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3. Riha HM, Erdman MJ, **Vandigo J**, Kimmons LA, Goyal N, Davidson EK, Pandhi A, Jones, GM. Impact of Moderate Hyperchloremia on Clinical Outcomes in Intracerebral Hemorrhage Patients Treated with Continuous Infusion Hypertonic Saline: A Pilot Study. *Critical Care Medicine.* 2017;45(9):e947-53.
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ABSTRACT

Title of Dissertation: The Impact of Medicare Contracting Reform on Metastatic Colon Cancer Treatment, Survival, and Costs

Joseph E. Vandigo, Doctor of Philosophy, 2018

Dissertation Directed by: Professor C. Daniel Mullins, PhD

Background: Receipt of metastatic colon cancer (mCC) treatment for Medicare beneficiaries varies across geography, potentially due to claims processors. Medicare contracting reform consolidated legacy claims processors, known as fiscal intermediaries (Part A) and carriers (Part B) into larger entities known as Medicare Administrative Contractors (MACs), responsible for both Part A and B claims.

Methods: This retrospective study used Surveillance, Epidemiology and End Results (SEER) and Medicare claims data to examine the effect of Medicare contracting reform using a difference-in-differences approach. Outcomes included the receipt of guideline-recommended chemotherapy and biologic therapy, overall survival, and mean costs for Medicare beneficiaries over age 66, diagnosed with mCC between 2005 and 2009. A generalized linear model estimated receipt of therapy and mean costs. An inverse-probability of treatment weighted Cox proportional-hazards regression modeled adjusted hazard ratios for predictors of mortality.

Results: Among 4,030 mCC patients, there was no statistically significant association between MAC implementation and patient receipt of guideline chemotherapy (Odds Ratio [OR]: 1.00; 95% Confidence Interval [CI] 0.65, 1.56) or biologic therapy (OR:

0.90; 95% CI: 0.57, 1.39). No impact of MAC implementation was observed on overall survival (Hazard Ratio: 1.14; 95% CI: 0.92, 1.41) or mean total costs, regardless of number of treatment lines received. Patients diagnosed in regions where the MAC was a new entity were more likely to receive biologic therapy and had higher costs as compared to patients diagnosed in regions where a legacy contractor became the MAC. Findings were robust to changing assumptions regarding timing of MAC implementation.

Conclusions: Receipt of treatment and total costs varied by geographic region in both the pre-implementation and post-implementation periods. However, Medicare contracting reform did not impact mCC patients' access to guideline therapy, survival, or total costs. Future research on geographic variation should focus on later stages of contractor consolidation and disease states vulnerable to local coverage decisions.

The Impact of Medicare Contracting Reform on Metastatic Colon Cancer Treatment,
Survival, and Costs

by
Joseph Edward Vandigo

Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, Baltimore in partial fulfillment
of the requirements for the degree of
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To my family –

Summer, Mom, Dad, Jackie, Micah and a Yorkshire Terrier named Captain Albert

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List of Abbreviations

ACS	American Cancer Society
CCI	Charlson Comorbidity Index
CMMI	Center for Medicare & Medicaid Innovation
CMS	Centers for Medicare & Medicaid Services
DID	Difference-in-differences
EGFR	Epidermal Growth Factor Receptor
FDA	United States Food and Drug Administration
FI	Fiscal Intermediary
GLM	Generalized Linear Model
HMO	Health Maintenance Organization
ICC	Intraclass Correlation Coefficient
IPTW	Inverse Probability of Treatment Weight
IPW	Inverse Probability Weight
IQR	Interquartile Range
LPM	Linear Probability Model
MAC	Medicare Administrative Contractor
MACRA	Medicare Access and CHIP Reauthorization Act
MMA	Medicare Prescription Drug, Improvement, and Modernization Act
mCC	Metastatic Colon Cancer
MAC	Medicare Administrative Contractor
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute

OCM	Oncology Care Model
RFP	Request for Proposal
PEDSF	Patient Entitlement and Diagnosis Summary File
SEER	Surveillance, Epidemiology, and End Results

Chapter One: Study Background and Aims

The background chapter begins with a description of metastatic colon cancer (mCC), treatments for mCC, and geographic variation in treatment receipt for Medicare beneficiaries. The subsequent sections explain fiscal intermediaries and carriers, and describe how Medicare Administrative Contractors replaced these entities during Medicare contracting reform. The chapter concludes with a description of Medicare Administrative Contractors and the aims of this research.

Colon Cancer and Colon Cancer Epidemiology

Colon cancer is cancer that develops in the first six feet of the large intestine.¹ In reported statistics, it is commonly grouped with cancers that develop in the rectum (the last 6 inches of the large intestine) as colorectal cancer; however, these cancers are separate and treatment regimens differ significantly between the two.^{2,3} The American Cancer Society (ACS) estimates there were 95,520 new, or incident, cases of colon cancer in the United States in 2017 and approximately 50,260 deaths.⁴ The National Cancer Institute (NCI) reports the median age at diagnosis and death for cases from 2006-2010 at 69 and 74 years old, respectively. NCI data also indicate that the incidence rate for cases diagnosed in 2009 through 2013 from the 18 Surveillance, Epidemiology, and End Results (SEER) Program regions was 29 cases per 100,000 people per year. This incidence increases to 153 per 100,000 people per year among individuals age 65 and older; the population covered by Medicare insurance coverage in the United States.²

The NCI also provides information on stage at diagnosis. Among individuals diagnosed from 2009-2012, 22% were diagnosed with distant disease (“*cancer that has spread from the primary site to distant organs or distant lymph nodes*”).^{1,5} This research focused on

individuals with distant disease, also referred to as metastatic or stage IV disease. The overall age-adjusted incidence rates of colon cancer have decreased gradually since the SEER registry began collecting data in 1975; (from 59.54 per 100,000 in 1975 to 54.04 per 100,000 in 1995, and 37.87 per 100,000 in 2013). The American Cancer Society also presents evidence that overall incidence of colon cancer is not distributed evenly between genders or geographically across the United States. Males represent a disproportionate number of new incident cases (52.7%) and deaths (54%) estimated to occur in 2017. Incidence and death rates are also generally higher in the Midwestern and Southern regions of the country as opposed to the East and West Coasts⁶

The overall 5-year survival rate for all colon cancer cases diagnosed from 2006-2012 (65.5%) has improved compared to earlier time periods; 50.6% for individuals diagnosed in 1975-1977 and 59.8% for individuals diagnosed between 1996-1998. Among individuals diagnosed from 2006-2012 who were age 65 or older, 5-year survival was 62.6%; the rate of survival among whites age 65 and older during this time was 63.3% as compared with 53.1% for blacks.² Stage of disease also has an impact on 5-year survival probability. Data from 2006-2012 indicate that 91.1% of individuals diagnosed with localized disease will be alive in five years, compared to 13.3% of those diagnosed with mCC. Racial disparities noticed in incidence rates also persist in survival. Fourteen percent (14%) of whites diagnosed with mCC will survive 5 years or longer as compared with only 9.4% of blacks.²

Treatment of Metastatic Colon Cancer

In mCC, there are two primary treatment options: chemotherapy and biologic therapy. Surgery at this stage of disease is conducted only among the healthiest patients who have

metastasis to the liver or lung, and is typically more palliative than curative in intent.⁷

Chemotherapies are medicines that indiscriminately kill cancer and certain quickly dividing non-cancer cells in the body.⁸ Chemotherapy has been used to treat mCC since fluorouracil, also known as 5-fluorouracil or 5-FU, received Food and Drug Administration (FDA) approval in 1958.⁹ Biologic therapies, a more recent addition to the mCC treatment arsenal, utilize the patient's immune system to fight cancer and offer a slightly improved side-effect profile over traditional chemotherapy.¹⁰ Table 1 lists chemotherapy and biologic therapies used in the treatment of mCC.

Table 1. National Comprehensive Chemotherapy Network listed chemotherapy and biologic therapy for the treatment of metastatic colon cancer

Name	Description	Method of Administration
Chemotherapies		
<i>fluorouracil</i>	Interferes with DNA/RNA creation	Intravenous
<i>capecitabine</i>	(Converted to 5FU)	Oral (tablet)
<i>floxuridine</i>	(Converted to 5FU)	Arterial Pump
<i>leucovorin</i>	Enhances activity of 5FU	Multiple ^a
<i>irinotecan</i>	Blocks enzyme necessary for cell division	Intravenous
<i>oxaliplatin</i>	Inhibits DNA repair/synthesis	Intravenous
Biologic Therapies		
<i>bevacizumab</i>	Stops creation of new blood vessels in tumor	Intravenous
<i>cetuximab</i>	Binds with cancer cells to signal immune response	Intravenous
<i>panitumumab</i>	Deactivates protein necessary for cancer cell growth	Intravenous
Note: National Comprehensive Cancer Network-recommended chemotherapies, biological therapies, and combination regimens for treatment of metastatic colon cancer in 2010 ¹¹⁻¹³		
^a Oral (tablet or solution), intravenous infusion, intramuscular injection		

As illustrated in Table 2, treatment regimens consisting of chemotherapies combined with one another and biologic therapies are also utilized. The concept of combination therapy is based on evidence indicates a synergistic effect when using certain chemotherapy and biological therapy of different classes in combination. This effect is attributed to

suppressive effect combination therapy has on a tumor’s ability to build resistance to medicines.¹⁴

Table 2. NCCN-recommended treatment regimens for metastatic colon cancer

Regimen	Abbreviation
Oxaliplatin + Leucovorin + Fluorouracil ± [<i>Bevacizumab OR Panitumumab</i>]	FOLFOX
Irinotecan + Leucovorin + Fluorouracil ± [<i>Bevacizumab OR Cetuximab OR Panitumumab OR Ziv-Aflibercept</i>]	FOLFIRI
Fluorouracil + Leucovorin	5-FU/LV
Oxaliplatin + Capecitabine ± [<i>Bevacizumab</i>]	CapeOX
Capecitabine + <i>Bevacizumab</i>	-
Oxaliplatin + Irinotecan	IROX
Oxaliplatin + Irinotecan + Leucovorin + Fluorouracil	FOLFOXIRI

In addition to combination therapy, patients who are healthy enough are also likely to receive more than one treatment regimen following “failure” (due to non-responsiveness of the tumor, concerns about toxicity, or patient preference) of the previous line of treatment.¹⁵ Evidence from Medicare patients diagnosed from 2003-2007 indicates that approximately 41% of patients receive initial chemotherapy or biologic therapy. Fewer than 1 in 5 (18%) receive second-line therapy and only 3% of all patients receive third line treatment.¹⁶ The National Comprehensive Cancer Center (NCCN) Guidelines provide an evidence-based framework on the use of a variety of different combinations of chemotherapy (with or without a biologic therapy) in patients based upon stage, prior treatments received, and comorbid conditions.¹¹ In the elderly Medicare population, the majority of patients begin treatment with a combination of fluorouracil and leucovorin (27%) or oxaliplatin with (24%) or without (21%) bevacizumab.¹⁶ Among the 18% of

patients who do receive second-line therapy, 61% will receive irinotecan (IRI) with or without a biologic therapy and 26% will receive oxaliplatin with or without a biologic therapy. This choice of second line therapy depends upon the therapy chosen for first line. A patient receiving oxaliplatin first line will not receive oxaliplatin in any subsequent line. Similarly, patients beginning therapy with IRI will receive another non-IRI chemotherapy in subsequent lines¹⁶

A degree of uncertainty in the decision-making process exists when an oncologist is selecting a treatment for an elderly patient. This uncertainty arises primarily due to the presence of comorbid chronic disease in geriatric populations, such as hypertension, diabetes, or chronic obstructive pulmonary disorder, and other physiologic changes that occur as an individual ages. As a result of these differences, elderly patients are systematically underrepresented in traditional randomized clinical trials and the evidence base for use of therapy in this population is not as robust as for younger populations.¹⁷

This uncertainty results in oncologists having latitude in selecting an appropriate treatment for a patient based on a patient's specific characteristics.¹⁸ The variety of treatment options for which there is an evidence base can lead to situation where reimbursement incentives influence treatment patterns in cancer. This typically occurs when a provider moves away from a fee-for-service environment and towards a capitated or episode-based payment mechanism, which disincentivizes the use of high-cost care.^{19,20} Complete lack of reimbursement has also been identified by oncologists internationally as the major barrier to patient access for bevacizumab specifically.²¹

Financial incentives are not the only mechanism that can impact prescribing patterns. Prior authorization, in which a provider must receive approval before prescribing a

medicine to a patient, is the most commonly used method of utilization method in oncology.²² There is evidence that the delays in treatment that result from prior authorization lead to shifts in treatment patterns, often towards guideline-recommended care not requiring authorization.²³ Therefore, any characteristics of the reimbursement environment that an oncologist practices in that impede the oncologist from prescribing a medicine have the potential to impact patient access to care.

Genetic Testing for Biologic Therapies

Cetuximab was the first biologic therapy approved by the FDA (2004) for use in mCC.²⁴ It works by targeting a protein, epidermal growth factor receptor (EGFR) that enables cancer cells to grow.²⁵ Panitumumab, approved more than two years later, also works by targeting EGFR.²⁶ In 2005, evidence began to accumulate that indicated that a specific mutation to the V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS) gene, found in approximately 40% of colon cancers, prevented gefitinib, an EGFR inhibitor, from working correctly in individuals with non-small cell lung cancer.²⁷ In 2007, researchers discovered a link between wild-type (non-mutated) KRAS genes and improved response to cetuximab as compared with individuals with KRAS mutation.²⁸ A year later, researchers found a similar relationship between wild-type KRAS and the efficacy of panitumumab; for individuals with KRAS mutations, the hazard of death [0.99; 95% CI, 0.73 to 1.36] was twice that found in the wild-type group [0.45; 95% CI: 0.34 to 0.59].²⁹ In 2009, the FDA labeling of cetuximab and panitumumab changed to show that neither was recommended for use in patients whose tumors had KRAS mutations.^{30,31} FDA subsequently removed patients with KRAS mutations from cetuximab's and panitumumab's indications in 2012.^{32,33} The clinical efficacy of

bevacizumab is not dependent on a tumor's KRAS mutation status as it targets vascular endothelial growth factor (VEGF) and prevent tumors from forming new blood vessels.²⁵

Medicare and Geographic Variation in Oncology Treatment

Medicare was established by the Social Security Amendments of 1965 to provide elderly and disabled Americans with access to adequate, federally-funded health insurance.^{34,35}

However, despite equivalent coverage, geographic location has been shown to introduce variations in treatments and spending for Medicare patients.^{36,37} Explanations for

variation in Medicare spending and utilization range from illness distribution,

demographics and physician practice style.³⁸⁻⁴² However, even after adjusting for these

factors, regional variation in Medicare spending, utilization, and treatment remains. As

Table 3 illustrates, variation in chemotherapy receipt exists in the mCC Medicare

population. There is also evidence that among the population represented by SEER-

Medicare, racial disparities exist in the stage at diagnosis and receipt of chemotherapy for prostate cancer patients with identical Medicare coverage.^{43,44} Research has demonstrated

treatment variation attributable to rural/urban status, survival differentials due to

urban/rural status, an association between treatment line receipt and SEER-region, and a

relationship between impoverished census tract and geographic region with reduction in

the likelihood of receiving chemotherapy.⁴⁵⁻⁴⁸

Table 3. Observational studies examining geographic variation in care for Medicare colon cancer patients

Study (Year)	Data Source (Years) n	Cancer (Stage)	Geographic Difference Found
Lund (2013) ⁴⁷	SEER/Medicare (2004-2007) n=4388	Colorectal (II, III)	<i>“Patients who were older; diagnosed before 2006; separated, divorced, or widowed; living in a higher poverty census tract or in the East or Midwest; or with higher levels of comorbidity were less likely to receive oxaliplatin.”</i>
Panchal (2013) ⁴⁶	SEER/Medicare (2003-2005) n=4106	Colon (III)	<i>“Patients in less urban regions were approximately 42% less likely to receive oxaliplatin chemotherapy than those residing in a big metro region.”</i>
Reese (2013) ⁴⁸	SEER/Medicare (2003-2007) n=7952	Colon (IV)	<i>“Compared with individuals living in the Connecticut SEER-region, patients living in other regions (except Los Angeles) were less likely to receive first or second line chemotherapy.”</i>
Panchal (2016) ⁴⁵	SEER/Medicare (2004-2009) n=8275	Colon (III)	<i>“Rural regions showed lowest 3-year survival, whereas big metro regions showed better 3-year survival rate than any other region (67.3% in rural regions vs. 69.5% in big metro regions).”</i>

Medicare Claims Processing in Part A and Part B

Private health care insurers have processed medical claims for Medicare beneficiaries since the program’s inception. These insurers, known as fiscal intermediaries (FIs) and carriers, processed all fee-for-service Medicare claims. Carriers were responsible for claims from physicians and laboratories (primarily Part B) while fiscal intermediaries managed Part A and B claims from hospitals and skilled nursing facilities. In 2003, there were 25 fiscal intermediaries and 18 carriers, also known now as legacy contractors. These legacy contractors varied significantly in respects to both volume of services provided and geographic spread. Legacy contractor jurisdictions could “encompass a single county, a single state, a block of states, or several states in different areas of the country.”⁴⁹ Furthermore, some legacy contractors served as both FIs and carriers in

separate geographic regions. As an example of this scenario, Noridian Healthcare Solutions served as both the fiscal intermediary and carrier in North Dakota, but only as the carrier in South Dakota, Wyoming, and Arizona.⁵⁰

Medicare Contracting Reform

Legacy contractors enjoyed a unique position among government contractors. As a concession to gain the approval of providers during the creation of Medicare, and to calm fears of government overreach, hospitals had the ability to select their own fiscal intermediary without input from the government.⁵¹ Carriers were similarly selected, primarily from among Blue Shield and large commercial plans.⁵² This meant that legacy contractors did not face a competitive bidding process and there was no performance-based incentive to improve service quality. In addition, legacy contractors could terminate their contracts with CMS for any reason by providing notice 180 days in advance while CMS was required to document significant performance issues and had to allow legacy contractors a hearing before contract termination.⁵³

These inefficiencies, as well as an aging information technology infrastructure, led to the call for reforms to the way in which Medicare claims were processed. In 2003, the Centers for Medicare & Medicaid Services (CMS) was directed via Section 911 (Increased Flexibility in Medicare Administration) of Subtitle B (Contracting Reform) of the Medicare Prescription Drug Improvement, and Modernization Act (MMA) of 2003 to replace the Part A FIs and Part B carriers with A/B Medicare Administrative Contractors (MACs). This act required competition for contracts and set contract length at five years between re-competition. The policy change also instituted quality measurement and performance incentives, and consolidated the number of jurisdictions.⁵⁴ The MMA

called for CMS to dissolve the relationships with the current fiscal intermediaries/carriers and create new contracts with a system involving fewer Medicare administrative contractors (MACs). Under the legislation, MACs retained the authority to make local coverage determinations (LCDs) previously held by FIs. For this research, coverage is assumed identical across regions as there were no LCDs on any medicines included in the analysis during the period under study. CMS began awarding MAC contracts in mid-2006 and to date, there are 15 MACs for Part A/B Claims, with plans to consolidate to 10 MACs in the future. Because the process of awarding MAC jurisdictions was now competitive, competing contractors had the right to protest contract awards, leading to delays in implementation in Washington, Louisiana, Michigan, and Kentucky.

Table 4. Key dates in Medicare contracting reform in SEER-Medicare states

State	Fiscal Intermediary	Carrier	MAC	RFP Issued	Award Date	Full Responsibility Date
CA HI	UGS	NHIC	Palmetto GBA	12/2006	10/2007	10/2008
WA	Premera	Noridan		-	-	*
UT	Regence	Noridan	Noridian	9/2005	7/2006	3/2007
NM	TrailBlazer	BCBS AR	Trailblazer	9/2006	8/2007	3/2008
IA	Cahaba	Noridan	Wisconsin Physicians Service	9/2006	9/2007	9/2008
LA	BCBS MS	BCBS AR	Novitas Solutions	-	-	*
MI	UGS	Wisconsin Physicians Service	Wisconsin Physicians Service	-	-	*
GA	BCBS GA	Cahaba	Cahaba	8/2007	1/2009	9/2009
NJ	BCBS TN (Riverbend)	Empire	Highmark Medicare Services	9/2006	10/2007	1/2009
CT	Anthem NH	NHIC	National Government Services	12/2007	3/2008	11/2008
KY	Anthem AdminaStar	Anthem AdminaStar	CGS Aministrators	-	-	*

Abbreviations: RFP=Request for Proposal, BCBS=Blue Cross Blue Shield, NHIC= National Heritage Insurance Company, UGS= United Government Services

*Contract award protested, no implementation in study period

Goals of Contracting Reform and Stakeholder Feedback

The United States Department of Health and Human Services (HHS) explicitly stated that “[c]ontracting reform was intended to improve Medicare’s administrative services to beneficiaries and health care providers through the use of new contracting tools including competition and performance incentives.”⁴⁹ Further down in this same report to Congress, HHS indicates that implementing changes to Medicare contracting will “[. . .] improve beneficiary and provider access to information through consolidated, standardized administrative services, all of which will result in the ability to provide more comprehensive and higher-quality care for beneficiaries.”⁴⁹ However, both immediately following the passage of the MMA and immediately following the first round of MAC implementation, evidence exists of provider concern with the potential negative impact. Three physician groups, the American College of Radiology, the Alliance of Specialty Medicine, and the American Medical Association submitted comment letters that provide insight into the mechanism by which administrative contracting reform could directly influence patient treatment and outcomes. The largest concern was the delayed payments due to the mishandling of claims resulting from the new competitive bidding process underfunding the MACs relative to the legacy contractors. Prior research has demonstrated that oncologists respond to reimbursement changes in terms of prescribing. Prior research has demonstrated that oncologists respond to reimbursement changes in terms of prescribing chemotherapy.⁵⁵ Delaying payments could therefore, act as an unintended reimbursement change and subsequently impact patient access. On the inverse, consolidation has the potential to improve coverage and

reimbursement due to economies of scale and scope, potentially reducing uncertainty concerning access barriers, such as provider enrollment and appeals management.

