# DECLINING OVERUSE OF HORMONE THERAPY FOR LOCALIZED PROSTATE CANCER: PREDICTORS OF REIMBURSEMENT RESPONSIVENESS AND EMERGING PATTERNS OF CARE

**Shellie Dawn Ellis**

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Health Policy and Management in the Gillings School of Global Public Health.

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Approved by:

William R. Carpenter

George L. Jackson

Matthew Nielsen

Morris Weinberger

Stephanie Wheeler

## ABSTRACT

Shellie Dawn Ellis: Declining Overuse of Hormone Therapy for Localized Prostate Cancer: Predictors of Reimbursement Responsiveness and Emerging Patterns of Care
(Under the direction of William R. Carpenter)

This research examines the effects of reimbursement policy as a strategy to improve quality of care. We estimated the degree to which physician characteristics are associated with declining androgen deprivation therapy (ADT) overuse; identified the effect of reimbursement changes on ADT overuse; and, evaluated the impact of changing patterns of ADT overuse on quality of care in localized prostate cancer.

We used SEER-linked Medicare claims and American Medical Association data to create three distinct longitudinal cohorts of individuals diagnosed with incident prostate cancer in the 2000s and their physicians. Multilevel logistic regression modeling controlled for patient and physician characteristics associated with overuse of medical care and prostate cancer treatment selection, and clustering of patients within physicians.

In the first study, time in practice was not associated with ADT overuse, but three patterns of ADT overuse were observed. We could not distinguish urologists who increased ADT overuse from those who decreased ADT overuse after MMA based on physician characteristics. Our findings suggest that: 1) new types of interventions will be needed to address persistent overuse; 2) guidelines should underscore treatment strategies for vulnerable patients; and 3) economic theory may need to consider clinic explanations for the volume response.

The second study suggests that, among urologists treating early-stage and lower grade prostate cancer, variation in reimbursement was not associated with overuse of ADT during a period of guideline stability. There was a small but significant negative association between ADT

overuse and excess reimbursement relative to all treatments: urologists in favorable reimbursement climates had lower odds of ADT overuse. Multi-specialty group practice type was associated with lower odds of ADT overuse. Reimbursement cuts may not be effective strategy to reduce overuse in all clinical scenarios.

Finally, physicians' pre-MMA ADT overuse was negatively associated with delivering guideline-concordant care post-MMA. High users of ADT pre-MMA were also more likely to overuse ADT and provide guideline–discordant care post-MMA. Reducing reimbursement for inappropriate therapy will not necessarily improve quality of care. Physicians unable to provide guideline-concordant care may need additional resources to align with guidelines or to adopt guideline-concordant technologies.

To my beautiful, intelligent, and gifted daughters, Sylvie and Stella.
Thank you for inspiring me to be nothing less than the accomplished role model you deserve.

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**TABLE OF CONTENTS**

## LIST OF TABLES

## LIST OF FIGURES

## LIST OF ABBREVIATIONS

| | |
|---|---|
| ACA | Patient Protection and Affordable Care Act |
| ADT | Androgen Deprivation Therapy |
| AMA | American Medical Association |
| AS | Active Surveillance |
| ASCO | American Society of Clinical Oncology |
| ASTRO | American Society of Therapeutic Radiation and Oncology |
| CMS | Centers for Medicare and Medicaid Services |
| CPT | Current Procedure Terminology |
| CRT | Conventional Radiation Therapy |
| GnRH | Gonadotropin-Releasing Hormone |
| HCPCS | Healthcare Common Procedure Code System |
| ICC | Intra-class Correlation |
| ICISS | Integrated Cancer Information and Surveillance System |
| ICD-9 | International Classification of Disease, 9$^{th}$ edition |
| IMRT | Intensity Modulated Radiation Therapy |
| MIRP | Minimally Invasive Radical Prostatectomy |
| MMA | Medicare Modernization Act of 2003 |
| NCCN | National Comprehensive Cancer Network |
| NCI | National Cancer Institute |
| RP | Radical Prostatectomy |
| RT | Radiation Therapy |
| PSA | Prostate Specific Antigen |
| RGI | Reimbursement Generosity Index |
| SEER | Surveillance, Epidemiology, and End Results |

# CHAPTER 1 INTRODUCTION

The federally mandated *National Quality Strategy* has designated the overuse of health care as a national priority. Currently 30%–40% of health care spending in the U.S. is for the provision of unnecessary care. Such overuse results in patient harms, health disparities, and waste in a healthcare system already stretched to capacity. Overuse is of particular concern within the context of cancer care. Emerging evidence in cancer screening, control, and treatment increasingly results in situations in which providers and patients must alter their behavior to *abandon* established practices. Although strategies to address overuse in cancer care are becoming increasingly relevant, little research exists to guide the development of interventions to address overuse. New studies are needed to enable intervention development and understand the impact of such strategies.

The overuse of androgen deprivation therapy (ADT) in the treatment of localized prostate cancer provides a model for understanding strategies to address healthcare overuse. ADT overuse is a harmful, costly, and persistent problem in prostate cancer treatment: 25.7% of men for whom it is not recommended still received it in 2005. Reimbursement cuts mandated by the Medicare Modernization Act (MMA) were associated with a 34% decline in ADT overuse; however, physician and practice characteristics that facilitated reimbursement responsiveness; the direct role of reimbursement in changing patterns of care; and the full impact on changing patterns of care on quality of care are not known. Nonetheless, sharp declines in overuse provide an opportunity to study the factors and consequences associated with declining overuse.

The objective of this dissertation was to 1) describe changes in physician-level ADT overuse associated with the MMA and identify physician characteristics associated with persistent ADT overuse; 2) explore the extent to which physicians may have been responsive to differences in reimbursement, rather than other trends in evidence, guidelines, and practice

change occurring coincident with MMA; and, 3) assess the impact of changes in ADT overuse on contemporary quality of care.

We matched American Medical Association physician and practice data to SEER–linked Medicare data for all three studies. We used distinct samples of men with clinically localized, incident adenocarcinoma of the prostate. Each sample was drawn from a time period appropriate to the research question. The aim 1 sample included 12,943 men diagnosed with early-stage and lower grade localized adenocarcinoma of the prostate between 2000 and 2007, and treated by 2,138 urologists through 2008, so that we could study change over the MMA implementation. Our second sample included the 2,213 urologists of 16,790 men diagnosed with early-stage and lower grade localized prostate cancer between January 1, 2000 and December 31, 2003 to exploit unintentional variation in ADT reimbursement that ended in late 2002. The third sample included 27,315 men diagnosed with incident low-, intermediate-, or high-risk localized prostate cancer between 2005 and 2007, treated by 4,104 physicians of all specialties, selected so we could study care delivered post-MMA implementation. Each study used a retrospective, longitudinal observational design; however, the second study also took advantage of a natural experiment, allowing for difference-in-difference design features. Statistical analysis consisted of descriptive analysis and multilevel mixed effects logistic regression models, which adjusted standard errors for clustering of patients within physicians and repeated physician measures over time and controlled for tumor, patient, provider, and practice characteristics known to be associated with ADT use or reimbursement responsiveness.

This research advances previous work studying the effect of MMA on ADT overuse. We followed patients for 2 years longer than previous studies to further understand the trends surrounding MMA. In addition, we explored physician-level changes in ADT use, rather than aggregated changes, to identify distinct patterns of response over the MMA period. Furthermore, our study is the first to assess physician-level factors and practice-level organizational characteristics associated with responsiveness to MMA. In Aim 2 we used

difference-in-difference study design features to better identify the role of reimbursement in ADT overuse. Where previous study designs had allowed only observation of associations between reimbursement change and ADT overuse, our study exploited reimbursement variation between and within physicians to better assess the effect of reimbursement change. Finally, our study is the first to assess the effects of pre-MMA ADT overuse on the global quality of care in a post-MMA population.

Our original hypotheses were that:

*Hypothesis 1A*: Urologists with greater time in practice would be less responsive to reimbursement changes;

*Hypothesis 1B*: Urologists would respond to reimbursement changes uniformly;

*Hypothesis 2A*: More generous reimbursement would be associated with greater overuse of ADT;

*Hypothesis 2B*: Single specialty urology practices would be more likely to persistently overuse ADT than multi-specialty groups;

*Hypothesis 3A*: High levels of pre-MMA primary ADT use would be associated with guideline-concordant care in the post-MMA period;

*Hypothesis 3B*: Patient race would be associated with greater odds of receipt of guideline-concordant care in the post-MMA period; and,

Hypothesis 3C: Pre-MMA ADT overuse would be negatively associated with uptake of new treatment modalities.

This work is relevant to current healthcare policy. Recent health policy legislation seeks to cut costs within Medicare while simultaneously improving healthcare quality. Several experimental innovations are proposed, but fee-for-service remains the payment mechanism for the majority of the Medicare population. The Patient Protection and Affordable Care Act (ACA) will limit increases in payment to physicians across the board. Better understanding of the nuances of how changes in the Medicare payment structure might work across a variety of health conditions, each with their own set of treatment alternatives, treating physician conventions, and practice milieu can better inform the policy debate with regard to how best to transform a system on which patients, physicians, and a large healthcare industry rely.

Sections of the dissertation are organized as follows. Chapter 2 describes the complexities of prostate cancer and discusses current literature regarding prostate cancer treatments, quality of care, and recent reimbursement policy affecting prostate cancer treatment. It further discusses alternative explanations for the declining use of ADT and factors associated with ADT overuse and reimbursement responsiveness. Chapter 3 provides an overview of the methods used throughout the dissertation. It includes the underlying conceptual model on which the work is based, a discussion of study design and rationale, data sources, hypotheses, and analytical approaches. Chapters 4–6 are manuscripts corresponding to Aims 1–3, respectively, and are intended for submission for peer-reviewed publication. Chapter 7 summarizes the findings of this dissertation, its policy relevance, and research gaps identified. References are provided in a comprehensive bibliography at the conclusion of the dissertation.

# CHAPTER 2 LITERATURE REVIEW

## The Burden of Prostate Cancer

Prostate cancer is the second most common cancer diagnosis in men. It is diagnosed in an estimated 217,730 men in the United States annually (1). Although common, relatively few men die from the disease. Between 2003 and 2007, an estimated 32,050 men died of prostate cancer each year (1). Although 4% of prostate cancers are detected after they have metastasized, a stage in which 5-year survival is only 30.2% (1), most men are diagnosed with localized and regional disease, for which the survival rate is nearly 100% (1). In the recent era of widespread prostate specific antigen (PSA) screening, 94% of men diagnosed with prostate cancer have clinically localized disease (2) in which the cancer is confined within the prostate gland. In some areas of the country, even greater numbers of men are diagnosed in this early stage. For example, in a North Carolina cohort of men diagnosed between 2004 and 2007, 97% of men had localized disease (3). Several factors contribute to its favorable prognosis: 1) most disease is diagnosed in the earliest, most curable stages; 2) it is primarily an indolent cancer; and 3) median age of diagnosis is 67 years (1, 4). Thus, most men diagnosed with prostate cancer die from other causes.

However, the favorable prognosis is not distributed equally among the population in the United States. Significant disparities in prostate cancer incidence and outcome in the United States are apparent. Age-adjusted incidence is higher among African-American men—150.4 per 100,000 white men versus 234.6 per 100,000 black men (1). In addition, African-American men are often diagnosed at an earlier age than white men and have a higher prevalence of high grade neoplasia, suggesting that they present with a more aggressive type of cancer (5). Death rates are

also significantly higher among African-American men—22.8 per 100,000 white men versus 54.2 per 100,000 black men (1)—and are particularly high in the South (6).

For the substantial number of men who live with prostate cancer, its costs are high. Compared to men without prostate cancer, those diagnosed with it can experience declines in physical health and emotional health, and social function (7). Many suffer increased incontinence and major depressive disorder, with some of these effects lasting more than a year after diagnosis and treatment (7). With early screening, men live many years with the knowledge of having a cancer, albeit a slow-growing one. Coupled with the ambiguity of appropriate treatment, this may lead to high psychological costs, although little research addresses this aspect of the disease.

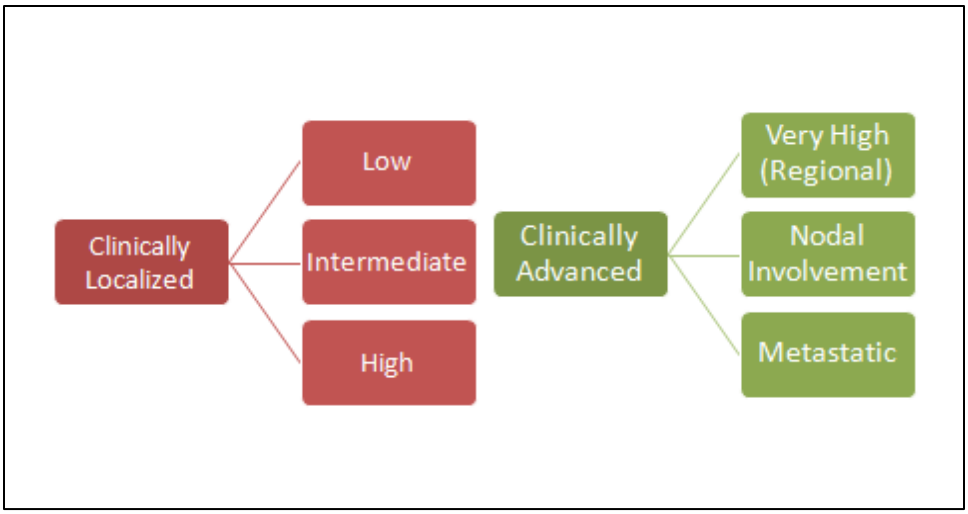
Although the full burden of patient suffering is unknown, the financial costs to patients and society are high and continue to grow. Accumulated costs of treatment 5.5 years after diagnosis range from $32,135 to $69,244, depending on the treatment selected (8). In 1994, Medicare expenditures alone for the treatment of prostate cancer was $1.4 billion (8). By 2006, total prostate treatment costs had grown to $9.9 billion, (4) and by 2010 the treatment of the 2.3 million prostate cancer survivors in the United States was estimated to be $11.9 billion (9). Costs are expected to grow 42% by 2020 for the care of an estimated 3.1 prostate cancer patients, giving prostate cancer the distinction of having the highest rate of increasing medical care costs among several prevalent cancers (9). A significant part of the costs of prostate cancer treatment is that spent on androgen deprivation therapy (ADT). Of the total prostate treatment costs paid by Medicare in 1994, $4.8 million was for androgen suppression therapy using luteinizing hormone-releasing hormone agonists, the treatment with the highest accumulated treatment cost (8). By the early 2000s, ADT use was responsible for almost $1 billion of annual Medicare spending (10). Thus, understanding how prostate cancer treatment, especially ADT, is selected and how treatment selection affects quality of care are crucial to improving the value of healthcare.

## The Treatment of Prostate Cancer

### *Risk Stratification and Classification*

Prostate cancer is an indolent disease with a long natural history, but the specific course of the disease depends on the stage of diagnosis. Prognosis for cancers confined to the prostate gland (*localized disease*) is better than that of cancers that have spread outside the gland (*regional disease*), and much better than that of cancers that have metastasized to the lymph nodes or to other organs (*metastatic disease*). Thus, each of these types of disease has distinct treatment goals. Since 1986 and the advent of widespread PSA screening, the majority of men have been diagnosed with localized disease, and even finer gradations of disease prognosis have been made. Figure 2.1 shows the six mutually exclusive prostate cancer recurrence risk categories generally used. Those highlighted in red are the focus of this dissertation.

**Figure 2.1. Prostate Cancer Recurrence Risk Categories**

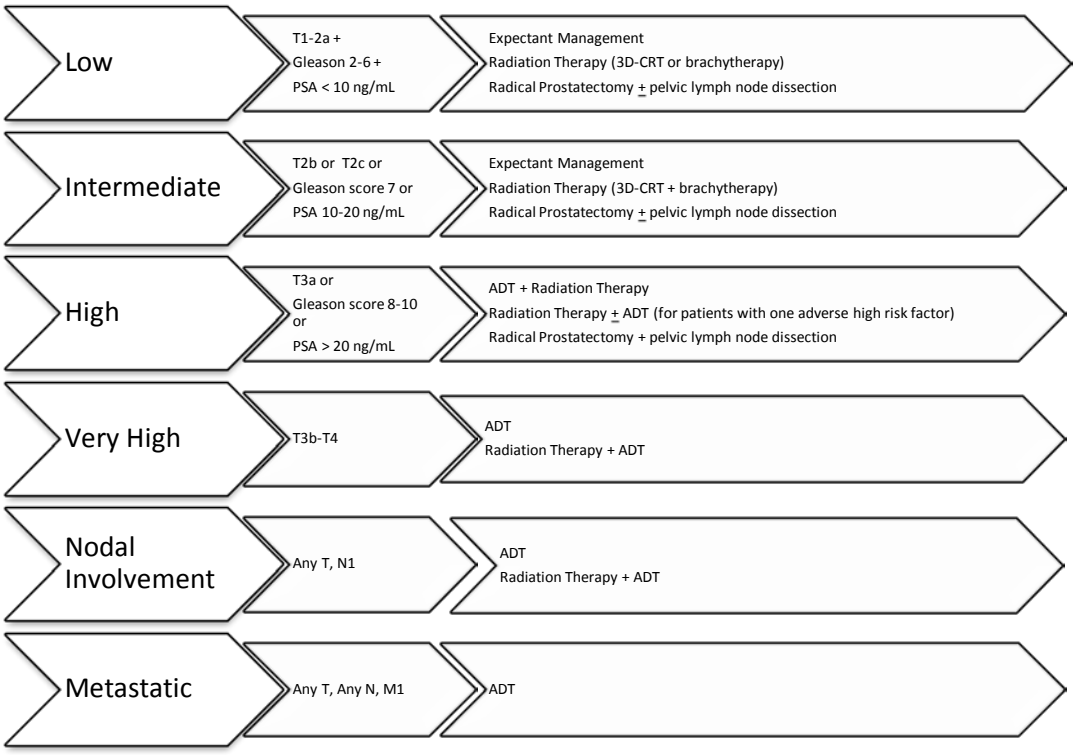



In contemporary prostate cancer, 94% of men have clinically localized disease, and less than 30% of these men have disease that is considered at high risk for progression, requiring definitive therapy. Aims 1 and 2 of this study focus on the other 70% of men, whose risk for

recurrence is not considered high; and Aim 3 studies all recurrence risk groups of localized disease.

Since the late 1990s, the prostate cancer recurrence risk for localized disease has been formally calculated and codified as the D'Amico risk classification. Based on clinical stage, grade, and PSA at diagnosis, the combination of risk factors has been shown to predict early PSA failure, a sign of disease progression (11). Figure 2.2 shows the six recurrence risk categories, their qualifying risk factors, and the treatments recommended by the National Comprehensive Cancer Network (NCCN) since 2004 (12).

**Figure 2.2. Prostate Cancer Treatment Algorithm**




### *Quality of Care in Prostate Cancer*

Although few national prostate cancer quality measures exist (13), as recurrence risk classifications, and subsequently, evidence of treatment effectiveness based on these risk stratifications has evolved, quality of care standards have emerged. Several professional

societies and RAND Corporation investigators have developed quality of care guidelines. Investigators at RAND sought to develop quality of care indicators for prostate cancer focusing on structural features and processes of care delivery but without specifying appropriate treatment (14, 15). The American Urological Association (AUA), American Society of Clinical Oncology (ASCO), and American Society for Therapeutic Radiology and Oncology (ASTRO) have developed consensus- or evidence-based guidelines, but most apply to narrow therapeutic indications (16, 17). The only evidence-based comprehensive treatment guideline for all prostate cancer stages and recurrence risk categories are those developed by the NCCN. Widely accepted as the standard for prostate cancer treatment (3, 18), NCCN guidelines are available for prostate cancer screening, staging, initial treatment, and salvage therapy.

Initial treatment guidelines, the focus of this dissertation, are based on the patient's life expectancy and recurrence risk categories (12, 19). Together these criteria are used to differentiate appropriate from inappropriate treatment options. NCCN guidelines for prostate cancer treatment are complex. Mainly because of the typical indolence of prostate cancer, no current course of treatment for early-stage disease provides any incremental benefit (19), and current guidelines for treating early-stage disease provide multiple options.

