Ayanian, J. Z. (2008). Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *Journal of Clinical Oncology,* 26(23), 3860-3866.

Earle, C. C., Neville, B. A., Landrum, M. B., Ayanian, J. Z., Block, S. D., & Weeks, J. C. (2004). Trends in the aggressiveness of cancer care near the end of life. *Journal of Clin ical Oncology,* 22(2), *3*15-321.

Earle, C. C., Park, E. R., Lai, B., Weeks, J. C., Ayanian, J. Z., & Block, S. (2003). Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *Journal of Clinical Oncology,* 21(6), *11*33-1138.

Emanuel, E. J., Young-Xu, Y., Levinsky, N. G., Gazelle, G., Saynina, O., & Ash, A. S. (2003). Chemotherapy use among Medicare beneficiaries at the end of life. *Annals of Internal Medicine*, 138(8), 639-643.

Ferrell, B., Connor, S, R., Cordes, A., Dahlin, C.M., Fine, P.G., Hutton, N., Leenay, Lents. J., Person, J.L., ,Meier, D.E., Zuroski,K. (2007). The National Agenda for Quality Palliative Care : the National Consensus project and the National Quality Forum. Journal of Pain and Symptom Management, 33(6), 737-744.

Ferguson,T. (2012). Improving Health Outcomes and Promoting Stewardship of Resources:ABIM Foundation's Choosing Wisely Campaign.*Virtual Mentor,*14 (11), 880-884.

Field, M. J., & Cassel, C. K. (2011). Approaching death: improving care at the end of life. *Health Progress,* 92(1), 25.

Finlay, E., & Casarett, D. (2009). Making difficult discussions easier: using prognosis to facilitate transitions to hospice. *CA: A Cancer Journal for Clinicians,* 59(4), *25*0-263.

Freeborn,N., Lynn,J., & Desbiens,N,A.(2000). Insights about Dying from the SOPPORT project.The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *Journal of the American Geriatric Society,* 48(5), S199-205.

Friedman, J. Y., Curtis, L. H., Hammill, B. G., Dhillon, J. K., Weaver, C. H., Biswas, S., Schulman, K. A. (2007). The Medicare Modernization Act and reimbursement for outpatient chemotherapy: do patients perceive changes in access to care? *Cancer,* 110(10), 2304-2312.

Glare, P., Virik, K., Jones, M., Hudson, M., Eychmuller, S., Simes, J., & Christakis, N. (2003). A systematic review of physicians' survival predictions in terminally ill cancer patients. *British Medical Journal,* 327(7408), 195-198.

Gonsalves, W. I., Tashi, T., Krishnamurthy, J., Davies, T., Ortman, S., Thota, R., Subbiah, S. (2011). Effect of palliative care services on the aggressiveness of end-of-life care in the Veteran's Affairs cancer population. J*ournal of Palliative Medicine,* 14(11), 1231-1235.

Gray, D., MacAdam, D., & Boldy, D. (1987). A comparative cost analysis of terminal cancer care in home hospice patients and controls. *Journal of Chronic Diseases,* 40(8), 801-810.

Gripp, S., Moeller, S., Bölke, E., Schmitt, G., Matuschek, C., Asgari, S., Willers, R. (2007). Survival prediction in terminally ill cancer patients by clinical estimates, laboratory tests, and self-rated anxiety and depression. *Journal of Clinical Oncology,* 25(22), 3313-3320.

Hanchate, A., Kronman, A.C., Young-Xu, Y., Emanuel.E.(2009). Racial and Ethnic Differences in end=of-life costs;Why do Minorities cost more than Whites? *Archives of Internal Medicine,* 169 (5), 493-501.

Hoel, D. G., Ron, E., Carter, R., & Mabuchi, K. (1993). Influence of death certificate errors on cancer mortality trends. *Journal of the National Cancer Institute,* 85(13), 1063-1068.

Hogan, C., Lunney, J., Gabel, J., & Lynn, J. (2001). *Health Affairs* , 20(4), 188-195.