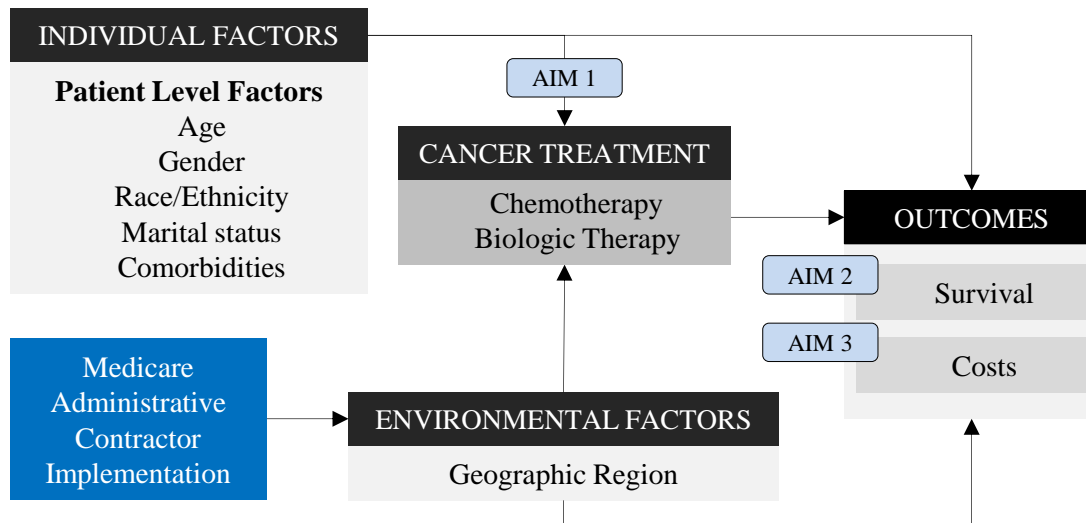
Table 5. Stakeholder responses to Medicare contracting reform

Stakeholder (Year)	Verbatim Comments
American College of Radiology ⁵⁶ (2004)	“[...] in order to ensure that beneficiary care is not disrupted, CMS should continue to ensure timely and accurate payments during and after the transition between the old and new contractors. CMS should anticipate possible software system problems and address these issues prior to the transition.”
Alliance of Specialty Medicine ⁵⁷ (2004)	<p>A. “The award of MAC contracts will end the historical separation of contractors administering Part A and Part B of the Medicare. It will change long-standing relationships with physicians, contractors, and CMS that are extremely complex and valuable.”</p> <p>B. “Claims payment must be timely and accurate. New contractor systems should be thoroughly pilot tested before national implementation. Every transition to new Medicare payment systems has been fraught with contractor software problems, which adversely affect provider cash flow.”</p>
American Medical Association ⁵⁸ (2011)	<p>A. “The AMA is concerned that as a result of a competitive bidding process, the MACs are funded at levels significantly lower than the previous carriers. This is having a significant impact on physicians’ ability to deliver high quality patient care”</p> <p>B. “The AMA continues to learn of numerous problems with the Center for Medicare and Medicaid Services’ (CMS) transition to these MACs. Complaints are widespread and include problems such as mishandling physician claims—both paper and electronic—leading to significant delays in payment. Physician offices are also facing significant and frustrating delays in the timeliness and accuracy of the MAC’s customer service to address these mishandled claims. These issues are drastically affecting physicians’ ability to provide high quality patient care. In some instances, physician offices have even had to seek private loans to cover the lost cash flow directly due to the MACs mishandling of their claims”</p>

Conceptual Framework

A conceptual framework based on Anderson's behavioral model of health services utilization framed the relationship between Medicare Administrative contractor implementation and patient-level outcomes.^{59,60} This framework, shown in Figure 2 below, identifies the relationship between MAC implementation and individual and environmental factors that determine treatment and outcomes for Medicare mCC patients. [1], [2], and [3] correspond to the specific aims of this dissertation work.

Figure 1. Conceptual framework for the research



Specific Aims and Hypotheses

Aim 1: To determine the extent to which Medicare contracting reform influenced a Medicare mCC patient's likelihood of receiving NCCN-guideline chemotherapy and/or biologic therapy.

Testable Hypothesis: Medicare Contracting Reform increased the number of patients receiving NCCN-guideline chemotherapy and/or biologic therapy.

Aim 2: To identify the impact of MAC implementation on overall mortality among Medicare mCC patients.

Testable Hypothesis: Medicare patients with mCC experienced a reduction in mortality associated with MAC implementation, suggesting that quality of care improved due to Medicare contracting reform.

Aim 3: To determine the impact of MAC implementation on the mean direct medical costs associated with the treatment of Medicare mCC patients.

Testable Hypothesis: Mean direct medical costs increased as a result of MAC implementation, primarily driven by an increase in the proportion of receiving treatment and improvements in survival.

Chapter Two: Study Design and Cohort

Study Cohort

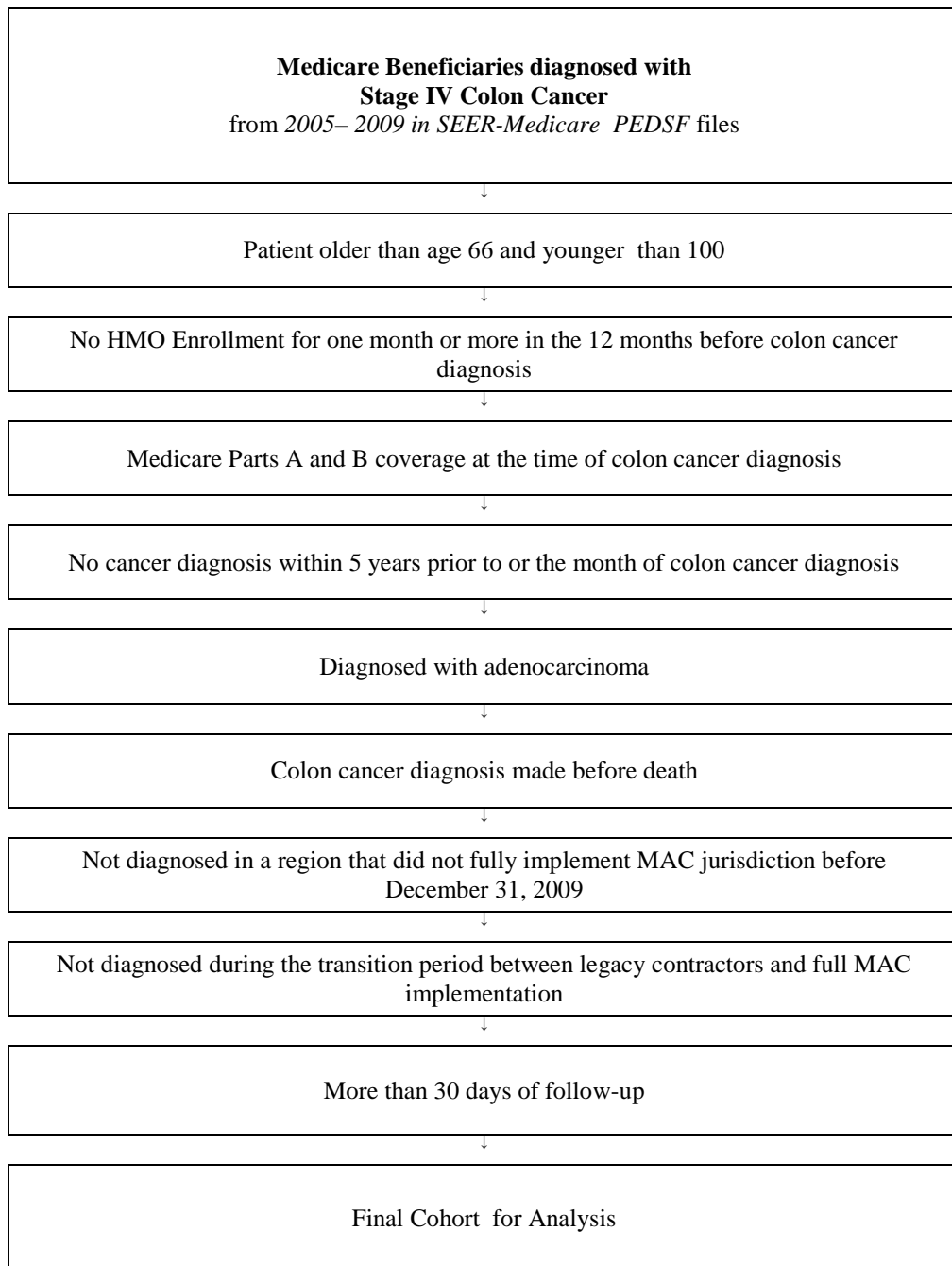
The SEER-Medicare Dataset

This analysis utilized the data available in the Surveillance, Epidemiology and End-Results (SEER)-Medicare database. The SEER-Medicare database combines SEER cancer registry data with longitudinal Medicare claims for individuals in areas that participate in the SEER-Registry program. SEER-Medicare is comprised of several files, linked by a patient-level identifier. This linkage is successful in links incident cases of cancer to a patient's Medicare files, a process that is successful for more than 93% of SEER cases.⁶¹ The data files available in SEER-Medicare combine clinical and resource utilization information for Medicare-enrolled patients with cancer. Each Medicare file contains claims generated from services available through Medicare Parts A, B, and D. Detailed descriptions of the files included in the SEER-Medicare datasets are presented in Appendix 1, Table 35. Analyses of SEER-Medicare data are the basis of 1621 peer-reviewed studies from 1993 to 2017, supporting its use as a resource to study cancer care and related outcomes in the elderly.⁶²

Inclusion / Exclusion Criteria

This study included Medicare beneficiaries in the SEER-Medicare database diagnosed with mCC between 2005 and 2009 who were between 66 and 100 years old at the time of cancer diagnosis. Although eligibility for Medicare begins at age 65, Medicare beneficiaries without continuous enrollment in Medicare Parts A and B in the year prior to cancer diagnosis were excluded, as these patients would lack information required to assess baseline comorbid burden. Patients in the 65-66 year old age range would not have the information to make this determination. Management of colon cancer is complicated by age. Colon cancer treatment in the elderly is more complex than in the non-elderly population and age is positively correlated with refusal of treatment; patients over 100 years old were excluded to make the sample representative of patients who would likely receive treatment.^{17,63-65} Patients with a history of cancer within the last five years were excluded to remove potential confounding from prior treatment or recurrence. A diagnosis of adenocarcinoma, which represents 96% of colon cancer diagnoses, was required for study inclusion as the remaining 4% includes a heterogeneous group of tumor types.^{66,67} Patients diagnosed after death were excluded as these individuals would not have had the opportunity to receive treatment. Evidence indicates that cohorts of patients with metastatic disease who survive beyond the first thirty days of diagnosis differ, primarily in respect to comorbidity burden, from individuals surviving beyond the first thirty days of diagnosis.⁶⁸ Patients diagnosed in a region where MAC implementation did not occur during the study period and patients diagnosed during the transition from FI/Carrier to MAC were excluded. Full inclusion and exclusion criteria, including order of application, are shown in Figure 2.

Figure 2. Flowchart of study inclusion/exclusion criteria



Difference-in-Differences (DID) Framework

In economics, the difference-in-differences (DID) estimator has been used to analyze a wide range of causal relationships associated with policy change; from the relationship between employment levels and increase in minimum wage to outcomes related to provisions of the Patient Protection and Affordable Care Act of 2010.⁶⁹⁻⁷¹ Recent examples of regional and national healthcare analyses conducted using the DID framework are presented in Table 6. This framework, also known as effect modification in the epidemiology literature, is appropriate for the analyses conducted in this dissertation. Patients receiving care in regions where their legacy contractor became the MAC are considered not exposed to the “treatment” of Medicare contracting reform as the same entity maintained responsibility for claims processing throughout. Patients diagnosed in regions where the legacy contractor was not a legacy contractor have a similar “untreated” experience in the period before implementation but become exposed to “treatment” following the transition to the MAC in the post-implementation period. Taking the difference between the expected outcomes between these two groups provides an estimate of the impact of contracting reform on patient outcomes. Regression models utilizing a DID framework were used to estimate the impact of Medicare contracting reform on treatment receipt and outcomes. The results of this analysis provide the average treatment effect on the treated (ATT); in this instance the impact of a new contractor entering a region during Medicare administrative contractor reform among regions where a new entity replaced the legacy contractors.⁷²

Table 6. Studies applying difference-in-differences approach to analyze United States health care policy

Author (Year) Journal	Policy Analyzed	Statistical Analysis	Results
Mullins et al. ⁷³ (2013) Transplantation	Benefits Improvement and Protection Act (BIPA)	Generalized logistic regression	<i>“Evidence indicated that BIPA increased the likelihood patients over age 65 received a kidney transplant and decreased the likelihood for patients under age 65.”</i>
Robbins et al. ⁷⁰ (2015) JAMA	Affordable Care Act Dependent Coverage Expansion (ACA-DCE)	Linear probability model	<i>“2 years post ACA-DCE, women aged 21 - 25 were more likely to be diagnosed with early-stage disease and receive fertility-sparing treatment as compared with 26-34 year olds”</i>
Hall et al. ⁷¹ (2016) American Journal of Public Health	Affordable Care Act (ACA) Medicaid Expansion	Multivariate regression model	<i>“After the ACA, respondents in expansion states were significantly more likely to be employed compared with those in non-expansion states”</i>
Ho et al. ⁷⁴ (2016) Med Care Research and Review	State Smoking Bans and Cigarette Taxes	OLS regressions	<i>“Smoking bans were not associated with heart failure outcomes. Higher cigarette taxes were associated with lower heart failure hospitalizations. Both bans and taxes resulted in fewer pneumonia hospitalizations for adults aged 60 to 74”</i>
Hu and Mortensen ⁷⁵ (2016) Health Services Research	Statewide Medicaid Managed Care Program (Florida)	Linear probability models	<i>“The Statewide Medicaid Managed Care Program contributed to slower growth in overall and chronic-disease related ambulatory care sensitive conditions”</i>
Loeher et al. ⁷⁶ (2016) Journal of Clinical Oncology	Massachusetts health care reform (2006)	Poisson regression models	<i>“Massachusetts health care reform was associated with increased rates of resection and decreased probability of emergent resection for colorectal cancer.”</i>
Sommers et al. ⁷⁷ (2016) Health Affairs	Affordable Care Act Medicaid /Private Insurance Expansion	Multivariate regressions	<i>“In ACA expansion states, the underinsurance rate declined, skipping medicines because of cost and trouble paying medical bills also declined, the proportion of individuals with chronic conditions receiving regular care increased”</i>
Dudith et al. (2017) ⁷⁸ Journal of Women’s Health	School-entry HPV vaccine mandate	Logistic regression	<i>“Virginia’s HPV vaccine mandate for school-entry did not lead to a significant increase in HPV vaccination among adolescent females.”</i>
Raifman et al. ⁷⁹ (2017) JAMA Pediatrics	State same-sex marriage policies	Linear regression	<i>“State same-sex marriage policies were associated with a reduction in the proportion of high school students reporting suicide attempts.”</i>

Operationalization of Difference-in-Differences Framework

Identifying Implementation Timeline

The study period, as shown in Table 7, was divided into three segments, determined in the base case by dates of contract award (pre-implementation to MAC transition) and CMS full implementation date (transition to post-implementation). In sensitivity analyses, the threshold defining the pre/transition period changed to: (1) 6 months prior to contract award or (2) the posting of the MAC request for proposal (RFP) to account for any anticipatory effects. As noted previously, all analyses excluded individuals diagnosed in the transition period.

Table 7. Visualization of the division of the study period, including cut-offs for sensitivity analysis.

2005	Patients Diagnosed	2009
2004	Medicare Claims	2010
BASE CASE		
PRE End defined by CMS contract award date	TRANSITION	POST Start defined by CMS full implementation date
SENSITIVITY ANALYSIS – 6 Months Prior to Contract Award		
PRE End defined as six months prior to contract award date	TRANSITION	POST Start defined by CMS full implementation date
SENSITIVITY ANALYSIS 2 – Request for Proposal Posted		
PRE End defined as request for proposal date	TRANSITION	POST Start defined by CMS full implementation date

Abbreviations: *CMS=Centers for Medicare and Medicaid Services*

Note: Data availability timeline shown for reference only and does not correspond to scenario analysis dates in the bottom half of the table due to varying dates of contract award and implementation across Medicare Administrative Contractor regions.

Defining Pre and Post Period

In the analyses, a binary variable, *implementation*, indicated whether a patient was diagnosed before or after the transition period in their region, using the thresholds described in Table 7 and exact dates are shown in Table 4. The coefficient of this variable indicated if outcomes varied based upon whether a patient began treatment in the period prior to implementation in their region or following implementation of the MAC.

Equation 1. Operationalization of *implementation* variable

$$implementation = \begin{cases} 1 & \text{if date of diagnosis} \geq \text{date of MAC award in region} \\ 0 & \text{if date of diagnosis} < \text{date of MAC award in region} \end{cases}$$

Defining Change in Contractor

The second component of the DID analysis was a variable indicating that neither legacy contractor became the MAC. The coefficient on this variable will reveal if treatment receipt differed for MACs that had no prior established relationships in a region before implementation (i.e. the MAC was a new entity in that state).

Equation 2. Operationalization of *region* variable

$$region = \begin{cases} 1 & \text{if region where MAC was not a legacy contractor} \\ 0 & \text{if region where MAC was a legacy contractor} \end{cases}$$

Interaction Approach to Difference-in-Difference Estimation

The simple form of the DID equation, using variable names relevant to this analysis, is shown in Equation 3. The variable of interest for all models in this analysis is β_3 ; however, this variable is not meaningfully interpretable in non-linear models.^{87,88}

Equation 3. General difference-in-differences equation

$$Y = F(X\beta + \beta_1 implementation + \beta_2 region + \beta_3(implementation * region))$$

As a result, in addition to reporting statistical testing on the coefficient, results are presented in both marginal effects and using predicted probabilities. Using the logistic regression equations below to model the four levels of interaction possible in the model in Equation 3 demonstrates the potential hurdle in interpretation. The coefficient on β_3 represents the ratio between the odds ratio of an outcome occurring post-implementation in a region where the MAC was not a legacy contractor with the odds ratio of an event occurring pre-implementation in a region where the legacy contractor became the MAC; a ratio of odds ratios.

Equation 4. Interpretation of differences-in-differences coefficients

$$\begin{aligned} P(y = 1 | X, implementation = 0, region = 0) &= F(X\beta) \\ P(y = 1 | X, implementation = 1, region = 0) &= F(X\beta + \beta_1) \\ P(y = 1 | X, implementation = 0, region = 1) &= F(X\beta + \beta_2) \\ P(y = 1 | X, implementation = 1, region = 1) &= F(X\beta + \beta_1 + \beta_2 + \beta_3) \end{aligned}$$

Measurement of Outcome Variables

Aim 1: Treatment Receipt

The primary outcomes in the first aim were a pair of binary endpoints that indicate whether a patient has received: (1) NCCN-guideline chemotherapy, with or without biologic therapy or (2) NCCN-guideline biologic therapy, with or without chemotherapy. These two outcomes were combined to serve as the outcome for the inverse probability of treatment weights for Aim 2.

Aim 2: Survival

The outcome for the second aim was time from diagnosis to death, operationalized using length of follow-up combined with a binary endpoint that indicated if the patient's death was observed within the study period or if that patient's death was observed or unobserved (censored).

Aim 3: Costs

The dependent variable in the third aim was the total, inflation adjusted, direct medical costs of treatment (physician office, inpatient hospital, outpatient hospital, skilled nursing facility, home health agency, durable medical equipment, and hospice) costs of treatment. Total costs were calculated as the sum of all payments beginning with diagnosis and ending upon death or censoring.

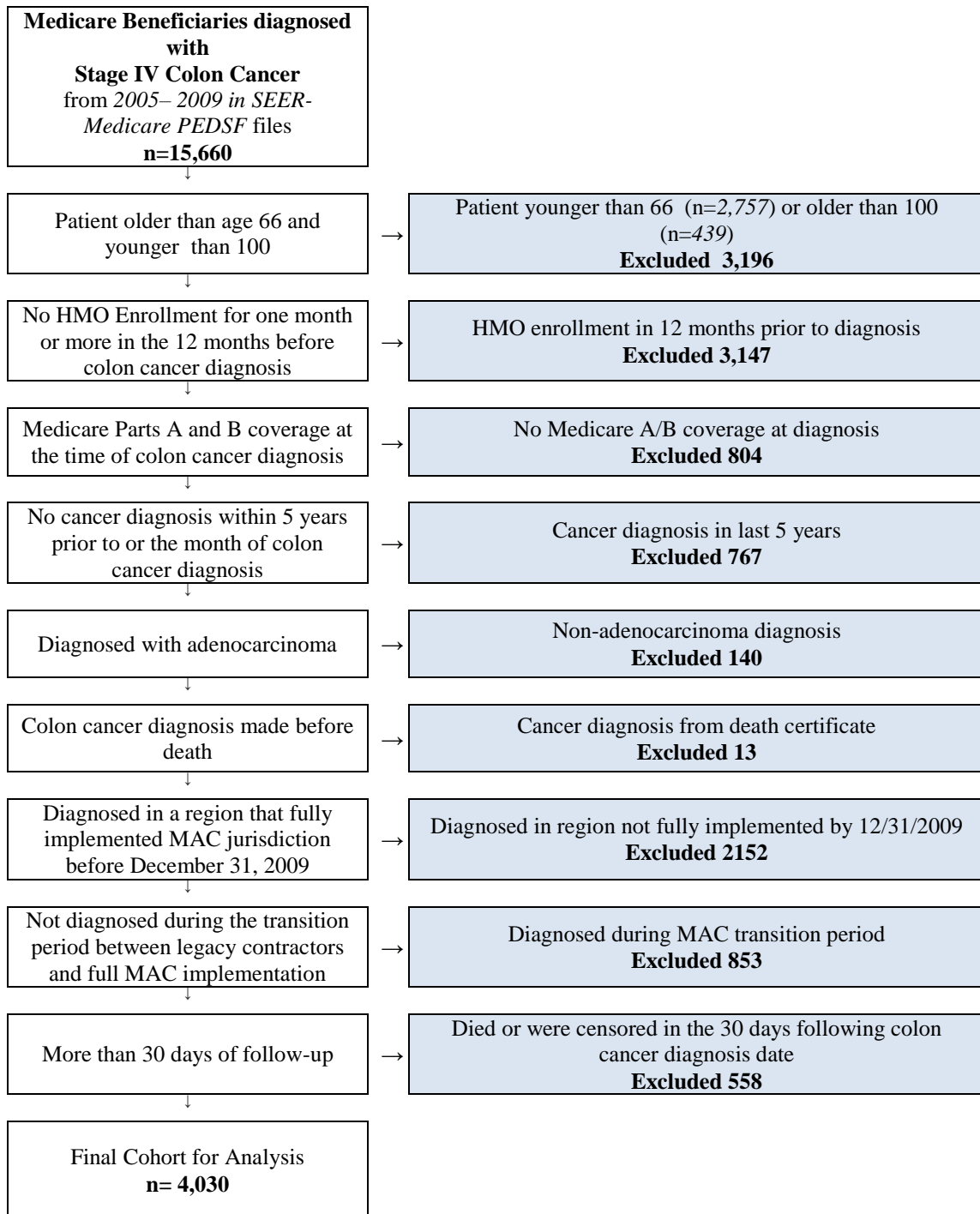
Measurement of Covariates

The analytical models also accounted for potential confounders. All models were adjusted for patient demographic characteristics: age at diagnosis, gender, race, marital status. Models also controlled for dual-eligibility with Medicare as a proxy for socioeconomic status. Three measures of comorbidity burden and overall patient health were also included in all models: the Charlson Comorbidity Index (CCI), a proxy for poor performance status, and receipt of surgery at the primary site. Table 36 describes the operationalization of these potential variables.