Because of rapidly emerging treatment evidence, NCCN guidelines have been updated frequently, in 2000, 2004, 2008, and 2010 (12, 20-22). Table 2.1 describes key differences in treatment that resulted from guideline changes during the period that is the focus of this research. Absent from Table 2.1 is the full description of the impact of treatment recommendations on life expectancy on treatment recommendation. Patients who have long life expectancies at the time of diagnosis are recommended for definitive treatment, rather than observation. One notable change during the period is that prior to 2004, primary ADT was recommended for high-risk patients expected to survive less than 5 years. Further, in 2004, guidelines changed in response to new evidence for the benefit of ADT adjuvant to radiation therapy for men with stage T3a cancers, higher grade tumors, or PSA >20 ng/mL.

**Table 2.1. NCCN Treatment Guidelines by Recurrence Risk Category and Year**

| Recurrence Risk Category | Risk Classification Criteria | 2000–2003 NCCN Treatment Options | 2004–2007 NCCN Treatment Options |
|---|---|---|---|
| Low | T1-2a +<br>Gleason 2-6 +<br>PSA <10 ng/mL | Expectant Management<br>Radiation Therapy (EBRT or brachytherapy)<br>Radical Prostatectomy | Expectant Management<br>Radiation Therapy (3D-CRT or brachytherapy)<br>Radical Prostatectomy |
| Intermediate | T2b or T2c* or<br>Gleason score 7 or<br>PSA 10–20 ng/mL | Expectant Management<br>Radiation therapy (EBRT)<br><br>Radical Prostatectomy | Expectant Management<br>Radiation Therapy (3D-CRT + brachytherapy)<br>Radical Prostatectomy |
| High | T3a or<br>Gleason score 8–10 or<br>PSA >20 ng/mL | ADT + Radiation Therapy<br>Radiation Therapy Alone<br>Radical Prostatectomy<br>Primary ADT if <5 yr life expectancy<br>Observe if <5 yr life expectancy | ADT + Radiation Therapy<br>Radiation Therapy + ADT<br>Radical Prostatectomy + pelvic lymph node dissection |

*T2c added in 2004

***Treatment***

Three guideline-recommended treatment options are available in localized prostate cancer: surgery, radiation, and active surveillance (Figure 2.2, above). However, the appropriateness of each of these treatments depends on the patient's prostate cancer recurrence risk and life expectancy (11). Surgery and radiation are recommended alternatives for all risk levels, but following men with active surveillance is a treatment option only for some men in certain circumstances. Men with low-risk disease who are treated by active surveillance, radiation therapy, or surgery are shown to have similar mortality (4). Thus, all three therapies are valid treatment options for the low-risk group, and active surveillance is thought to be underused (4, 12).

*Active surveillance* sometimes is used interchangeably with *expectant management* and *watchful waiting*. All are therapeutic options that avoid definitive treatment, but they have distinct meanings, although the definitions have been fluid over time (4). The main distinction is that watchful waiting generally represents an approach in which the patient is not actively

followed but waits for symptoms to develop before treatment is considered, whereas active surveillance represents regular monitoring for changes in biopsy results, PSA levels, or tumor growth. Under NCCN definitions, active surveillance includes PSA testing and/or digital rectal exams and repeated biopsies at regular intervals to monitor disease progression. For men with an intermediate risk of recurrence, active surveillance is a recommended option only for those with less than 10 years of remaining life expectancy. For men with a high risk of recurrence, initial treatment with active surveillance in lieu of definitive treatment is not recommended, regardless of remaining life expectancy (12).

A fourth treatment, ADT, has been the primary treatment for metastatic prostate cancer since the 1940s (23), originally as surgical castration and increasingly, almost exclusively, as medical castration in the form of gonadotropin-releasing hormone (GnRH) agonists. ADT was recommended for localized prostate cancer for a brief period, and even then, only under very narrow clinical circumstances. However, for most men during most of the last 20 years, ADT has not been recommended. Although ADT is effective at stopping cancer growth, among men with localized disease for whom there are multiple treatment alternatives, the benefits of *primary ADT*—the use of ADT in the absence of other definitive therapies—have not been shown to outweigh its harms.

These harms include well-known side effects such as: hypotestosteronemia, impotence, weight gain, mood lability, gynecomastia, fatigue, lassitude, cognitive changes, loss of libido, and gastrointestinal and hematological effects (17, 24). In addition to the well-known side effects and resulting poor quality of life (7, 17, 24, 25), iatrogenic effects have been documented including increased incidence of cardiovascular risk factors (e.g., rising serum lipoproteins, insulin sensitivity, and obesity) and greater risk of cardiovascular disease, diabetes, osteoporosis, fractures, thromboembolic events, and cardiovascular death (26-28). Moreover, ADT has a limited window of effectiveness for tumor control; therefore, its initiation early in the disease trajectory limits future more definitive treatment options (29).

Surgical therapy for prostate cancer is generally defined as radical prostatectomy, which can be accomplished through open techniques (retropubic radical prostatectomy and radical perineal prostatectomy) or minimally invasive techniques such as minimally invasive radical prostatectomy (MIRP) (30). Radiation therapies can be either external beam radiation or surgically implanted radioactive pellets, known as brachytherapy. There are several modalities of external beam radiation including conventional two-dimensional radiation therapy, three-dimensional conformal radiation therapy (3D CRT), intensity modulated radiation therapy (IMRT), stereotactic body radiation therapy, and proton therapy (30).

Several other treatments are used in the initial treatment of prostate cancer, although at low frequency and without the recommendation of the NCCN (12, 31). In addition to ADT, chemotherapy is used as salvage therapy when initial therapy fails (22). Emerging therapies include cryosurgery and high-intensity focused ultrasound, the newest therapy currently available only through clinical trials. Although these therapies are not the focus of this dissertation, they are relevant in understanding the changes occurring in the initial treatment of prostate cancer.

### *Preference- and Supply-sensitive Care in Localized Prostate Cancer*

Two distinct quality of care problems have emerged in localized prostate cancer care over the last two decades, partly because evidence for effective treatment is equivocal. Of the four treatments for prostate cancer, only three are currently guideline-recommended for localized disease: active surveillance, radical prostatectomy, and radiation therapy. Selecting among these options is *preference-sensitive*. That is, because no treatment provides a survival advantage, treatment selection should be based on the patients' willingness to experience the unique adverse risk profile associated with the chosen therapy. However, one patient survey demonstrates the role of physicians in prostate treatment selection: 57% of patients cited a doctor's suggestion as the most influential reason for selecting a prostate cancer treatment (32).

These preference-sensitive treatments are provided at the discretion of the treating physician. Because few demonstrated clinical and patient characteristics influence treatment choice, current quality improvement interventions focus on improving risk communication and increasing patient involvement in decision making in an effort to allow patient tolerance for the varied side effects to guide treatment choice.

Less recognized in prostate cancer, however, is a second *supply-sensitive* quality problem that arose over the last two decades: the overuse of ADT. Despite increasing evidence that men with localized prostate cancer should not receive ADT (12, 22), its use is substantial among this population. Economic principles can be used to describe this quality problem. Supply-sensitive services are those for which the supply of a specific resource has a major influence on utilization rates. Variations in supply-sensitive care are due primarily to differences in local capacity, coupled with a payment system that ensures that existing capacity remains fully deployed (33). Situations in which supply and demand are not independently determined can also lead to supply-sensitive care (34, 35). Such situations occur commonly in medical decision making. Physicians, who must act dually as agents for themselves and for their patients, are not considered perfect agents in advising patients on their care. A perfect agent would recommend only the treatment a fully informed patient would demand (34). Instead, physicians, as providers of health services, are in a position of potential conflict of interest, in which they must choose between the most clinically efficacious treatment for the patient and the treatment that provides the best financial reward for the physician, given the marginal cost of treatment (36). Moreover, physicians set the quantity of health services needed and thus are able to induce demand, persuading patients to use services they do not need (36). Thus, in reimbursement environments in which the provision of the service exceeds the cost to deliver the service, supply-sensitive care can lead to overuse and physicians recommending treatments to patients who may not need them.

**ADT Overuse in Localized Prostate Cancer**

*ADT overuse* in prostate cancer (i.e., the use of ADT in patients for whom it is not recommended) is widely believed to be an example of physician-induced demand. ADT use in localized prostate cancer grew steadily from the 1990s: the adjusted odds of medical ADT use increased almost seven fold between 1991 and 1999. By the year 2000, ADT use was seen in as many as 3.2% of all male Medicare beneficiaries (37, 38); and, by 2002, 44.9% of men diagnosed with prostate cancer, and for whom ADT was not recommended, received this treatment (39). ADT use peaked in 2003 and then sharply declined after 2005 (10, 40-42). Even though use declined in the last decade, 25.7% of men for whom it is not recommended still receive primary ADT (39, 40).

The sharp declines in ADT observed in 2005 coincided with significant Medicare reimbursement changes for the administration of GnRH and has therefore been thought to be causal (42). Weight et al. provide a list of potential confounders to their observational study of declining ADT use in the full Medicare population (42), most of which are addressed by later studies that show persistent declines in the cohort for which ADT was not indicated (10, 39). That is, ADT use occurred among men for whom this treatment is not indicated—without changes in use among men for whom the treatment is clearly beneficial—suggesting that healthcare providers were indeed responsive to reimbursement changes in their treatment decisions (10, 39).

However, no study evaluating the impact of the MMA to date has demonstrated that physicians were responding directly to the reimbursement changes. Notably, some evidence suggests that reimbursement changes may not have been responsible for changing ADT use. Trends in Canada and the U.S. Veterans Administration, health systems in which Medicare reimbursement changes would not affect use, have also experienced declining ADT use. In Canada, use of primary ADT has been declining since the 1990s (43). Declining use of ADT in the Veterans Administration Health System has been shown to mirror declines among Medicare

beneficiaries (44). Further, the most recent evidence suggests that even among Medicare beneficiaries in the United States, declines in overall ADT use among all prostate cancer patients, not just those with localized disease, appear to have begun prior to 2004 (40).

As the use of primary ADT decreased up to 34% from 2003 to 2005 among men with incident localized prostate cancer (10, 39), active surveillance may have replaced ADT use. Recent analysis of Medicare claims suggest that for elderly men across all levels of prostate cancer risk and severity, reductions in ADT use occurred simultaneously with an increase in "no active therapy" (40). Moreover, the magnitude of the change was similar—a 44% decrease in ADT use accompanied by a 44% increase in no active therapy. These data suggest that the quality of care for men with localized prostate cancer may be improving. Other trends in prostate cancer patterns of care include the shifting of surgical and radiation therapy modalities. Although overall rates of surgery and radiation have remained constant, minimally invasive surgery has begun to offset closed surgical techniques, and newer radiation modalities such as IMRT and proton therapy have begun to replace other delivery methods (40). However, whether quality of care actually is improving depends on the patients' recurrence risk and what treatments have replaced ADT.

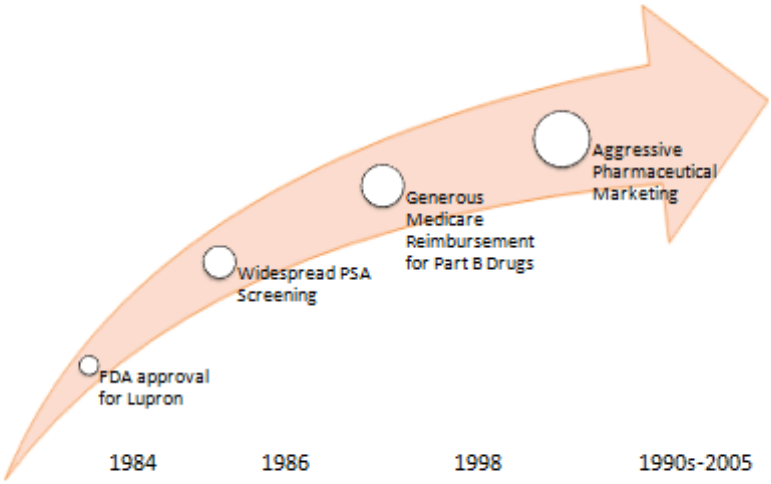
In addition, it is not known whether these changes in patterns of care affected all patients equally or were uniform among all types of providers. While ADT is underused among African-American men with metastatic prostate cancer (41), it is overused among African-American men with localized prostate cancer (45). Whether African-American men were affected by changes in ADT use to the same degree as white men is unknown.

### *Contributors to Changing Patterns of Care*

Several factors likely contributed to ADT's rise in use (Figure 2.3). First, since its advent in 1986, widespread use of PSA screening led to a large increase in the number of men diagnosed with low- and intermediate-risk localized prostate cancer. The lack of severity of their disease may have not yet been fully appreciated, leading to the application of treatments known

to be effective in metastatic disease. In addition, many of these men, which some consider to have been overdiagnosed (46), may not have been candidates for surgical therapy, the main therapy for localized disease at the time. Secondly, aggressive (and illegal) pharmaceutical marketing practices coupled with liberal Medicare reimbursement for Part B drugs made ADT administration extremely profitable for physicians administering the drug (47, 48).

**Figure 2.3. Timeline of Increasing ADT Use**




As with its rise in use, several factors likely contributed to the decline in ADT use. First, because Medicare reimbursement for ADT and other physician-administered cancer drugs far exceeded physician costs (49), the Medicare Modernization Act of 2003 revised reimbursement policy for all Part B drugs (50), reducing the profitability of ADT administration in two phases. Effective January 1, 2004, Medicare changed reimbursement for Part B drugs from 95% of the average wholesale price to 85% of the wholesale price. Effective January 1, 2005, the formula was changed again to reimburse physicians at 106% of the average national sales price of the previous two quarters (47). Together these changes were associated with a 65% decrease in Medicare reimbursement for medical ADT from 2003 to 2005 (47). The second change is

thought to have cut reimbursement the most (51). However, changes in prescribing began at least 1 month prior to Medicare implementation in anticipation of the cuts, since physicians purchase the drugs they administer to patients in advance (51).

Secondly, although affecting only a small group of patients, clinical practice guidelines for the treatment of high-risk localized prostate cancer also changed during the same time. From 2000 to 2004, ADT was recommended for men with less than 5 years life expectancy whose risk for prostate cancer recurrence was categorized as high (20). This recommendation was dropped in 2004 (12). Finally, evidence of the long-term harms of ADT that predated guideline changes began appearing in the 1990s; thus, physicians may have been responding to new harm calculations and proceeding more cautiously (43).

**Reimbursement as a Quality of Care Intervention**

Although many questions remain about the cause of declining use, ADT overuse remains a serious quality problem, and addressing it and other overuse problems through reimbursement policy is a promising strategy. Although ADT use has declined since 2003, 25.7% of men for whom it is not recommended currently receive ADT (39). Reimbursement policy, if it were responsible for the reduction in overuse, is a promising quality intervention. The 34% reduction in ADT use attributed to the policy is large relative to intensive behavioral and systems interventions designed to improve quality of care, which are shown to induce median changes of only 10% (52). Further, pay-for-performance is increasingly advocated to improve quality (53). However, despite emerging interest in provider responsiveness to reimbursement policies, evidence is lacking with regard to whether and how these policies might work (54, 55).

Fortunately, opportunities exist to explore further the role of reimbursement in ADT overuse. Prior to MMA implementation and during a period of guideline stability (2000–2004), substantial variation in ADT reimbursement existed within Medicare. Although Congress sets reimbursement policy nationally, national policy is implemented locally among the contractors

responsible for paying Medicare claims—*fiscal intermediaries* for Part A claims and *carriers* for Part B claims. Although geographically fixed, carriers are regional and do not have uniform policies regarding reimbursements (56). In particular, from 1997 to October 2002, Medicare carriers were responsible for translating Part B drug Healthcare Common Procedure Coding System (HCPCS) claims into National Drug Code (NDC) indices (57). Although some HCPCS had only one equivalent NDC, others had 10 or more matches in 2000, resulting in substantial variation among carriers (49). The GnRH agonist leuprolide acetate was one of the drugs identified that had a more than 10% variation in reimbursement across Medicare. In contrast, another GnRH agonist, goserelin acetate, was uniformly reimbursed across the carriers (49). In addition to the variability among regional carriers, reimbursements changed at different rates over time based on revisions to the average wholesale price for specific NDCs (57). Exploiting this variation in ADT reimbursement enables one to isolate the effect of ADT reimbursement changes in urologists' use of ADT between 2000 and 2003.

**Determinants of ADT Overuse**

In general, overuse is believed to derive from both provider and patient demand (35). Providers may suggest non-indicated treatments in the course of 1) early innovation; 2) practicing defensive medicine, or 3) inducing demand to increase their profitability. Patient demand for specific treatments arises from health education efforts, direct-to-consumer advertising, prior treatment experiences (such as with antibiotics), and the treatment experiences of others.

Although clinical characteristics and patient preferences may have influenced the medical decision to prescribe ADT to men with localized prostate cancer, there is little evidence to support this supposition. In fact, most variation in prostate cancer treatment has been attributed to the physician. Research in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) cohort, a national registry of prostate cancer treatment, found high variation among healthcare practices in the selection of therapy (31). The wide variations in care

delivered were not explained by disease characteristics as measured by the CAPRA score, an indicator of disease severity.

In particular, variation in ADT use in the 1990s can be explained by physician characteristics. A study among urologists identified in the Surveillance, Epidemiology, and End Results-linked Medicare claims database found substantial variation in ADT use by provider. The authors partitioned the variance by three categories and found that only 4% was due to patient characteristics and 10% was due to tumor characteristics, whereas the largest part of the variance that could be explained (23%) was due to the urologist (58).

Patient reports support these findings: 57% of men report their physician as being most influential in their prostate cancer treatment decision (32). Thus, understanding provider characteristics associated with ADT overuse are crucial to developing interventions for its elimination (59).

### *Urologist Characteristics Associated with ADT Overuse*

Urologists provide the majority of prostate cancer care as they perform the biopsy necessary for confirming the prostate cancer diagnosis. Although patients are referred to medical oncologists in late-stage disease and increasingly to radiation oncologists in localized disease, most primary ADT is prescribed by urologists (58). Among fee-for-service Medicare patients, overall ADT use (across all recurrence risk categories) between 1992 and 2002 was associated with female, non-board–certified, and non-academically affiliated urologists. However, among patients for whom the benefit of ADT was uncertain, physician characteristics associated with ADT overuse shifted over time. Both the least and most clinically experienced physicians prescribed more ADT than their moderately experienced peers. Across the period of 1992 to 2002, physicians with no or minor academic affiliation were more likely to overuse ADT, and increasing panel size was associated with greater odds of overuse. Lack of strong academic affiliation was the strongest predictor of ADT overuse from 1992–1995, but lack of board certification, lack of academic affiliation, and increasing panel size did increase the odds of ADT

overuse by the 1996–2002 period. Together, these patterns of ADT use suggest that either physicians with greater knowledge and professional affiliations were more cautious in adopting ADT or that non-academic physicians were more responsive to financial incentives (60).

Although this single study provides important information regarding ADT use and overuse, no research to date describes characteristics associated with *change in overuse*. Previous studies clarify the clinical population for which ADT use declined (10, 39). Sharp declines in ADT use occurred among men for whom it is not indicated, without changes in use among men for whom the treatment is clearly beneficial. However, no information is available that indicates whether the change was universal among all physicians or occurred among isolated pockets of physicians or practices. Nor have the characteristics of physicians who eliminated overuse and those who did not been explained.

### *Clinical Experience as an Indicator of Quality of Care*

Although counterintuitive, clinical experience has been found to be associated with lower quality of care (61). Physicians with greater amounts of clinical experience are believed to neglect maintenance of their technical knowledge, missing changes in clinical practice guidelines and emerging technology. These physicians experience clinical inertia, practicing as they always have done. For prostate cancer, established physicians may be less likely to be aware of and responsive to emerging evidence and recommendations against ADT in men with low-risk prostate disease. In addition, physicians later in their career are thought to be less responsive to reimbursement cuts, because they are more likely to have repaid educational and business loans, personal mortgages, and their children's college expenses (57).