Hornbrook, M.C., Malin, J., Weeks, J.C., Makgoeng, S. B., Keating, N. L., & Potosky, A. L. (2014).Did changes in drug reimbursement after the Medicare Modernization Act affect chemotherapy prescribing? *Journal of Clinical Oncology*, 32(6),4042-9.

Hui, D., Elsayem, A., De la Cruz, M., Berger, A., Zhukovsky, D. S., Palla, S., . . . Bruera, E. (2010). Availability and integration of palliative care at US cancer centers. *Journal of the American Medical Association*, 303(11), 1054-1061.

Huskamp, H.A., Buntin, M.B., Wang, V., & Newhouse, J.P (2001). Providing care at the end of life: do Medicare rules impede good care? *Health Affairs, 2*0(3), 204-211.

Jacobson, M., O'Malley, A. J., Earle, C. C., Pakes, J., Gaccione, P., & Newhouse, J. P. (2006). Does reimbursement influence chemotherapy treatment for cancer patients? *Health Affairs,* 25(2), 437-443.

Jenkins, V., Fallowfield, L., & Saul, J. (2001). Information needs of patients with cancer: results from a large study in UK cancer centres. *British Journal of Cancer,* 84(1), 48-51.

Kao, S., Shafiq, J., Vardy, J., & Adams, D. (2009). Use of chemotherapy at end of life in oncology patients. *Annals of Oncology,* 20(9), 1555-1559.

Kao, S. C., Butow, P., Bray, V., Clarke, S. J., & Vardy, J. (2011). Patient and oncologist estimates of survival in advanced cancer patients. *Psychooncology,* 20(2), 213-218.

Kheirbek,R. E., Fletcher, R.D., Bakitas, M.A., Fonarow, G.C., Parvateneni, S., Bearden, D., Bailey, F.A., Morgan, C.J., Singh, S., Blackman, M.R., Zile, M.R., Patel, K., Ahmed, M.B., Tucker, R.O., Brown, C.J., Love, T.E., Aronow, W.S., Roseman, J.M., Rich, M.W., Allman, R.M., & Ahmed,A (2015). Discharge Hospice Referral and Lower 30-Day All-cause Readmission in Medicare bBneficiaries Hospitalized for Heart Failure. *Circulation Heart Failure*, 8(4), 733-740.

Kilgore, M.L., Grabowski, D.C., David, C., Morrisey, M.A., Ritchie, C.S., Yun, H., & Locher, J.L (2009).The Effects of the Balance3d Budget Act of 1997 on Home Health and Hopsice in Older Adult Cancer Patients. *Medical Care*, 47(3), 279-285.

Kidder, D. (1992). The effects of hospice coverage on Medicare expenditures. *Health Services Research,* 27(2), 195-217.

Knaus, W. A., Harrell, F. E., Lynn, J., Goldman, L., Phillips, R. S., Connors, A. F., Wagner, D. P. (1995). The SUPPORT prognostic model. Objective estimates of survival for seriously ill hospitalized adults. Study to understand prognoses and preferences for outcomes and risks of treatments. *Annals of Internal Medicine,* 122(3), 191-203.

Lin, R. Y., Levine, R. J., & Scanlon, B. C. (2012). Evolution of End-of-Life Care at United States Hospitals in the New Millennium. *Journal of Palliative Medicine,* 15(5), 592-601.

Loggers,E.T., Maciejewski, P.K., Paulk, E., DeSanto-Madeya, S., Nilsson, M., Viswanath, K., Wright, A. A.,Balboni, T.A., Temel, J., Stieglitz, H., Block, S., & Prigerson, H,G (2009). Racial Differences in Predictors of Intensive End-of-Life Care in patients with Advanced Cancer. *Journal of Clinical Oncology,* 27 (33), 5559-64.

Lorenz, K., Lynn, J., Dy, S., Hughes, R., Mularski, R. A., Shugarman, L. R., & Wilkinson, A. M. (2006). Cancer care quality measures: symptoms and end-of-life care. *Evidence Report/ Technology Assessment,* (137), 1-77.

Lowes,R.(2015). Medicare Approves Payment for End-of-life Counseling.*Medscape Medical News* .Retrieved from http://www.medscape.com/viewarticle/853541 10.10.16.