Chapter Three: Analytical Cohort

A total of 15,660 Medicare beneficiaries in the SEER-Medicare were diagnosed with mCC from January 1, 2005 to December 31, 2009. From this cohort, 2,757 patients younger than 66 years old were excluded; also excluded were 439 patients more than 100 years old; 3,147 patients who were enrolled in a Medicare HMO at any point during the year prior to diagnosis; 804 patients who lacked Medicare Part A or Part B coverage at diagnosis; 767 individuals diagnosed with cancer in the 5 years prior to the month of their colon cancer diagnosis; 140 patients with non-adenocarcinoma type mCC, 13 patients who were diagnosed with mCC post-mortem; 853 patients who were diagnosed during the transition period between legacy contractors and full MAC implementation; and 558 individuals who died or were censored in the 30 days immediately following the mCC diagnosis. The final analytical cohort, shown in Table 8, consisted of 4,030 patients.

Table 8. Flowchart of the final analytical cohort



Cohort Descriptive Characteristics

The baseline demographic and clinical characteristics of the final cohort are shown in Table 10 and Table 11 respectively. Approximately a third of the sample was diagnosed between ages 66-74 (33.8%), 44.7% were diagnosed between ages 75-84, and only 22.6% of patients were diagnosed at age 85 or older. The cohort contained a slightly higher number of females (54.7%) in the cohort as compared with males (45.3%). The cohort was predominantly non-Hispanic white (77.6%), 9.3% black, 6.8% Hispanic, and 6.3% individuals of other races. Nearly half of the cohort (45.4%) was currently married at the time of diagnosis. Approximately two out of every five patients in the cohort (43.2%) were diagnosed in MAC Jurisdiction 1 (California, Hawaii), 2.9% in Jurisdiction 3 (Utah), 3.28% in Jurisdiction 4 (New Mexico), 10.5% in Jurisdiction 5 (Iowa), 8% in Jurisdiction 10 (Georgia), 22.4% in Jurisdiction 12 (New Jersey), and 9.9% in Jurisdiction 14 (Connecticut). The majority of the cohort (85%) was diagnosed in a region where the MAC was a new entity. Fifteen percent (15%) were diagnosed in a jurisdiction where the FI/Carrier became the MAC. In the year of diagnosis, 19.4% of patients had at least one month of dual-eligibility with Medicaid and Most patients.

Clinically, 47.8% of the cohort received any NCCN-guideline chemotherapy, with or without a biologic therapy. Nearly one in three (31.7%) received an NCCN-guideline biologic, with or without chemotherapy. Prior studies in this population found a treatment receipt rate of approximately 41% for chemotherapy and biologic therapy.^{16,48,80,81} This analysis required patients to remain alive and uncensored 30 days post-diagnosis and this likely led to the slight disparity between the prior studies, which did not have this threshold. In terms of treatment lines, 28.3% of patients received only one line of

chemotherapy or biologic therapy and 20.8% received two or more lines of chemotherapy or biologic therapy. Patients in the sample were scored based on the comorbidities in the Charlson comorbidity index (CCI) and the majority (52.3%) had a comorbidity score of zero (0), 24.2% had one comorbid condition, 17.7% had two or more comorbid conditions, and 5.8% of the cohort did not have clinical information to calculate the CCI. Davidoff and colleagues developed an additional claims-based measure to capture poor-performance status.⁸² Using this measure, 8.7% of the cohort had an indicator of poor performance status. Inversely, 61.3% of the cohort had surgery on the primary tumor site; an intervention associated with superior baseline performance status, low overall comorbid burden, and improved overall survival.^{83,84}

Table 9. Demographic descriptive characteristics of the analytical cohort

Variable	N	(%)
<i>Entire Cohort</i>	4,030	
Age at diagnosis		
66-74	1,360	33.8
75-84	1,759	43.7
≥85	911	22.6
Gender		
Male	1,826	45.3
Female	2,204	54.7
Race		
Non-Hispanic White	3,126	77.6
African American	376	9.3
Hispanic	274	6.8
Other	254	6.3
Marital status at diagnosis		
Married	1,830	45.4
Not Married	2,200	54.6
MAC Jurisdiction of diagnosis (State)		
1 (California, Hawaii)	1,739	43.2
3 (Utah)	115	2.9
4 (New Mexico)	132	3.28
5 (Iowa)	423	10.5
10 (Georgia)	323	8.0
12 (New Jersey)	901	22.4
14 (Connecticut)	397	9.9
MAC relationship with legacy contractor		
New Entity (Neither FI nor Carrier)	3460	85.0
Previously legacy contractor	570	15.0
Any Medicaid coverage in diagnosis year		
No	3,250	80.7
Yes	780	19.4
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary		

Table 10. Clinical descriptive characteristics of the analytical cohort

Variable	N	(%)
<i>Entire Cohort</i>	4,030	
Received any NCCN chemotherapy		
No	2,104	52.2
Yes	1,926	47.8
Received any NCCN biologic therapy[◇]		
No	2,753	68.3
Yes	1,277	31.7
Lines of NCCN-guideline therapy		
0	2,053	50.9
1	1,139	28.3
≥2	838	20.79
CCI		
CCI=0	2,108	52.3
CCI=1	977	24.2
CCI≥2	712	17.7
CCI=Missing	233	5.8
Poor performance indicators[‡]		
No	3680	91.3
Yes	350	8.7
Surgery of primary tumor site		
No	1561	38.8
Yes	2469	61.3

Abbreviations: *NCCN=National Comprehensive Cancer Network, CCI=Charlson Comorbidity Index*
[‡]Indicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis
[◇]With or without chemotherapy

Descriptive Statistics by Implementation Status

Table 11 and Table 12 show the distribution of demographic and clinical characteristics, respectively, of the final cohort by whether diagnosis occurred prior to MAC implementation or after MAC implementation in the state where the patient received treatment. Examining the frequency distributions indicates that significant differences in age at diagnosis, receipt of biologic therapy, number of lines of therapy received, CCI, and surgery of the primary tumor site exists between the pre-implementation and post-implementation cohort. Patients in the post-implementation period were more likely to be older at diagnosis, have supplemental Medicaid coverage, have comorbid conditions and surgery at the primary tumor site as compared to the pre-implementation period. In addition, a smaller proportion of patients diagnosed in the post-implementation period received NCCN-guideline biologic therapy or two or more lines of therapy than in the pre-implementation period. A greater proportion of patients diagnosed in the post-implementation period received at least one line of NCCN-guideline therapy compared to individuals in the pre-implementation period. There were also variations in the geographic location between pre-implementation and post-implementation. This is attributable to the variations in MAC implementation due to award protests shown in Table 4.

Table 11. Descriptive demographic characteristics stratified by diagnosis before or after Medicare Administrative Contractor full implementation

Variable	Before Implementation		After Implementation		p-value
	N	Col %	N	Col %	
<i>Entire Cohort</i>	2,817		1,213		
Age at diagnosis					
66-74	967	34.3	393	32.4	<0.01
75-84	1,256	44.6	503	41.5	
≥85	594	21.1	317	26.1	
Gender					
Male	1,259	44.7	567	46.7	0.23
Female	1,558	55.3	646	53.3	
Race					
Non-Hispanic White	2,177	77.3	949	78.2	0.11
African American	281	9.9	95	7.8	
Hispanic	191	6.8	83	6.8	
Other	168	5.9	86	7.1	
Marital status at diagnosis					
Married	1,274	45.2	556	45.8	0.72
Not Married	1,543	54.8	657	54.2	
MAC Jurisdiction of diagnosis (State)					
1 (California, Hawaii)	1199	42.6	540	44.5	<0.01
3 (Utah)	41	1.5	74	6.1	
4 (New Mexico)	79	2.8	53	4.4	
5 (Iowa)	267	9.5	156	12.9	
10 (Georgia)	282	10.0	41	3.4	
12 (New Jersey)	656	23.3	245	20.2	
14 (Connecticut)	293	10.4	104	8.6	
MAC relationship with legacy contractor					
New Entity (Neither FI nor Carrier)	2415	85.7	1045	86.2	0.73
Previously legacy contractor	402	14.3	168	13.9	
Medicaid coverage in diagnosis year					
No	2,247	79.8	1003	82.7	0.03
Yes	570	20.2	210	17.3	

Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary

Table 12. Descriptive clinical characteristics stratified by diagnosis before or after Medicare Administrative Contractor full implementation

Variable	Before Implementation		After Implementation		p-value
	N	Col %	N	Col %	
<i>Entire Cohort</i>	2,817		1,213		
Received any NCCN chemotherapy					
No	1,478	52.5	626	51.6	0.61
Yes	1,339	47.5	587	48.4	
Received any NCCN biologic therapy[◊]					
No	1,895	67.3	858	70.7	0.03
Yes	922	32.7	355	29.3	
Lines of NCCN-guideline therapy					
0	1,445	51.3	608	50.1	<0.01
1	744	26.4	395	32.6	
≥2	628	22.3	210	17.31	
CCI					
CCI=0	1,494	53.0	614	50.6	0.01
CCI=1	684	24.3	293	24.2	
CCI≥2	465	16.5	247	20.4	
CCI=Missing	174	6.2	59	4.9	
Poor performance indicators[‡]					
No	2,580	91.6	1,100	90.7	0.35
Yes	237	8.4	113	9.3	
Surgery of primary tumor site					
No	1045	37.1	516	42.5	<0.01
Yes	1772	62.9	697	57.5	

Abbreviations: NCCN=National Comprehensive Cancer Network , CCI Charlson comorbidity index, Col column

[‡]Indicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Chapter Four: Aim 1 – Receipt of NCCN-Guideline Therapy

Analytical Approach

We first compared the socio-demographic and clinical characteristics of patients who received NCCN-guideline chemotherapy before and after MAC implementation. We then examined the odds of treatment receipt using a logistic regression model with a difference-in-differences estimator, as shown in Equation 5:

Equation 5. Log-linear regression model for receipt of therapy

$$\text{logit}\{\text{Pr}(\text{Receipt of therapy} = 1)\} = \beta_0 + \theta_1 \text{implementation} + \theta_2 \text{region} + \theta_3 \text{implementation} * \text{region} + \sum (\beta_k X_k) + \epsilon$$

Alternative Analytical Approaches

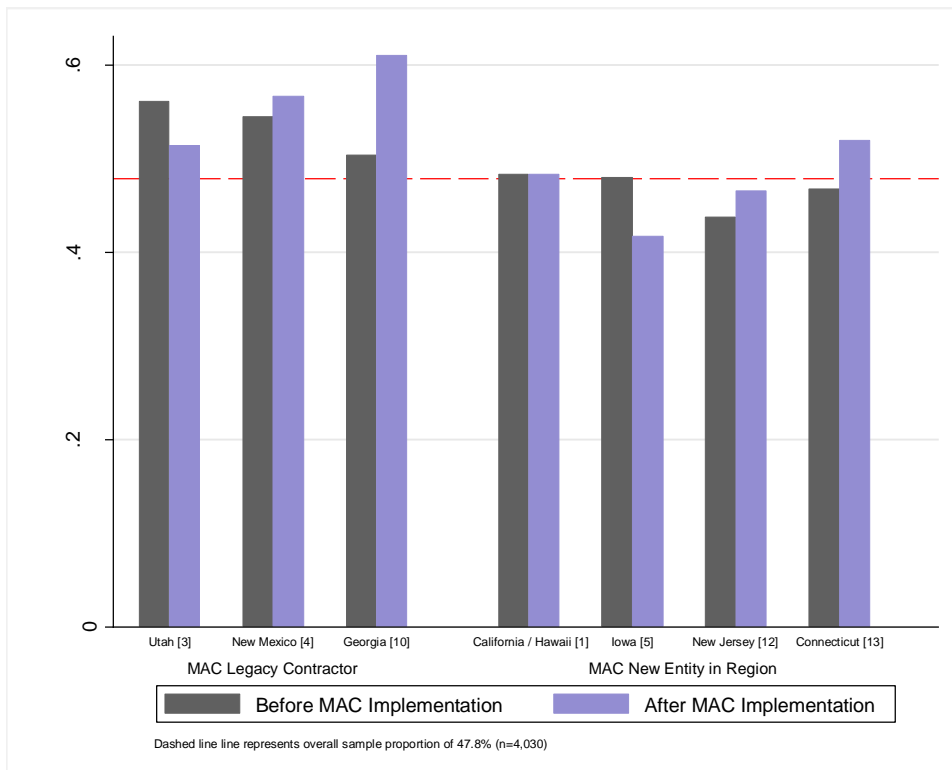
Given the large proportion of chemotherapy and biologic therapy receipt in this population, a traditional logistic regressions approach could produce odds ratios that overestimate the true effect of Medicare administrative contracting reform.^{85,86} Zou presents an approach, operationalized in SAS by Lindquist, using a Poisson model with robust error variances, to address this issue and estimate risk ratios.^{87,88} As an additional check on the validity of the estimates produced in the logistic regression and modified-Poisson estimation, we estimated a linear probability model, which has a more direct interpretation than the interaction coefficient in the main models.⁸⁹

Receipt of NCCN-Guideline Chemotherapy

Descriptive Results

Nearly half of patients in the cohort (48%) received NCCN-guideline chemotherapy. Statistically significant age, gender, geographic (Table 13) and clinical (Table 14) differences exist between patients who received chemotherapy and those who did not. Patients diagnosed in a region where the legacy contractor became the MAC represented 16% of those receiving chemotherapy and only 13% of individuals not receiving chemotherapy. Figure 3 highlights the variation in chemotherapy receipt by implementation status and region.

Figure 3. Proportion of patients receiving NCCN-guideline chemotherapy before and after Medicare contracting reform, by Medicare Administrative Contractor jurisdiction and legacy contractor status



Patients who received chemotherapy were significantly younger than those who did not – one in five (20%) individuals in the non-chemotherapy group was age 66-74 compared to almost half (48%) of individuals who received chemotherapy. The chemotherapy group also had a larger proportion of men and individuals married at diagnosis than the non-chemotherapy cohort did. There was no statistically significant variation in the racial composition of the chemotherapy and non-chemotherapy groups. Patients who received Medicaid coverage and those with higher comorbidity burden were more common in the non-chemotherapy group than in the chemotherapy group. More than one in ten patients (12%) who did not receive chemotherapy had an indicator of poor performance status, compared to only 5% of patients who received chemotherapy. The majority of patients who received an NCCN-guideline biologic also received NCCN-chemotherapy. Only 25 patients (1.2%) who did not receive chemotherapy received biologic therapy. Almost two thirds of patients who received chemotherapy (65%) also received biologic therapy. The chemotherapy group also included a higher proportion of patients who received primary tumor surgery (72%) than the non-chemotherapy group (51%).

Table 13. Descriptive demographic characteristics stratified by receipt of NCCN-guideline chemotherapy

Variable	No NCCN Chemotherapy		NCCN Chemotherapy		<i>p-value</i>
	N	Col %	N	Col %	
Entire Cohort	2104		1926		
Age at diagnosis					
66-74	429	20.4	931	48.3	<0.01
75-84	926	44.0	833	43.3	
≥85	749	35.6	162	8.4	
Gender					
Male	885	42.1	941	48.9	<0.01
Female	1,219	57.9	985	51.1	
Race					
Non-Hispanic White	1,629	77.4	1,497	77.7	0.09
African American	216	10.3	160	8.3	
Hispanic	131	6.2	143	7.4	
Other	128	6.1	126	6.5	
Marital status at diagnosis					
Married	756	35.9	1074	44.2	<0.01
Not Married	1,348	64.1	852	55.8	
MAC Jurisdiction of diagnosis (State)					
1 (California, Hawaii)	899	42.7	840	43.6	0.08
3 (Utah)	54	2.6	61	3.2	
4 (New Mexico)	59	2.8	73	3.8	
5 (Iowa)	230	10.9	193	10.0	
10 (Georgia)	156	7.4	167	8.7	
12 (New Jersey)	500	23.8	401	20.8	
14 (Connecticut)	206	9.8	191	9.9	
MAC history as legacy contractor					
New Entity (Neither FI nor Carrier)	1835	87.2	1625	84.4	<0.01
Previously FI or Carrier	269	12.8	301	15.6	
Medicaid coverage in diagnosis year					
No	1628	77.4	1,622	84.2	<0.01
Yes	476	22.6	304	15.8	

Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary

Table 14. Descriptive clinical characteristics stratified by receipt of NCCN-guideline chemotherapy

Variable	No NCCN Chemotherapy		NCCN Chemotherapy		<i>p-value</i>
	N	Col %	N	Col %	
<i>Entire Cohort</i>	2104		1926		
Received any NCCN biologic therapy^o					
No	2,079	98.8	674	35.0	<0.01
Yes	25	1.2	1252	65.0	
CCI					
CCI=0	1,015	48.2	1,093	56.8	<0.01
CCI=1	489	23.2	488	25.3	
CCI≥2	464	22.1	248	12.9	
CCI=Missing	136	6.5	97	5.0	
Poor performance indicators[‡]					
No	1,846	87.7	1,834	95.2	<0.01
Yes	258	12.3	92	4.8	
Surgery of primary tumor site					
No	1025	48.7	536	27.8	<0.01
Yes	1079	51.3	1,390	72.2	

Abbreviations: *NCCN*=National Comprehensive Cancer Network, *CCI*=Charlson Comorbidity Index, *Col*=column

^oIndicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Multivariable Regression Results

Logistic regression results of the model predicting receipt of chemotherapy are shown in Table 15. The odds ratio on the *implementation* variable (Odds Ratio [OR]: 1.18; 95% Confidence Interval [CI]: 0.79, 1.78) indicates that patients in regions where the legacy contractor became the MAC had the same odds of receiving NCCN-guideline chemotherapy before and after the transition from legacy contractors to MACs. The odds ratio for the *region* variable (OR: 0.87; 95% CI: 0.69, 1.11) indicates that in the pre-implementation period, patients diagnosed in regions where the MAC was not a legacy contractor did not have statistically-different odds of receiving biologic therapy relative to patients diagnosed in a region where the MAC was the legacy contractor. The interaction effect (*implementation* region*) indicates to what extent the effect of implementation differed for patients diagnosed in regions where a legacy contractor became the MAC and regions where the MAC was a new entity. This effect represents the difference-in-difference analysis. As an alternative interpretation, this variable represents the extent to which the MAC being a new entity modifies the effect of implementation.⁹⁰ The effect of implementation for patients diagnosed in a region where the MAC was a new entity (OR: 1.00; 95% CI: 0.65, 1.56) is equal to the effect of implementation on diagnosed in regions where a legacy contractor became the MAC. That this effect is not statistically different from one indicates no differential effect of implementation based on if the MAC was a legacy contractor. This estimate was consistent with results from the modified-Poisson regression (Risk Ratio [RR]: 0.94; 95% CI 0.75, 1.18) , reported in Table 42. We found implementation associated with a non-significant 3% decrease in probability of receiving chemotherapy (95% CI: -9%, +8%)

using the LPM (Table 44). Changes in assumptions regarding the timing of implementation did not affect the findings (Table 51).

Table 15. Multivariate correlations between receipt of chemotherapy (with or without biologic therapy) and clinical and demographic factors

genyt	Receipt of chemotherapy (with or without biologic therapy)		
	Odds Ratio	95% CI	<i>p</i>
<i>Difference-in-differences estimators</i>			
θ_1 - Post Implementation (v. Pre)	1.18	(0.79, 1.78)	0.27
θ_2 - New MAC (v. Legacy contractor became MAC)	0.87	(0.69, 1.11)	0.42
θ_3 - Interaction	1.00 ^a	(0.65, 1.56)	0.99
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.42	(0.36, 0.49)	<0.01
≥85	0.11	(0.09, 0.14)	<0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	0.82	(0.64, 1.05)	0.12
Hispanic	1.11	(0.83, 1.48)	0.47
Asian and others	1.10	(0.82, 1.49)	0.53
Married at diagnosis (v. Not Married)	1.64	(1.42, 1.91)	<0.01
Female (v. Male)	0.99	(0.86, 1.15)	0.93
Any Medicaid buy-in during diagnosis year	0.67	(0.55, 0.82)	<0.01
<i>Clinical characteristics</i>			
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	1.04	(0.87, 1.23)	0.68
CCI≥2	0.70	(0.57, 0.86)	<0.01
CCI=Missing	0.51	(0.38, 0.69)	<0.01
Proxy for poor performance status ^b	0.44	(0.33, 0.58)	<0.01
Surgery of primary site	2.12	(1.84, 2.46)	<0.01

Abbreviations: MAC= Medicare Administrative Contractor, CI=confidence interval

^aInterpreted as how much the effect of implementation differs between patients diagnosed in regions where the MAC was a new entity and patients diagnosed in a region where a legacy contractor became the MAC, in multiplicative terms.

^bIndicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Comparing the difference between the expected odds of patients receiving chemotherapy in both the pre-implementation and post-implementation period, return consistent results (Table 16). The odds of receiving chemotherapy for patients diagnosed in the pre-implementation period in regions where the legacy contractor became the MAC are 1.66. This indicates that, holding other variables at their reference categories, one would expect to find 166 patients receiving chemotherapy for every 100 patients who did not receive chemotherapy. The odds of receiving chemotherapy for patients diagnosed in the post-implementation period in regions where the legacy contractor became the MAC is 2.00. The difference between the pre- and post-implementation odds (0.35) indicates a non-statistically significant trend towards increasing use of chemotherapy therapy following MAC implementation in regions where the legacy contractor became the MAC. The marginal effect of implementation for patients receiving treatment in regions where the MAC was a new entity was 0.10 (1.45 minus 1.35), indicating increasing use of chemotherapy as well in the regions. The DID between these marginal effects (-0.25) was not statistically significant from zero, indicating no variation in the odds of receiving chemotherapy associated with the implementation of Medicare contracting reform. The effects of region were not significantly different in either the pre-implementation and post-implementation period, indicating that patients in regions where the MAC was a legacy contractor had similar odds of receiving biologic therapy both before and after implementation relative to patients diagnosed in regions where the MAC was a new entity.

Table 16. Marginal effects of logistic regression model assessing the correlations between receipt of chemotherapy therapy (with or without biologic therapy) and clinical and demographic factors

Time	Geography		Difference [i - ii] (iii)
	Region where MAC was a legacy contractor (i)	Region where MAC was not a legacy contractor (ii)	
Before MAC implementation (a)	1.66* (1.27, 2.03)	1.35* (1.21, 1.50)	-0.31 (-0.69, 0.08)
After MAC implementation (b)	2.00* (1.30, 2.70)	1.45* (1.23, 1.67)	-0.55 (-1.27, 0.16)
Difference [a-b] (c)	0.35 (-0.43, 1.12)	0.10 (-0.13, 0.33)	-0.25 (-1.06, 0.56)

Note: Values reported as: Estimate (95% Confidence Interval)

Abbreviations: MAC=Medicare Administrative Contractor

*p-value <0.05

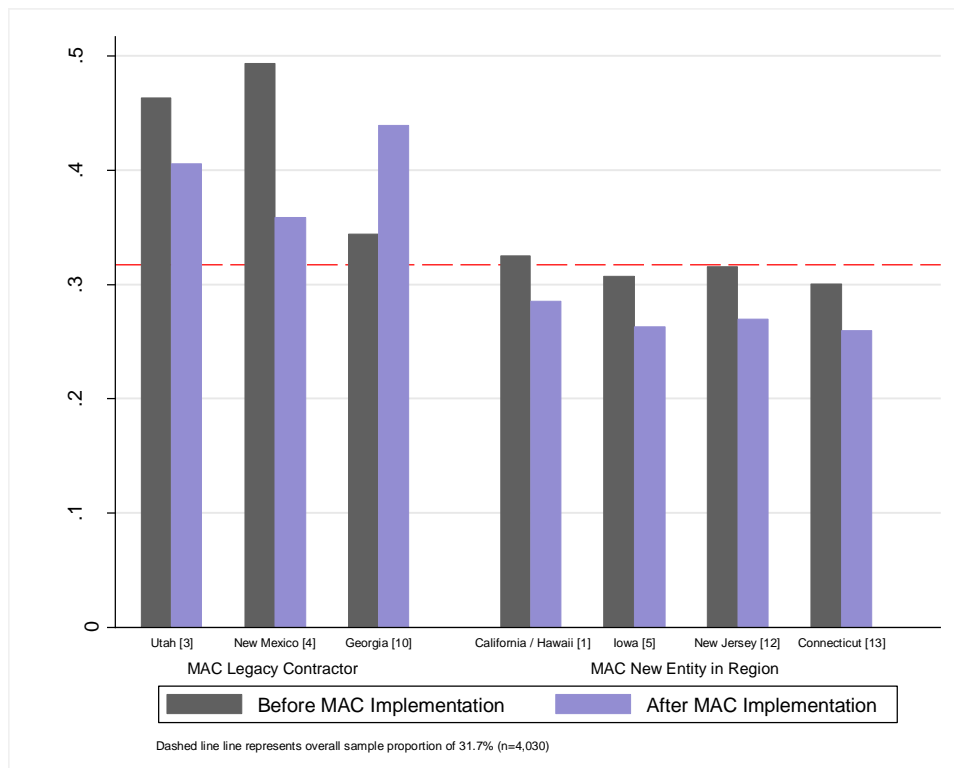
^aModel controlled for age, race, sex, marital status, dual eligibility with Medicare, an indicator for poor performance status, Charlson Comorbidity Index, and surgery at primary tumor site.

Receipt of NCCN-Guideline Biologic Therapy

Descriptive Results

Approximately one third of patients in the cohort (32%) received NCCN-guideline biologic therapy. A greater proportion of patients diagnosed in regions where the MAC was the legacy contractor received biologic therapy both before and after implementation (Figure 4). Patients diagnosed in a region where the legacy contractor became the MAC represented 17% of those receiving biologic therapy and only 13% of individuals not receiving biologic therapy.

Figure 4. Proportion of patients receiving NCCN-guideline biologic therapy before and after Medicare contracting reform, by Medicare Administrative Contractor jurisdiction and legacy contractor status



Variation in socio-demographic and clinical characteristics by those who received NCCN biologic therapy and those who did not is shown in Table 17 and Table 18. Patients who received biologic therapy were significantly younger than those who did not. The biologic therapy group also had a larger proportion of men and individuals married at diagnosis than the non-biologic therapy cohort did. There was no association between race and receipt of biologic therapy. Patients who received Medicaid coverage and those with higher comorbidity burden were more common in the non-biologic therapy group than in the biologic therapy group. Eleven percent (11%) of patients who did not receive biologic therapy had an indicator of poor performance status, compared to only 4% of patients who received biologic therapy. The majority of patients who received an NCCN-guideline biologic also received NCCN-chemotherapy. Only 2% of individuals who received biologic therapy did so without chemotherapy. The biologic therapy group also included a higher proportion of patients who received primary tumor surgery (73%) than the non-chemotherapy group (56%).

Table 17. Descriptive demographic characteristics stratified by receipt of NCCN-guideline biologic therapy

Variable	No NCCN Biologic		NCCN Biologic		p
	N	Col %	N	Col %	
Entire Cohort	2,753		1,277		
Age at diagnosis					
66-74	675	24.5	685	53.6	<0.01
75-84	1,246	45.3	513	40.2	
≥85	832	30.2	79	6.2	
Gender					
Male	1,197	43.5	629	49.3	<0.01
Female	1,556	56.5	648	50.7	
Race					
Non-Hispanic White	2,110	76.6	1,016	79.6	0.06
African American	280	10.2	96	7.5	
Hispanic	188	6.8	86	6.7	
Other	175	6.4	79	6.2	
Marital status at diagnosis					
Married	1,107	40.2	723	56.6	<0.01
Not Married	1,646	59.8	554	43.4	
MAC Jurisdiction of diagnosis (State)					
1 (California, Hawaii)	1,195	43.4	544	42.6	<0.01
3 (Utah)	66	2.4	49	3.8	
4 (New Mexico)	74	2.7	58	4.5	
5 (Iowa)	300	10.9	123	9.6	
10 (Georgia)	208	7.6	115	9.0	
12 (New Jersey)	628	22.8	273	21.4	
14 (Connecticut)	282	10.2	115	9.0	
MAC History as FI/Carrier					
New Entity (Neither FI nor Carrier)	2,405	87.4	1,055	82.6	<0.01
Previously FI or Carrier	348	12.6	222	17.4	
Any Medicaid coverage in diagnosis year					
No	2,147	78.0	1,103	86.4	<0.01
Yes	606	22.0	174	13.6	

Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary

Table 18. Descriptive clinical characteristics stratified by receipt of NCCN-guideline biologic therapy

Variable	No NCCN Biologic		NCCN Biologic		<i>p</i>
	N	Col %	N	Col %	
<i>Entire Cohort</i>	2,753		1,277		
Received any NCCN Chemotherapy					
No	2,079	75.5	25	2.0	<0.01
Yes	674	24.5	1,252	98.0	
Lines of NCCN Guideline Therapy					
0	2,053	74.6	0	-	<0.01
1	572	20.8	567	44.4	
≥2	128	4.7	710	55.6	
CCI					
CCI=0	1,351	49.1	757	59.3	<0.01
CCI=1	658	23.9	319	25.0	
CCI≥2	581	21.1	131	10.3	
CCI=Missing	163	5.0	70	5.5	
Poor performance indicators[‡]					
No	2,456	89.2	1,224	95.9	<0.01
Yes	297	10.8	53	4.2	
Surgery of primary tumor site					
No	1,216	44.2	345	27.0	<0.01
Yes	1,537	55.8	932	73.0	

Abbreviations: CCI=Charlson comorbidity index, Col=column,
[‡]Indicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Multivariable Regression Results

Logistic regression results are shown in Table 19. The odds ratio on the *implementation* variable (1.01: 95% CI 0.67, 1.51) indicates that patients in regions where the legacy contractor became the MAC had the same odds of receiving biologic therapy before and after the transition from FIs and carriers to MACs. The odds ratio for the *region* variable (0.76: 95% CI 0.59, 0.97) indicates that in the pre-implementation period, patients diagnosed in regions where the MAC was not a legacy contractor had 24% lower odds of receiving biologic therapy relative to patients diagnosed in a region where the MAC was the legacy contractor. The interaction effect (*implementation* region*) indicates to what extent the effect of implementation differed for patients diagnosed in regions where a legacy contractor became the MAC and regions where the MAC was a new entity. This effect represents the difference-in-difference analysis. As an alternative interpretation, this variable represents the extent to which the MAC being a new entity modifies the effect of implementation. The effect of implementation for patients diagnosed in a region where the MAC was a new entity (0.90: 95% CI 0.57, 1.39) is 10% lower than the effect of implementation on diagnosed in regions where a legacy contractor became the MAC. That this effect is not statistically different from one indicates no differential effect of implementation based on if the MAC was a legacy contractor. These findings were consistent with estimates of risk ratios (RR: 0.94; 95% CI: 0.75, 1.18) produced using the modified Poisson regression approach with robust error variance shown in Table 43. The results from the LPM reported in Table 44 indicate that MAC implementation was associated with a non-significant decrease in the probability of receiving biologic therapy of 2% (95% CI: -11%, +6%). Changes in assumptions regarding the timing of

implementation also did not affect the findings (Table 52). This estimate was consistent with results from the modified-Poisson regression (Risk Ratio [RR]: 0.94; 95% CI 0.75, 1.18), reported in Table 48. We found implementation associated with a non-significant 3% decrease in probability of receiving chemotherapy (95% CI: -9%, +8%).

Table 19. Multivariate correlations between receipt of biologic therapy (with or without chemotherapy) and clinical and demographic factors

	Receipt of biologic therapy (with or without chemotherapy)		
	Odds Ratio	95% CI	<i>p</i>
<i>Difference-in-differences estimators</i>			
θ_1 - Post Implementation (v. Pre)	1.01	(0.67, 1.51)	0.98
θ_2 - New MAC (v. Legacy contractor became MAC)	0.76	(0.59, 0.97)	0.03
θ_3 - Interaction	0.90 ^a	(0.57, 1.39)	0.63
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.41	(0.35, 0.48)	< 0.01
≥85	0.10	(0.08, 0.14)	< 0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	0.69	(0.53, 0.91)	< 0.01
Hispanic	0.89	(0.66, 1.21)	0.46
Asian and others	1.00	(0.73, 1.40)	0.99
Married at diagnosis (v. Not Married)	1.36	(1.16, 1.59)	< 0.01
Female (v. Male)	0.96	(0.83, 1.12)	0.62
Any Medicaid buy-in during diagnosis year	0.61	(0.49, 0.76)	< 0.01
<i>Clinical characteristics</i>			
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	0.96	(0.81, 1.15)	0.66
CCI≥2	0.55	(0.44, 0.70)	< 0.01
CCI=Missing	0.60	(0.44, 0.82)	0.02
Proxy for poor performance status ^b	0.50	(0.36, 0.70)	< 0.01
Surgery of primary site	1.77	(1.51, 2.06)	< 0.01

Abbreviations: MAC= Medicare Administrative Contractor, CI=confidence interval

^aInterpreted as how much the effect of implementation differs between patients diagnosed in regions where the MAC was a new entity and patients diagnosed in a region where a legacy contractor became the MAC, in multiplicative terms.

^bIndicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Marginal effects of the logistic model are reported in Table 20. The odds of receiving biologic therapy for patients diagnosed in the pre-implementation period in regions where the legacy contractor became the MAC are 0.83, indicating that one would expect to find 83 patients receiving biologic therapy for every 100 patients who did not receive biologic therapy. The odds of receiving biological therapy for patients diagnosed in the post-implementation period in regions where the legacy contractor became the MAC is 0.89. The marginal effect of 0.06 between the pre- and post-implementation odds indicates a non-statistically significant trend towards increasing use of biologic therapy following MAC implementation in regions where the legacy contractor became the MAC. The marginal effect of implementation for patients receiving treatment in regions where the MAC was a new entity was -0.11 (0.60 minus 0.49), indicating decreasing use of biologic therapy. The difference-in-differences between these marginal effects (-0.17) was not significantly different from zero, indicating no association between the implementation of Medicare contracting reform and the receipt of biologic therapy. The effects of region were significantly different ($p < 0.05$) in both the pre-implementation and post-implementation, indicating that patients in regions where the MAC was a legacy contractor had higher odds of receiving biologic therapy both before and after implementation relative to patients diagnosed in regions where the MAC was a new entity.

Table 20. Marginal effects of logistic regression model assessing the correlations between receipt of biologic therapy (with or without chemotherapy) and clinical and demographic factors

Time	Geography		Difference [i - ii] (iii)
	Region where MAC was a legacy contractor (i)	Region where MAC was not a legacy contractor (ii)	
Before MAC implementation (a)	0.83* (0.74, 0.92)	0.60* (0.54, 0.66)	0.23* (0.04, 0.43)
After MAC implementation (b)	0.89* (0.79, 0.99)	0.49* (0.42, 0.57)	0.40* (0.09, 0.71)
Difference [a-b] (c)	<i>0.06</i> (-0.30, 0.41)	-0.11* (-0.20, -0.02)	-0.17 (-0.53, 0.20)

Note: Values reported as: Estimate (95% Confidence Interval)

Abbreviations: MAC=Medicare Administrative Contractor

*p-value <0.05

^aModel controlled for age, race, sex, marital status, dual eligibility with Medicare, an indicator for poor performance status, Charlson comorbidity index, and surgery at primary tumor site.

Chapter Six: Aim 2 – Survival

Analytical Approach

We first performed a descriptive analysis of event times using Kaplan-Meier survival estimation. To test whether survival time varied across the four levels of the DID model, the log-rank was utilized to compare unadjusted survival across groups. We then assessed the impact of Medicare contracting reform on overall survival using an inverse probability of treatment weighted (IPTW) multivariable Cox proportional hazards model with an interaction term. To account for the fact that there is the potential for selection bias into receiving NCCN-guideline therapy, a potential confounder that has a significant impact on survival, a logistic regression model, shown in Equation 6, estimated the impact of covariates on the probability of receiving NCCN-guideline treatment, the dependent variable.^{91,92}

Equation 6. Calculation of probability of treatment logit estimation model

$$\text{Probability of NCCN – Guideline Treatment} = e(x_i) = P(\text{Treatment}_i = 1 | x_i)$$

Appendix 7 provides more details on the propensity score model coefficients and diagnostic testing results. Weights were calculated as in Equation 7, where Z is a binary variable denoting observed receipt of treatment and $p(X)$ is the predicted probability from the logistic regression estimation:

Equation 7. Calculation of inverse probability of treatment weights

$$w_i = \frac{Z}{p(X)} + \frac{(1 - Z)}{1 - p(X)}$$

For untreated individuals, the first component of the model will be equal to zero when $Z=0$ and for treated individuals, the second component will equal to zero (when $Z=1$), leading to two weights: $1/p(x)$ for individuals who were treated and $1/[1-p(x)]$ for individuals not receiving treatment. To maintain sample size, weights were normalized by dividing the each weight by the mean weight, resulting in weights that summed to 4,030.⁹³

The Cox proportional hazard model was then weighted by the normalized inverse of the probability of receiving NCCN– guideline treatment. The final Cox proportional hazard model is shown in Equation 8.

Equation 8. Cox proportional hazard interaction model

$$\lambda_i(t); = \lambda_0(t) \exp \left\{ \theta_1 \textit{implementation} + \theta_2 \textit{region} + \theta_3 (\textit{implementation} * \textit{region}) + \sum_{k=1}^n \beta_k X_k \right\}$$

In the model, λ_i represents the hazard for an individual at time period t . Baseline hazard for this individual is noted as λ_0 . The variable *implementation* indicates whether or not this patient was diagnosed before or after MAC implementation in their region, *region* denotes whether or not the patient lives in an area where the legacy contractor did not become the MAC, and the interaction represents the effect of MAC implementation on survival. Additional clinical and demographic variables included in the model are denoted by X_i . The variable of interest in this model is θ_3 . As illustrated in Equation 9,

this coefficient represents the incremental survival impact attributable to MAC implementation and represents the incremental reduction/increase in hazard for patients diagnosed post-implementation in regions where the MAC was a new entity relative to patients diagnosed pre-implementation in regions where the legacy contractor became the MAC.

Equation 9. Cox proportional hazard model interaction parameter of interest

$$INT_M = \frac{e^{(\theta_1 + \theta_2 + \theta_3)}}{e^{(\theta_1 + \theta_2)}} = e^{\theta_3}$$

Descriptive Results

During the study period, death was observed for 86% of the individuals in the cohort. Table 21 shows that the proportion censored was statistically-significantly lower in the pre-implementation than the post-implementation period. This is logical as the post-implementation period, by definition, is closer to the administrative censoring that occurred on December 31, 2010 (Table 7). No statistically significant differences in censoring were noted between regions within the same period.

Table 21. Percentage of cohort with observed and censored outcomes, stratified by contractor implementation status and region

	Overall	Pre-Implementation		Post-Implementation	
		Legacy ^a	New ^b	Legacy	New
Observed Outcome	3,461 (86%)	87%	93%	72%	74%
Censored	569 (14%)	13%	7%	28%	26%

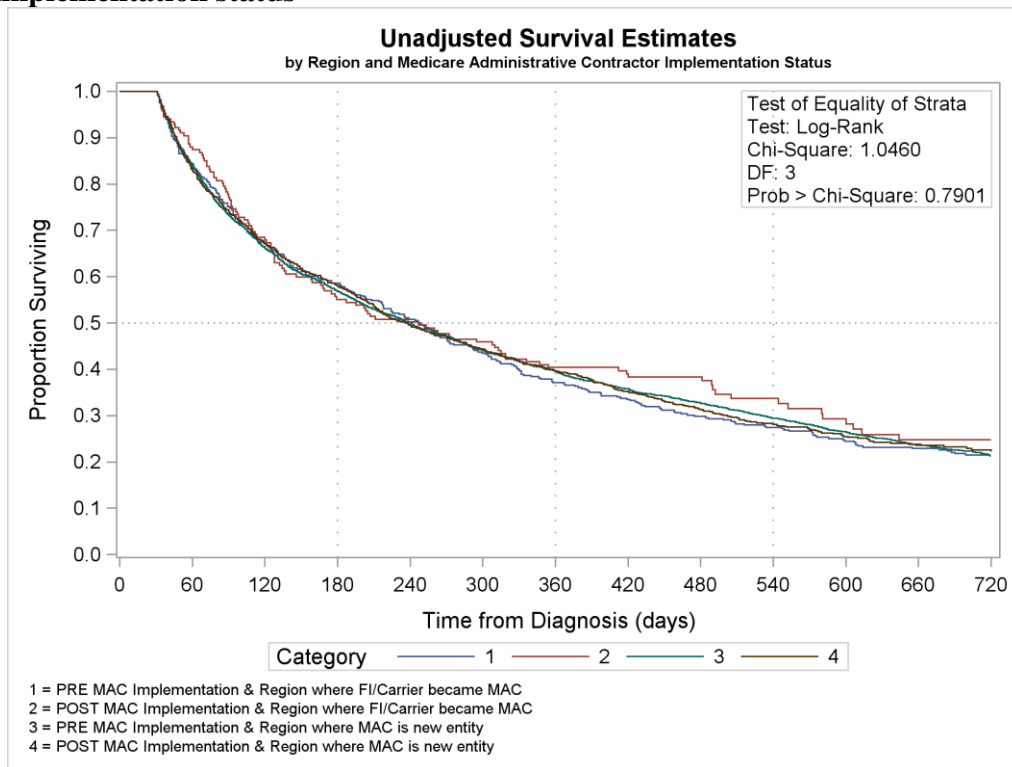
^aDenotes region where the legacy contractor became the Medicare Administrative Contractor

^bDenotes region where a new entity who was neither the fiscal intermediary nor carrier became the Medicare Administrative Contractor

Visually assessing the survival curves associated with the four combinations of implementation and region (Equation 4) implied a slight differential in survival in regions

where legacy contractors became the MAC in the post period; the non-significant p-value on the test statistic for the log-rank test provided no evidence to support this conclusion. Additional survival curves examined survival before and after implementation and compared regions where the MAC was a legacy contractor against regions where the MAC was a new entity. Neither curve, presented in Figure 11 and Figure 12, demonstrated significant unadjusted difference in survival.