A better understanding of the effects of clinical experience on efforts to address overuse among urologists is important not only because of the harms already described, but also because recent trends suggest urologists are staying in practice past traditional retirement age to address perceived physician shortages (62). If end of career issues influence quality of care, we can

expect the magnitude of the problem to persist, and further reimbursement cuts are unlikely to address the problem.

**Reimbursement Responsiveness**

Little is known about what might make providers more or less responsive to reimbursement changes. Nonetheless, variation in responsiveness to financial disincentives has been documented (35, 63). Previous observations of fee freezes or reimbursement cuts has shown that physicians generally increase the quantity of services provided (36, 51, 64, 65). This is so well established that reimbursement policy planners usually compensate for a set increase in volume when estimating the impact of a reimbursement cut (66). However, this volume response has not been demonstrated uniformly (36). Moreover, reasons for these variations have not been adequately explained (63). The proposed research fills this gap by addressing factors associated with variation in response to reimbursement changes.

***Practice Factors Associated with Patterns of Care***

The prostate cancer treatment decision is strongly associated with preferences of the treating physician (58, 60, 67). However, different models of practice organization may affect responsiveness to reimbursement by shaping the kinds of care that can be substituted when certain therapeutic options are discounted. In particular, physicians in certain types of multi-specialty practices are expected to have a greater number of treatment options to offer their patients and subsequently be more likely to lower ADT use. However, it is not known how different models of multi-specialty group practice organization influence changes in care.

Depending on the specialty configuration, one might expect different degrees of change in ADT use. For example, one might expect healthcare providers in comprehensive multispecialty practices to be insulated from reimbursement policy as they are more likely to provide patient-centered care, coordinate decision making, and optimize informed decision making. Therefore, they would be more likely to have low levels of baseline ADT overuse and to maintain those low levels over time. Single-specialty group practices may have high levels of

baseline use and *increase* their overuse of ADT, as that strategy may be their only means of replacing revenue.

An emerging type of multi-specialty practice organization, in which a urology group practice hires a radiation oncologist to provide IMRT, may have a different response. Because of the substantial investment required to build IMRT facilities, this treatment is well reimbursed. However, to justify the investment, a certain number of referring urologists are needed to support the optimal use of the equipment. Thus, a new urologist-centric practice organization has developed (68, 69). Subsequently, IMRT is more readily available in select group practices that organize in this way and may lead to physician inducement (69, 70). Physicians in urologist-centric multi-specialty practices might have the greatest levels of early ADT use and be very responsive to reimbursement policy changes because they have other options for replacing revenue. However, it not known whether physicians in these types of practices were more likely to replace ADT use with IMRT and less likely to adopt active surveillance.

**Significance and Innovation**

The proposed research is significant in several respects: it addresses a prevalent condition for which the treatment varies by patient race; it investigates the mechanisms by which federal reimbursement policy designed to reduce healthcare costs may also improve quality of care; and it will improve understanding of the moderating effects on reimbursement policy. Moreover, it will enable future quality of care interventions to target a harmful, costly, and persistent problem. Localized prostate cancer treatment quality drastically improved in 2000s. However, the problem remains that 25.7% of men for whom it is not recommended still receive ADT, and racial differences may persist. Continued efforts are needed to further understand barriers and facilitators to change. The relative contributions of physician and practice factors to responsiveness to reimbursement disincentives are not known, but efforts to reach remaining urologists are critical. Although overuse remains substantial, the 34%

reduction in use from 2003 to 2005 provides an opportunity to identify facilitators and barriers to treatment discontinuation.

Moreover, the approach to the proposed research is innovative. This study addresses a poorly studied quality of care issue: overuse. Approximately 30% to 40% of healthcare spending in the U.S. has been attributed to *overuse*, the provision of unnecessary care or care for which the harms outweigh the benefits (71-73). Overuse results in patient harms, health disparities and waste in a healthcare system already stretched to capacity (73). As a result, overuse recently has been designated one of six national priorities in the National Quality Strategy, a strategic plan mandated by the 2010 Patient Protections and Affordable Care Act (74). Overuse is particularly important to address within the context of cancer care, because changes in evidence supporting cancer screening and control increasingly result in situations in which providers and patients must alter their behavior to *abandon* established practices. Thus, strategies to address overuse in cancer care are becoming increasingly relevant.

Despite the recent spotlight on overuse as a significant quality problem, relatively little research actually focuses on this problem (71, 75). Few quality measures assess overuse, and most of the research that is available describes the degree to which overuse exists in a few distinct clinical areas. Although broad strategies such as academic detailing have been used successfully to limit prescribing (76), few studies evaluate interventions designed to limit overuse. As a whole, the field lacks overarching models that consolidate empirical findings into principals for addressing the problem. Even reviews of successful quality improvement strategies do not differentiate whether the goal is to stop an established behavior or start a new one (77-79).

Yet overuse is a distinct quality problem with potentially different determinants than underuse. Whereas *adopting new* behaviors requires that the new behavior be: 1) advantageous to the intended user; 2) compatible with the users' culture and values; 3) minimally complex; 4) easy to test prior to adoption; and 5) easy to observe prior to adoption (80), little is known about

principles of *relinquishing established* behaviors. Thus, interventions to reduce overuse may be quite different in their structure as well as their goals (76, 81). Implementation research suggests the factors that facilitate adoption of new technology, but we know little about factors that facilitate or impede discontinuation of disproven technology (Rogers 2003).

In summary, the current healthcare environment is faced with reducing costs while increasing healthcare quality. Yet our tool kit to address these simultaneously is limited. Quality interventions are known to work modestly, and little effort has been made to delineate the contexts in which they may be successful. Misaligned incentives are cited as a substantial impediment to quality care (82), but little research focuses on *how* change in reimbursement policy affects quality. The proposed research will address these problems and identify ways to improve quality while reducing overall healthcare costs, addressing key national priorities to improve quality of care for all Americans.

# CHAPTER 3 STUDY DESIGN AND METHODS

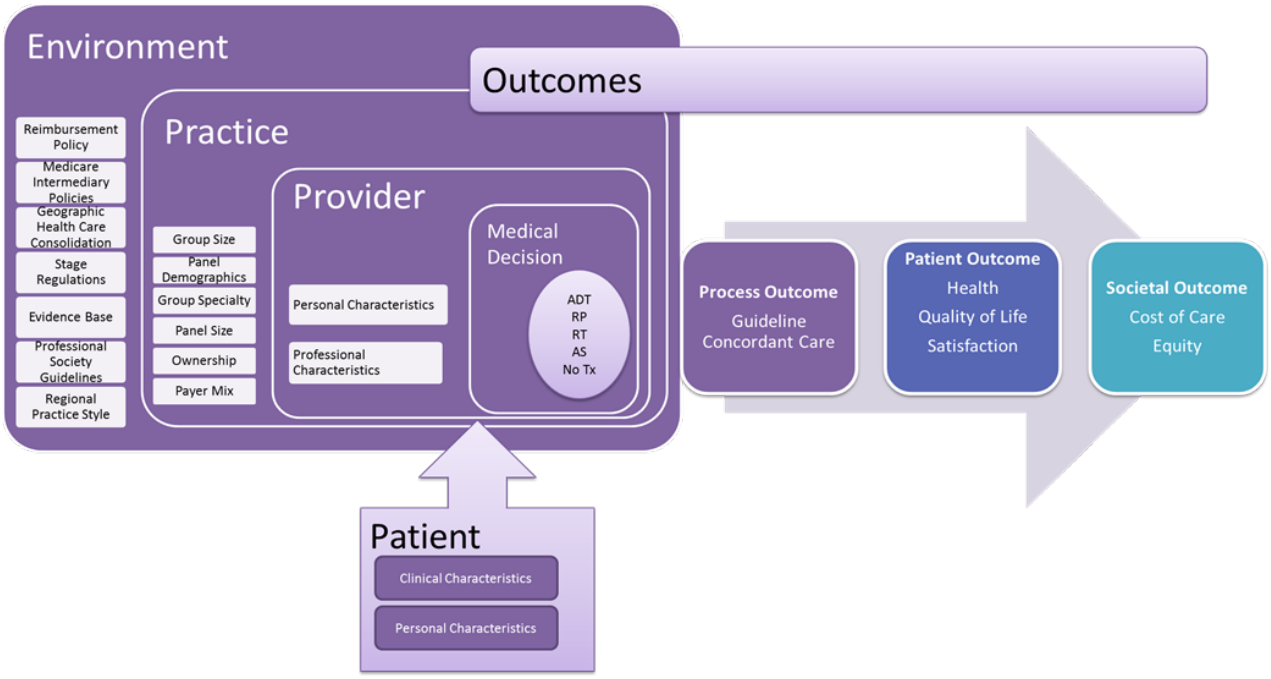
## Overview and Rationale

The three aims of this dissertation are executed as longitudinal, retrospective analyses of three distinct cohorts of men diagnosed with incident adenocarcinoma of the prostate and treated by physicians participating in fee-for-service Medicare. Aim 2 additionally exploits a natural experiment producing exogenous variation in reimbursement and allows for difference-in-difference design features. Data come from SEER-linked Medicare claims and the American Medical Association's physician Masterfile. Three unique study cohorts are formed including patients diagnosed from 2000–2007 (Aim 1); 2000–2003 (Aim 2); 2005–2007 (Aim 3); and their treating physicians. Aim 1 uses the binary outcome ADT use measured at the patient level. Aim 2 also uses the binary outcome ADT use, also measured at the patient level. Aim 3 uses the binary outcome NCCN guideline concordance measured at the patient level. Aim 1 analyses include the explanatory variables *time in practice,* a dichotomous measure of physicians' length of time since graduating from medical school, and *group practice type*, a categorical indicator of the multi-specialty organization of urology group practices. In Aim 2, the explanatory variables are *reimbursement generosity*, an index that measures excess reimbursement relative to the national average spending on ADT, and *group practice type*. The explanatory variables of Aim 3 is *pre-MMA ADT use*, measured as a physicians' average ADT use among non-metastatic T1 and T2 well- and moderately differentiated incident prostate cancer patients between 2000 and 2003, and patient *race*, a categorical indicator of five race/ethnic groups. Each of the three analyses uses multilevel mixed logistic regression to control for tumor, patient, physician, practice, and environmental characteristics and to account for clustering of patients within physician and physicians across time.

## Conceptual Foundation

The overall model of medical decision making that underlies this research (Figure 3.1) is derived from Andersen and Aday's *Behavioral Model of Health Service Use* (83, 84), which identifies the external, macro-, and micro-level factors that affect processes of care. The *Behavioral Model of Health Service Use* is adapted to consider the influences on medical decision making *from the healthcare provider's perspective*. The conceptual model is further informed by more recent efforts to incorporate economic theory into medical decision making (85) and draws more directly from economic and behavioral response theory to conceptualize how both the reimbursement context and reimbursement changes may influence physicians to induce demand for health services and respond to reimbursement changes (64, 86).

**Figure 3.1. Conceptual Model**




*Outcomes.* In this physician-centric model of medical decision making, the ultimate *outcomes* are process outcomes—what care is delivered and whether it is guideline-concordant

(85). More distal (and less controllable) outcomes from the physician perspective are the patient and societal outcomes traditionally studied. Quality of care is judged relative to the concordance of the care that is delivered with national prostate cancer guidelines.

*Medical Decision*. The outcome guideline-concordant care is derived from the *medical decision* that is made for each patient. Although care delivered, as measured in claims data, may not fully represent the care recommended, it does represent the care recommended by the physician that the patient consented to receive. For men with localized prostate cancer there is an array of treatment options including surgery, radiation therapy, active surveillance, ADT, no treatment, and several other treatments including combinations of these frequently used treatments and other less frequently used treatments such as cryosurgery and high-intensity focused ultrasound.

Multiple patient-, provider-, practice-, and environmental-level factors directly or indirectly influence the medical decision.

*Patient Factors.* Patient factors influence each medical decision through both clinical presentation and personal circumstances and preferences. Patients present with prostate cancer of varying levels of severity, which warrant different treatment approaches. However, their life expectancy, other health concerns, and physical and emotional stamina may all be considered in the treatment decision, as some therapies have different cost/benefit trajectories or require different levels of commitment to complete. Different therapies also require varying levels of social support to either complete treatment or endure treatment side effects; thus the patients' level of social support and community resources are also important. Physicians also may integrate their patients' preferences for the treatment options presented in the medical decision.

*Physician Factors.* Physician's treatment decisions and willingness to change prescribing behavior are influenced by their own personal perceptions of disease and treatment risk, their personal valuation of individual patients, and their personal comfort with inducing demand. Economic theory suggests that physicians' treatment decisions are also influenced by their

economic self-interest. Physicians act as imperfect agents for their patients. They are ethically bound to choose the best treatment for their patients, but they also must balance their own financial solvency against the "costs" of the treatments offered. Because they rely on the delivery of healthcare for their livelihood and well-being, they may respond to incentives from the healthcare delivery system to optimize their income. In balancing these varying influences, physicians may be more motivated to treat African-American patients medically with ADT if they perceive that these patients are at higher risk of death from their disease and if they perceive that these patients are not candidates for surgery or radiation therapy. Physicians' medical decisions are also influenced by professional characteristics, such as medical professionalization, specialty professionalization, and experience (55).

*Practice Factors.* Medical decisions also are influenced by the practice milieu indirectly shaping the physicians' opportunities for treatment and behavior change, thereby shifting their perspectives of disease and treatment risk and their personal comfort with inducing demand. The size of the practice, number and types of other physicians in the environment, types and volume of patients seen in the practice, and compensation arrangements all contribute to the weighting of patient and clinical factors for any treatment decision. The specialty organization of the practice in particular is expected to contribute to the treatment decision. Multi-disciplinary teams have been shown to improve treatment outcomes (87, 88) and are generally believed to improve the quality of cancer care by increasing coordination, communication, and decision making (89). However, some multidisciplinary groups are organized around particular treatment modalities, which may lead to inducement of certain services the practices are organized to deliver (69), possibly at the expense of other treatment options.

Compensation arrangements include both the physician's compensation structure as well as the physicians' and practices' combination of healthcare payers and plans that affect the way care is compensated. Depending on how they are paid, individual physicians may balance varying amounts of leisure time and personal income against their moral and professional

obligation to do no harm. Under fee-for-service payment arrangements, physicians are paid based on the quantity of service provided, and their income increases when they provide more services (when cost for providing the services remains the same). Physicians may therefore recommend more services to optimize income (36). However, the extent to which they do this is also influenced by the relative influence of the reimbursement policies of a particular payer. Providers see patients insured by a variety of payers, each with different payment levels. Although physicians are thought to optimize income (whether stopping at an income target or increasing to a maximum), response to change in reimbursement may produce varying behaviors (36). Although it seems that physicians would induce demand when faced with decreases in reimbursement, instead multiple behavioral responses can result from a decrease in reimbursement: providers can increase, replace, or drop the discounted service (36).

*Environmental Factors.* Medical decisions are also influenced by environmental factors. Within the prostate cancer treatment decision, environmental factors include the reimbursement policy of individual payers, especially Medicare; local coverage determinations of the Medicare fiscal intermediaries; business trends that affect the structure of treating practices (86); state policies that affect practice structures; research that provides evidence of harms and informs clinical practice guidelines (which in turn defines the appropriate patient for treatment); and, the community practice patterns that are informed by and influence the individual physicians' practice styles.

**Specific Aims**

Following from this conceptual model and evidence from the published literature presented above are testable hypotheses, organized into the specific aims proposed in this dissertation.

**Aim 1: Estimate the degree to which physician characteristics are associated with changes in ADT overuse.**

*Hypothesis 1A: Among urologists treating ADT-ineligible men from 2000 to 2009, urologists with more time in practice will be less likely to reduce ADT overuse following reimbursement changes.*

*Hypothesis 1B: Among urologists in group practice treating ADT-ineligible men from 2000 to 2008, urologists will respond to reimbursement changes uniformly.*

**Aim 2: Estimate the degree to which reimbursement changes are associated with ADT overuse.**

*Hypothesis 2A: Among urologists of ADT-ineligible prostate cancer patients, reimbursement will be positively associated with ADT overuse.*

*Hypothesis 2B: Among urology group practices, physicians in single-specialty group practice will be more likely to overuse ADT than physicians in multi-specialty group practice.*

**Aim 3: Assess the impact of pre-MMA ADT overuse on the quality of post-MMA prostate cancer treatment for localized prostate cancer.**

*Hypothesis 3A: Among clinically localized prostate cancer patients, physicians' pre-MMA ADT overuse will be positively associated with receipt of guideline-concordant care in the post-MMA period.*

*Hypothesis 3B: Patterns of care associated with changes in ADT use will be similar for African-American men compared to white men, resulting in similar levels of guideline concordance for African-American men.*

*Hypothesis 3C: Pre-MMA ADT overuse will be negatively associated with uptake of new treatment modalities.*

## Data

This study links two datasets to accomplish its aims: 1) the most recent Surveillance, Epidemiology and End Results (SEER)-linked Medicare database, co-developed by the National Cancer Institute (NCI) and the Centers for Medicare and Medicaid Services (CMS), and 2) data on physicians and practices from the American Medical Association.

### *Surveillance, Epidemiology, and End Results-Medicare Linked Database (SEER-Medicare)*

The SEER registry is a collection of 17 population-based registries of all diagnosed cancers in 14 geographic areas, currently representing 26% of the U.S. population (90). Patients in the SEER 17 grouping are drawn from nine states (California (in 4 registries), New Mexico, Hawaii, Utah, Connecticut, Iowa, Kentucky, Louisiana, and New Jersey); three metropolitan areas (Metro Atlanta, Seattle and Detroit); one rural area (rural Georgia); and one ethnic group population registry (Alaska Natives). Although the SEER population tends to be more urban and has a higher proportion of foreign-born persons than the general U.S. population, SEER data are comparable with regard to measures of poverty and education. As of the 2000 census, when the SEER registry included 11 registries, it represented 26.3% of the African-American population in the U.S. (90). SEER data include patient demographics, primary tumor site, morphology, stage at diagnosis, first course of treatment, and vital status follow-up. Routine quality control activities ensure highly reliable data (90).

SEER data from 16 of the registries are linked to Medicare data. Medicare is an administrative claims database covering hospital services, physician services, some drug therapy, and other medical services for more than 97% of the U.S. population 65 years of age and older. Provided by CMS, Medicare claims are linked to registry data and packaged as de-identified SEER-Medicare files linked by a SEER case identifier (91). Thus, for each elderly prostate cancer patient identified in one of the SEER registries and covered by Medicare fee-for-service, virtually complete claims for treatment are available.

We used Medicare Provider Analysis and Review (MEDPAR), outpatient claims, durable medical equipment (DME), and carrier files for sample selection, outcome, and treating provider identification, but used only carrier files to study response to reimbursement in Aim 2, because other files do not identify physicians, reimbursement, or both.

### *The American Medical Association (AMA) Masterfile*

The AMA Masterfile is a comprehensive database of physician and practice characteristics, covering approximately 800,000 member and non-member practicing, retired, and deceased physicians in the U.S. Most data originate from training records collected annually with 96%–98% response rates. American Board of Medical Specialties certification data are collected annually. These data are confirmed and supplemented by annual surveys of one-third of physicians each year (response rate approximately 40%) and other physician regulatory agencies (92). Prostate cancer patients' physicians were identified within the Medicare data by Unique Physician Identification Number (UPIN) and sent to AMA to provide a matched file of physician personal characteristics. Physician matching has been reported to be 98.7% complete and consistent across SEER site and geographic areas for the six most common cancers, including prostate cancer (92).

Although some practice-level data are available within the AMA Masterfile, additional practice data are available for a subset of group practices. Data are collected by survey every 3 years. Data completion in this subset ranges from 20% to 100% complete and for many variables approximates the proportion of urologists in group practice.