Mack, J. W., Weeks, J. C., Wright, A. A., Block, S. D., & Prigerson, H. G. (2010). End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. *Journal of Clinical Oncology,* 28(7), 1203-1208

Maltoni, M., & Amadori, D. (2002). Prognosis in advanced cancer. *Hematology Oncology Clinics of North America,* 16(3), 715-729.

Martin, M.Y., Pisu, M., Oster, R.A., Urmie, J.M., Schrga, D., Huskamp, H.A., Lee, J., Kiefe, C.I., Fouad, M.N. (2011). Racial Variation in Willingness to Trade Financial Resources for life-prolonging cancer treatment (2011). *Cancer*, 117(15), 3476-84.

Mc Donald, J.C., du Manoir, J.M., Kevork, N., Le, L.W., & Zimmermann, C.(2016). Advanced Directives in patients with Advanced cancer receiving Active Treatment: Attitudes, Prevalence and Barriers. S*upportive Care in Cancer,* October 7. Epub ahead of print.

McKinney, M.(2010).Where you Live= How you Die. *Modern Healthcare*, 40(47), 6-8.

Mitchell, J. J. (2011). The findings of the Dartmouth Atlas Project: a challenge to clinical and ethical excellence in end-of-life care. *Journal of Clinical Ethics,* 22(3), 267-276.

Morden, N. E., Chang, C. H., Jacobson, J. O., Berke, E. M., Bynum, J. P., Murray, K. M., & Goodman, D. C. (2012). End-of-life care for medicare beneficiaries with cancer is highly intensive overall and varies widely. *Health Affairs,* 31(4), 786-796.

Moroni,M., Zocchi, D., Bolognesi, D., Abernethy, A., Rondeli, R., Savorani, G., Salera, M., Dall'Olio, F.G., Galli, G., (2014). The "Surprise" Question in Advanced Cancer Patients: A Prospective Study Among General Practitioners. *Palliative Medicine*, 28(7), 959-964.

Obermeyer, Z., Makar, M., Abujaber, S., Dominici, F., Block, S., & Cutler, D.M. Association between Medicare Hospice Benefit and Health Care Utilization and Costs for Patients with poor Prognosis Cancer (2014). *Journal of the American Medical Association*, 312 (18), 1888-1896.

Riley, G.F., Lubitz, J.D (2010). Long-term trends in Medicare payments in the last year of life. *Health Services Research*, 45(2), 565-576.

Shea,A. M., Curtis, L.H., Hammill, B.G., DiMartino, L.D., Abernethy, L.D., & Schilman, K.A.(2008). Association between the Medicare Modernization Act of 2003 and Patient Wait Times and Travel Distance for Chemotherapy. *Journal of the American Medical Association*, 300(2), 189-196.

Schnipper, L. E., Smith, T. J., Raghavan, D., Blayney, D. W., Ganz, P. A., Mulvey, T. M., & Wollins, D. S. (2012). American society of clinical oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *Journal of Clinical Oncology,* 30(14), 1715-1724.

Schulman-Green, D., Ercolano, E., Jeon, S., & Dixon, J. (2012). Validation of the Knowledge of Care Options Instrument To Measure Knowledge of Curative, Palliative, and Hospice Care. *Journal of Palliative Medicine*, (10) 1091-9.

Seow, H., Snyder, C. F., Shugarman, L. R., Mularski, R. A., Kutner, J. S., Lorenz, K. A., Dy, S. M. (2009). Developing quality indicators for cancer end-of-life care: proceedings from a national symposium. *Cancer*, 115(17), 3820-3829.

Siegel, J (2006). Impact of the Medicare Prescription Drug Improvement and Modernization Act on the Management of Colorectal Cancer.*American Journal of Health System Pharmacy*, 63(9), 518-521.

Sington, J. D., & Cottrell, B. J. (2002). Analysis of the sensitivity of death certificates in 440 hospital deaths: a comparison with necropsy findings. *Journal of Clinical Pathology*, 55(7), 499-502.

Sporn, M. B. (1996). The war on cancer. *Lancet*, 347(9012), 1377-1381.