Figure 5. Unadjusted 2-year survival curves comparing region and contractor implementation status



The median time from diagnosis to death in the overall cohort was 249 days. As Table 23 shows, there was limited variation across time and region. Survival probabilities were similarly consistent before and after MAC implementation and between regions where the legacy contractor became the MAC and regions where the MAC was a new

entity. The one-year survival estimates for this cohort was 39%, the 5-year survival estimate was 12%, consistent with current SEER estimates using 2007-2013 that indicate 5-year relative survival is 13.9% for individuals diagnosed at the distant stage.²

Table 22. Median survival (days) and 95% confidence intervals stratified by implementation status and region

Overall	Pre-Implementation		Post-Implementation	
	<i>Legacy^a</i>	<i>New^b</i>	<i>Legacy</i>	<i>New</i>
239	248	239	247	236
(224 – 227)	(208 – 290)	(220– 261)	(168 – 319)	(212 – 271)

^aDenotes region where the legacy contractor became the Medicare Administrative Contractor

^bDenotes region where a new entity who was neither the fiscal intermediary nor carrier became the Medicare Administrative Contractor

Table 23. Unadjusted Kaplan-Meier survival probabilities stratified by implementation status and region

Time Period	Overall	Pre-Implementation		Post-Implementation	
		<i>Legacy^a</i>	<i>New^b</i>	<i>Legacy</i>	<i>New</i>
60 day	0.84	0.83	0.84	0.87	0.83
90 day	0.74	0.75	0.73	0.77	0.74
180 day	0.57	0.59	0.57	0.55	0.58
239 day	0.50	0.51	0.50	0.50	0.50
1 year	0.39	0.37	0.39	0.40	0.39
5 year	0.12	0.12	0.21	0.13	0.11

^aDenotes region where the legacy contractor became the Medicare Administrative Contractor

^bDenotes region where a new entity who was neither the fiscal intermediary nor carrier became the Medicare Administrative Contractor

Cox Proportional Hazard Model Results

Results from the IPTW Cox-Proportional Hazard Model are shown in Table 24.

Diagnostic testing indicated no significant violations of the proportional hazards assumption. The hazard ratio comparing survival in the post-implementation period in regions where the MAC was a new entity against the pre-implementation period in regions where the MAC was a legacy contractor was not statistically significantly different from zero (Hazard Ratio [HR] 1.03; 95% CI: 0.91, 1.16). No comparison of any combination of implementation status and MAC status as a legacy contractor provided evidence of differential survival. Full survival model results are presented in Table 26. Findings were not sensitive to changes to the definition of the cutoff for the pre/transition period (Table 7). Results of sensitivity analyses are shown in Table 53.

Table 24. Cox proportional hazards survival analysis full difference-in-difference results

Post Implementation	MAC Status in Region	Hazard Ratio	(95% CI)
No	Legacy contractor	<i>Reference</i>	-
No	New entity	0.96	(0.84, 1.06)
Yes	Legacy contractor	0.94	(0.79, 1.17)
Yes	New entity	1.03	(0.91, 1.16)

Abbreviations: MAC= Medicare Administrative Contractor, CI=confidence interval

Table 25. Results from inverse probability of treatment weighted Cox proportional hazards model

	IPTW Cox Proportional Hazards Model		
	Hazard Ratio	95% CI	P
<i>Difference in Difference Analysis</i>			
θ_1 - Post implementation	0.94	(0.79, 1.17)	0.31
θ_2 - MAC new entity	0.96	(0.84, 1.06)	0.67
θ_3 - Interaction	1.14	(0.92, 1.41)	0.52
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	1.43	(1.33, 1.54)	<0.01
≥85	2.06	(1.87, 2.28)	<0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	1.08	(0.96, 1.22)	0.19
Hispanic	0.97	(0.84, 1.11)	0.62
Asian and others	1.06	(0.91, 1.21)	0.46
Married	0.83	(0.77, 0.89)	<0.01
Female	1.05	(0.98, 1.13)	0.17
Dual-eligibility with Medicaid	1.14	(1.04, 1.26)	<0.01
<i>Clinical Characteristics</i>			
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	1.02	(0.94, 1.11)	0.57
CCI≥2	1.15	(1.03, 1.27)	0.01
CCI = Missing	1.32	(1.13, 1.53)	<0.01
Proxy for poor performance status	1.34	(1.16, 1.55)	<0.01
Surgery of primary site	0.47	(0.44, 0.51)	<0.01

Abbreviations: IPTW=Inverse Probability of Treat Weight, MAC=Medicare Administrative Contractor, FI=fiscal intermediary, CI=Confidence Interval
‡Detects any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Chapter Seven: Aim 3 – Costs

Analytical Approach

Cost analyses were conducted using a generalized linear model with a log link and a gamma distribution.⁹⁴ As shown in Equation 10 below, we utilized a DID regression framework to determine the impact of Medicare contracting reform on total direct medical costs.

Equation 10. Log-linear regression model for cost estimation

$$\begin{aligned} \text{logit} \{(Total\ Cost | X_{ik})\} = \\ \beta_0 + \sum (\beta X_i) + \theta_1 implementation_k + \theta_2 region_k + \theta_3 (implementation_k * region_k) \\ + \epsilon_{ik} \end{aligned}$$

Several methods were considered to control for the presence of censoring, approximately 14%, observed during the descriptive analysis of Aim 2 (Table 21). Given that this censoring was likely administrative in nature and not as extreme as would be found in conditions with longer median survival, we decided to utilize Lin's simplified regression approach in the main analyses.^{95,96} This approach weighs each complete observation (where death is observed in the study period) by the inverse probability of being censored at the end of the study period.⁹⁷ Additionally, to assess the extent to which choice of model influenced cost results, two additional methods were used to estimate total mean costs. The first was not accounting for the presence of censoring, which evidence indicates can be a valid approach as a primary analysis depending on the underlying nature of the cost data, and the second approach was estimation using only completed cases. Model specification was performed as previously described in Appendix 4. In addition to the previously described sensitivity analyses that varied the length of the

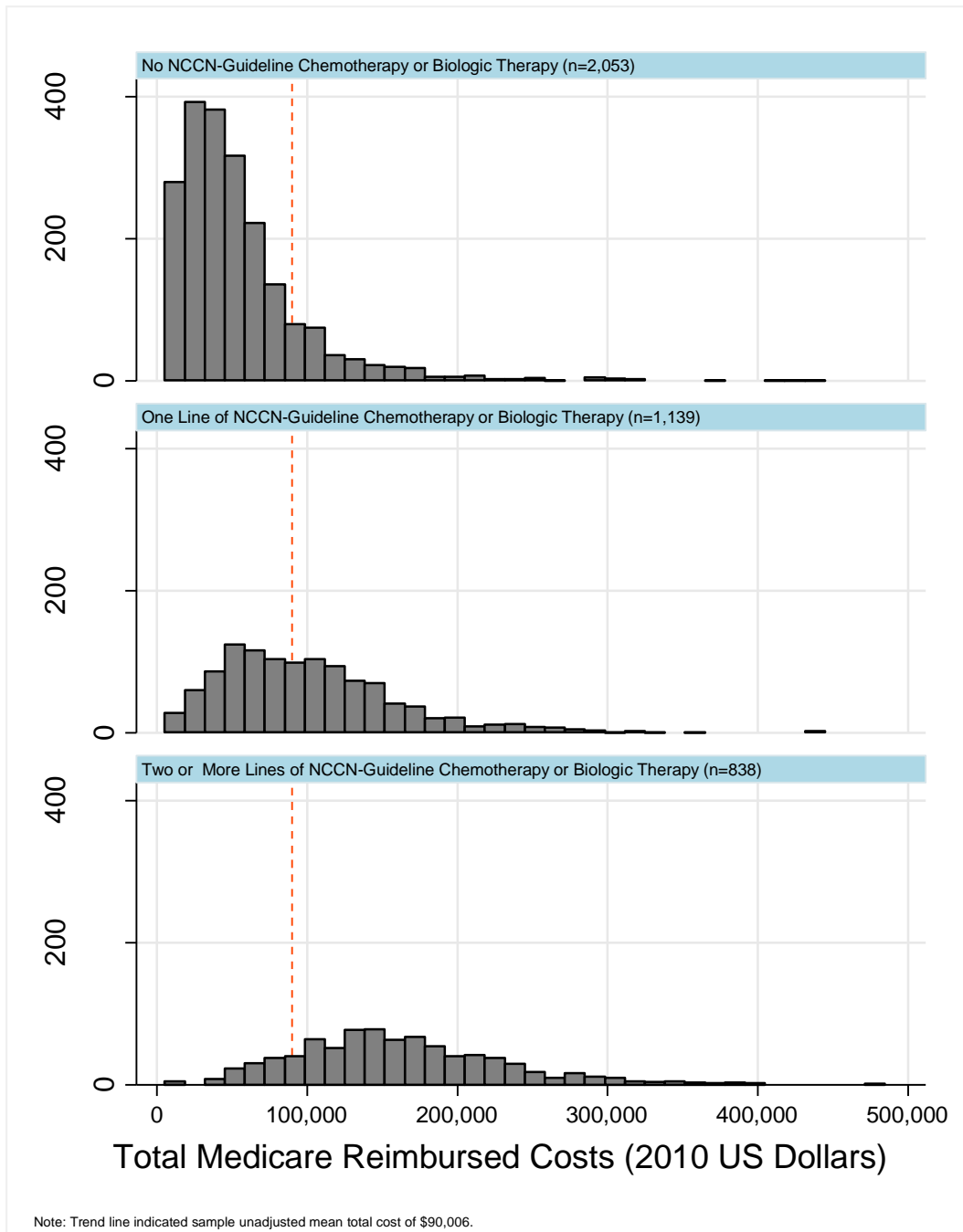
transition period, we performed an additional sensitivity analyses on total costs. We excluded patients diagnosed before January 1, 2006 to account for another policy enacted as part of the MMA: Part D prescription drug coverage. The rationale for removing these patients is that not having retail pharmacy prescription drug coverage may have impacted their overall spending patterns.

Distribution of Costs

Visual overview of total cost data suggested that the Gamma distribution fit the underlying cost data for the entire cohort. Statistical testing utilizing the Kolmogorov-Smirnov test did not support the null hypothesis that the cost data was drawn from a Gamma distribution. Given the variation in cost attributable to lines of therapy, as defined using the algorithm developed by Bikov et al., the study was then stratified into three categories: (1) patients who did not receive any NCCN-guideline recommended chemotherapy or biologic therapy, (2) patients who received one line of NCCN-guideline therapy (chemotherapy and/or biologic therapy), and (3) patients who received two or more lines of NCCN-guideline therapy (chemotherapy and/or biologic therapy).¹⁶

Diagnostic testing supported that using these strata; there was no evidence to reject that the cost data came from the Gamma distribution. The distinct distributions are shown below in Figure 6 were used to model the impact of Medicare contracting reform on total costs. Additional detail on the assessment of the distribution of costs for the cohort can be found in Appendix 11.

Figure 6. Total cost distributions by number of lines of NCCN-guideline therapy received



Descriptive Results

Mean total direct medical costs for the entire cohort are shown in Table 26. Unadjusted IPW-estimates indicate that regions where MAC was not a legacy contractor had consistently higher mean patient costs than regions where the MAC was a legacy contractor, regardless of time period or estimation method. Before MAC implementation, mean total costs in regions where the MAC was the legacy contractor were \$79,143 (Interquartile range [IQR]: \$37,088 - \$107,266) compared to \$95,199 (IQR: \$43,208 - \$131,549) in regions where the MAC was a new entity. In the post period, costs decreased in both regions, likely due to biologic use peaking early in the period covered by this analysis and slowly declining as genetic testing became more prevalent and physicians were better able to target therapy.⁹⁸ Mean total costs after MAC implementation in regions where the MAC was a legacy contractor were \$63,492 (IQR: \$29,973 - \$82,862) compared to \$72,859 (IQR: \$34,824 - \$101,178) in regions where the MAC was a new entity. Figure 7 visually highlights the overall decline in unadjusted full-sample total costs and the persistent differential between regions. Appendix 16 includes additional descriptive cost analyses by potential confounding variables.

Table 26. Descriptive mean total direct medical costs (interquartile range in parentheses), by implementation status and region

	Full-sample estimation ^a	Uncensored cases estimation ^b	Inverse probability weighted estimation ^c
Full Cohort	\$90,006 (\$38,736 - \$126,338)	\$85,427 (\$36,070 - \$118,094)	\$87,494 (\$40,037 - \$121,557)
<i>Before MAC Implementation</i>			
Region where MAC was a legacy contractor	\$81,035 (\$35,559 - \$112,159)	\$77,372 (\$32,581 - \$106,871)	\$79,143 (\$37,088 - \$107,266)
Region where MAC was not a legacy contractor	\$94,951 (\$40,457, \$134,193)	\$92,988 (\$39,042 - \$129,767)	\$95,199 (\$43,208 - \$131,594)
<i>After MAC Implementation</i>			
Region where MAC was a legacy contractor	\$76,807 (\$30,755 - \$111,710)	\$64,458 (\$27,959 - \$84,351)	\$63,492 (\$29,973 - \$82,862)
Region where MAC was not a legacy contractor	\$84,152 (\$39,792 - \$119,950)	\$70,683 (\$31,542 - \$98,680)	\$72,859 (\$34,824 - \$101,178)

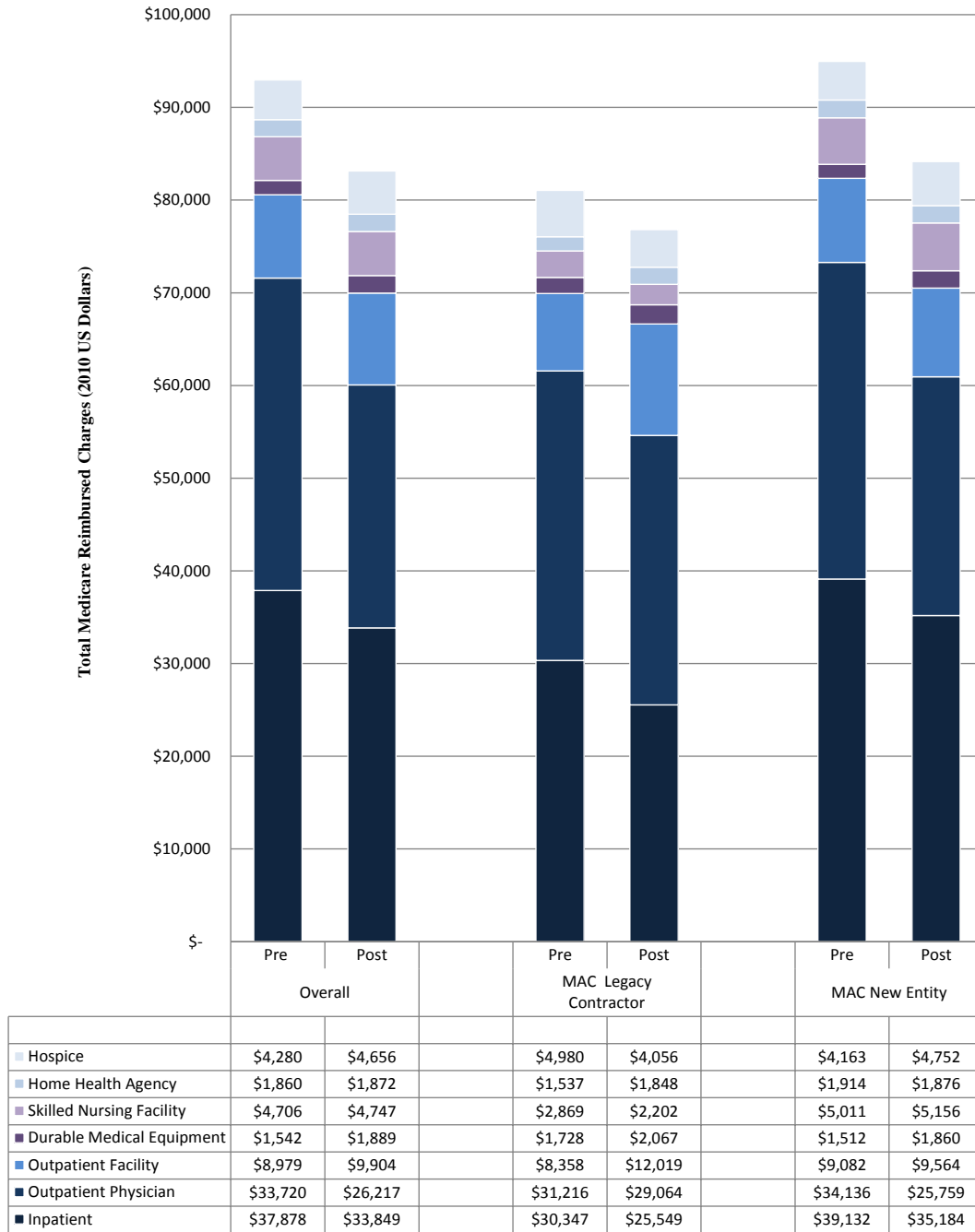
Abbreviations: MAC=Medicare Administrative Contractor

^aFull sample analysis represents total costs for all individuals in the cohort, regardless of whether patients died or were censored

^bUncensored case estimation includes total costs for individuals whose death was observed during the study period

^cInverse probability weighted estimation utilizes total costs accumulation weighted by the inverse probability of not being censored at the end of the observation period (12/31/2010) among patients for whom death was observed

Figure 7. Mean total costs stratified by implementation timing and region



Resource Utilization and Costs

No Chemotherapy or Biologic Therapy

Results of the generalized linear model (weighted by the inverse probability of censoring at the end of the study period) for patients who did not receive NCCN-guideline chemotherapy or biologic therapy are shown in Table 27. The coefficient on the implementation variable (0.91; 95% CI: 0.77, 1.07) indicates that for patients who did not receive NCCN-guideline chemotherapy and were diagnosed in a region where the Legacy contractor became the MAC, costs did not change after implementation. The coefficient on the region variable indicates that (1.27; 95% CI: 1.13, 1.44) indicates that, all else equal, patients diagnosed before implementation in regions where the MAC was not a legacy contractor had costs 26% higher than in regions where the MAC was a legacy contractor. The interaction effect is also multiplicative and indicates that implementation did not differentially affect patients diagnosed in a region where the MAC was not a new entity. These findings were robust to changes in assumptions about timing of the transition period (Table 54) and shortening the pre-implementation period to exclude patients who did not have access to Part D prescription drug coverage. Cost results for patients who did not receive chemotherapy or biologic therapy were the most resistant to different methods to estimate costs – coefficients and intercept values were consistent for the full sample estimate, complete case estimate, and both IPW models (Table 50).

Table 27. Cost estimates from Lin's Regression model for patients not receiving treatment

	Simplified Lin's Regression Model [#] for Costs		
	Exponentiated Coefficient*	95% CI	P
<i>Intercept</i>	\$33,350	(\$28,439, \$39,109)	<0.01
<i>Difference in Difference Analysis</i>			
Post Implementation (v. Pre)	0.91	(0.77, 1.07)	0.25
New MAC (v. FI/Carrier became MAC)	1.27	(1.13, 1.44)	<0.01
Interaction	1.12	(0.93, 1.35)	0.24
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.86	(0.78, 0.96)	<0.01
≥85	0.82	(0.74, 0.91)	<0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	1.29	(1.13, 1.46)	<0.01
Hispanic	0.98	(0.82, 1.17)	0.80
Asian and others	0.92	(0.81, 1.05)	0.21
Married	0.96	(0.88, 1.05)	0.41
Female	0.99	(0.91, 1.08)	0.84
Medicaid buy-in during diagnosis year	1.17	(1.03, 1.32)	0.01
<i>Clinical Characteristics</i>			
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	1.01	(0.91, 1.11)	0.89
CCI≥2	1.06	(0.97, 1.17)	0.19
CCI = Missing	0.95	(0.82, 1.09)	0.45
Proxy for poor performance status [†]	1.03	(0.93, 1.15)	0.56
Surgery of primary site	1.84	(1.71, 1.97)	<0.01

Abbreviations: IPW=Inverse Probability Weight, MAC=Medicare Administrative Contractor, FI= fiscal intermediary

[#]Weighted regression model is fitted to patients with complete cost information is available (death observed in study period). Weights applied to the cost regression model are $1/[\text{Prob}(\text{Censoring}=0)]$ at the end of the study period.

Marginal effects from the cost model for patients who received no NCCN-guideline chemotherapy or biologic therapy are reported in Table 28. With all other variables at their reference category (a 66-74 year old patient, white, not married, male, with no Medicaid dual-eligibility, a CCI=0, no indicators of poor-performance status and no surgery of primary site), the estimated average total direct medical costs for a patient diagnosed before implementation in a region where the MAC was a legacy contractor is \$52,424 (95% CI: \$46,540, \$58,307). These costs decrease by -\$9,046 (95% CI: -15,867, -2,723) following MAC implementation for patients diagnosed in a region where the MAC was the legacy contractor. Estimated average total costs for patients diagnosed in a region where the MAC was not a legacy contractor were \$61,718 (95% CI: \$58,368, \$65,070) in the pre-implementation period and \$57,018 (95% CI: \$52,904, \$61,131) in the post implementation period; this difference was not statistically significant. Regions where the MAC was not the legacy contractor were associated with significantly higher costs in both the pre- and post-implementation period. The DID estimate of -\$4,344 (95% CI: - \$13,735, \$5,046) was not statistically significant and suggests that MAC implementation was associated with between a \$13,735 reduction in costs and a \$5,046 increase in costs for patients who did not receive NCCN-guideline chemotherapy or biologic therapy.

Table 28. Marginal effects of generalized linear model assessing relationship between contracting reform and costs for patients who did not receive an NCCN-guideline chemotherapy or biologic

Time	Geography		Difference [i – ii] (iii)
	Region where MAC was a legacy contractor (i)	Region where MAC was not a legacy contractor (ii)	
Before MAC implementation (a)	\$52,424 (\$46,540, \$58,307)	\$61,718 (\$58,368, \$65,070)	-\$9,295* (-\$15,867, -\$2,723)
After MAC implementation (b)	\$43,378 (\$37,829, \$48,928)	\$57,018 (\$52,904, \$61,131)	-13.639* (-\$20,382, -6,896)
Difference [a-b] (c)	-\$9,046* (-\$17,068, -\$1,024)	-\$4,701 (-9,709, \$306)	-\$4,344 (-\$13,735, \$5,046)

Abbreviations: MAC=Medicare Administrative Contractor

*p-value <0.05

^aModel controlled for age, race, sex, marital status, dual eligibility with Medicare, an indicator for poor performance status, Charlson comorbidity index, and surgery at primary tumor site.