## Study Sample and Inclusion/Exclusion Criteria

For Aim 1, we identified all men diagnosed with incident adenocarcinoma of the prostate between January 1, 2000 and December 31, 2007. Only patients experiencing their first and only cancer, as indicated by SEER, were included. We excluded patients whose comorbidities could not be ascertained and/or whose initial treatment could not be ascertained including those who were younger than 66 years and lacking a complete year of claims; diagnosed at

autopsy, by death certificate, or at a nursing/convalescent facility; not enrolled in fee-for-service (defined as continuous Part A and B coverage and not in a Health Maintenance Organization (HMO) for at least 12 months post diagnosis; died within 12 months of diagnosis; and/or diagnosed in Louisiana (due to disruptions in health services cause by Hurricane Katrina). The Tumor Node Metastasis (TNM) staging system was used to restrict the cohort conservatively to patients for whom ADT is not a NCCN guideline-recommended treatment across the study period. Men in the ADT-ineligible sample were those who lacked evidence of nodal or metastatic involvement and had no greater than unilateral, stage T2 tumors and World Health Organization grades 1–2 (10). Thus, we excluded men diagnosed with 1) T1 or T2 cancers with Gleason scores 8–10; 2) T2b tumors before 2002 when the staging definition changed; 3) T2c tumors after 2002 when the category was added; or, 4) T3a tumors. Men receiving external beam radiation therapy were also excluded, because the appropriateness of their ADT receipt could not be ascertained. Treating physicians were identified from claims. After limiting claims to those submitted for initial prostate cancer treatment, the physician responsible for the majority of prostate cancer-related treatment claims was considered the treating physician.

For Aim 2, we identified all patients in the SEER registries who had an incident diagnosis of adenocarcinoma of the prostate (ICD-9 diagnosis code 185 and histology code 8140) between January 1, 2000 and December 31, 2002. Only patients experiencing prostate cancer as their first and only cancer, as identified by SEER, were included. We excluded patients younger than 66 years of age at diagnosis because their comorbidities could not be ascertained. We excluded those whose initial treatment decision could not be ascertained because they lacked observation throughout the full treatment window and were 1) were diagnosed at autopsy, death certificate, or at a nursing/convalescent facility; 2) died within 12 months of diagnosis; 3) were not continuously enrolled in fee-for-service (defined as Part A and B coverage and not in an HMO for 12 months post diagnosis); or 4) had no treatment claims. The TNM staging system was used to restrict the patient sample to those ineligible for ADT. Following

previous work, men in the ADT-ineligible sample were limited to those who lacked evidence of nodal or metastatic involvement and who had no greater than unilateral, stage T2 tumors and WHO grades 1–2 (10). In addition, we excluded men with less than 5 years actuarial life expectancy following an algorithm used previously (93), because NCCN guidelines for this period allowed for the use of primary ADT in men with limited life expectancy (20, 93). Because urologists prescribe 95% of primary ADT to localized prostate cancer patients (37, 93), we excluded non-urologists based on specialty information in the AMA data.

In Aim 3, we identified all men diagnosed with incident adenocarcinoma of the prostate between January 1, 2005 and December 31, 2007. Only patients experiencing their first and only cancer were included. We excluded patients whose comorbidities and/or initial treatment could not be ascertained including those who were younger than 66 years; diagnosed at autopsy, death certificate, or at a nursing/convalescent facility; not enrolled in fee-for-service (defined as continuous Part A and B coverage and not in an HMO for at least 12 months post diagnosis); or died within 12 months of diagnosis. The TNM staging system was used to restrict the cohort to men with clinically localized prostate cancer. We excluded men with 1) tumors clinically staged T3b or greater; 2) any evidence of nodal involvement; or, 3) any evidence of metastases. Treating physicians were identified in Medicare claims. After limiting claims to those submitted for initial prostate cancer treatment and identifying the primary therapy received, the physician responsible for the most primary therapy treatment claims was considered the treating physician.

***Physician Assignment***

Treating physicians were identified from claims files. After limiting claims to those submitted for primary prostate cancer treatment, the provider responsible for the most initial treatment claims was considered the treating provider, consistent with most studies identifying providers (28). Providers identified in claims were matched by encrypted Unique Physician Identifier Number (UPIN) or National Provider Identifier (NPI) to AMA data, a process which

excluded non-physician providers. Because we excluded non-urologists as treating providers, no patients receiving external beam radiation were included.

## Variables and Measurement

### *Dependent Variables*

Aims 1 and 2 use ADT use as the dependent variable. ADT in conjunction with radiation is recommended therapy for some men with high-risk disease; however, ADT alone is not recommended. Thus, the outcome, *primary ADT use*, is a binary variable defined for each patient as initial treatment claim for a Healthcare Common Procedure Coding System (HCPCS) code for medical ADT administered within 1 year from the SEER date of diagnosis without another non-surveillance prostate treatment administered within the treatment window. Non-surveillance treatments included orchiectomy, radical prostatectomy, all forms of radiation therapy planned or delivered (brachytherapy, conformal, IMRT, proton therapy), chemotherapy, and cryotherapy. All claims files were used to identify treatment delivered. Codes for other hormonal treatments were not considered part of the primary ADT definition. Table 3.1 lists procedure codes used.

**Table 3.1. Treatment Claims**

| Treatment | ICD-9 Codes | CPT/HCPCS Codes |
|---|---|---|
| Active Surveillance-Standard | | [84152-84154, G0103 (PSA) OR G0102 (DRE)] + 99201-99215 (E&M) |
| Active Surveillance-NCCN | 60.1, 60.11 (biopsy) | [84152-84154, G0103 (PSA) OR G0102 (DRE) OR + 99201-99215 (E&M)] + 55700, 55705, 55706, 76942, 10021, 10022, 88172, 88173, C1710, or G0416-9 (Biopsy) |
| Radical Prostatectomy | 60.4, 60.5, 60.60-60.69 | 55801, 55810, 55812, 55815, 55821, 55831, 55840, 55842, 55845, 00865 |
| Minimally Invasive Radical Prostatectomy | | 55866 |
| Radiation Planning and Management | | 77261, 77262, 77263, 77299, 77427, 77431, 77499 |
| Conformal Radiation | Revenue center 330, 333, 339 | 77310, 77315, 77321, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416 |

| | | |
|---|---|---|
| Brachytherapy | 92.20, 92.27, 92.28 | 55860, 55875, 55876, 76873, 77326, 77327, 77328, 77761, 77762, 77763, 77776, 77777, 77778, 77781, 77782, 77783, 77784, 77785, 77786, 77787, 77789, 77790, 77799, Q3001, A9527, C1715, C1716, C1717, C1719, C1728,C2616, C2634, C2635, C2636, C2637, C2638, C2639, C2640, C2641, C2642, C2643, C2698, C2699, C9725, 0182T |
| IMRT | | 77301, 77338, 77418, 0073T, G0174, G0178 |
| Proton Therapy | 92.24, 92.26 | 77380, 77381, 77520, 77522, 77523, 77525 |
| Androgen Deprivation Therapy (GnRH agonist) | | J0128, J9202, J1950, J9217, J9218, J9219, J3315, J9225, J9226 or C9216, C9430, S0165 |
| Orchiectomy | 62.3, 62.41, 62.42 | 54520, 54522, 54530 54535, or 54690 |
| Other | 99.25, V58.1x, V66.2, V67.2 (chemotherapy); 92.24, 92.26 (other radiation); 60.21, 60.29 (other prostatectomy); 92.21, 92.22, 9233, 92.25, 92.29, V58.0, V6.61, V6.71 (other radiation) | 55873 (cryosurgery), 96400-96549, Q0083-Q0085 (chemotherapy); J9999 (unspecified); 77432, 77435 (stereotactic radiation); 77371, 77372, 77373, 0082T, 0083T, G0251, 77750-60, 77774, 77775, 77779, 77780, 77791-98, 77305, 77402, 77403, 77404, 77406, 77423, G0339, G0340 (other radiation) |
| Abbreviations: ICD-9: International Classification of Diseases, 9th Revision; CPT: Current Procedural Terminology; HCPCS: Healthcare Common Procedure Coding System; PSA: Prostate-specific Antigen; E&M: Evaluation and Management | | |

Because reimbursement may affect the prescription of both primary ADT and adjuvant ADT, we also created an outcome variable for Aim 2 sensitivity analysis that captured any ADT used alone or in conjunction with any other therapy. Neither primary nor adjuvant ADT was guideline-recommended for our cohort during the study period.

The binary outcome used in Aim 3, *guideline concordance,* was derived from the 2004 NCCN prostate cancer treatment algorithm effective throughout the study period (12). The algorithm stratifies patients by stage, grade, PSA, and in some cases, the presence of multiple risk factors. The low-risk group includes men with T1–2a stage, Gleason grade 2–6, and PSA <10 ng/mL. The intermediate-risk group includes men with T2b or T2c stage, Gleason grade 7,

or PSA 10–20 ng/mL. The high-risk group includes men with PSA >20 ng/mL, Gleason grade >7, or stage T3a. Concordant treatments are assigned for each risk category. To identify the *initial treatment received*, we reviewed patients' claims to categorize initial treatment into one of five mutually exclusive options: 1) active surveillance; 2) radiation therapy; 3) radical prostatectomy; 4) primary ADT; and, 5) other less frequently used treatments (See Table 3.1 above for relevant codes). Where two treatment modalities were possible, we further split the category to distinguish them for some analyses, but excluded non-concordant modalities based on NCCN recommendations. Only treatment received within 18 months of diagnosis and only the first treatment following diagnosis was considered as the initial treatment decision, except where ADT was considered adjuvant to another therapy. Although SEER registry data and Medicare claims are roughly comparable for radiation therapy and surgery (94, 95), and their use in combination ascertains additional treatment, SEER data tend to underestimate use of medical therapies including ADT (37). In addition, registry data may inaccurately represent active surveillance (96). Thus, for consistency, treatment was derived from Medicare claims only. Each treatment is defined as follows:

- *Active surveillance* was defined in two ways: 1) <u>standard surveillance</u> was defined as at least one claim for PSA or digital rectal exam (DRE), at least two prostate cancer specialist visits within the initial treatment window, and the absence of any other definitive prostate therapy; 2) <u>NCCN surveillance</u> was defined as at least two claims for PSA or DRE and at least one claim for needle biopsy of the prostate, in the absence of other definitive treatment (12). Although DRE claims are rarely coded, some claims did include them, which we counted as a component of surveillance, but neither definition required a DRE claim.
- *Radiation therapy* was defined as either EBRT (two- or three-dimensional conformal radiation therapy), IMRT, or brachytherapy, with or without ADT, from claims definitions used in prior studies (18, 97, 98) and from search of International

Classification of Disease-9 (ICD-9) and Current Procedural Terminology (CPT) dictionaries (99). Other forms of radiation (stereotactic-body radiation and proton therapy) are not guideline-recommended and were not included in this category but were considered as "other" therapy.

- *Radical prostatectomy* consisted of 1) open prostatectomy (retropubic, or perineal radical prostatectomy); and 2) MIRP, distinguished from other prostatectomies by CPT code.
- *Primary ADT* was considered ADT use in the absence of other definitive therapy. ADT included either orchiectomy or a GnRH agonist, as neither are guideline-concordant for clinically localized disease (39, 100).
- *Other therapy* included cryosurgery, chemotherapy, and therapy combinations not included in the NCCN guidelines (e.g., radical prostatectomy with adjuvant ADT).

***Key Explanatory Variables***

In Aim 1, the explanatory variables included *time in practice* and *group practice type*. *Time in practice* was calculated as the difference between a patient's SEER diagnosis date (averaged as the 15th day of the month) and the date of a physicians' medical degree (from the AMA Masterfile). We dichotomized time in practice as <20 versus ≥20 years. Previous studies assessing practice outcomes have defined time in practice as a continuous variable (101), dichotomized as we have done (102) as a categorical variable with cut points at 5- or 10-year increments (103-105), or as categories of low, medium, and high experience (60), with little theoretical rationale. We tested model fit for all specifications, including a quadratic term. The dichotomized specification best fit our data reflecting urology practice patterns.

*Group practice organizational type* is a series of mutually exclusive indicator variables denoting the treating practice as a single specialty urology group, multi-specialty group, or urology-radiation oncology group (all urologists with two or fewer radiation oncologists).

Variables in this construct were self-reported by practice representatives to the AMA and provide a practice-level description.

The key explanatory variable in Aim 2 is *reimbursement generosity*. *Group practice organizational type*, defined above, is also used. Although Congress sets reimbursement policy nationally, the national policy is implemented locally among contractors responsible for paying claims (fiscal intermediaries for Part A claims and carriers for Part B claims). Often, regional carriers do not have uniform implementation policies (56). In particular, from 1997 through 2002, carriers were responsible for translating Part B drug Healthcare Common Procedure Coding System (HCPCS) claims into National Drug Code (NDC) indices (57). Although some HCPCS had only one equivalent NDC, others had 10 or more matches, resulting in substantial reimbursement variation (49). Reimbursement for the GnRH agonist leuprolide acetate varied more than 10%, whereas another GnRH agonist, goserelin acetate, was uniformly reimbursed (49). In addition to variability among carriers, reimbursements changed at different rates over time due to changes in the average wholesale price for specific NDCs (57).

Exploiting this variation and following the method developed by Jacobson and colleagues (57), the key explanatory variable, reimbursement generosity, was operationalized as the sum of the weighted average difference between the urologists' reimbursement and the national mean reimbursement for each agent the urologist prescribed. Weights were derived as the ratio of SEER registry-wide spending on a regimen to total spending on all ADT agents. Differences in the index reflect the variation in reimbursement specific to each carrier, so that a positive association between reimbursement generosity index (RGI) and ADT use would indicate that urologists are inducing demand. Any score greater than one indicates excess reimbursement, or reimbursement greater than the national average.

Unlike in Jacobson's study of chemotherapy use in late-stage cancers, in our study some urologists may not have prescribed ADT for any of their patients; RGI was mathematically undefined (0/0) for those urologists. Thus, we created two additional constructs to be used in

sensitivity analyses. First, we calculated a second RGI that included the costs of each ADT modality relative to all other care provided to this population, with weights adjusted to capture this additional "non-ADT treatment" category. This measure allowed us to assess the question of substitution, because urologists can substitute lost income not only from increasing the quantity of discounted services, but also by increasing or selecting alternate treatments they can offer (106), especially in localized prostate cancer where there are multiple treatment options. However, although there are multiple treatment options, a given patient may not be eligible for all of them. For that reason, we also created a third version of the RGI, which assumed the SEER average reimbursement for urologists who did not prescribe any ADT.

The RGI was calculated as:

$$R_{it} = \frac{\sum_{g \in g(i,t)} (P_{itg} - P_{tg}) W_{tg}}{\sum_{g \in g(i,t)} W_{tg}}$$

where $P_{itg}$ is the average reimbursement for patients receiving GnRH agonist $g$ prescribed by provider $i$ in year $t$, and $P_{tg}$ is the SEER average reimbursement of GnRH agonist $g$ in year $t$. $W_{tg}$, the weight for GnRH agonist $g$, is the ratio of SEER-wide spending on that regimen to total spending on all GnRH agonists. Each medical ADT regimen was dose-standardized by converting each instance of GnRH agonist in use on separate days to a monthly dosing regimen. Intended duration was determined from the unit designation of the "carrier miles/time/units/serv count" field in carrier claims or the "revenue center unit count" field in outpatient claims. Claims for 12-month implant were assumed to represent 12 months of therapy regardless of unit designation.

The key explanatory variable for Aim 3, *pre-MMA ADT use*, is a provider-level measure based on the 3-year period of time preceding the first MMA implementation in 2004. It is calculated as each physicians' average annual proportion of patients receiving primary ADT, defined as GnRH agonists claims only, during the pre-MMA years 2000–2003. Orchiectomy is excluded from the independent variable definition, because MMA affected only reimbursement

for medical ADT and not surgical ADT. Thus, we would not expect orchiectomy to be displaced by other care. Patient race is defined from SEER data and measured by five categories: 1) Non-Hispanic White; 2) Black or African-American; 3) Hispanic; 4) Other; or 5) Unknown.

***Control Variables***

In addition, we included physician, practice, and patient constructs associated with prostate treatment decision, quality of care, or responsiveness to incentives in all three aims.

*Patient Factors*

Clinical Factors: Because staging systems used in SEER changed over the study period, Extent of Disease-1988 3rd edition variables for patients diagnosed from 2000–2003 and Collaborative Staging variables for patients diagnosed 2004–2007 were mapped to American Joint Committee on Cancer staging variables used for treatment by the National Comprehensive Cancer Network guidelines (12, 20). We included age and the NCI Comorbidity Index (NCI CI), which is derived from relevant medical conditions appearing in hospital and physician claims; it predicts mortality in prostate cancer with greater statistical efficiency than other common comorbidity measures such as the Charlson Comorbidity Index (107).

*Treatment Support*: We compared men married/living with a partner to those single, widowed or divorced, and those with missing marital status. We also assessed their use of consultations in the prostate cancer treatment decision (108). Primary Care Use was >1 visit to the same primary care physician occurring in 1) the 12 months prior to diagnosis; and, 2) the window between diagnosis and treatment. Specialist Care Use was three binary variables indicating presence of >1 prostate-related carrier claim filed by a radiation oncologist, urologist, or medical oncologist between diagnosis and the earliest of first treatment date or 12 months (108).

*Healthcare access*: We included several geographic indicators: SEER region, collapsed by state; rurality of the community in which the patient resided at diagnosis (<2,500 residents versus >2,500 residents); and community deprivation defined as quartile of median income of

the patients' zip code of residence and as quartiles of proportion of adults residing in the patients' zip code with less than high school education.

*Provider Factors*

Using data available from the AMA and Medicare Hospital files, we controlled for: (1) physician gender; (2) medical professionalization defined by a binary indicator of board certification and a categorical indicator measuring the degree of affiliation with an academic institution (none, some, or missing) (109, 110); and (3) training location (U.S. versus non-U.S.).

*Practice Factors*

We controlled for *panel size*, measured by tertiles of the number of Medicare fee-for-service prostate cancer patients/year/physician (60). A providers' ability to spread practice income losses across other providers may affect his or her ability to compensate for reimbursement cuts and may limit exposure to emerging research. Thus, we controlled for *practice type* (solo practitioner, group practice or missing). Finally, because a physician's patient panel also affects decision making, we controlled for the *proportion of a practice's Medicare patients that are minority*, categorized into tertiles following other studies of prostate cancer care in minority-enriched practices (111).

The degree to which providers are reliant on a particular payer will influence the providers' responsiveness to reimbursement cuts. Thus, for the analyses assessing group practices, we also controlled for the practices' self-reported *proportion of Medicare and Medicaid patients*. We expected those with greater proportions of Medicare patients to change overuse to a greater degree. We also controlled for practice size, a practice-reported count of the number of providers in each practice.

*Environmental factors*

In Aim 1, we controlled for changes due to MMA and other temporal factors by including indicator variables for diagnosis in each MMA implementation period: pre-MMA, 2000–2003;

MMA implementation, 2004–2005; and, post-MMA, 2006–2007. In Aims 2 and 3, we controlled for time by including variables for each year of the study.

**Statistical Analyses**

Across all Aims, bivariate analyses were conducted with t-tests and analysis of variance (continuous variables) and Pearson chi-squared tests (binary and categorical variables), as appropriate. In Aim 1, descriptive statistics are shown by patient for patient-level factors and by physician for physician-level factors (rather than patient-physician observations). Previous studies demonstrate high intraclass correlation among providers in prostate cancer treatment (58). Thus, to test the main hypotheses we used multilevel mixed logistic regression models that controlled for clustering of patients within provider and for repeated measures of physicians over time to calculate odds ratios and differential effects. We calculated the fixed portion of marginal effects for time in practice in each MMA period using mean and modal values of covariates. Interaction terms were constructed to test differential effects by MMA implementation period.

Model fit was tested in a 50% random sample. Likelihood ratio tests were used to determine appropriateness of inclusion of constructs in the model and of allowing both intercepts and slopes to vary randomly by physician. We compared random slope and random intercept model fit with the Bayesian Information Criterion (BIC). Stata/SE 12.1 was used for all analyses (112).