Stewart, A. L., Teno, J., Patrick, D. L., & Lynn, J. (1999). The concept of quality of life of dying persons in the context of health care. *Journal of Pain and Symptom Managment*, 17(2), 93-108.

Tanneberger, S., Malavasi, I., Mariano, P., Pannuti, F., & Strocchi, E. (2002). Planning palliative or terminal care: the dilemma of doctors' prognoses in terminally ill cancer patients. *Annals of Oncology*, 13(8), 1320-1322.

Teno, J,M., Gozalo, L., Bynum, J.P., Leland,N.E., Miller, S.C., Morden, N.E., Scupp, T., Goodman, D.C., & Mpr, V.M. Change in end-of-life care for Medicare Beneficiaries (2013).*Journal of the American Medical Association*, 309(5), 470-477.

Teno, J.M., Freedman, V.A., Kasper, J.D., Gozalo, P., & Mor, V. (2015). Is Care for the Dying Improving in the United States?. *Journal of Palliative Medicine*, 18(8), 662-666.

Thompson, J. W., Carlson, M. D., & Bradley, E. H. (2012). US hospice industry experienced considerable turbulence from changes in ownership, growth, and shift to for-profit status. *Health Affairs*, 31(6), 1286-1293.

Vogelzang, N. J., Benowitz, S. I., Adams, S., Aghajanian, C., Chang, S. M., Dreyer, Z. E., Kris, M. G. (2012). Clinical cancer advances 2011: Annual Report on Progress Against Cancer from the American Society of Clinical Oncology. *Journal of Clinical Oncology*, 30(1), 88-109.

von Gruenigen, V., Daly, B., Gibbons, H., Hutchins, J., & Green, A. (2008). Indicators of survival duration in ovarian cancer and implications for aggressiveness of care. *Cancer*, 112(10), 2221-2227.

Warren, J. L., Barbera, L., Bremner, K. E., Yabroff, K. R., Hoch, J. S., Barrett, M. J., . Krahn, M. D. (2011). End-of-life care for lung cancer patients in the United States and Ontario. *Journal of the National Cancer Institute,* 103(11), 853-862.

Weeks, J.C., Catalano, P.J., Cronin, A., Finkelman, M.D., Mack, J.W., Keating, N.L., & Schrag, D. Patient's expectations about effects of chemotherapy for advanced cancer (2012). *New England Journal of Medicine*, 367(17), 1616-25

Wright, A. A., Zhang, B., Ray, A., Mack, J. W., Trice, E., Balboni, T., Prigerson, H. G. (2008). Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *Journal of the American Medical Association,* 300(14), 1665-1673.

Zhang, B., Wright, A. A., Huskamp, H. A., Nilsson, M. E., Maciejewski, M. L., Earle, C. C., Prigerson, H. G. (2009). Health care costs in the last week of life: associations with end-of-life conversations. *Archives of Internal Medicine*, 169(5), 480-488.

Wang, SY., Hall, J., Pollack, C.E., Adelson, K., Long, J.B., Gross, C.P.(2016). Trends in end-of-life cancer care in the Medicare program. *Journal of Geriatric Oncology* 7 (2), 116-25.

World Health Organization-WHO Definition of Palliative Care –retrieved from http://www.who.int/cancer/palliative/definition/en/ 10.10.16

APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL FORM

THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM
Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on January 24, 2017. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator: JOOSTE, RENE
Co-Investigator(s):
Protocol Number: **X121009004**
Protocol Title: *Comparing the Quality of End-of-Life Cancer Care in the Medicare Population Prior to and Afte the Enactment of the Medicare Prescription Drug, Improvement and Modernization Act of 2003*

The IRB reviewed and approved the above named project on 10-11-16. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.
IRB Approval Date: 10-11-16
Date IRB Approval Issued: 10-11-16
IRB Approval No Longer Valid On: 10-11-17
HIPAA Waiver Approved?: Yes

Marilyn Doss
Expedited Reviewer
Member - Institutional Review Board
for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