One Line of Therapy

Results of the generalized linear model (weighted by the inverse probability of censoring at the end of the study period) for patients who received one line of NCCN-guideline chemotherapy or biologic therapy are shown in Table 29. The coefficient on the implementation variable (1.02; 95% CI: 0.81, 1.27) indicates that for patients who received one line of NCCN-guideline therapy and were diagnosed in a region where the legacy contractor became the MAC, costs did not change after implementation. The coefficient on the region variable (1.25; 95% CI: 1.10, 1.42) indicates that, similar to the findings among individuals who did not receive NCCN-chemotherapy or biologic therapy, patients diagnosed before implementation in regions where the MAC was not a legacy contractor had costs 25% higher than in regions where the MAC was a legacy contractor. The interaction effect is also multiplicative and indicates that implementation did not differentially affect patients diagnosed in a region where the MAC was not a new entity. These findings were robust to changes in assumptions about timing of the transition period (Table 54). Shortening the pre-implementation period to exclude patients who did not have access to Part D prescription drug coverage (Table 59) resulted in no change to the estimate on the base case model; however, in sensitivity analyses where the pre-period was redefined, the difference in region was no longer statistically significant. Cost results for patients who did not receive chemotherapy or biologic therapy were the most resistant to different methods to estimate costs – coefficients and intercept values were consistent for the full sample estimate, complete case estimate, and both IPW models (Table 50).

Table 29. Cost estimates from Lin's Regression model for patients receiving one line of chemotherapy, with or without biologic therapy

	Simplified Lin's Regression Model [#] for Costs		
	Exponentiated Coefficient*	95% CI	P
<i>Intercept</i>	\$57,989	(\$49,284, 68,230.13)	< 0.01
<i>Difference in Difference Analysis</i>			
Post Implementation (v. Pre)	1.02	(0.81, 1.27)	0.89
New MAC (v. FI/Carrier became MAC)	1.25	(1.10, 1.42)	< 0.01
Interaction	0.94	(0.74, 1.20)	0.64
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.86	(0.79, 0.93)	< 0.01
≥85	0.74	(0.66, 0.84)	< 0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	0.96	(0.86, 1.08)	0.51
Hispanic	0.92	(0.79, 1.08)	0.32
Asian and others	1.01	(0.85, 1.18)	0.95
Married	0.97	(0.90, 1.05)	0.50
Female	0.98	(0.91, 1.06)	0.63
Medicaid buy-in during diagnosis year	1.00	(0.90, 1.11)	0.97
<i>Clinical Characteristics</i>			
Addition of biologic therapy	1.43	(1.32, 1.54)	< 0.01
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	1.11	(1.02, 1.22)	0.02
CCI≥2	1.18	(1.05, 1.32)	< 0.01
CCI = Missing	0.96	(0.84, 1.09)	0.51
Proxy for poor performance status [†]	1.06	(0.89, 1.26)	0.52
Surgery of primary site	1.42	(1.31, 1.54)	< 0.01

Abbreviations: IPW= Inverse Probability Weight, MAC=Medicare Administrative Contractor, FI=fiscal intermediary,

[#]Weighted regression model is fitted to patients with complete cost information is available (death observed in study period). Weights applied to the cost regression model are $1/[\text{Prob}(\text{Censoring}=0)]$ at the end of the study period.

Marginal effects from the cost model for patients who received one line of NCCN therapy are shown in Table 30. The estimated average total direct medical costs for a patient diagnosed before implementation in a region where the MAC was a legacy contractor is \$84,329 (95% CI: \$74,264, \$94,393). These costs decrease by -\$2,021 (95% CI: -\$21,817, -\$17,776) following MAC implementation for patients diagnosed in a region where the MAC was the legacy contractor. Estimated average total costs for patients diagnosed in a region where the MAC was not a legacy contractor were \$97,234 (95% CI: \$91,988, \$102,480) in the pre-implementation period and \$92,746 (95% CI: \$86,482, \$99,010) in the post implementation period; this difference was not statistically significant. While there was a statistically significant difference in mean total costs pre-implementation between regions where the legacy contractor became the MAC and regions where the MAC was not a legacy contractor, in the post-implementation period the difference (-\$10,438; 95% CI: -\$28,522, \$7,646) is not statistically significant. The DID estimate of -\$2,467 (95% CI: -\$18,995, \$23,930) was not statistically significant either and suggests that MAC implementation was associated with between a -\$18,995 reduction in costs and a \$23,930 increase in costs for patients who received one line of NCCN-guideline therapy.

Table 30. Marginal effects of generalized linear model assessing relationship between contracting reform and costs for patients who received one line of NCCN-guideline therapy

Time	Geography		Difference [i - ii] (iii)
	Region where MAC was a legacy contractor (i)	Region where MAC was not a legacy contractor (ii)	
Before MAC implementation (a)	\$84,329 (\$74,264, \$94,393)	\$97,234 (\$91,988, \$102,480)	-\$12,905* (-\$24,403, -\$1,407)
After MAC implementation (b)	\$82,308 (\$65,466, \$99,150)	\$92,746 (\$86,482, \$99,010)	-\$10,438 (-\$28,522, \$7,646)
Difference [a-b] (c)	-\$2,021 (-\$21,817, -\$17,776)	-\$4,488 (-12,909, \$3,934)	-\$2,467 (-\$18,995, \$23,930)

Abbreviations: MAC=Medicare Administrative Contractor

*p-value <0.05

^aModel controlled for age, race, sex, marital status, dual eligibility with Medicare, an indicator for poor performance status, Charlson comorbidity index, and surgery at primary tumor site.

Two or More Lines of Therapy

Results of the generalized linear model (weighted by the inverse probability of censoring at the end of the study period) for patients who received two or more lines of NCCN-guideline chemotherapy or biologic therapy are shown in Table 31. The coefficient on the implementation variable (0.97; 95% CI: 0.81, 1.15) indicates that for patients who received two or more lines of NCCN-guideline therapy and were diagnosed in a region where the Legacy contractor became the MAC, costs did not change after implementation. The coefficient on the region variable (1.30; 95% CI: 1.13, 1.44) indicates that, as with the prior two analyses, patients diagnosed before implementation in regions where the MAC was not a legacy contractor had costs 30% higher than in regions where the MAC was a legacy contractor. The interaction effect indicates that implementation did not differentially affect patients diagnosed in a region where the MAC was not a new entity. These findings were robust to changes in assumptions about timing of the transition period (Table 56) and shortening the pre-implementation period to exclude patients who did not have access to Part D prescription drug coverage (Table 59). Costs for individuals receiving two or more lines of chemotherapy were also robust to changes in methods for addressing censored costs (Table 50).

Table 31. Cost estimates from Lin's Regression model for patients receiving two or more lines of chemotherapy, with or without biologic therapy

	Simplified Lin's Regression Model [#] for Costs		
	Exponentiated Coefficient*	95% CI	P
<i>Intercept</i>	\$101,239	(\$87,034, \$117,762)	<0.001
<i>Difference in Difference Analysis</i>			
Post Implementation (v. Pre)	0.97	(0.81, 1.15)	0.72
New MAC (v. FI/Carrier became MAC)	1.30	(1.20, 1.42)	<0.01
Interaction	0.87	(0.72, 1.05)	0.14
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.84	(0.79, 0.89)	<0.01
≥85	0.70	(0.61, 0.81)	<0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	1.01	(0.91, 1.13)	0.80
Hispanic	0.94	(0.83, 1.06)	0.30
Asian and others	0.95	(0.84, 1.08)	0.42
Married	1.01	(0.96, 1.07)	0.98
Female	0.98	(0.92, 1.04)	0.53
Medicaid buy-in during diagnosis year	1.05	(0.95, 1.16)	0.33
<i>Clinical Characteristics</i>			
Addition of biologic therapy	1.33	(1.21, 1.46)	<0.01
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	1.03	(0.96, 1.10)	0.38
CCI≥2	1.00	(0.91, 1.11)	0.98
CCI = Missing	1.08	(0.93, 1.25)	0.30
Proxy for poor performance status [‡]	1.09	(0.97, 1.24)	0.16
Surgery of primary site	1.14	(1.07, 1.22)	<0.01

Abbreviations: IPW=Inverse Probability Weight, MAC=Medicare Administrative Contractor, FI=fiscal intermediary,

[#]Weighted regression model is fitted to patients with complete cost information is available (death observed in study period). Weights applied to the cost regression model are $1/[\text{Prob}(\text{Censoring}=0)]$ at the end of the study period.

Marginal effects from the cost model for patients who received two or more lines of NCCN-guideline therapy are reported in Table 32. The estimated average total direct medical costs for a patient diagnosed before implementation in a region where the MAC was a legacy contractor is \$132,610 (95% CI: \$121,830, \$143,391). These costs decrease by -\$5,502 (95% CI: -\$28,458, -\$17,454) following MAC implementation for patients diagnosed in a region where the MAC was the legacy contractor. Estimated average total costs for patients diagnosed in a region where the MAC was not a legacy contractor were \$165,769 (95% CI: \$159,658, \$171,879) in the pre-implementation period and \$135,552 (95% CI: \$126,913, \$144,192) in the post implementation period; this difference (-\$30,216; 95% CI: -\$40,967, -\$19,466) was statistically significant. This supports the conclusion that total costs for patients receiving two or more lines of NCCN-guideline therapy in regions where the MAC was not a legacy contract had significantly lower direct medical costs post-implementation. While there was a statistically significant difference in mean total costs pre-implementation between regions where the legacy contractor became the MAC and regions where the MAC was not a legacy contractor (-\$33,158; 95% CI: -\$45,663, -\$20,654), in the post-implementation period the difference (-\$8,444; 95% CI: -\$30,472, \$13,584) is not statistically significant. Regions where the MAC was not the legacy contractor were associated with significantly higher costs in both the pre- and post-implementation period.

Table 32. Marginal effects of generalized linear model assessing relationship between contracting reform and costs for patients receiving two or more lines of NCCN-guideline therapy

Time	Geography		Difference [i - ii] (iii)
	Region where MAC was a legacy contractor (i)	Region where MAC was not a legacy contractor (ii)	
Before MAC implementation (a)	\$132,610 (\$121,830, \$143,391)	\$165,769 (\$159,658, \$171,879)	-\$33,158* (-\$45,663, -\$20,654)
After MAC implementation (b)	\$127,108 (\$106,930, \$147,286)	\$135,552 (\$126,913, \$144,192)	-\$8,444 (-\$30,472, \$13,584)
Difference [a-b] (c)	-\$5,502 (-\$28,458, -\$17,454)	-\$30,216* (-\$40,967, -\$19,466)	\$24,714 (-\$571, \$49,999)

Abbreviations: MAC=Medicare Administrative Contractor

*p-value <0.05

^aModel controlled for age, race, sex, marital status, dual eligibility with Medicare, an indicator for poor performance status, Charlson comorbidity index, and surgery at primary tumor site.

Chapter Four: Discussion

In this retrospective cohort study of Medicare beneficiaries with mCC, Medicare contracting reform does not appear to have negatively impacted patients although significant variation in biologic therapy receipt and costs remain. This research found that Medicare administrative contracting reform did not reduce patient access to NCCN-guideline treatment. There was also no evidence of an implementation impact on overall survival or costs.

Medicare contracting reform is ongoing and impacted by recent legislation. Section 509 of the Medicare Access and Children's Health Insurance Program Reauthorization Act (MACRA) of 2015 makes several additional changes to the Medicare Administrative contracting reform landscape.⁹⁹ The most significant change is the extension of MAC contracts from five to ten years between re-competition. In a sense, this moves MACs closer to the legacy contractor environment in terms and underscores the need for the other component of MACRA relevant to MACs: the requirement for CMS to publish performance information on MACs for transparency. The currently available quality measures cover eleven business functions of MACs: appeals, audit and reimbursement, beneficiary customer service, claims processing, debt management, financial management, Freedom of Information Act, medical review, Medicare secondary payer, provider customer service program, and provider enrollment. The data released under this mandate indicates that while over time MAC overall performance has improved, likely due to the clarity around the quality measures themselves, not all MACs are reaching their overall compliance goals and there is variation among the MACs in respects to quality.¹⁰⁰ As shown in Table 33 below, the Alliance of Specialty Medicine noted this in

their comments on the MACRA legislation, implying both an overall declining trend in quality as well as failure by MACs to make evidence-based local coverage decisions.

Table 33. Alliance of Specialty Medicine comments in response to a request for information regarding the awarding and the administration of Medicare administrative contractor contracts (CMS-1653-NC)

Stakeholder (Year)	Verbatim Comments
Alliance of Specialty Medicine (2016) ¹⁰¹	<p>A. Alliance member organizations have noted significant performance deterioration on key administrative activities by multiple MACs.</p> <p>B. “We also note that MAC LCDs can vary significantly across regions without any clear rationale or supportive evidence to justify the stark differences in coverage for certain items and services”</p> <p>C. “MACs are developing ‘other’ coverage and payment policies, which they deem are not LCDs and as a result, circumvent the require notice and comment period”</p>

Treatment options in oncology are evolving and are placing additional pressure on public programs to control costs beyond what is likely possible through consolidation of claims processing. In the time from the end of follow-up for this study to the present, five new medicines have been approved for the treatment of metastatic colon cancer: nivolumab, bevacizumab-awwb, trifluridine and tipiracil, regorafenib, and ziv-aflibercept. Only one product is considered traditional chemotherapy (trifluridine and tipiracil), the other four medicines are biologic therapies, or in the case of bevacizumab-awwb, a biosimilar.

Given the high costs associated with these innovative therapies, CMS has proposed implementing evidence developed by a European-style health-technology assessment agency into decision-making by Medicare Part B as part of a demonstration withdrawn in 2017.¹⁰² Further cost pressures could lead to the development of local coverage decisions

at the MAC level that would directly result in policy changes that could impact practice patterns and subsequently, patient care.^{103,104}

Table 34. United States Food and Drug Administration approvals for colon and colorectal cancer since January 2012

Name (Approval Month/Year) Method of Administration	Description / Mechanism of Action
nivolumab (08/2017) Intravenous infusion	Monoclonal antibody that attaches to PD-1 receptor to block proteins (PD-L1 / PD-L2) from interfering with immune system cells, increasing the body's ability to kill cancer cells
bevacizumab-awwb (07/2017) Intravenous infusion	First oncology biosimilar approved in the United States; inhibits human vascular endothelial growth factor (VEGF), slowing the growth of new blood vessels
trifluridine and tipiracil (07/2015) Oral- tablet	Cytotoxic fixed-dose combination that interferes with DNA function to prevent cancer cells from dividing and multiplying
regorafenib (07/2012) Oral - tablet	Biologic protein kinase inhibitor (TKI) that blocks multiplication of cancer cells and creation of new blood vessels
ziv-aflibercept (08/2012) Intravenous infusion	Biologic therapy that stops creation of new blood vessels in tumor by inhibiting vascular endothelial growth factor (VEGF)

Study Strengths and Limitations

A particular strength of this work is that it is the first study to assess the impact of Medicare contracting reform on treatment receipt and outcomes using the same framework (difference-in-differences) that the Center for Medicare and Medicaid Innovation utilizes when it is assessing the impact of innovative payment and service delivery models.¹⁰⁵ However, this work is not without limitations. While this study analyzes the first cycle of MAC implementation, a well-documented component of the transition process for new MACs assuming responsibility in a jurisdiction is the sharing of “lessons learned” throughout the transition process.¹⁰⁶ While this component was part

of the initial transition from fiscal intermediaries and carriers to MACs as well, it does indicate a mechanism for incorporating and disseminating best practices, which could result in this analysis lacking generalizability to the implementation of future MACs, who would be better prepared by learning from their predecessors. This impact is expected to be minimal as due to the resources and experience necessary to administer claims across a region the size of the new jurisdictions, it is highly unlikely that an unsophisticated entity would be awarded a contract.

The SEER-Medicare dataset, while a nationally representative and valuable data source, has several known limitations that can reduce the generalizability of findings. If chemotherapy or biologic therapy was provided in the inpatient setting, it was not captured in this analysis as hospital inpatient claims do not capture that level of detail.¹⁰⁷ However, it is not likely that this was a significant source of bias as the majority of oncology care occurs in the physician office or hospital outpatient department.¹⁰⁸ SEER-Medicare also has data limitations that prevent potentially additional useful analyses, particularly genetic test results and accurate patient out-of-pocket information.¹⁰⁹ The availability of genetic testing results would indicate the appropriateness of biologic therapy and serve as a measure to indicate quality care. Calculating the patient proportion of costs would also help determine if Medicare contracting reform impacted patient cost sharing responsibility; however, estimations of true patient responsibility would be unreliable due to supplemental Medigap policies.

Chapter Five: Conclusions and Future Research

This dissertation examined whether or not the consolidation of claims processors for Medicare Parts A and B influenced the treatment mCC patients received and subsequently, their overall survival and total direct medical costs. While external groups have expressed concern, it appears that CMS was successful in transitioning the first round of legacy contractors to MACs while neither restricting patient access to NCCN-guideline therapy nor increasing direct medical costs. However, systematic differences remain between regions where the legacy contractor became the MAC and where the MAC was a new entity to the region. Variation at the MAC level has also been found in patient receipt of hemodialysis but to date no other research examines the impact of MACs on the receipt of therapy for cancer patients.¹¹⁰ This variation does not necessarily denote disparity although impacts beyond variability driven by underlying case mix differences should be further investigated.

Future research is necessary as CMS continues to consolidate MAC jurisdictions and decisions made at the regional level could result in patients with the same Medicare insurance receiving different treatments, and experiencing different outcomes simply based on what entity is reimbursing their claims. This is particularly important as Medicare beneficiaries cannot feasibly change the MAC to which their claims are submitted. Doing so would require physical relocation to another jurisdiction, an impractical solution at best. As the most logical extension, future research should examine subsequent cycles of implementation, now that several rounds of contracting have occurred, increasing the potential sample size and allowing for alternate modeling approaches as well as analysis of specific types of chemotherapy and biologic therapy, as

well as the inclusion of Part D medicines. This analysis would also enable examination of heterogeneity of the impact of contracting reform to determine if there are subgroups of patients for whom contracting reform affected differentially so that future reforms can account for this variation. As the broadest extension, further analyses on consolidation's impact on disease states beyond mCC would also prove valuable. This could either take the form of an analysis of patients diagnosed with earlier stages of disease, or in more prevalent, chronic conditions, such as muscular sclerosis and rheumatoid arthritis, where LCDs made at the MAC level could either restrict or expand patient access to medicines to improve quality of life.

Appendices

Appendix 1. Detail on SEER-Medicare Dataset

Table 35. Summary table of SEER-Medicare data files used for analysis

Name of File	Information in File
Patient Entitlement and Diagnosis Summary File (PEDSF) ¹¹¹	<i>The PEDSF file includes SEER diagnostic information (for up to ten diagnosed cancers), date of birth, date of death (if applicable), sex, race, and state of residence. This file also includes non-SEER variables including Medicare eligibility, reason for Medicare entitlement, and health maintenance organization (HMO) enrollment.</i>
Medicare Claims Files¹¹²	
Medicare Provider Analysis and Review (MEDPAR)	<i>The MEDPAR file includes all Part A short stay, long stay, and skilled nursing facility (SNF) bills for each calendar year. MEDPAR contains one summarized record per admission. Each record includes up to 10 ICD-9 diagnoses and 10 ICD-9 procedures provided during the hospitalization</i>
National Claims History (NCH)	<i>A file exists for each calendar year that contains all Medicare Part B claims generated due to physician (or non-institutional provider) services in clinics, hospitals, or other sites.</i>
Outpatient Files (OUTPT)	<i>A file exists for each calendar year, containing all Medicare Part B claims from institutional outpatient providers.</i>
Home Health Agencies (HHA)	<i>Information on number of visits, type of visits, and diagnosis is contained for home healthcare.</i>
Hospice (HOSP)	<i>Information on type of care (inpatient care or routine home care) as well as terminal diagnosis associated with that care.</i>
Durable Medical Equipment (DME)	<i>Contains information on use of oral and intravenous chemotherapeutic agents, as well as infusion pumps used.</i>
Prescription Drug Event (PDE)	<i>Contains information about drug utilization: date of prescription fill, drug dispensed (identified by National Drug Code), quantity dispensed, days supplied, total cost and out-of-pocket cost. The SEER-Medicare data includes Part D PDE data from 2007 onward.</i>

Appendix 2. Summary of regression model covariates

Table 36. Operationalization of covariates used in analysis

Variable Name	Source	Type	Operationalization ^a
Age at diagnosis	SEER	Categorical	0=66-74 , 1=75-84, 2 ≥85
Sex	SEER	Binary	0=Male , 1=Female
Race	SEER	Categorical	0=Non-Hispanic White , 1=Black, 2= Hispanic, 3= Other [Includes Asian, Native American, Hawaiian, Unknown]
Marriage status	SEER	Binary	0=Not married [Includes single, separated, divorced and widowed], 1= Married
Dual-eligibility with Medicaid	SEER	Binary	0=No Medicaid buy-in for the patient in the 12 months prior to diagnosis , 1= one or more months of Medicaid buy-in
Charlson Comorbidity Index (CCI)	Medicare	Categorical	0=No comorbid conditions , 1=One comorbid condition, 2= Two or more comorbid conditions, 3= Unknown/Missing
Indicators of Poor Performance Status ⁸²	Medicare	Binary	0=No indicators of poor performance status , 1=One or more indicator of poor performance status
Surgery of primary tumor site ^b	SEER	Binary	0=No surgery on primary tumor site , 1=Surgery on primary tumor site
Receipt of NCCN guideline chemotherapy*	Medicare	Binary	0=No NCCN Guideline chemotherapy (with or without biologic therapy) received , 1=NCCN Guideline chemotherapy (with or without biologic therapy) received
Receipt of NCCN guideline biologic therapy*	Medicare	Binary	0=No NCCN Guideline biologic therapy (with or without chemotherapy) received , 1=NCCN Guideline chemotherapy (with or without chemotherapy) received

^aReference Category in Bold

^bDefined as: “[A] surgical procedure that removes and/or destroys tissue of the primary site that is performed as part of the initial diagnostic and staging work-up or first course of therapy” This does not include removal, biopsy, or aspiration of regional lymph nodes.¹¹³

Appendix 3. Analysis of variance and model adjustment

This analysis uses patient-level data to determine the impact of a policy change at the regional/MAC level. As such, the potential exists for unit-of-analysis error as described by Whiting-O'keefe, Henke, and Simborg in 1984.¹¹⁴ To assess for unit-of-analysis error, initial analyses examined to what extent variability in treatment is accounted for by MAC region-level (as opposed to patient-level) factors.¹¹⁵ This was accomplished by fitting a multi-level model and analyzing the intraclass correlation coefficient (ICC) where:

Equation 11. Intraclass correlation coefficient

$$ICC = \frac{\sigma_{clustering}}{\sigma_{clustering} + \sigma_{residual}}$$

If the resulting value is 0, this indicates independence as there is no variance attributable to the clustering (in this instance SEER region). Using methods operationalized by Ene and colleagues for interpreting covariance parameter estimates from PROC GLIMMIX procedure, it is possible to assess how much of the total variation of treatment receipt is accounted for by a patient's MAC region.¹¹⁶ Given the operationalization of the primary outcome of interest is dichotomous and follows a logistic distribution ($\mu = 0, \sigma^2 = 3.29$), the value of $\sigma_{residual}$ in Equation 5 above will be substituted with 3.29 and the level-2 error variance will be estimated from the regression models.¹¹⁷

The initial models proposed included a random effect for SEER-Medicare region under the assumption that each region in the analysis is drawn from a larger population of regions; a logical assumption given that SEER-Medicare covers a sample of the United States. This effect would cause incorrect inference at the patient level, the unit of analysis for this research, as patients would experience differential impact in their regions, much as the patients in Whitting and O’Keefe’s work experienced variation in outcomes dependent upon seeing a nurse at their place of work as compared with a physician office provider.¹¹⁴ To determine the presence of a SEER-Medicare region-level effect in the study data, the ICC was calculated for receipt of chemotherapy (Table 27) and biologic therapy (Table 28). In the null models shown, approximately 0.3% of the variability in the receipt of NCCN-guideline chemotherapy and 0.07% of the variability in the receipt of NCCN-guideline biological therapy is accounted for by SEER-Medicare region. In the final, full models, this variability increases to 0.09% for receipt of NCCN-guideline chemotherapy and decreases for receipt of biologic therapy (0.03%). This analysis, demonstrating that less than 1% of the variation in chemotherapy and biological therapy receipt is attributable to SEER-Medicare region, provided evidence that the proportion of patients receiving either therapy within a SEER-Medicare region is no more similar than the proportion of patients receiving therapy in any other region. These analyses supported the transition to a simplified model without random effects.