*Aim 1 Sensitivity Analysis*. Only 14% of all prostate cancer patients (including those with advanced disease) are thought to have prostate-specific antigen (PSA) levels greater than 20 ng/mL—the cut point qualifying localized prostate cancer patients for high-risk disease. In addition, a sizeable number of men qualify for high-risk disease based on more than one risk factor. Thus, some men in our sample may have been eligible for ADT. Because we cannot exclude men based on PSA levels, the analysis was repeated in a subsample of men with <5 years actuarial life expectancy at year of diagnosis and age <88 for most years, except 2004, when 5-

year life expectancy was reached at age 89, and 2005, when 5-year life expectancy was reached at age 87 (113-120).

For Aim 2, we used multiple imputation to impute missing values of the proportions of Medicare patients seen within practices. We categorized RGI dichotomously, dividing the sample into a group whose reimbursement generosity was negative or zero and a group whose reimbursement generosity was positive, and then conducted bivariate analyses with Pearson's chi-squared tests and t-tests to describe sample differences by reimbursement level. Descriptive statistics are presented for the sample of patients, the main unit of analysis, but physician characteristics are aggregated by physician. Due to high intraclass correlation among providers in prostate cancer treatment (58), we used multilevel mixed logistic regression models that controlled for clustering of patients within provider and for repeated measures of physicians over time. We created a sub-sample, further limiting the cohort to urologists identified by the AMA as practicing in a group practice to study the moderating effect of group practice organizational type on RGI and included an interaction term to capture it. Statistical significance was evaluated at $\alpha=0.05$ for all tests. Stata/SE 12.1 was used for all analyses (112).

For Aim 3, we stratified the patient sample by physician guideline concordance and assessed differences between groups by comparing the frequencies and proportions of binary and categorical variables and the means and standard deviations of each continuous variable. We used a common benchmark (121) to stratify physician guideline concordance; physicians were defined as high-concordance when 80% or more patients received guideline-concordant care, or alternatively defined as non-high concordance. Multilevel logistic regression was used to model the association between pre-MMA ADT use on guideline-concordant care. Separate multilevel logistic regression models comparing the effect of pre-MMA use on each modality alternative within multi-modality treatment options were run. Statistical significance was determined at $\alpha=0.05$, and Stata/SE 12.1 was used for all analyses (112).

# CHAPTER 4 CHANGES IN PRIMARY ANDROGEN DEPRIVATION THERAPY OVERUSE: RESPONSE TO REIMBURSEMENT AND CHARACTERISTICS ASSOCIATED WITH CHANGE

## Introduction

Prostate cancer is a prevalent and costly disease for which the guideline-recommended treatment options are equivocal for most men (1, 9, 19). Nonetheless, the harms of one widely used treatment in the previous two decades, primary androgen deprivation therapy (PADT), are known to outweigh its benefits among men with localized disease (22, 26-29). Although ADT, a long-lasting physician-administered drug that blocks testosterone to slow tumor growth, is recommended for some men receiving radiation, ADT by itself was recommended only for a small group of patients with localized disease in the early 2000s.

Despite the paucity of data supporting its clinical effectiveness in localized disease, PADT use in localized prostate cancer grew steadily from the 1990s, peaking in 2003 (10, 18, 40-42). Although clinical characteristics and patient preferences were thought to influence ADT overuse, most variation in prostate cancer treatment has been attributed to physician practice style (31, 58). Aggressive pharmaceutical marketing practices and liberal Medicare reimbursement for Part B drugs made ADT extremely profitable for physicians administering the drug (47, 48), costing Medicare more than $1 billion annually. Because Medicare reimbursement for physician-administered drugs covered under Medicare Part B (including ADT) far exceeded physician costs, the Medicare Modernization Act (MMA) of 2003 reduced the profitability of ADT administration in two phases implemented January 1, 2004 and January 1, 2005. Together these policies were associated with a 65% decrease in physician reimbursement for ADT from 2003 to 2005 (47). Subsequently, ADT use declined 34% after 2005. Although most of the decline occurred among men for whom ADT was not indicated (10, 39), 25.7% of men for whom

it is not recommended received PADT in 2005 (39, 40). Thus, understanding characteristics of physicians who persistently overuse ADT—despite reimbursement changes—is essential to improving quality of care.

Although prior results are mixed, physicians with the longest time in practice may be the least receptive to reimbursement changes (57). Experienced physicians' lack of response is concerning. Urologists are delaying retirement due to perceived physician shortages (62), and the delay might further slow quality improvement in prostate cancer care. In addition, a decrease in reimbursement can result in multiple behavioral responses, motivating providers to increase, replace, or drop the discounted service (36). Previous analysis of cancer specialists' response to the MMA suggests that physicians increased the use of discounted treatments (51, 57), so it is possible that reimbursement changes may have intensified ADT overuse.

This study sought to investigate the role of physician characteristics in persistent ADT overuse in localized prostate cancer by: 1) developing a model of physician characteristics associated with persistent and increasing overuse; 2) assessing whether time in practice was associated with persistent and increasing overuse; and, 3) identifying patterns of response to reimbursement changes. We hypothesize that physicians with greater time in practice may be less responsive to reimbursement changes.

## Methods

We conducted a retrospective, longitudinal analysis using a large, national population-based sample of elderly prostate cancer patients. The study was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

### *Data Sources*

We linked the Surveillance, Epidemiology and End Results (SEER)-Medicare database to the American Medical Association (AMA) physician Masterfile. SEER is a collection of population-based cancer registries in 17 geographic areas (90). Data are linked to administrative claims of Medicare, which covers medical services for more than 97% of the U.S. population 65

years of age and older, approximately 81% of whom are covered under fee-for-service (91, 122). The AMA Masterfile is a comprehensive database describing approximately 800,000 member and non-member physicians in the United States. Confirmed data originate from training and certification records and are supplemented by data from annual surveys of one-third of physicians and other physician regulatory agencies (92).

### *Cohort Definition*

*Patient Selection Criteria.* We identified all men diagnosed with incident adenocarcinoma of the prostate between January 1, 2000 and December 31, 2007. Only patients experiencing their first and only cancer, as indicated by SEER, were included. We excluded patients whose comorbidities could not be ascertained and/or whose initial treatment could not be ascertained including those who were younger than 66 years and lacking a complete year of claims; diagnosed at autopsy, death certificate, or at a nursing/convalescent facility, for similar reasons; not enrolled in fee-for-service (defined as continuous Part A and B coverage and not in an HMO for at least 12 months post diagnosis); died within 12 months of diagnosis; and/or diagnosed in Louisiana (due to disruptions in health services cause by Hurricane Katrina). The Tumor Node Metastasis (TNM) staging system was used to restrict the cohort conservatively to patients for whom ADT is not NCCN guideline-recommended across the study period. Men in the ADT-ineligible sample were those who lacked evidence of nodal or metastatic involvement and had no greater than unilateral, stage T2 tumors and World Health Organization grades 1–2 (10). Thus, we excluded men diagnosed with 1) T1 or T2 cancers with Gleason scores 8–10; 2) T2b tumors before 2002 when the staging definition changed; 3) T2c tumors after 2002 when the category was added; or, 4) T3a tumors. Men receiving external beam radiation therapy were also excluded, because the appropriateness of their ADT receipt could not be ascertained.

*Physician Inclusion Criteria.* Treating physicians were identified from claims. After limiting claims to those submitted for prostate cancer treatment, the physician responsible for

the majority of prostate cancer-related initial treatment claims was considered the treating physician.

***Measures***

*Dependent Variable.* ADT in conjunction with radiation is recommended therapy for some men with high-risk disease; however, ADT alone is not recommended. Thus, the outcome *primary ADT use* is a binary variable defined for each patient as an initial treatment claim for a HealthCare Common Procedure Coding System (HCPCS) code for medical ADT administered within 1 year from the SEER date of diagnosis without another non-surveillance prostate treatment administered within the treatment window. Non-surveillance treatments included orchiectomy, radical prostatectomy, all forms of radiation therapy planned or delivered (brachytherapy, conformal, IMRT, proton therapy), chemotherapy, and cryotherapy. All claims files were used to identify treatment delivered. Codes for other hormonal treatments were not considered part of the primary ADT definition. Appendix A lists the procedure codes used.

*Explanatory Variables. Time in practice* was calculated as the difference between a patient's SEER diagnosis date (averaged as the 15th day of the month) and the date of a physicians' medical degree (from the AMA Masterfile). We dichotomized time in practice as <20 versus ≥20 years. Previous studies assessing practice outcomes have defined time in practice with little theoretical rationale as: a continuous variable (101); dichotomized as we have done (102); a categorical variable with cut points at 5- or 10-year increments (103-105); or, as categories of low, medium, and high experience (60). We tested model fit for all specifications, including a quadratic term. The dichotomized specification best fit our data reflecting urology practice patterns.

*Control Variables.* We controlled for changes due to MMA and other temporal factors by including indicator variables for diagnosis in each MMA implementation period: pre-MMA, 2000–2003; MMA implementation, 2004–2005; and post-MMA, 2006–2007. In addition, we

included physician, practice, and patient constructs associated with prostate treatment decision, quality of care, or responsiveness to incentives.

Provider Factors: Using data available from the AMA and Medicare Hospital files, we controlled for: (1) *physician gender;* (2) *medical professionalization* defined by both a binary indicator of board certification and a categorical indicator measuring the degree of affiliation with an academic institution (none, some, or missing) (109, 110); and, (3) *training location* (U.S. versus non-U.S.). Practice factors included *panel size* (58), measured by tertiles of the number of Medicare fee-for-service prostate cancer patients/year/physician (60); *practice type* (solo practitioner, group practice or missing); and tertiles of *proportion of a practice's Medicare patients that are minority* (111).

Patient Factors:

*Clinical Factors*: Because staging systems used in SEER changed over the study period, Extent of Disease-1988 3rd edition variables for patients diagnosed from 2000–2003 and Collaborative Staging variables for patients diagnosed 2004–2007 were mapped to American Joint Committee on Cancer staging variables used for treatment by the National Comprehensive Cancer Network guidelines (12, 20). We included age and the NCI Comorbidity Index (NCI CI) with uniform weights, which is derived from relevant medical conditions appearing in hospital and physician claims (107, 123).

*Treatment Support:* We compared men married/living with a partner to those single, widowed, or divorced and those with missing marital status. We also assessed proclivity to seek care and men's use of consultations in the prostate cancer treatment decision (108). *Primary Care Use* was any claim in the 12 months prior to diagnosis (86). *Primary care consultation* was >1 visit to the same primary care physician occurring in both 1) the 12 months prior to diagnosis; and, 2) the window between diagnosis and treatment (108). *Specialist Care* was three binary variables indicating the presence of ≥1 prostate-related carrier claim filed by a radiation

oncologist, urologist, or medical oncologist between diagnosis and the first treatment date or 12 months, whichever is earlier (108).

*Patients' healthcare access*: We included several geographic indicators: *SEER region*, collapsed by state; *rurality* of the community in which the patient resided at diagnosis (<2,500 residents versus ≥2,500 residents); and *community deprivation*, defined as quartile of median income of the patients' zip code of residence and as quartiles of proportion of adults residing in the patients' zip code with less than high school education.

*Analysis*

Bivariate analyses were conducted with t-tests and analysis of variance (continuous variables) and Pearson chi-squared tests (binary and categorical variables). Descriptive statistics are shown by patient for patient-level factors and by physician for physician-level factors (rather than patient-physician observations). Previous studies demonstrate high intraclass correlation among providers in prostate cancer treatment (58). Thus, to test the main hypotheses we used multilevel mixed logistic regression models that controlled for clustering of patients within provider and for repeated measures of physicians over time to calculate odds ratios and differential effects. We calculated the fixed portion of marginal effects for time in practice in each MMA period using mean and modal values of covariates. Interaction terms were constructed to test differential effects by MMA implementation period.

Model fit was tested in a 50% random sample. Likelihood ratio tests were used to determine the appropriateness of inclusion of constructs in the model and of allowing both intercepts and slopes to vary randomly by physician. We compared random slope and random intercept model fit with the Bayesian Information Criterion (BIC). Stata/SE 12.1 was used for all analyses (112).

*Sensitivity Analysis.* Only 14% of *all* prostate cancer patients (including those with advanced disease) are thought to have prostate-specific antigen (PSA) levels >20 ng/mL—the cut point qualifying localized prostate cancer patients for high-risk disease. In addition, a

sizeable number of men qualify for high-risk disease based on more than one risk factor. Thus, some men in our sample may have been eligible for ADT. Because we cannot exclude men based on PSA levels, the analysis was repeated in a subsample of men with <5 years actuarial life expectancy at year of diagnosis: age <88 for most years, except 2004, when 5-year life expectancy was reached at age 89, and 2005, when 5-year life expectancy was reached at age 87 (113-120).

**Results**

Urologists prescribed 94.6% of the primary ADT observed in the cohort. Thus, we excluded other physicians from the main analysis. Consequently, the final sample included 12,943 men diagnosed with T1 and T2 well- or moderately-differentiated prostate cancer from 2000 through 2007, and treated through 2008 by 2,138 urologists (Figure 4.1).

*ADT Overuse.* Among the men treated by urologists from 2000–2008, 18.5% received primary ADT (Table 4.1). However, primary ADT overuse decreased from 21.0% before MMA implementation to 17.6% during the implementation phase, and ultimately to 13.6% following full deployment of the policy (Figure 4.2).

*Time in Practice.* In the unadjusted analysis, more experienced urologists' rates of ADT overuse declined less sharply over time compared to their less experienced counterparts (Figure 4.2). Overall, 19.4% of patients of more experienced urologists received primary ADT whereas 16.9% of patients of less experienced urologists received this treatment (Table 4.1). However, the patients of more experienced physicians differed from patients seen by their less experienced peers. Experienced physicians' patients were slightly older, spread disproportionately across SEER regions, and were more likely to be non-Hispanic black, Hispanic, unmarried, or live in communities with fewer resources (Table 4.1). Slightly less than two-thirds of urologists had been in practice ≥20 years, and they were more likely to be male or U.S.-trained; lack medical school affiliation; or be solo practitioners than physicians with fewer years in practice (Table 4.2).

*Adjusted Analysis.* A multilevel random intercepts model best fit the training data; coefficients were similar in the validation data. The interaction of time in practice and MMA period was not jointly significant and therefore not included in the final model (Table 4.3). After adjusting for patient and physician characteristics and secular changes, time in practice was not associated with primary ADT overuse or increasing overuse (OR 0.89, 95% CI 0.75, 1.05). However, being a solo practitioner substantially increased the odds of primary ADT overuse compared to urologists in group practice (OR 1.65, 95% CI 1.34, 2.02). In addition, having a medical school affiliation was associated with lower odds of overuse (OR 0.65, 95% CI 0.55, 0.77), compared to those with no affiliation.

At the patient level, increased age, greater comorbidity, being in a racial/ethnic minority, high utilization of primary care in the prior year, and receiving a radiation oncology consultation prior to treatment were associated with increased odds of primary ADT overuse (Table 4.3). Non-Hispanic blacks (OR 1.76; 95% CI 1.37-2.27), Hispanics (OR 1.41; 95% CI 1.12, 1.79), and men of "other" race (OR 1.44; 95% CI 1.04, 1.99) all had greater odds of receiving unnecessary ADT compared to Non-Hispanic whites. Receiving a primary care consultation and being in the highest income category was associated with lower odds of ADT overuse.

In sensitivity analysis, removing 453 men who were NCCN guideline-ineligible for primary ADT by virtue of their age and year of diagnosis produced no difference in the size or significance of effects (analysis not shown). When examining differential effects for the fixed effects portion of provider and practice characteristics (Table 4.4), partial effects of time in practice were not significant and did not differ by MMA period (confidence intervals not shown). In contrast, differential effects of practice type and medical school affiliation were significant.

*Physician Practice Changes.* Although overall primary ADT use declined incrementally over the period, in unadjusted analysis three patterns of physician response appeared (Figure 4.3). *Static users* (n=1,478) had low levels of ADT use at entry into the cohort and either

continued to use primary ADT infrequently following MMA implementation or contributed data in only one MMA period. This group treated the most patients (n=5,809). Among those who had the highest levels of primary ADT use in 2000 (n=394), overuse averaged 23.1% over the period but decreased sharply in 2004, and by 2008 these *decreasing users* had levels of use similar to static users. A third group of urologists (n=276), *increasing users*, sharply increased their use of primary ADT in 2004 and maintained even higher levels of primary ADT use after MMA implementation. Their average overuse was 32.6% among the 2,817 patients they treated over the study period.

**Discussion**

The purpose of this study was to create a model of physician characteristics associated with changes in ADT overuse; test the association of time in practice with ADT overuse; and, describe physician-level changes in ADT use. Contrary to some previous work (61), time in practice was not associated with urologists' overuse of ADT in localized prostate cancer after adjusting for other physician and patient factors. Two prevailing theories offer insight into why this may be so. Economic theory suggests that physicians' treatment decisions and willingness to change prescribing habits are influenced by their need to balance ethical obligations to choose the best treatment for their patients and their own financial interests to limit the marginal "costs" of the treatments offered (86). Although this suggests physicians may respond to financial incentives to optimize income, physicians later in their career may be less responsive to reimbursement cuts because they are more likely to have repaid major debts (57). Educational theory suggests more experienced physicians may be less aware of and responsive to emerging evidence and guideline recommendations. Thus, even if more experienced physicians were not responding to reimbursement, they still may not have changed their patterns of ADT overuse.

Our results are similar to an earlier study (60) in which the least and most experienced urologists were more likely to use ADT for treating prostate cancer patients. However, when the sample was restricted to patients for whom ADT had uncertain benefit (similar to our cohort),

time in practice was not a significant factor. Studies that have found time in practice to be associated with poor quality of care have not been conducted in fee-for-service Medicare, but in HMOs and the Canadian health system (124-128). These differences in findings based on reimbursement context suggest that more experienced physicians may succumb to clinical inertia or lapsed technical skill, but this may be overcome by changing or aligning financial incentives. Interestingly, our study differs from a recent study that found a significant inverse relationship between time in practice and cost across treatments and physician specialties (105). Of note, that cross-sectional study was limited to between-physician comparisons and care delivered in the state of Massachusetts, a state with the third highest HMO penetration among the United States (129). Our study assessed not only between-physician differences among urologists with varying experience levels but also within-physician differences (i.e., changes in physicians' treatment decisions for similar patients as they gained time in practice).

Although our study design did not rule out cohort effects in which the training experience imprints a physician signature, time in practice by itself does not appear to affect overuse. Instead, we found that ADT overuse was concentrated in solo practitioners. Other studies assessing physician characteristics of ADT overuse have not considered practice type in their analyses (60), although solo practice has been identified as a barrier to innovation adoption (130). Whether these physicians are isolated from other physicians who might influence them to align with guidelines or are more motivated by financial factors to prescribe ADT is unknown. Nonetheless, because ADT overuse was found among 25.7% of patients seen in solo practices (compared to 17.1% of patients seen in group practices), and more urologists (23%) practice as solo practitioners than any other surgical specialty (131), they are an important target for quality improvement.

Urologists who overuse ADT also were more likely to lack professional affiliation with a medical school, which may make them hard to reach for intervention. Other studies have also found professional affiliation to be associated with higher quality of care (132). Physicians

affiliated with medical schools may have resources (e.g., trainees, tumor boards) that encourage guideline-concordant practice. Alternately, physicians who affiliate with a medical school may lack motivation for financial gain, as it is well established that academic physicians forgo compensation (133, 134). We cannot identify reasons for this association, but either motivation could make it difficult to engage these physicians in traditional quality improvement efforts.

Consistent with other studies, we found that ADT overuse declined precipitously over the 2000s, a drop that was coincident with reimbursement policy changes (10, 39). Our study shows that ADT overuse continued on a downward trajectory in the 2 years following full MMA implementation. Nonetheless, ADT overuse remains a problem even in the post-MMA period, in which 14% of men with T1 or T2 tumors and well- or moderately differentiated cancer were prescribed primary ADT. Post-MMA consensus guidelines do not recommend PADT for these men, as harms are well-recognized without evidence of benefit (21, 22, 26-28). Of concern, primary ADT use among men with high-risk localized prostate cancer is even higher (135); thus the problem may extend to an even larger group of men than studied here. Moreover ADT overuse remains costly. Direct Medicare costs—not including the treatment of adverse events attributable to ADT—have been estimated at $42 million per year for all risk groups (135).