APPENDIX B

2 X 2 AND REGRESSION TABLES

2 X 2 TABLES

```
                                The SAS System

                              The FREQ Procedure

           Frequency   Table of three_day_to_death by mmr2005_date
           Percent     three_day_to_death        mmr2005_date
           Row Pct                                 0        1      Total
           Col Pct                        1    31613    34431      66044
                                               27.54    29.99      57.53
                                               47.87    52.13
                                               59.42    55.91

                                          0    21594    27156      48750
                                               18.81    23.66      42.47
                                               44.30    55.70
                                               40.58    44.09

                       Total                   53207    61587     114794
                                               46.35    53.65     100.00


             Statistics for Table of three_day_to_death by mmr2005_date
             Statistic                      DF      Value     Prob
             Chi-Square                      1   143.8451   <.0001
             Likelihood Ratio Chi-Square     1   143.9545   <.0001
             Continuity Adj. Chi-Square      1   143.7015   <.0001
             Mantel-Haenszel Chi-Square      1   143.8438   <.0001
             Phi Coefficient                       0.0354
             Contingency Coefficient               0.0354
             Cramer's V                            0.0354
```

Fisher's Exact Test	
Cell (1,1) Frequency (F)	31613
Left-sided Pr <= F	1.0000
Right-sided Pr >= F	1.955E-33
Table Probability (P)	3.042E-34
Two-sided Pr <= P	3.842E-33

Sample Size = 114794

REGRESSION TABLES

```
                              The SAS System

                            The FREQ Procedure

Frequency     Table of chemo_2wks by MMR2005_date

Percent        chemo_2wks        MMR2005_date

Row Pct                               0          1       Total

Col Pct                      1     7950      11398       19348

                                  37.33      53.51       90.84

                                  41.09      58.91

                                  90.33      91.20

                             0      851       1100        1951

                                   4.00       5.16        9.16

                                  43.62      56.38

                                   9.67       8.80

              Total                8801      12498       21299

                                  41.32      58.68      100.00


              Statistics for Table of chemo_2wks by MMR2005_date

                Statistic                    DF     Value     Prob

                Chi-Square                    1    4.6755   0.0306
```

Statistic	**DF**	**Value**	**Prob**
Likelihood Ratio Chi-Square	1	4.6541	0.0310
Continuity Adj. Chi-Square	1	4.5717	0.0325
Mantel-Haenszel Chi-Square	1	4.6753	0.0306
Phi Coefficient		-0.0148	
Contingency Coefficient		0.0148	
Cramer's V		-0.0148	

Fisher's Exact Test

Cell (1,1) Frequency (F)	7950
Left-sided Pr <= F	0.0164
Right-sided Pr >= F	0.9855
Table Probability (P)	0.0019
Two-sided Pr <= P	0.0318

The LOGISTIC Procedure

Model Information

Data Set	_EXP0_.RJNOSKIN_HOSPICEFINAL_TREND
Response Variable	three_day_to_death
Number of Response Levels	2
Model	binary logit
Optimization Technique	Fisher's scoring

Number of Observations Read	114794
Number of Observations Used	114794

Response Profile

Ordered Value	three_day_to_death	Total Frequency
1	0	48750
2	1	66044

Probability modeled is three_day_to_death=1.

Model Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Intercept Only	Intercept and Covariates
AIC	156524.95	155490.31
SC	156534.60	155625.42
-2 Log L	156522.95	155462.31

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	1060.6329	13	<.0001
Score	1056.7983	13	<.0001

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Wald	1048.1413	13	<.0001

Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	0.5571	0.0371	225.5385	<.0001
mmr2005_date	1	-0.4326	0.0233	344.7578	<.0001
time_trend1	1	0.0573	0.00382	224.9907	<.0001
race_white	1	-0.0700	0.0190	13.6079	0.0002
sex_male	1	-0.2096	0.0131	257.5694	<.0001
gi_ca	1	-0.2880	0.0286	101.7435	<.0001
gu_ca	1	-0.3328	0.0327	103.3675	<.0001
lung_ca	1	-0.3213	0.0283	128.9173	<.0001
other_ca	1	-0.4304	0.0292	218.0046	<.0001
breast_ca	1	-0.2566	0.0363	50.1003	<.0001
younger_sixtyfive	1	0.2678	0.0294	82.9159	<.0001
seventy_seventyfour	1	-0.00812	0.0209	0.1511	0.6975
seventyfive_seventyn	1	0.0784	0.0198	15.7468	<.0001
eighty_older	1	0.1762	0.0161	120.1764	<.0001