Table 37. Estimates from two- level generalized linear model predicting probability receiving NCCN-guideline chemotherapy

	Model 1	Model 2 ^c
<i>Fixed Effects</i>		
Intercept	-0.06 (0.5)	-2.55* (0.28)
Implementation		0.06 (0.22)
Region		-0.24 (0.18)
Interaction		0.02 (0.24)
<i>Error Variance</i>		
Level-2 Intercept ^a	0.012 (0.014)	0.032 (0.024)
ICC ^b	0.0036	0.0097
<i>Model Fit</i>		
-2LL	5576.60	4658.55**

Values based on SAS PROC GLIMMIX. Entries show parameter estimates with standard errors in parentheses. Estimation Method = Laplace.

*p< .05

**=likelihood ratio test significant

^aSEER-Medicare Region

^bIntraclass Correlation Coefficient - calculated as: $[ICC = \text{Covariance Parameter Estimate} / (\text{Covariance Parameter Estimate} + 3.29)]$

^cModel includes covariates for age, gender, race, marital status, Medicaid coverage, Charlson Comorbidity Index, an indicator for poor performance status, and receipt of surgery at the primary site.

Table 38. Estimates from two- level generalized linear model predicting probability receiving NCCN-guideline biologic therapy

	Model 1	Model 2 ^c
<i>Fixed Effects</i>		
Intercept	-0.73* (0.6)	-2.95* (0.30)
Implementation		-0.16 (0.22)
Region		-0.48* (0.15)
Interaction		-0.11 (0.23)
<i>Error Variance</i>		
Level-2 Intercept ^a	0.024 (0.024)	0.011 (0.014)
ICC ^b	0.0072	0.0039
<i>Model Fit</i>		
-2LL	5031.05	4304.52**

Values based on SAS PROC GLIMMIX. Entries show parameter estimates with standard errors in parentheses. Estimation Method = Laplace.

*p < .05

**=likelihood ratio test significant

^aSEER-Medicare Region

^bIntraclass Correlation Coefficient - calculated as: $ICC = [Covariance\ Parameter\ Estimate / (Covariance\ Parameter\ Estimate + 3.29)]$

^cModel includes covariates for age, gender, race, marital status, Medicaid coverage, Charlson Comorbidity Index, an indicator for poor performance status, and receipt of surgery at the primary site.

Appendix 4. Generalized Linear Model Diagnostic Testing

Goodness-of-fit of logistic regression models was examined using the Hosmer-Lemeshow test.¹¹⁸ The Ramsey Regression Equation Specification Error Test (RESET) was performed to detect functional form misspecification.^{119,120} As an example, the initial logistic regression model used to predict receipt of biologic therapy was expanded as shown in Equation 12 below:

Equation 12. The Ramsey Regression Equation Specification Error Test

$$\begin{aligned} \text{logit}\{\text{Pr}(\text{Receipt of Biologic Therapy} = 1)\} = \\ \beta_0 + \theta_1 \text{implementation} + \theta_2 \text{region} + \theta_3 \text{implementation} * \text{region} + \sum (\beta_k X_k) \\ + \delta_1 \hat{Y}^2 + \delta_2 \hat{Y}^3 + \epsilon \end{aligned}$$

In this model, \hat{Y} represents the linear prediction derived from the model, making \hat{Y}^2 and \hat{Y}^3 are non-linear functions of the explanatory variables. Under the null hypotheses, the model is correctly specified and a non-significant test statistic indicates there is no evidence of a functional form problem.

The Pregibon link test was used to select the appropriate link function for each monthly regression model.¹²¹ As before, the model used to predict receipt of biologic therapy is used as an example:

Equation 13. Pregibon link test

$$\text{logit}\{\text{Pr}(\text{Receipt of Biologic Therapy} = 1)\} = \beta_0 + \delta_1 \hat{Y}^2 + \delta_2 \hat{Y}^2 + \delta_3 \hat{Y}^3 + \epsilon$$

Similar to the RESET test, \hat{Y} represents the linear prediction derived from the model and \hat{Y}^2 and \hat{Y}^3 are non-linear functions of the explanatory variables. Under the null

hypotheses, the model is correctly specified and a significant test statistic on δ_2 or δ_3 indicates a lack of linearity.

The Modified Park Test was used to determine the appropriate family distribution for cost models following distributional analysis.¹²² As outlined by Glick et al., following the initial GLM model estimation based on the descriptive overview of the data, squared residuals were regressed against the log-transformed cost predictions in GLM with a “*log link gamma distribution, and robust variance/covariance matrix.*”¹²³

Equation 14. Modified Park test

$$\text{Untransformed Residuals} = \beta_0 + \alpha(\ln\hat{Y}) + \epsilon$$

The resulting coefficient was tested against several null hypotheses based on the expected values of the coefficient for family distributions, as shown in Table 39 below.¹²⁴

Table 39. Test values for modified Park test

Coefficient*	Family	Null Hypothesis
0	Gaussian	$H_0: \alpha = 0$
1	Poisson	$H_0: \alpha = 1$
2	Gamma	$H_0: \alpha = 2$
3	Inverse Gaussian or Wald	$H_0: \alpha = 3$

* α in Equation 14

A significant test statistic providing evidence to reject the null hypotheses indicates that the distribution is a poor fit for the underlying data.

Appendix 5. Logistic regression diagnostic testing for receipt of treatment

Receipt of Chemotherapy Model

Table 40. Results from model misspecification tests for logistic regression model examining the relationship between MAC implementation and likelihood of receiving NCCN-recommended chemotherapy

Goodness of fit statistic	AIC ^a	BIC ^b	-2 log L ^c	H-L ^d (χ^2 ; Pr > χ^2)	c-statistic ^e
Intercept-only model	5580.90	5587.20	-2789.45	10.11; 0.26	-
Intercept with main effects ^a	4701.84	4808.96	-2333.92		0.761
Goodness of link test (<i>p-values</i>) ^f	Linear predictor	Squared linear predictor	Cubed linear predictor		
Pregibon link test	< 0.001	0.61	0.34		
Ramsey RESET ^g	-	0.93	0.57		
^a Akaike's information criteria ^b Schwarz's Bayesian information criteria ^c Log likelihood ^d Hosmer-Lemeshow test; a p-value > 0.05 indicates no evidence of poor model fit ^e Indicates the probability that a patient who received NCCN-guideline chemotherapy will have a higher predicted probability from the regression model than a patient who did not receive NCCN-guideline chemotherapy ^f p-values < 0.05 indicate that combinations, both linear and non-linear, of the explanatory variables included in the model have explanatory power. If p < 0.05 for non-linear combinations, this indicated that the receipt of NCCN-guideline chemotherapy would better be approximated by a non-linear predictor. ^g Regression Equation Specification Error Test					

Receipt of Biologic Therapy Model

Table 41. Results from model misspecification tests for logistic regression model examining the relationship between MAC implementation and likelihood of receiving NCCN-guideline biologic therapy

Goodness of fit statistic	AIC ^a	BIC ^b	-2 log L ^c	H-L ^d (χ^2 ; Pr > χ^2)	c-statistic ^e
Intercept-only model	5035.39	5041.69	-2516.70	6.07; 0.64	-
Intercept with main effects ^a	4353.49	4460.62	-2159.74		0.748
Goodness of link test (<i>p-values</i>) ^f	Linear predictor	Squared linear predictor	Cubed linear predictor		
Pregibon link test	< 0.001	0.99	0.73		
Ramsey RESET ^g	-	0.90	0.88		
^a Akaike's information criteria ^b Schwarz's Bayesian information criteria ^c Log likelihood ^d Hosmer-Lemeshow test; a p-value > 0.05 indicates no evidence of poor model fit ^e Indicates the probability that a patient who received NCCN-guideline biologic therapy will have a higher predicted probability from the regression model than a patient who did not receive NCCN-guideline biologic therapy ^f P-values < 0.05 indicate that combinations, both linear and non-linear, of the explanatory variables included in the model have explanatory power. If p < 0.05 for non-linear combinations, this indicated that the receipt of NCCN-guideline biologic therapy would better be approximated by a non-linear predictor. ^g Regression Equation Specification Error Test					

Appendix 6. Alternate models for receipt of therapy

Table 42. Modified Poisson regression model estimates of correlations between receipt of chemotherapy therapy (with or without biologic therapy) and clinical and demographic factors

	Receipt of Chemotherapy (with or without biologic therapy)		
	Risk Ratio	95% CI	<i>p</i>
<i>Difference-in-differences estimators</i>			
θ_1 - Post Implementation (v. Pre)	1.07	(0.96, 1.19)	0.23
θ_2 - New MAC (v. Legacy contractor became MAC)	0.94	(0.84, 1.07)	0.36
θ_3 - Interaction	1.01	(0.89, 1.15)	0.90
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.72	(0.69, 0.75)	< 0.01
≥85	0.29	(0.26, 0.34)	< 0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	0.92	(0.84, 1.00)	0.04
Hispanic	1.05	(0.96, 1.15)	0.31
Asian and others	1.03	(0.91, 1.17)	0.60
Married at diagnosis (v. Not Married)	1.23	(1.18, 1.29)	< 0.01
Female (v. Male)	0.99	(0.94, 1.04)	0.73
Any Medicaid buy-in during diagnosis year	0.84	(0.75, 0.94)	< 0.01
<i>Clinical characteristics</i>			
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	1.02	(0.96, 1.09)	0.47
CCI≥2	0.84	(0.77, 0.92)	< 0.01
CCI=Missing	0.75	(0.66, 0.85)	< 0.01
Proxy for poor performance status [‡]	0.64	(0.53, 0.76)	< 0.01
Surgery of primary site	1.42	(1.34, 1.51)	< 0.01

Abbreviations: MAC= Medicare Administrative Contractor, CI=confidence interval

[‡]Indicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis

Table 43. Modified Poisson regression model estimates of correlations between receipt of biologic therapy (with or without chemotherapy) and clinical and demographic factors

	Receipt of Biologic Therapy (with or without chemotherapy)		
	Risk Ratio	95% CI	<i>p</i>
<i>Difference-in-differences estimators</i>			
θ_1 - Post Implementation (v. Pre)	0.99	(0.81, 1.23)	0.99
θ_2 - New MAC (v. Legacy contractor became MAC)	0.85	(0.76, 0.97)	0.01
θ_3 - Interaction	0.94	(0.75, 1.18)	0.59
<i>Demographic characteristics</i>			
Age at time of diagnosis			
66-74		Reference	
75-84	0.60	(0.56, 0.64)	< 0.01
≥85	0.20	(0.15, 0.25)	< 0.01
Race/ethnicity			
Non-Hispanic White		Reference	
African American	0.80	(0.68, 0.95)	< 0.01
Hispanic	0.94	(0.76, 1.17)	0.59
Asian and others	0.99	(0.80, 1.24)	0.99
Married at diagnosis (v. Not Married)	1.19	(1.12, 1.28)	< 0.01
Female (v. Male)	0.97	(0.86, 1.09)	0.64
Any Medicaid buy-in during diagnosis year	0.74	(0.61, 0.90)	< 0.01
<i>Clinical characteristics</i>			
Charlson comorbidity index (CCI)			
CCI=0		Reference	
CCI=1	0.98	(0.90, 1.07)	0.71
CCI≥2	0.68	(0.62, 0.74)	< 0.01
CCI=Missing	0.75	(0.59, 0.95)	0.02
Proxy for poor performance status [‡]	0.62	(0.46, 0.84)	< 0.01
Surgery of primary site	1.42	(1.27, 1.59)	< 0.01
Abbreviations: MAC= Medicare Administrative Contractor, CI=confidence interval			
‡Indicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis			

Table 44. Linear probability model coefficient estimates for receipt of chemotherapy and biologic therapy

	Linear Probability Model with Robust Standard Errors	
	Coefficient ^a	95% Confidence Interval
Receipt of NCCN-guideline chemotherapy (with or without biologic)		
θ_1 - Post Implementation (v. Pre)	0.035	(-0.05, 0.12)
θ_2 - New MAC (v. Legacy contractor became MAC)	-0.026	(-0.07, 0.02)
θ_3 - Interaction	-0.032	(-0.09, 0.08)
Receipt of NCCN-guideline biologic therapy (with or without chemotherapy)		
θ_1 - Post Implementation (v. Pre)	0.004	(-0.08, 0.09)
θ_2 - New MAC (v. Legacy contractor became MAC)	-0.051*	(-0.09, -0.004)
θ_3 - Interaction	-0.024	(-0.11, 0.06)

^a Interpreted as the impact on probability of receiving treatment
Statistical significance: *p < .05

Appendix 7. Inverse Probability of Treatment Weight Model

Table 45. Results of inverse probability of treatment weight logistic regression model

	Logistic Regression Model*		
	<i>Odds Ratio</i>	95% Confidence Interval	<i>p-value</i>
Socio-demographic Characteristics			
Age at time of diagnosis (<i>Continuous</i>)			
Per additional year of age	0.89	(0.88, 0.90)	<0.01
Race/ethnicity			
Non-Hispanic White		<i>Reference</i>	
African American	0.80	(0.63, 1.03)	0.08
Hispanic	1.07	(0.80, 1.43)	0.65
Asian and others	1.12	(0.83, 1.52)	0.64
Married (<i>vs. Unmarried</i>)	1.57	(1.35, 1.82)	<0.01
Female (<i>vs. Male</i>)	1.00	(0.86, 1.16)	0.97
Medicaid (<i>vs. no Medicaid</i>)	0.63	(0.52, 0.77)	<0.01
Clinical Characteristics			
Charlson comorbidity index (CCI)			
CCI=0		<i>Reference</i>	
CCI=1	1.05	(0.88, 1.25)	0.57
CCI≥2	0.71	(0.58, 0.87)	<0.01
CCI = Missing	0.51	(0.38, 0.70)	<0.01
Proxy for poor performance status present (<i>vs. absent</i>)	0.47	(0.36, 0.62)	<0.01
Surgery of primary site (<i>vs. no surgery of primary site</i>)	2.09	(1.81, 2.41)	<0.01
*Modeling probability of receiving any NCCN-guideline treatment – either chemotherapy or biologic therapy.			
†Indicates any hospital bed use, oxygen use, walking aid use, wheel chair use or home health claim within 3 months prior to cancer diagnosis			

Figure 8. Area under the receiver operating characteristic curve for inverse probability of treatment logistic regression model

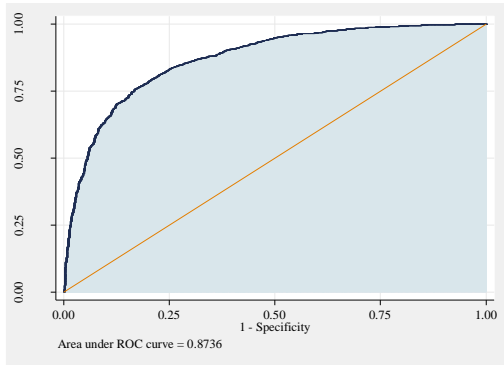


Figure 9. Probability distribution for receipt of NCCN-guideline treatment before application of normalized inverse probability of treatment weights

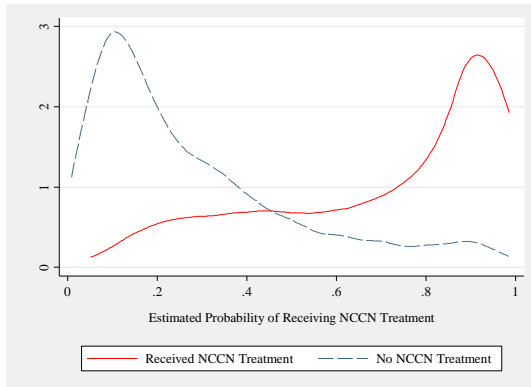
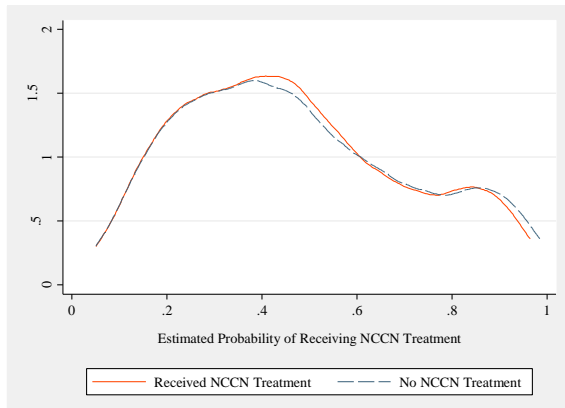


Figure 10. Probability distribution for receipt of NCCN-guideline treatment after application of normalized inverse probability of treatment weights



Appendix 8. Unadjusted Kaplan-Meier survival analyses

Figure 11. Kaplan-Meier survival curves comparing survival before and after contracting reform

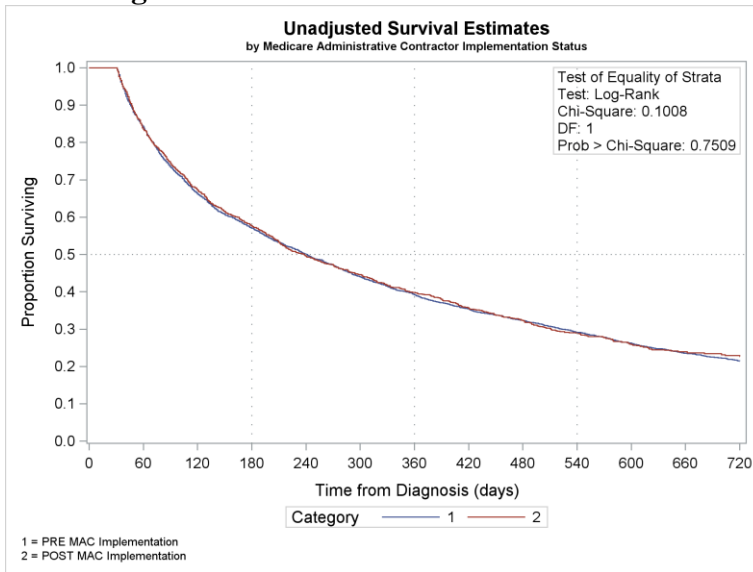
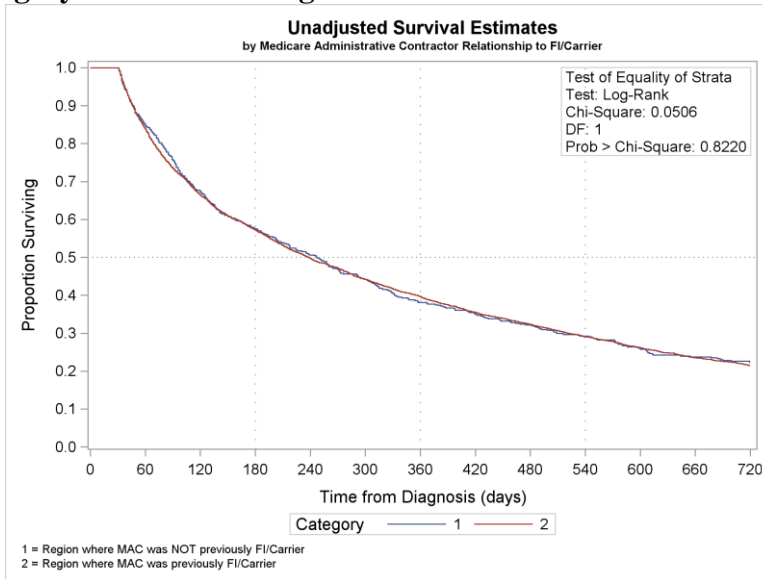


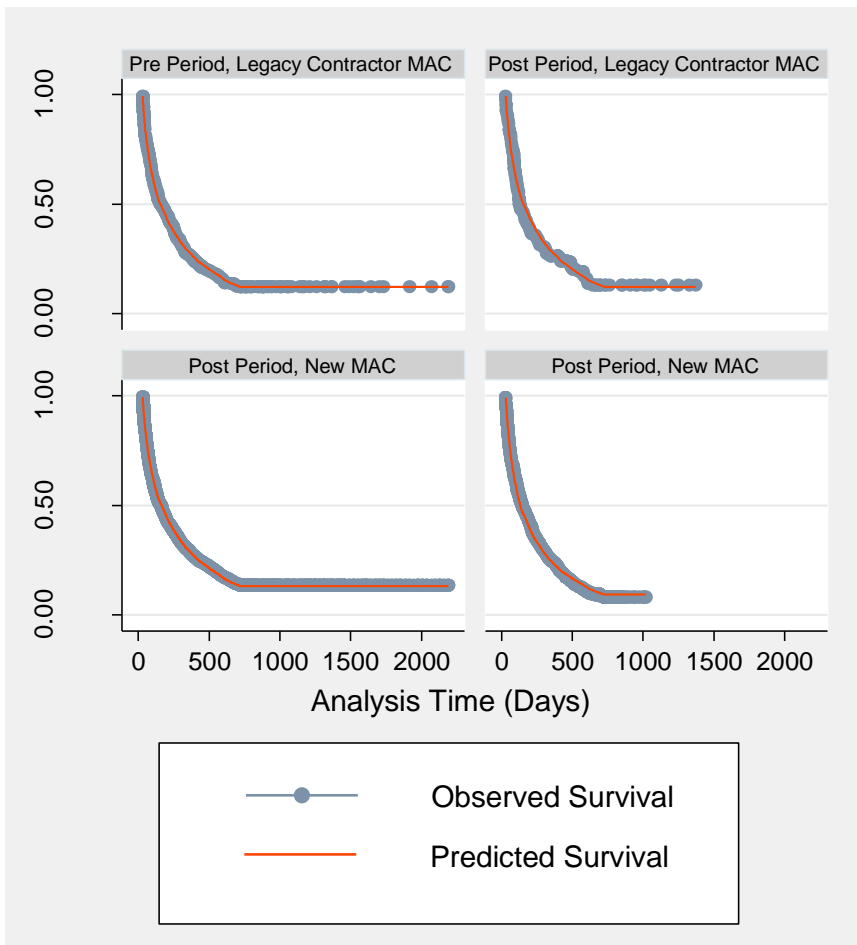
Figure 12. Kaplan-Meier survival curves comparing regions where MAC was a legacy contractor to regions where MAC was a new entity



Appendix 9. Diagnostics for Cox Proportional Hazards Model

We assessed the proportional hazards assumption in two ways. The initial test was performed by plotting the observed Kaplan-Meier estimates for all four combinations of timing (pre, post) and region (legacy contractor became MAC, legacy contractor was new entity) against the predicted estimates from the IPTW Cox proportional model. If the predicted and observed values are closely aligned, this indicates that the proportional hazard assumption has not been violated. Table 46 below indicates that for all groups, the observed and predicted values are consistent across all four groups.