We also hypothesized that urologists might intensify ADT overuse in response to the reimbursement cut. Although ADT overuse significantly declined, in this study we identified three distinct types of volume response: 1) static use; 2) decreasing use; and, 3) increasing use. Economists have observed a volume response to other cancer care reimbursement changes (51, 57), but interestingly, not among urologists in other reimbursement contexts (64, 65, 136, 137). Because we identified differing responses among physicians in a single specialty subject to the same reimbursement change, we further explored characteristics of these physicians. Non-responders, those who had low rates of use that remained stable over time, differed from responders in both physician characteristics and patient panels (data not shown).

Although we observed two distinct patterns among responders, we could not distinguish urologists who increased from those who decreased ADT utilization based on physician characteristics. The largest group of responders, urologists who decreased ADT overuse, began the study period with high rates of overuse but sharply decreased use to that of non-responders. However, a sizeable group of urologists sharply increased ADT overuse coincident with reimbursement cuts. Although increasing users diminished in number over the study period, they saw a large number of patients and are a cause for concern and a target for intervention: their ADT overuse remains over 30%. Responders—both increasing and decreasing users—shared statistically similar physician characteristics (Table 4.5). The patient panels of increasing users were significantly different than those of decreasing users (Table 4.6); however, increasing users' patients were older, had more comorbid conditions, and were more likely to be non-Hispanic black or "other" race. They resided in communities with fewer resources and were less likely to receive radiation oncology consultations. Although we cannot distinguish whether urologists were responding to their changing patient population or were more likely to have more socially vulnerable patients, the characteristics of patients within these practices may point toward another source of prostate cancer treatment disparities. In addition, our study suggests an alternative explanation for volume response. Economic studies rarely assess patient-level factors in accounting for induced demand following reimbursement cuts (138). Urologists who increased ADT overuse coincident with reimbursement cuts had older patients than urologists who decreased ADT overuse after MMA implementation. Studies consistently show that older patients are more likely to be prescribed ADT, despite the lack of recommendation for this treatment. Our study suggests that increasing overuse could be a rational but clinically inappropriate response to a changing patient panel. For increasing overusers, the lack of treatment alternatives, and possibly referral options, for older patients may encourage overuse. Future assessments of volume response should consider characteristics of the patient panel to better understand responsiveness to financial incentives.

There are several limitations of our study. First, we excluded patients treated by non-physician providers. As a result, our sample disproportionately excluded younger men, minorities, patients in the lower median income quartiles, those with well-differentiated or T1 tumors, and those not receiving primary ADT. Thus, our findings do not represent the full experience of these patients and cannot be extrapolated to treatment decisions made by mid-level providers, even in a fee-for-service environment. Secondly, we restricted our study to urologists because they make most treatment decisions about ADT for patients with localized prostate cancer. Thus, our findings may not be generalizable to other physician specialties. Third, PADT was recommended for a small group of men in the early 2000s. However, in sensitivity analysis, removing patients likely to have fewer than 5 years life expectancy did not change the results. Finally, although we used a national registry, patients in SEER are not selected randomly. Nonetheless, the SEER population is comparable to the U.S. population in terms of poverty and education, and represents more than 26% of the African-American population in the U.S. (90). Further, characteristics of urologists in our study mirror national trends (139), suggesting that these results are generalizable.

***Research and Policy Implications***

Approximately 30%–40% of healthcare spending in the U.S. has been attributed to *overuse*, the provision of unnecessary care for which harms outweigh benefits (71-73). Overuse results in patient harms, health disparities, and waste in a healthcare system already stretched to capacity (73). Despite being designated a significant quality problem and national priority (74), relatively little research focuses on the problem of overuse or strategies to address it (71, 75). We found that among urologists providing care in fee-for-service Medicare, physicians' time in practice, whether a proxy for diminishing economic motivation or educational disinterest, was not associated with overuse. Physician retirement, even if delayed, may not result in improving prostate cancer quality. Future studies should compare the effect of time in practice

among physicians practicing in multiple payer environments, or control for the proportion of care that is delivered under fee-for-service mechanisms.

In addition, we found that reimbursement policies may not have uniform results in some physician populations, suggesting that additional research assessing physician response to reimbursement is necessary. Reimbursement strategies may need to be tailored to physician specialty, practice dynamics, and patient panels to reduce overuse overall. We also demonstrated that the patient panels of increasing users differ significantly from that of urologists who responded to reimbursement cuts in the expected direction. Of concern, older patients and minority patients were more vulnerable to overuse, despite reimbursement changes to disincentivize ADT use. Quality in prostate cancer care may be improved by discouraging the use of primary ADT in the oldest patients, but research and guidelines are needed to address appropriate treatment for the oldest patients. No localized prostate cancer studies of which we are aware adequately account for the overuse of ADT in ethnic and racial minorities. Whether unmeasured frailty, incomplete reporting of disease severity, patient preference, or physician bias is responsible should be determined. Finally, we identified an important group of physicians who may need additional support in reducing overuse. Although ADT overuse has declined significantly during and after MMA implementation, overuse remains high among professionally isolated urologists. Most physician intervention studies target all physicians or work through networks of physicians affiliated with academic research partners. Few studies focus on the needs of solo practitioners who lack these affiliations. Finally, understanding the characteristics of group practice that make it protective against primary ADT overuse could be instructive. Whether the added financial vulnerability of physicians practicing on their own engenders this behavior or whether isolation from timely and relevant knowledge prevents adoption of quality of care practices should be determined.

**Figure 4.1. Cohort Exclusions**

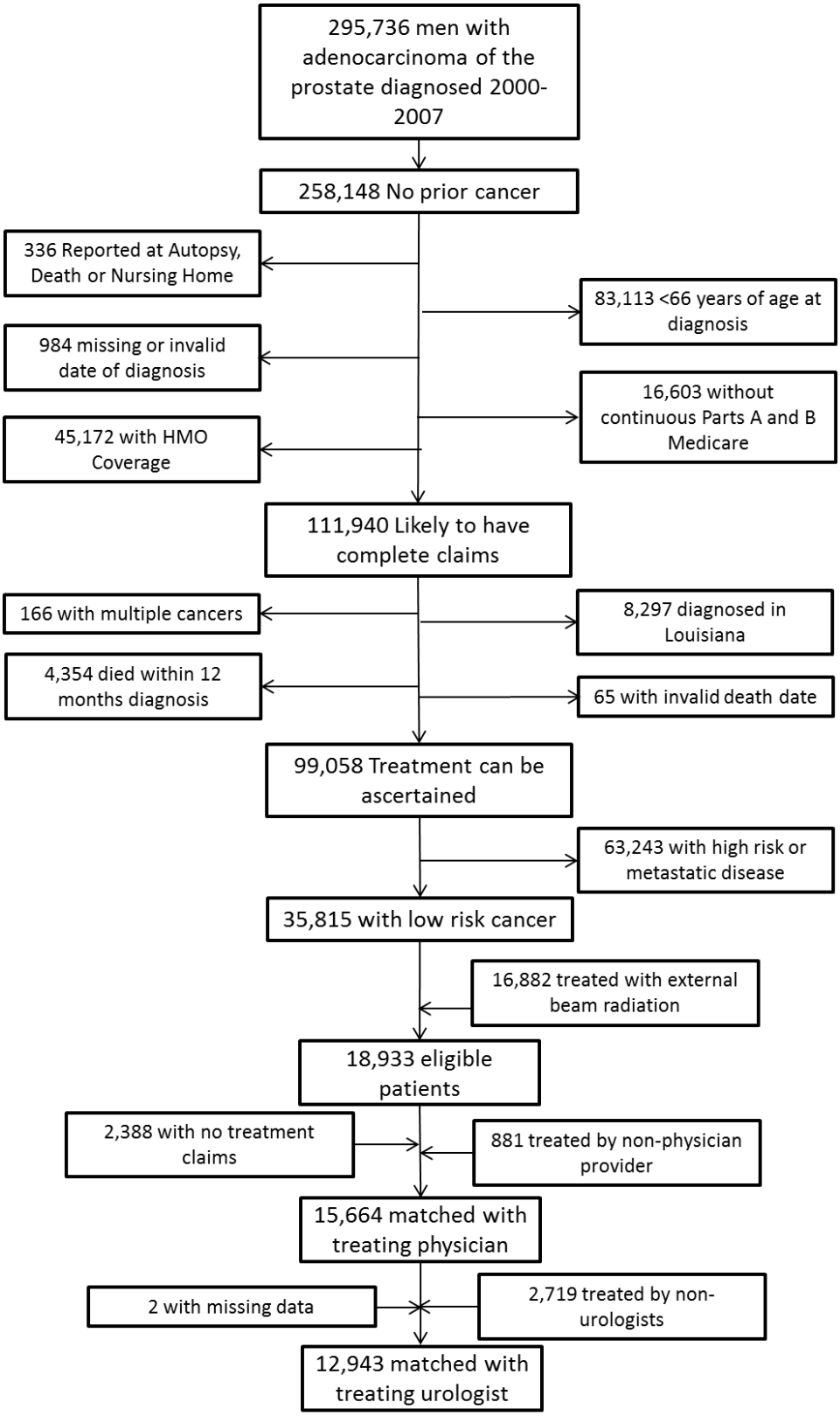
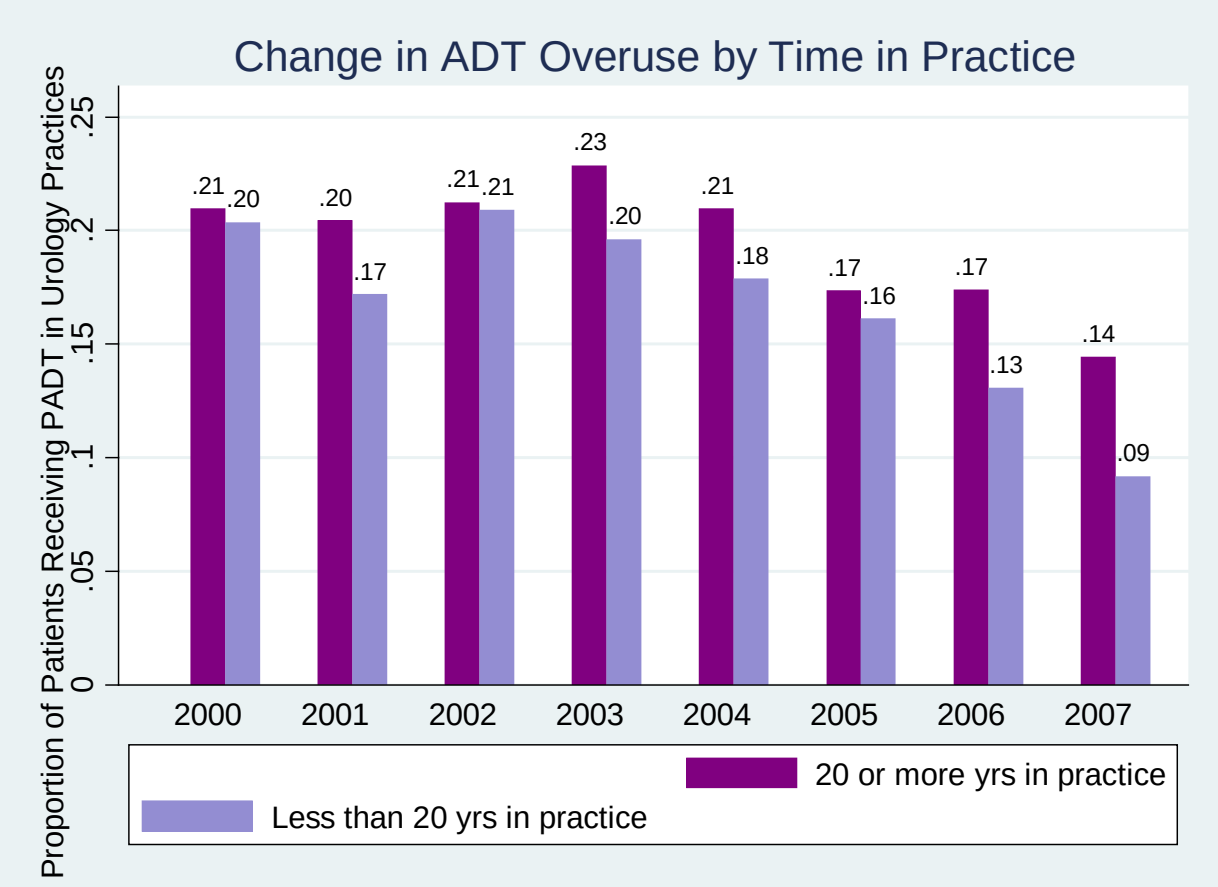
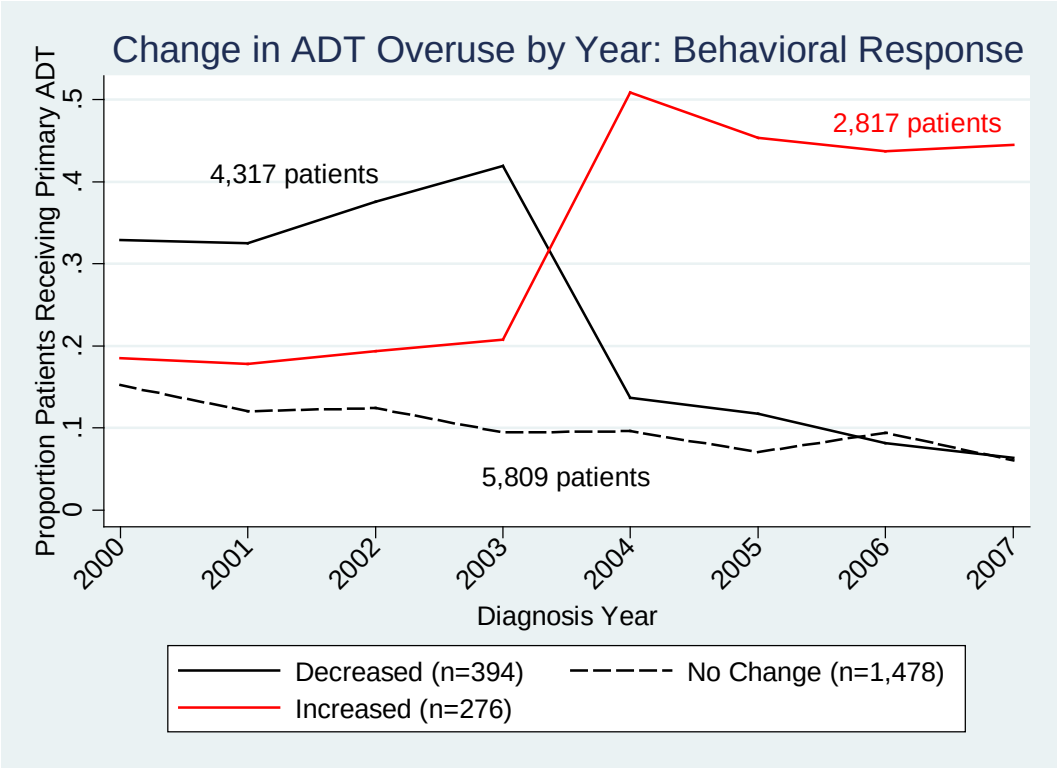


**Figure 4.2. Change in ADT Overuse by Time in Practice**




*unadjusted

**Figure 4.3. Change in ADT Overuse by Year: Behavioral Response**




*unadjusted

**Table 4.1. Sample Characteristics by Physician Time in Practice—Patient Characteristics**

| | Overall | <20 years | ≥20 years | |
|---|---|---|---|---|
| | N (%) or Mean (Standard Deviation) | | | *p-value* |
| | **N=12,943** | **N=4,273** | **N=8,670** | |
| **Primary ADT** | 18.5 | 721 (16.9%) | 1,679 (19.4%) | *<0.001* |
| **Period of MMA Implementation** | | | | *0.51* |
| Pre-MMA Implementation | 54.3 | 2,290 (53.6%) | 4,734 (54.6%) | |
| MMA Implementation Period | 23.1 | 1,009 (23.6%) | 1,981 (22.8%) | |
| Post-MMA Implementation | 22.6 | 974 (22.8%) | 1,955 (22.5%) | |
| **T Stage** | | | | *0.48* |
| T1 | 79.9 | 3,428 (80,2%) | 6,910 (79.7%) | |
| T2 | 20.1 | 845 (19.8%) | 1,760 (20.3%) | |
| **Grade** | | | | *0.009* |
| Well differentiated, 2–4 | 5.0 | 179 (4.2%) | 471 (5.4%) | |
| Moderately differentiated 5–7* | 92.9 | 4,008 (93.8%) | 8,017 (92.5% | |
| Missing | 2.1 | 86 (2.0%) | 182 (2.1%) | |
| **Comorbidities** | | | | *0.14* |
| 0 | 67.3 | 2,930 (68.6%) | 5,778 (66.6%) | |
| 1 | 21.4 | 891 (20.9%) | 1,882 (21.7%) | |
| 2 | 6.7 | 268 (6.3%) | 602 (6.9%) | |
| ≥3 | 4.6 | 184 (4.3%) | 408 (4.7%) | |
| **Mean Age (SD)** | 74.1 (6.1) | 73.4 (6.0) | 74.4 (6.2) | *<0.001* |
| **Race/ethnicity** | | | | *0.004* |
| Non-Hispanic White | 77.8 | 2,298 (79.5%) | 6,678 (77.0%) | |
| Non-Hispanic Black | 6.6 | 273 (6.4%) | 586 (6.8%) | |
| Hispanic | 7.5 | 280 (6.6%) | 688 (7.9%) | |
| Other | 4.1 | 177 (4.1%) | 350 (4.0%) | |
| Missing | 4.0 | 145 (3.4%) | 368 (4.2%) | |
| **Marital Status** | | | | *0.04* |
| Not Married | 19.7 | 799 (18.7%) | 1.751 (20.2%) | |
| Married | 68.4 | 2934 (68.7% | 5920 (68.3% | |
| Missing | 11.9 | 540 (12.6%) | 999 (11.5%) | |
| **Pre-treatment Primary Care Use** | | | | *0.49* |
| 0–2 visits in prior year | 18.9 | 805 (18.8%) | 1,645 (19.0%) | |
| 3–5 visits in prior year | 43.6 | 1,892 (44.3%) | 3,747 (43.2% | |
| ≥6 visits in prior year | 37.5 | 1,576 (36.9% | 3,278 (37.8%) | |
| **Primary Care Consultation** | | | | *0.08* |
| No | 43.9 | 1,831 (42.9%) | 3,854 (44.5%) | |
| Yes | 56.1 | 2,442 (57.1%) | 4,816 (55.5%) | |

| | | | | |
|---|---|---|---|---|
| **Radiation Oncology Consultation** | | | | *0.41* |
| No | 84.9 | 3,610 (84.5%) | 7,373 (85.0%) | |
| Yes | 15.1 | 663 (15.5%) | 1,297 (15.0%0 | |
| **Medical Oncology Consultation** | | | | *0.63* |
| No | 96.4 | 4,122 (96.5%) | 8,349 (96.3%) | |
| Yes | 3.6 | 151 (3.5%) | 321 (3.7%) | |
| **Urology Consultation** | | | | *0.41* |
| No | 1.0 | 49 (1.1%) | 86 (1.0%) | |
| Yes | 99.0 | 4,226 (98.9%) | 8,584 (99.0%) | |
| **Rural Residence** | | | | *0.83* |
| No | 98.1 | 4,193 (98.1% | 8,503 (98.1%) | |
| Yes | 1.9 | 80 (1.9%) | 167 (1.9%) | |
| **SEER Region** | | | | *<0.001* |
| Seattle | 4.4 | 226 (5.3%) | 345 (4.0%) | |
| Connecticut | 6.0 | 274 (6.4% | 508 (5.9%) | |
| Detroit | 7.0 | 291 (6.8% | 617 (7.1%) | |
| Hawaii | 0.9 | 45 (1.1%) | 77 (0.9%) | |
| Iowa | 6.2 | 261 (6.1% | 538 (6.2% | |
| New Mexico | 3.8 | 144 93.4%) | 347 (4.0%) | |
| California | 39.2 | 1,597 (37.4%) | 3,479 (40.1%) | |
| Utah | 4.3 | 223 (5.2%) | 333 (3.8%) | |
| Georgia | 2.7 | 108 (2.5%) | 236 (2.7%) | |
| Kentucky | 9.7 | 373 (8.7%) | 887 (10.2%) | |
| New Jersey | 15.7 | 731 (17.1%) | 1,303 (15.0%) | |
| **Median Income of Patients' Communities** | | | | *<0.001* |
| <$35,031 | 20.7 | 759 (17.8%) | 1923 (22.2%) | |
| $35,051–$46,079 | 24.8 | 1,033 (24.2%) | 2,181 (25.2%) | |
| $46,084–$60,668 | 24.3 | 1,103 (25.8%) | 2,040 (23.5%) | |
| $60,669–$200,008 | 25.8 | 1,182 (27.7%) | 2,163 (24.9%) | |
| Missing | 4.3 | 196 (4.6%) | 363 (4.2%) | |
| **Proportion of Patient's Community w/o High School Education** | | | | *<0.001* |
| 0%–9.7% | 25.7 | 1,166 (27.3%) | 2,163 (24.9%) | |
| 9.7%–15.5% | 24.3 | 1,126 (26.4%) | 2,014 (23.2%) | |
| 15.5%–25.2% | 23.1 | 966 (22.6%) | 2,019 (23.3%) | |
| 25.2%–100% | 22.7 | 821 (19.2%) | 2,116 (24.4%) | |
| Missing | 4.3 | 194 (4.5%) | 358 (4.1%) | |