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
mmr2005_date	0.649	0.620	0.679
time_trend1	1.059	1.051	1.067
race_white	0.932	0.898	0.968
sex_male	0.811	0.790	0.832
gi_ca	0.750	0.709	0.793
gu_ca	0.717	0.672	0.764
lung_ca	0.725	0.686	0.767

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
other_ca	0.650	0.614	0.688
breast_ca	0.774	0.721	0.831
younger_sixtyfive	1.307	1.234	1.385
seventy_seventyfour	0.992	0.952	1.033
seventyfive_seventyn	1.082	1.040	1.124
eighty_older	1.193	1.156	1.231

Association of Predicted Probabilities and Observed Responses

Percent Concordant	54.8	**Somers' D**	0.110
Percent Discordant	43.8	**Gamma**	0.112
Percent Tied	1.3	**Tau-a**	0.054
Pairs	3219645000	**c**	0.555

```
                              The SAS System

                          The LOGISTIC Procedure
                            Model Information

    Data Set                      _EXP0_.RJNOSKINCHEMO_TIMETREND1
    Response Variable             chemo_2wks
    Number of Response Levels     2
    Model                         binary logit
    Optimization Technique        Fisher's scoring

                 Number of Observations Read   21299
                 Number of Observations Used   21299

                             Response Profile

                   Ordered  chemo_2wks        Total
                     Value               Frequency
                         1  0                 1951
                         2  1                19348

                   Probability modeled is chemo_2wks=1.

                        Model Convergence Status

              Convergence criterion (GCONV=1E-8) satisfied.

                          Model Fit Statistics

               Criterion  Intercept Only  Intercept and
                                             Covariates
               AIC             13046.587      12977.213
               SC              13054.554      13088.742
               -2 Log L        13044.587      12949.213

                 Testing Global Null Hypothesis: BETA=0

            Test               Chi-Square  DF  Pr > ChiSq
            Likelihood Ratio      95.3745  13      <.0001
            Score                 95.3834  13      <.0001
```

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Wald	94.5543	13	<.0001

Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	2.3729	0.1044	516.5934	<.0001
MMR2005_date	1	-0.2324	0.0937	6.1514	0.0131
time_trend1	1	0.0608	0.0149	16.6846	<.0001
race_white	1	-0.1714	0.0721	5.6580	0.0174
sex_male	1	-0.0778	0.0502	2.4027	0.1211
GI_ca	1	-0.2881	0.0757	14.4883	0.0001
gu_ca	1	-0.0925	0.0893	1.0728	0.3003
lung_ca	1	-0.4433	0.0720	37.9434	<.0001
other_ca	1	-0.2181	0.0819	7.0970	0.0077
breast_ca	1	-0.3833	0.1075	12.7058	0.0004
younger_sixtyfive	1	0.1140	0.0879	1.6818	0.1947
seventy_seventyfour	1	0.00398	0.0671	0.0035	0.9528
seventyfive_seventyn	1	0.1345	0.0714	3.5423	0.0598
eighty_older	1	0.2427	0.0684	12.5882	0.0004

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
MMR2005_date	0.793	0.660	0.952
time_trend1	1.063	1.032	1.094
race_white	0.842	0.732	0.970
sex_male	0.925	0.838	1.021
GI_ca	0.750	0.646	0.870
gu_ca	0.912	0.765	1.086
lung_ca	0.642	0.557	0.739

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
other_ca	0.804	0.685	0.944
breast_ca	0.682	0.552	0.842
younger_sixtyfive	1.121	0.943	1.331
seventy_seventyfour	1.004	0.880	1.145
seventyfive_seventyn	1.144	0.994	1.316
eighty_older	1.275	1.115	1.458

Association of Predicted Probabilities and Observed Responses

Percent Concordant	55.1	**Somers' D**	0.132
Percent Discordant	42.0	**Gamma**	0.136
Percent Tied	2.9	**Tau-a**	0.