Table 46. Plot comparing Kaplan-Meier and Cox Regression estimates



The second test of the proportional hazards-assumption was performed statistically at the covariate level using Schoenfeld residuals. The Schoenfeld residual (r_i) is calculated as shown in Equation 15 as the difference between the observed covariate and the expected value for every observed failure time:

Equation 15. Calculation of the Schoenfeld residual

$$r_i = Z_i(X_i) - \bar{Z}(X_i\hat{B})$$

Schoenfeld visuals are uncorrelated with an expected mean of zero. This test diagnostic test estimates a linear regression of the scaled Schoenfeld residuals against time. The null hypothesis is that the slope parameter estimated in this regression is equal to zero. Evidence that supports the rejection of this hypothesis indicates a violation of the proportional hazards assumption. As shown in Table 47 below, there is no evidence that either individual covariates or the overall model violate the proportional hazards assumption.

Table 47. Test of proportional hazards assumption with Schoenfeld residuals

Variable*	χ^2	DF	Pr > χ^2
Post Implementation	0.40	1	0.5275
New MAC	0.04	1	0.8427
Interaction	1.08	1	0.2982
Age 75-84	0.08	1	0.7729
Age \geq 85	1.18	1	0.2779
African American	0.01	1	0.9287
Hispanic	3.37	1	0.0963
Asian and others	0.09	1	0.7667
Married	0.37	1	0.5409
Female	0.02	1	0.8992
Dual-Eligibility with Medicaid	0.07	1	0.7962
CCI=1	0.54	1	0.4609
CCI=2	2.83	1	0.0925
CCI=3	0.00	1	0.9779
Proxy for poor performance status present	1.00	1	0.3163
Surgery of primary tumor site	0.27	1	0.6048
Global Test	18.21	16	0.3119

Abbreviations: MAC=Medicare Administrative Contractor, CCI=Charlson comorbidity index

Note: Reference categories shown in main model output and omitted from diagnostic table.

Appendix 10. Adjustment for inflation

Costs were adjusted to 2010 United States dollars, using the medical care component of the Consumer Price Index published by the United States Department of Labor Bureau of Labor Statistics.¹²⁵ Adjustments were made annually at the regional level (Northeast, Midwest, South, West) using archived annual average index tables.¹²⁶ Adjustments ranged in magnitude from 1.03 (2009: Midwest, West, South) to 1.21 (2005: West, South). Table 48 contains the medical care CPI values and calculated adjustment factors, by year and region used in the analysis.

Table 48. Inflation factors used to adjust costs to 2010 United States dollars

YEAR	Northeast		Midwest	
	Medical Care CPI	Adjustment Factor	Medical Care CPI	Adjustment Factor
2005	348.8	1.19	327.6	1.19
2006	361.2	1.14	340.8	1.15
2007	380.5	1.09	357.6	1.09
2008	390.3	1.06	365.7	1.07
2009	398.9	1.04	378.9	1.03
2010	413.5	-	390.6	-

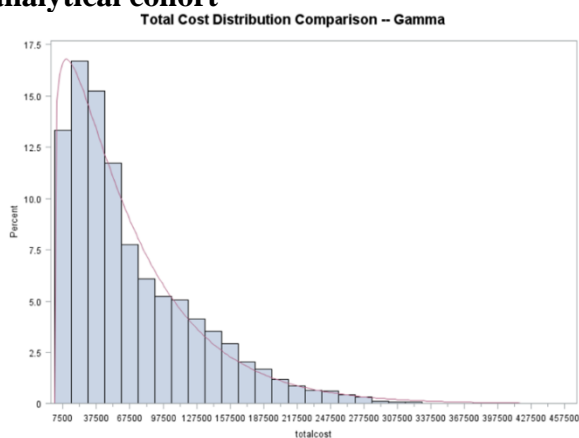
YEAR	West		South	
	Medical Care CPI	Adjustment Factor	Medical Care CPI	Adjustment Factor
2005	328.6	1.21	328.6	1.21
2006	340.9	1.17	340.9	1.17
2007	360.7	1.11	360.7	1.11
2008	371.6	1.07	371.6	1.07
2009	387.7	1.03	387.7	1.03
2010	399.2	-	399.2	-

Appendix 11. Cost Model Specification

Initial analysis of the overall cost distribution found that the Gamma distribution, while an approximate fit, was not statistically appropriate to model the underlying cost data. Using the Kolmogorov-Smirnov test, the p-value (< 0.001) on the test statistic (0.064) provided evidence supporting the alternate hypothesis that the overall cohort cost data for this dissertation does not follow a Gamma distribution. This lack of fit is visually apparent in the histogram of the full cohort cost data presented in Figure 13 below.

Stratifying the sample by lines of treatment received (detailed in Appendix 14), resulted in three Gamma distributions (shown in Figure 6 in the main text) that returned non-significant Kolmogorov-Smirnov test statistics: no chemotherapy or biologic therapy (0.026, $p > 0.25$); one line of therapy (0.02, $p = 0.223$); and two or more lines of therapy (0.027, $p = 0.13$). Non-significant p-values on the modified Park test, shown in Table 49 support the appropriateness of the Gamma distribution to model costs in this analysis.

Figure 13. Cost histogram for assessing fit of Gamma distribution in entire analytical cohort



Appendix 12. Cost Model Diagnostic Testing

Table 49. Results from model misspecification tests for generalized linear cost models examining the relationship between costs and Medicare contracting reform

Model 1: No NCCN-guideline chemotherapy or biologic therapy			
Goodness-of-link test (<i>p-values</i>)	Linear predictor	Squared linear predictor	Cubed linear predictor
Pregibon link test	0.02	0.25	0.52
Ramsey RESET ^a	-	0.76	0.58
Distributional Assumptions	Regression Coefficient	χ^2	<i>p-value</i>
Gamma	1.89	0.15	0.70
Poisson		8.98	0.003
Inverse Gaussian or Wald		14.15	<0.001
Model 2: One line of NCCN-guideline chemotherapy or biologic therapy			
Goodness-of-link test (<i>p-values</i>)	Linear predictor	Squared linear predictor	Cubed linear predictor
Pregibon link test	0.06	0.89	0.78
Ramsey RESET	-	0.87	0.53
Distributional Assumptions	Regression Coefficient	χ^2	<i>p-value</i>
Gamma	1.94	0.03	0.87
Poisson		9.77	0.002
Inverse Gaussian or Wald		11.97	<0.001
Model 3: Two or more lines of NCCN-guideline chemotherapy or biologic therapy			
Goodness-of-link test (<i>p-values</i>)	Linear predictor	Squared linear predictor	Cubed linear predictor
Pregibon link test	0.05	0.14	0.22
Ramsey RESET	-	0.19	0.27
Distributional Assumptions	Regression Coefficient	χ^2	<i>p-value</i>
Gamma	1.87	0.22	0.64
Poisson		11.01	<0.001
Inverse Gaussian or Wald		18.12	<0.001
^a Regression Equation Specification Error Test			

Appendix 13. Alternate Approaches to Adjust for Censored Costs

Table 50. Comparison of alternate approaches to adjust for censored costs

	Unadjusted Models		Adjusted Models	
	Uncensored Cases	Full Sample	Uncensored Case IPW (Lin's Method) ^a	Full Sample IPW
No NCCN-Guideline Chemotherapy or Biologic Therapy	<i>n</i> =1,894	<i>n</i> =2,053	<i>n</i> =1,894	<i>n</i> =2,053
Intercept	\$32,858	\$33,193	\$33,091	\$33,350
Post Implementation (v. Pre)	0.98	0.96	0.91	0.91
New MAC (v. Legacy became MAC)	1.31*	1.30*	1.28*	1.27*
Interaction [†]	1.06	1.07	1.11	1.12
One Line of NCCN-Guideline Chemotherapy or Biologic Therapy	<i>n</i> =765	<i>n</i> =1,139	<i>n</i> =765	<i>n</i> =1,139
Intercept	\$71,196	\$79,178	\$70,355	\$77,322
Post Implementation (v. Pre)	0.89	0.98	0.88	1.01
New MAC (v. FI/Carrier became MAC)	1.24*	1.22*	1.21*	1.21*
Interaction [†]	1.03	1.00	1.03	0.94
Two or More Lines of NCCN-Guideline Chemotherapy or Biologic Therapy	<i>n</i> =402	<i>n</i> =838	<i>n</i> =402	<i>n</i> =838
Intercept	\$145,694	\$141,183	\$142,867	\$133,577
Post Implementation (v. Pre)	0.80	1.03	0.74	0.98
New MAC (v. FI/Carrier became MAC)	1.23*	1.27*	1.24*	1.30*
Interaction [†]	1.01	0.79	1.09	0.83

Abbreviations: MAC=Medicare Administrative Contractor, NCCN= National Comprehensive Cancer Network

^a Adjusted for censoring using Lin's regression method with one interval. Completed cases weighted by the inverse probability of not being censored at the end of the study period.

[†] Statistical significance determined with joint F-test

*Indicates statistical significance at the 0.05 level

Appendix 14. Sensitivity analyses varying pre-implementation period

Aim 1: Treatment Receipt

Table 51. Multivariate correlations between receipt of NCCN-guideline chemotherapy (with or without biologic therapy) and difference-in-differences estimators under three assumptions defining the end of the pre-implementation period

Variable (<i>Comparison Group</i>)	Logistic Regression Model	
	Odds Ratio	95% Confidence Interval
(A) Base Case -- Pre period defined by award date (n=4,030)		
θ_1 - Post-Implementation (<i>Pre-Implementation</i>)	1.18	(0.79, 1.78)
θ_2 - Region with new MAC (<i>Legacy contractor became MAC</i>)	0.87	(0.69, 1.11)
θ_3 - Interaction	1.00	(0.65, 1.56)
(B) Pre period defined by award date minus 6 months (n=3,534)		
θ_1 - Post Implementation (vs. Pre)	1.12	(0.99, 1.27)
θ_2 - New MAC (vs. Legacy contractor became MAC)	0.98	(0.87, 1.11)
θ_3 - Interaction	0.97	(0.84, 1.11)
(C) Pre period defined by Request for Proposal (RFP) issue (n=3,307)		
θ_1 - Post Implementation (vs. Pre)	1.11	(0.91, 1.36)
θ_2 - New MAC (vs. Legacy contractor became MAC)	0.97	(0.85, 1.10)
θ_3 - Interaction	0.98	(0.79, 1.20)
Abbreviations: MAC=Medicare Administrative Contractor		
Statistical significance: *p < .05		

Table 52. Multivariate correlations between receipt of NCCN-guideline biologic therapy (with or without chemotherapy) and difference-in-differences estimators under three assumptions defining the end of the pre-implementation period

Variable (<i>Comparison Group</i>)	Logistic Regression Model	
	Odds Ratio	95% Confidence Interval
(A) Base Case -- Pre period defined by award date (n=4,030)		
θ_1 - Post-Implementation (<i>Pre-Implementation</i>)	1.01	(0.67, 1.51)
θ_2 - Region with new MAC (<i>Legacy contractor became MAC</i>)	0.76*	(0.59, 0.97)
θ_3 - Interaction	0.90 ^a	(0.57, 1.39)
(B) Pre period defined by award date minus 6 months (n=3,534)		
θ_1 - Post Implementation (vs. Pre)	1.02	(0.80, 1.30)
θ_2 - New MAC (vs. Legacy contractor became MAC)	0.87	(0.74, 1.01)
θ_3 - Interaction	0.92	(0.71, 1.21)
(C) Pre period defined by Request for Proposal (RFP) issue (n=3,307)		
θ_1 - Post Implementation (vs. Pre)	0.95	(0.73, 1.24)
θ_2 - New MAC (vs. Legacy contractor became MAC)	0.81*	(0.67, 0.97)
θ_3 - Interaction	0.99	(0.75, 1.32)
Abbreviations: MAC=Medicare Administrative Contractor		
Statistical significance: *p < .05		

Aim 2: Survival

Table 53. Sensitivity analysis results from inverse probability of treatment weighted Cox Proportional Hazards model

	IPTW Cox Model for Mortality	
	Hazard Ratio	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=4,030)</i>		
Post Implementation (v. Pre)	0.94	(0.79, 1.17)
New MAC (v. FI/Carrier became MAC)	0.96	(0.84, 1.06)
Interaction	1.14	(0.92, 1.41)
<i>Pre period defined by award date minus 6 months (n=3,534)</i>		
Post Implementation (v. Pre)	1.05	(0.83, 1.21)
New MAC (v. FI/Carrier became MAC)	0.90	(0.80, 1.01)
Interaction	0.96	(0.78, 1.17)
<i>Pre period defined by Request for Proposal (RFP) issue (n=3,307)</i>		
Post Implementation (v. Pre)	0.99	(0.81, 1.22)
New MAC (v. FI/Carrier became MAC)	0.90	(0.78, 1.04)
Interaction	0.96	(0.77, 1.19)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary, IPTW=Inverse Probability of Treatment Weight		
Statistical significance: *p< .05		

Aim 3: Total Costs

Table 54. Sensitivity analysis of cost estimates from Lin's Regression model for patients not receiving treatment

	Simplified Lin's Regression Model for Costs	
	Exponentiated Coefficient	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=6790)</i>		
Post Implementation (v. Pre)	0.91	(0.77, 1.07)
New MAC (v. FI/Carrier became MAC)	1.27*	(1.13, 1.44)
Interaction	1.12	(0.93, 1.35)
<i>Pre period defined by award date minus 6 months (n=1803)</i>		
Post Implementation (v. Pre)	0.90	(0.75, 1.07)
New MAC (v. FI/Carrier became MAC)	1.26*	(1.09, 1.45)
Interaction	1.13	(0.92, 1.38)
<i>Pre period defined by RFP issue (n=1690)</i>		
Post Implementation (v. Pre)	0.95	(0.78, 1.15)
New MAC (v. FI/Carrier became MAC)	1.35*	(1.15, 1.58)
Interaction	1.06	(0.86, 1.31)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary		
Statistical significance: *p< .05		

Table 55. Sensitivity analysis of cost estimates from Lin's Regression model for patients receiving one line of chemotherapy, with or without biologic therapy

	Simplified Lin's Regression Model for Costs	
	Exponentiated Coefficient	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=6790)</i>		
Post Implementation (v. Pre)	1.02	(0.81, 1.27)
New MAC (v. FI/Carrier became MAC)	1.25*	(1.10, 1.42)
Interaction	0.94	(0.74, 1.20)
<i>Pre period defined by award date minus 6 months (n=1002)</i>		
Post Implementation (v. Pre)	0.96	(0.74, 1.24)
New MAC (v. FI/Carrier became MAC)	1.14	(0.96, 1.36)
Interaction	0.99	(0.75, 1.31)
<i>Pre period defined by RFP issue (n=929)</i>		
Post Implementation (v. Pre)	0.90	(0.68, 1.19)
New MAC (v. FI/Carrier became MAC)	1.08	(0.89, 1.31)
Interaction	1.05	(0.78, 1.41)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary		
Statistical significance: *p< .05		

Table 56. Sensitivity analysis of cost estimates from Lin's Regression model for patients receiving two or more lines of chemotherapy, with or without biologic therapy

	Simplified Lin's Regression Model for Costs	
	Exponentiated Coefficient	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=6790)</i>		
Post Implementation (v. Pre)	0.97	(0.81, 1.15)
New MAC (v. FI/Carrier became MAC)	1.30*	(1.20, 1.42)
Interaction	0.87	(0.72, 1.05)
<i>Pre period defined by award date minus 6 months (n=729)</i>		
Post Implementation (v. Pre)	0.98	(0.81, 1.18)
New MAC (v. FI/Carrier became MAC)	1.31*	(1.18, 1.45)
Interaction	0.82	(0.67, 1.01)
<i>Pre period defined by RFP issue (n=688)</i>		
Post Implementation (v. Pre)	1.00	(0.82, 1.23)
New MAC (v. FI/Carrier became MAC)	1.35*	(1.20, 1.52)
Interaction	0.85	(0.69, 1.01)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary		
Statistical significance: *p< .05		

Appendix 15. Results of Restricting Sample to Diagnosis Post-Part D

Table 57. Impact of Medicare contracting reform on total costs for patients diagnosed after 2006 receiving no NCCN-guideline therapy

	Simplified Lin's Regression Model for Costs	
	Exponentiated Coefficient	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=1559)</i>		
Post Implementation (v. Pre)	0.90	(0.75, 1.08)
New MAC (v. FI/Carrier became MAC)	1.30*	(1.12, 1.51)
Interaction	1.10	(0.89, 1.35)
<i>Pre period defined by award date minus 6 months (n=1309)</i>		
Post Implementation (v. Pre)	0.89	(0.72, 1.10)
New MAC (v. FI/Carrier became MAC)	1.29*	(1.07, 1.56)
Interaction	1.10	(0.87, 1.39)
<i>Pre period defined by RFP issue (n=1200)</i>		
Post Implementation (v. Pre)	0.94	(0.72, 1.22)
New MAC (v. FI/Carrier became MAC)	1.41*	(1.10, 1.80)
Interaction	1.02	(0.77, 1.35)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary		
Statistical significance: *p< .05		

Table 58. Impact of Medicare contracting reform on total costs for patients diagnosed after 2006 receiving one line of NCCN-guideline therapy

	Simplified Lin's Regression Model for Costs	
	Exponentiated Coefficient	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=870)</i>		
Post Implementation (v. Pre)	0.97	(0.76, 1.25)
New MAC (v. FI/Carrier became MAC)	1.20*	(1.03, 1.40)
Interaction	0.95	(0.72, 1.24)
<i>Pre period defined by award date minus 6 months (n=733)</i>		
Post Implementation (v. Pre)	0.88	(0.67, 1.17)
New MAC (v. FI/Carrier became MAC)	1.09	(0.89, 1.33)
Interaction	1.04	(0.77, 1.40)
<i>Pre period defined by RFP issue (n=660)</i>		
Post Implementation (v. Pre)	0.74	(0.55, 1.01)
New MAC (v. FI/Carrier became MAC)	0.93	(0.74, 1.16)
Interaction	1.23	(0.89, 1.70)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary		
Statistical significance: *p< .05		

Table 59. Impact of Medicare contracting reform on total costs for patients diagnosed after 2006 receiving two or more lines of NCCN-guideline therapy

	Simplified Lin's Regression Model for Costs	
	Exponentiated Coefficient	95% Confidence Interval
<i>Base Case -- Pre period defined by award date (n=605)</i>		
Post Implementation (v. Pre)	0.99	(0.82, 1.20)
New MAC (v. FI/Carrier became MAC)	1.31*	(1.18, 1.46)
Interaction	0.83	(0.68, 1.01)
<i>Pre period defined by award date minus 6 months (n=496)</i>		
Post Implementation (v. Pre)	0.98	(0.80, 1.21)
New MAC (v. FI/Carrier became MAC)	1.33*	(1.17, 1.50)
Interaction	0.81	(0.65, 1.01)
<i>Pre period defined by RFP issue (n=455)</i>		
Post Implementation (v. Pre)	1.05	(0.83, 1.32)
New MAC (v. FI/Carrier became MAC)	1.42*	(1.20, 1.68)
Interaction	0.77	(0.55, 1.03)
Abbreviations: MAC=Medicare Administrative Contractor, FI=Fiscal Intermediary, RFP=Request for Proposal		
Statistical significance: *p< .05		

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