P-values by t-test for continuous variables and chi$^2$ test for binary / categorical variables

**Table 4.2. Sample Characteristics by Physician Time in Practice—Physician Characteristics**

| | Overall | <20 years | ≥20 years | |
|---|---|---|---|---|
| | Mean (Standard Deviation) or Percent | | | *p-value* |
| | **N=2,138** | **N=923** | **N=1,215** | |
| **Mean Primary ADT Use 2000–2007 (SD)** | 0.2 (0.3) | 0.2 (0.3) | 0.2 (0.3) | *<0.001* |
| **Time in Practice** | 100.0% | 923 (38.8%) | 1215 (61.2%) | *<0.001* |
| **Physician Gender** | | | | *<0.001* |
| Male | 97.7% | 877 (95.0%) | 1212 (99.8%) | |
| Female | 2.3% | 46 (5.0%) | 3 (0.2%) | |
| **Board Certified** | | | | *0.65* |
| No | 6.8% | 60 (6.5%) | 85 (7.0%) | |
| Yes | 93.2% | 863 (93.5%) | 1130 (93.0%) | |
| **US Trained** | | | | *<0.001* |
| No | 15.9% | 39 (4.2%) | 301 (24.8%) | |
| Yes | 84.1% | 884 (95.8%) | 914 (75.2%) | |
| **Medical School Affiliation** | | | | *0.009* |
| None | 44.2% | 373 (40.4%) | 571 (47.6%) | |
| Some | 53.9% | 530 (57.4%) | 623 (51.3%) | |
| Missing | 1.9% | 20 (2.2%) | 21 (1.7%) | |
| **Physician Prostate Panel Size** | | | | *0.58* |
| 0–20 prostate patients/year | 64.3% | 589 (63.8%) | 785 (64.6% | |
| 21–37 prostate patients/year | 27.5% | 251 (27.2%) | 336 (27.7%) | |
| ≥38 prostate patients/year | 8.3% | 83 (9.0%) | 94 (7.7%) | |
| **Solo Practitioner** | | | | *<0.001* |
| No | 72.3% | 740 (80.2%) | 805 (66.3%) | |
| Yes | 21.6% | 89 (9.6%) | 373 (30.7%) | |
| Missing | 6.1% | 94 (10.2%) | 37 (3.0%) | |
| **Proportion of Patients Minority** | | | | *0.69* |
| 0%–6.1% | 38.0% | 360 (39.0%) | 453 (37.3%) | |
| 6.2%–19.5% | 27.5% | 253 (27.4%) | 336 (27.7%) | |
| ≥20.0% | 34.4% | 310 (33.6%) | 426 (35.1%) | |

P-values by t-test for continuous variables and $chi^2$ test for binary/categorical variables; time invariant physician measures described at first entry into cohort

**Table 4.3. Multilevel Logistic Regression Model of Time in Practice on Primary ADT Overuse**

| | Odds Ratio | 95% Confidence Limits | |
|---|---|---|---|
| **Time in Practice** | 0.89 | 0.75 | 1.05 |
| **Physician Gender** | 0.92 | 0.45 | 1.89 |
| **Board Certified** | 1.00 | 0.71 | 1.41 |
| **US Trained** | 0.78 | 0.62 | 0.99 |
| **Medical School Affiliation (compared to none)*** | | | |
| Some | 0.65 | 0.55 | 0.77 |
| Missing | 0.82 | 0.39 | 1.73 |
| **Prostate Patient Panel Size (compared to 0–20 patients/year)** | | | |
| 21–37 prostate patients/year | 1.04 | 0.89 | 1.21 |
| ≥38 prostate patients/year | 1.00 | 0.83 | 1.22 |
| **Solo Practitioner (compared to group practice)*** | | | |
| Yes | 1.65 | 1.34 | 2.02 |
| Missing | 0.82 | 0.55 | 1.23 |
| **Proportion of Patients Minority (compared to 0%–6.1% minority)*** | | | |
| 6.2%–19.5% | 0.79 | 0.66 | 0.93 |
| ≥20.0% | 0.81 | 0.66 | 1.00 |
| **Period of MMA Implementation (compared to Pre-MMA Implementation*** | | | |
| MMA Implementation Period | 0.78 | 0.68 | 0.91 |
| Post-MMA Implementation | 0.54 | 0.46 | 0.64 |
| **T Stage** | 1.36 | 1.19 | 1.57 |
| **Grade (compared to Well Differentiated)** | | | |
| Moderately differentiated 5–7* | 3.12 | 2.33 | 4.17 |
| Missing | 4.90 | 3.15 | 7.60 |
| **Comorbidities (Compared to None)** | | | |
| 1 | 1.29 | 1.13 | 1.48 |
| 2 | 1.25 | 1.01 | 1.55 |
| ≥3 | 1.46 | 1.14 | 1.87 |
| **Age (continuous)** | 2.30 | 1.88 | 2.82 |
| **Age squared** | 1.00 | 0.99 | 1.00 |
| **Race/ethnicity (compared to Non-Hispanic White)*** | | | |
| Non-Hispanic Black | 1.76 | 1.37 | 2.27 |
| Hispanic | 1.41 | 1.12 | 1.79 |
| Other | 1.44 | 1.04 | 1.99 |
| Missing | 1.84 | 1.40 | 2.41 |

| | | | |
|---|---|---|---|
| **Marital Status (compared to Unmarried)** | | | |
| Married | 0.91 | 0.79 | 1.05 |
| Missing | 1.64 | 1.34 | 1.99 |
| **Pre-treatment Primary Care Use (compared to 0–2 visits in prior year)*** | | | |
| 3–5 visits in prior year | 1.64 | 1.38 | 1.96 |
| ≥6 visits in prior year | 1.73 | 1.44 | 2.10 |
| **Primary Care Consultation** | 0.42 | 0.37 | 0.48 |
| **Radiation Oncology Consultation** | 1.73 | 1.47 | 2.05 |
| **Medical Oncology Consultation** | 1.03 | 0.76 | 1.40 |
| **Urology Consultation** | 6.03 | 2.93 | 12.41 |
| **Rural Residence** | 0.94 | 0.62 | 1.44 |
| **Region (compared to Seattle)** | | | |
| Connecticut | 4.45 | 2.56 | 7.74 |
| Detroit | 2.39 | 1.36 | 4.19 |
| Hawaii | 4.78 | 2.02 | 11.30 |
| Iowa | 3.38 | 1.90 | 6.01 |
| New Mexico | 2.63 | 1.37 | 5.04 |
| California | 2.54 | 1.56 | 4.15 |
| Utah | 1.46 | 0.76 | 2.83 |
| Georgia | 2.44 | 1.27 | 4.70 |
| Kentucky | 3.17 | 1.85 | 5.44 |
| New Jersey | 5.49 | 3.32 | 9.08 |
| **Median Income of Patients' Communities (compared to <$35,031)** | | | |
| $35,051–$46,079 | 0.83 | 0.69 | 1.00 |
| $46,084–$60,668 | 0.83 | 0.66 | 1.05 |
| $60,669–$200,008 | 0.66 | 0.50 | 0.88 |
| Missing | 6.60 | 0.72 | 60.11 |
| **Proportion of Patient's Community w/o High School Education (compared to <9.7%)** | | | |
| 9.7%–15.5% | 1.18 | 0.98 | 1.43 |
| 15.5%–25.2% | 1.24 | 0.99 | 1.55 |
| 25.2%–100% | 1.17 | 0.89 | 1.54 |
| Missing | 0.11 | 0.01 | 0.99 |
| **Constant** | 0.00 | 0.00 | 0.00 |

N=12,943 patients; 2,138 urologists

*Constructs tested for joint significance by likelihood ratio test of nested models:

Medical school affiliation—$X^2$=24.36, p<0.001
Solo practitioner— $X^2$=574.55, p<0.001
Proportion of patients minority— $X^2$=7.90, p=0.019
Period of MMA implementation— $X^2$=59.46, p<0.001
Race/ethnicity— $X^2$=39.33, p<0.001

**Table 4.4. Differential Effect of Physician Characteristics**

| Construct | MMA Period | Differential Effect | Standard Error | p-value |
|---|---|---|---|---|
| Time in Practice | Pre | -0.008 | 0.006 | 0.162 |
| | During | -0.007 | 0.005 | 0.165 |
| | Post | -0.005 | 0.004 | 0.169 |
| Solo Practice | Pre | 0.040 | 0.010 | 0.000 |
| | During | 0.033 | 0.009 | 0.000 |
| | Post | 0.025 | 0.007 | 0.000 |
| Some Medical School Affiliation | Pre | -0.024 | 0.005 | 0.000 |
| | During | -0.020 | 0.005 | 0.000 |
| | Post | -0.014 | 0.003 | 0.000 |

**Table 4.5. Comparison of Physician and Practice Characteristics of Behavioral Responders—Physician Characteristics**

| | Decreasing Users (N=394) | Increasing Users (N=276) | *p-value* |
|---|---|---|---|
| **Primary ADT** | 0.3 (0.2) | 0.3 (0.2) | *<0.001* |
| **Time in Practice** | | | *0.25* |
| <20 years | 36.5 | 32.2 | |
| ≥20 years | 63.5 | 67.8 | |
| **Gender** | | | *0.5* |
| Male | 98.7 | 99.3 | |
| Female | 1.3 | 0.7 | |
| **US Trained** | | | *0.34* |
| No | 15.0 | 17.8 | |
| Yes | 85.0 | 82.2 | |
| **Board Certified** | | | *0.34* |
| No | 4.8 | 6.5 | |
| Yes | 95.2 | 93.5 | |
| **Medical School Affiliation** | | | *0.37* |
| No | 54.8 | 59.4 | |
| Some | 44.9 | 40.6 | |
| Missing | 0.3 | 0.0 | |
| **Physician Prostate Panel Size** | | | *0.61* |
| 0–20 prostate patients/year | 32.5 | 30.4 | |
| 21–37 prostate patients/year | 42.9 | 46.7 | |
| ≥38 prostate patients/year | 24.6 | 22.8 | |
| **Solo Practitioner** | | | *0.89* |
| No | 72.1 | 71.4 | |
| Yes | 24.6 | 24.6 | |
| Missing | 3.3 | 4.0 | |
| **Proportion of Patients Minority** | | | *0.3* |
| 1 | 28.4 | 31.5 | |
| 2 | 36.5 | 30.8 | |
| 3 | 35.0 | 37.7 | |

**Table 4.6. Comparison of Physician and Practice Characteristics of Behavioral Responders—Patient Panel Characteristics**

| | Patients of Physicians who Increased ADT | Patients of Physicians who Decreased ADT | *p-value* |
|---|---|---|---|
| | Mean (Standard Deviation) or % | | |
| | (N=4,317) | (N=2,817) | |
| **Primary ADT** | 23.2 | 30.5 | *<0.001* |
| **Time in Practice** | | | *<0.001* |
| <20 years | 31.5 | 26.8 | |
| ≥20 years | 68.5 | 73.2 | |
| **T Stage** | | | *0.02* |
| T1 | 78.2 | 80.4 | |
| T2 | 21.8 | 19.6 | |
| **Grade** | | | *0.02* |
| Well differentiated, 2–4 | 4.5 | 5.9 | |
| Moderately differentiated 5–7* | 93.2 | 91.9 | |
| Missing | 2.3 | 2.1 | |
| **Comorbidities** | | | *0.18* |
| 0 | 65.8 | 63.8 | |
| 1 | 22.7 | 23.0 | |
| 2 | 6.8 | 7.7 | |
| ≥3 | 4.8 | 5.5 | |
| **Age (continuous)** | 74.6 (6.1) | 75.1 (6.3) | *<0.001* |
| **Race/ethnicity** | | | *<0.001* |
| Non-Hispanic White | 78.7 | 75.6 | |
| Non-Hispanic Black | 5.1 | 8.0 | |
| Hispanic | 8.7 | 6.8 | |
| Other | 2.9 | 5.3 | |
| Missing | 4.6 | 4.3 | |
| **Marital Status** | | | *0.75* |
| Not Married | 19.3 | 19.2 | |
| Married | 67.2 | 66.7 | |
| Missing | 13.5 | 14.2 | |
| **Pre-treatment Primary Care Use** | | | *0.15* |
| 0–2 visits in prior year | 18.6 | 17.5 | |
| 3–5 visits in prior year | 43.2 | 42.1 | |
| ≥6 visits in prior year | 38.2 | 40.4 | |
| **Primary Care Consultation** | | | *0.9* |
| No | 44.4 | 44.2 | |
| Yes | 55.6 | 55.8 | |

| | | | |
|---|---|---|---|
| **Radiation Oncology Consultation** | | | *<0.001* |
| No | 84.3 | 87.7 | |
| Yes | 15.7 | 12.3 | |
| **Medical Oncology Consultation** | | | *0.12* |
| No | 96.2 | 96.9 | |
| Yes | 3.8 | 3.1 | |
| **Urology Consultation** | | | *0.07* |
| No | 0.8 | 1.2 | |
| Yes | 99.2 | 98.8 | |
| **Rural Residence** | | | *0.38* |
| No | 98 | 97.7 | |
| Yes | 2.0 | 2.3 | |
| **SEER Region** | | | *<0.001* |
| Seattle | 2.3 | 2.4 | |
| Connecticut | 8.1 | 4.4 | |
| Detroit | 6.9 | 8.1 | |
| Hawaii | 0.3 | 1.4 | |
| Iowa | 6.9 | 5.6 | |
| New Mexico | 6.3 | 2.6 | |
| California | 39.1 | 34.4 | |
| Utah | 4.5 | 5.1 | |
| Georgia | 1.4 | 2.2 | |
| Kentucky | 9.2 | 15.1 | |
| New Jersey | 14.9 | 18.6 | |
| **Median Income of Patients' Communities** | | | *0.003* |
| $2,506–$35,031 | 21.2 | 24.6 | |
| $35,051–$46,079 | 26.4 | 25.7 | |
| $46,084–$60,668 | 23.3 | 23.6 | |
| $60,669–$200,008 | 24.9 | 22.7 | |
| Missing | 4.2 | 3.4 | |
| **Proportion of Patient's Community w/o High School Education** | | | *<0.001* |
| 0%–9.7% | 25.6 | 21.5 | |
| 9.7%–15.5% | 24.9 | 23.1 | |
| 15.5%–25.2% | 24.0 | 23.4 | |
| 25.2%–100% | 21.4 | 28.6 | |
| Missing | 4.1 | 3.4 | |

P-values by t-test for continuous variables and $chi^2$ test for binary / categorical variables

# CHAPTER 5 EFFECT OF REIMBURSEMENT CHANGES ON PRIMARY ANDROGEN DEPRIVATION THERAPY OVERUSE

## Introduction

Approximately 30-40% of healthcare spending in the U.S. has been attributed to *overuse*, the use of care in patients for whom it is not recommended (71-73). Overuse results in patient harms, health disparities and waste in a healthcare system already stretched to capacity (73). Despite being designated a significant quality problem and a national priority (74), relatively little research focuses on interventions to address overuse (71, 75). One strategy for limiting overuse is to decrease financial incentives. Specifically, limiting reimbursement is attractive because it may save money and simultaneously improve quality (39, 52).

Androgen deprivation therapy (ADT) in the form of Gonadotropin-releasing Hormone (GnRH) agonists is standard treatment for metastatic prostate cancer; however, primary ADT has not been guideline recommended for most men diagnosed with localized disease for a decade (12, 20). Nonetheless, by 2002, 44.9% of men diagnosed with prostate cancer, and for whom ADT was not recommended, received it (39). Because Medicare spent almost $1 billion annually on ADT (10, 37, 38), almost half of which was unnecessary, and Medicare reimbursement for physician-administered drugs, including ADT, far exceeded physician costs, the Medicare Modernization Act of 2003 (MMA) revised reimbursement policy for Part B drugs; this reduced reimbursement for ADT by 65% (47).

By 2005, sharp declines in ADT use were observed, suggesting reimbursement influenced treatment decisions (10, 39, 42). Other evidence suggests reimbursement changes may not have been responsible for this trend because: (1) declining ADT use also occurred in Canada and the Department of Veterans Affairs, health systems where Medicare policy should not affect use (43, 44) and (2) downward trends were observed among Medicare beneficiaries

prior to 2004 (40). However, no study has evaluated whether urologists were responding directly to MMA reimbursement policy. Thus, we investigate the effect of reimbursement on ADT overuse. In addition, we assess how the specialty organization of urology group practices may have affected the effect of reimbursement on ADT overuse. We hypothesize that more generous reimbursement will be associated with greater overuse of ADT and that single specialty urology practices will be more likely to overuse ADT than multi-specialty groups.

## Methods

Prior to MMA and during a period of clinical practice guideline stability (2000-2003), substantial variation in ADT reimbursement existed within Medicare. Differences in ADT reimbursement occurred because of the different drugs available, varying reimbursement by Medicare carriers which are grouped geographically, and by year of use. Exploiting this variation, this study examines the association of ADT reimbursement with urologists' use of ADT from January 2000 through December 2003, among clinically localized prostate cancer patients during a period of guideline stability. The study was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

### *Data Sources*

We linked the Surveillance, Epidemiology and End Results (SEER)-Medicare database to the American Medical Association (AMA) Masterfile. SEER data include patient demographics, primary tumor site, morphology, and stage at diagnosis for a population-based sample of U.S. residents diagnosed with cancer (90). Medicare administrative claims data include hospital services, physician services, physician-administered drug therapy and other medical services, regardless of where care was provided. We used Medicare Provider Analysis and Review, outpatient, Durable Medical Equipment, and Carrier files for sample selection, outcome and treating provider identification, but used only carrier files to study response to reimbursement, as other files do not identify physicians, reimbursement, or both (57). The AMA Masterfile includes physician and practice characteristics from approximately 800,000 US physicians.

Most data originate from training records collected annually (96-98% response rates). Data collected from physician regulatory agencies are confirmed and supplemented by annual surveys of one third of physicians each year (92). Additional group practice data, collected by survey of practice representatives, also were available from the AMA.

### *Cohort Definitions*

***Patients***. We identified all patients who had an incident diagnosis of adenocarcinoma of the prostate (International Classification of Disease, 9th Revision, Clinical Modification (ICD-9) diagnosis code 185 and International Classification of Diseases for Oncology, Third Edition histology code 8140) between January 1, 2000 and December 31, 2003. Only patients experiencing prostate cancer as their first and only cancer, as defined by SEER, were included. We excluded patients $\leq$ 66 years at diagnosis whose comorbidities could not be ascertained; and, men whose initial treatment decision could not be ascertained because they lacked observation throughout the full treatment window, including those who 1) were diagnosed at autopsy, death certificate, or at a nursing/convalescent facility; 2) died within 12 months of diagnosis; 3) were not continuously enrolled in fee-for-service; or 4) had no treatment claims. The Tumor Node Metastasis Staging System was used to restrict the cohort to those for whom ADT is not guideline-recommended (lacked evidence of nodal or metastatic involvement and who had no greater than unilateral, stage T2 tumors and World Health Organization grade 1-2) (3). In addition, we excluded men with less than five years actuarial life expectancy following an algorithm used previously (93), because National Comprehensive Cancer Network (NCCN) guidelines allowed for the use of primary ADT in men with limited life expectancy during this window (20, 93).

***Urologists***. Because they prescribe 95% of primary ADT to localized prostate cancer patients (37, 93), we restricted the cohort to treating urologists. First, we used patients' claims files to identify the treating provider, defined as the physician responsible for the most primary treatment claims (105). Providers identified in claims were matched by encrypted Unique

Physician Identifier Number or National Provider Identifier to AMA Masterfile data (which excluded non-physician providers).

***Measures***

***Dependent Variables***. The outcome, *primary ADT use,* is a binary variable defined as any claim for medical ADT administered within one year after the SEER date of diagnosis, unless another non-surveillance prostate treatment was also administered within the treatment window. Non-surveillance treatments included orchiectomy, radical prostatectomy, brachytherapy, chemotherapy, and cryotherapy. All claims files were used to identify treatment delivered using HealthCare Common Procedure Coding System (HCPCS), Current Procedural Terminology, and ICD-9-CM procedure and revenue center codes (93) (Appendix A).

Although primary ADT is the most prevalent form of ADT overuse, reimbursement also may affect other forms of overuse. Thus, we created an outcome that captured any ADT used in conjunction with any other therapy or alone for use in sensitivity analyses.

***Explanatory Variables***. Claims are paid by local *fiscal intermediaries* (Part A) and *carriers* (Part B), which lack uniform reimbursement policies (56). From 1997-2002, carriers were responsible for translating Part B drug HCPCS claims into National Drug Code (NDC) indices (57). While some HCPCS had only one equivalent NDC, others had $\geq$ 10 matches, resulting in substantial reimbursement variation (49). In addition to variability among carriers, reimbursements changed at different rates over time due to changes in average wholesale prices for specific NDCs (57).

To exploit this variation in ADT reimbursement, the key explanatory variable, *reimbursement generosity index (RGI)*, was operationalized as the sum of the weighted average difference between the urologists' and the national mean reimbursement for each drug the urologist prescribed (57). Weights were derived as the ratio of SEER registry-wide spending on a regimen to total spending on all ADT agents (see Appendix B). Differences in the index reflect variation in reimbursement specific to each carrier and over time as well as changes in the mix

of drugs prescribed by each physician in any year. Any score greater than one indicates *excess* (greater than the national average) reimbursement. Thus, a positive association between RGI and ADT use would indicate that urologists are inducing demand.

Some urologists may not have prescribed ADT for any of their patients. Because RGI could not be computed for these urologists, they were excluded from the analysis. Thus, we created two additional constructs for sensitivity analyses. First, we calculated a second RGI which included the costs of each ADT modality relative to all other care provided to this population, with weights adjusted to capture this additional "non-ADT treatment" category. This allowed us to assess whether urologists substituted for lost income by increasing the quantity of discounted services or selecting alternate treatments (106). Second, we created a revised RGI that assumed the SEER average reimbursement for urologists who did not prescribe any ADT.

*Group practice organizational type* is a series of mutually exclusive categories of the treating practice: single specialty urology group; multi-specialty group; or urology-radiation oncology group (all urologists with two or fewer radiation oncologists). This was self-reported by practice representatives to the AMA.

***Control Variables***. Patient, urologist, and practice variables were selected based upon the literature on prostate treatment decisions, quality of care, or responsiveness to incentives.

*Patient-Level Factors.* Disease severity included *tumor stage*, as measured by SEER Extent of Disease-1988 3rd edition variables, and *grade,* categorized as low (Gleason 2 to 4) or intermediate (Gleason 5 to 7) by SEER. Comorbidities were measured by the NCI Comorbidity Index (NCI CI) (107). Patient demographics included *age*; and *marital status* (married/living with a partner versus single, widowed or divorced, or missing). Healthcare use included: *prior primary care use* (any claim in the 12 months prior to diagnosis) (86); *specialist consultation* (three binary variables indicating presence of > 1 prostate-related carrier claim filed by a radiation oncologist, urologist or medical oncologist between diagnosis and the earliest of first treatment date or 12 months) (108); and, *primary care consultation* (>1 visit to the same

primary care physician occurring in both 1) the 12 months prior to diagnosis; and, 2) the window between diagnosis and treatment) (108). To control for environmental resources and community norms, we controlled for *SEER region*, collapsed by state, *rurality* of patient's residence (urban versus rural), and *community deprivation* (quartiles of median income and proportion of adults with less than 12 years of education in the patients' zip code of residence) (140).

*Provider-Level Factors*. Using data from the AMA and Medicare Hospital files, we measured: (1) *Physician gender;* (2) *time in practice*; and (3) medical professionalization (109, 110) defined as *board certification* (yes/no) and degree of *affiliation with an academic institution* (categorical); (4) *panel size* (number of prostate cancer patients/year/urologist); (5) *practice type* (solo; group practice; or missing); and (6) *proportion minority Medicare patients within a* practice (categorized into quartiles) (111). Using self-reported data from the AMA Masterfile, we included *proportion of Medicare patients* (<25%/≥25%) in group practice analyses.

Finally, we controlled for time by including variables for each year of the study.

### *Statistical Analysis*

We used multiple imputation for missing values of the proportions of Medicare patients seen within practices (141). We dichotomized RGI (negative or zero versus positive) and used Pearson's chi-squared tests and t-tests to compare across reimbursement levels. Descriptive statistics are presented for the sample of patients, the main unit of analysis, and the sample of physicians. Due to high intraclass correlation among patients treated by the same urologist (58), we used multilevel mixed logistic regression models which controlled for clustering of patients within provider. We conducted sensitivity analyses with alternate specifications of RGI and samples of urologists and with varying definitions of the outcome. We created a sub-sample, further limiting the cohort to urologists identified by the AMA as practicing in a group practice.

Statistical significance was evaluated at $\alpha = 0.05$ for all tests. Stata/SE 12.1 was used for all analyses (112).

**Results**

The final sample (Figure 1) included 15,128 men with T1 or T2 well- or moderately-differentiated prostate cancer treated by 1,800 ADT-using urologists between 2000 and 2003. Twenty four percent (3,653/15,128) of patients were treated with primary ADT. Among the ADTs used, goserelin acetate implants (3.6 mg) and leuprolide acetate injections (7.5 mg) were most frequently used. All other androgen deprivation modalities (leuprolide acetate implant, triptorelin pamoate injection, leuprolide acetate injection 3.5 mg, leuprolide acetate injection 1 mg, and orchiectomy) made up less than 3% of ADT use combined.

Average reimbursement generosity for all androgen deprivation therapy combined over the study period was 2.93, but fluctuated by treatment year and among urologists who prescribed ADT. Average reimbursement generosity among ADT-prescribing urologists for both ADTs and all other non-ADT treatments combined was -1.54.

In unadjusted analysis, among urologists who prescribed ADT, primary ADT use was higher among patients treated by urologists who received ADT reimbursement greater than the national average than it was among patients whose urologists received unfavorable reimbursement (i.e., negative or zero) (Table 1). However, at the physician level, there was no difference in the proportion of their fee-for-service localized prostate cancer patients prescribed primary ADT between urologists in unfavorable and favorable reimbursement climates (Table 2). Each group prescribed primary ADT to 30% of patients ($p=0.56$). ADT-prescribing urologists in favorable reimbursement areas were more likely to have some medical school affiliation ($p<0.001$) and more likely to be in group practice ($p=0.03$) than urologists in unfavorable reimbursement areas.

After controlling for patient, urologist, and practice characteristics and accounting for the correlation of patients within urologists, excess reimbursement for ADT, *relative to other*

*ADTs*, was not associated with ADT overuse among urologists who prescribed primary ADT to their T1 and T2 well- or moderately-differentiated prostate cancer patients (OR 1.00, 95% CI, 0.99, 1.00) (Table 3). However, the odds of primary ADT (OR 0.99; 95% CI 0.99, 0.99) use, *relative to all treatments,* decreased with an increase in RGI. Although the result was statistically significant, practically, the effect was very small. In additional sensitivity analysis, when considering all urologists (n=16,789) and assuming that non-prescribers were reimbursed at the SEER national average, primary ADT overuse was negatively associated with reimbursement, although the effect size was small and confidence intervals rounded to cross one (OR 0.99, 95% CI 0.99, 1.00). For every dollar of reimbursement above the national average, there was a 0.59 percentage point reduction in the odds of prescribing unnecessary (table not shown). Results for all models were qualitatively similar whether we used primary ADT or any ADT use as the outcome.

Results also were similar among urologists practicing in group settings (Table 4). Among the subset of urology group practices whose physicians prescribed ADT, reimbursement generosity was not associated with ADT overuse (OR 1.00; 95% CI 1.00, 1.00). Among all urologists in group practice selecting among all therapies, we found a very small, but significant, negative association of reimbursement with ADT overuse, but the confidence intervals rounded to one (OR 0.99; 95% CI 0.99, 1.00). Results from models considering any ADT use were similar. Physicians practicing in a multispecialty group environment were less likely to prescribe PADT (OR 0.79; 95% CI 0.64, 0.97). Urology group practices with at least one radiation oncologist did not differ in use of PADT from statistically urology group practices.

**Discussion**

Because Medicare reimbursement far exceeded the cost of physician-administered drugs such as ADT, the MMA of 2003 reduced reimbursement for Part B. While studies observed dramatic decreases in ADT use, no study has evaluated whether urologists were responding directly to MMA reimbursement policy. Contrary to our hypothesis, we found no evidence to

suggest excess reimbursement was associated with greater ADT overuse. The overuse of ADT in men with early stage and lower grade prostate cancer appeared at first to be greater for those who received more generous reimbursement. However, the relationship did not persist after adjusting for patient and physician factors known to be associated with ADT use. However, when we broadened our definition of reimbursement to be relative to all prostate cancer treatments, we observed a significant but small association in the unexpected direction. Excess reimbursement was associated with less overuse, not more, though the magnitude of this difference was nominal. Results were similar in sensitivity analysis that examined all urologists and assumed average ADT reimbursement for non-ADT users.

Our main findings differ from two studies which found the implementation of MMA to be associated with declining ADT use (10, 39). These observational studies assessed the change in ADT use over time. However, a wide range of factors—emerging evidence, guideline changes, prosecution of illegal marketing practices, and practice reorganization—could have led to the changes observed in the 2 studies (12, 20, 28, 43, 48, 69, 142). In contrast, we conducted our study during a period of guideline stability, controlled for other trends and exploited variation in reimbursement that occurred both within and between urologists. Thus, our study design isolated the effect of excess reimbursement, providing a stronger comparison than the within-provider comparison measured in earlier studies. Our study contributes to a body of work which does not support the hypothesis that reimbursement cuts alone drove down the overuse of ADT (43, 44). A more recent study using join point analysis found no association between MMA and decreasing use of ADT adjuvant to radical prostatectomy (143). Our findings are also consistent with other studies using the reimbursement generosity index to assess reimbursement changes. In a study assessing the effect of MMA on chemotherapy use in other cancers, reimbursement cuts were associated with increased use of chemotherapy, rather than the expected drop in use (51). The phenomenon of increasing the quantity of services when faced with a price reduction is well described in the economics literature (36, 51, 64, 65, 105). Our earlier study of response to

MMA demonstrated that while some urologists decreased ADT overuse coincident with MMA implementation, a smaller but substantial group of urologists increased ADT overuse during the same time (93). In the current study among ADT users, differential volume response may have negated any effect reimbursement differences may have had.

Because our findings differed based on our urologist sample and including only the reimbursement generosity of ADT versus reimbursement generosity relative to all treatments, we suspect that while at least some urologists who experienced lower or declining reimbursement may have intensified their overuse of ADT to make up for their declining revenues, others may have substituted other therapies for their lower stage and grade prostate cancer patients. Rather than ADT reimbursement affecting practice patterns, it is possible that other treatments urologists could offer their patients over the MMA implementation period—which on average were reimbursed with greater generosity than any ADT modality—may have impacted ADT overuse. Whether these alternate therapies may have been available only to a subset of urologists or limited by the types of patients seen in some urologists' practices is not known. But, the treatments patients received in the favorable and unfavorable reimbursement generosity areas differed slightly.

In other studies, physicians faced with differing reimbursement select the more highly reimbursed modality, suggesting that they are responsive to reimbursement within the bounds of treatments they are willing—or able—to prescribe (51). However, in some situations the physician may also alter the mix of treatments offered to align the care provided with better reimbursement (51, 105). We examined the effect of urology group practice organization on reimbursement generosity by repeating our analysis in a subset of urologists in group practices, expecting that practice organizational types suggestive of differing treatment resources, may have better access to alternative treatments and be less likely to overuse ADT. We found that physicians in multi-specialty group practices did offer less PADT, supporting our hypothesis. We did not find a similar effect among urology-radiation oncology practices, but the number of

urology-radiation oncology practices in our sample was small, partly because this practice type was just emerging in the beginning of the decade.

Our study has several limitations that warrant careful interpretation of results. First, from 2000-2004, primary ADT was recommended for men with less than five years of life expectancy whose risk for prostate cancer recurrence was high (20). We excluded men with stage and grade consistent with high recurrence risk. However, our cohort may have included men with high risk disease who could not be identified through SEER. To minimize this bias, we excluded men with less than five years of actuarial life expectancy, the target group to whom the ADT recommendation actually applied. Second, we were unable to control for the proportion of a physicians' patients who were in fee-for service Medicare in our main analysis. When this variable was included in the group practice analyses, we found that physicians with greater concentrations of Medicare patients had greater odds of ADT overuse, suggesting practices may switch to patients with other payers. However, few urology practices treat high proportions of Medicare patients and data collected during this time suggest that urologists' maintained stable portions of Medicare patients (62, 144, 145). Nonetheless, we used a dataset of practice information never before used for research, so results regarding organization type should be interpreted cautiously. Finally, measurement error and our sampling strategy may have interfered with our ability to detect a relationship between ADT overuse and reimbursement.

***Conclusions***

Despite declining use, ADT overuse remains a serious quality problem in 14% of patients in whom it is not clinically recommended (93). Although policy makers and payers may view changes in reimbursement as a promising strategy to reduce overuse, this was not the case in our study of ADT. In a large, national sample of urologists ADT reimbursement generosity was not associated with primary ADT use. We conducted multiple sensitivity analyses: varying our definition of ADT overuse; considering reimbursement relative to ADT; and, comparing among all urologists treating patients in our cohort and only those who prescribed ADT during the

study. In these analyses our findings were robust that ADT reimbursement changes were not associated with practice changes. However, in analyses comparing ADT relative to all treatments provided, we detected a small, but negative association with ADT use, suggesting that other treatments' reimbursement may have encouraged some physicians to limit their ADT overuse. Additional research on physician response to reimbursement when opportunities for treatment substitution are available should be investigated.

**Figure 5.1. Cohort Exclusions**

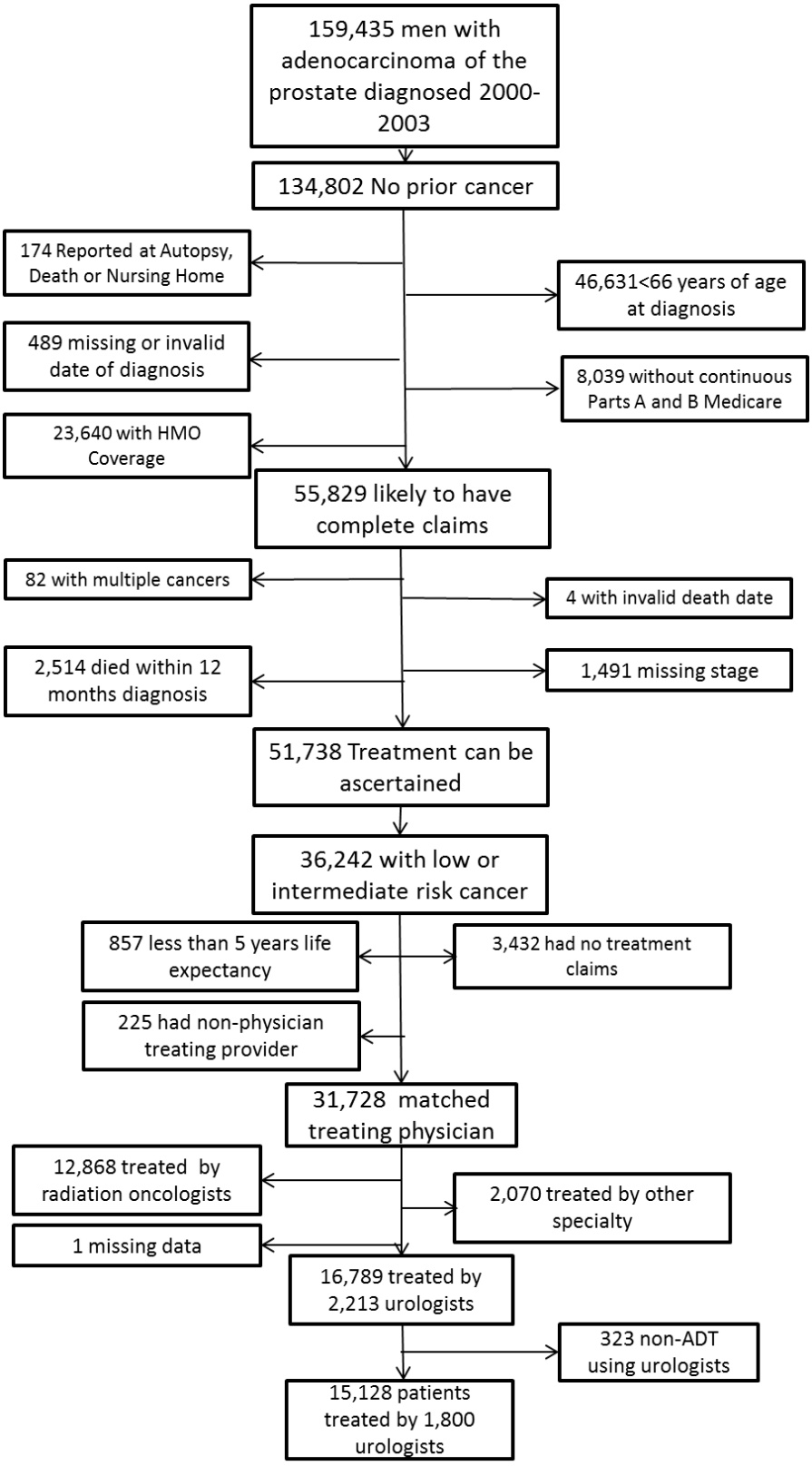


**Table 5.1. Characteristics of Patients of ADT-Prescribing Urologists**

| | Overall | ADT Reimbursement ≤ to National Average | ADT Reimbursement > National Average | |
|---|---|---|---|---|
| | Mean (Standard Deviation) or % | | | |
| | **N=15,128** | **N= 5,932** | **N= 9,196** | ***p*** |
| **Primary ADT Reimbursement Generosity Index** | 2.9 (69.6) | -48.0 (65.6) | 35.8 (49.5) | *<0.001* |
| **Year Treated** | | | | *<0.001* |
| 2000 | 3,317 (21.9%) | 1,332 (22.5%) | 1.985 (21.6%) | |
| 2001 | 3,894 (25.7%) | 1,618 (27.3%) | 2,276 (24.7%) | |
| 2002 | 4,421 (29.2%) | 1,890 (31.9%) | 2,531 (27.5%) | |
| 2003 | 3,496 (23.1%) | 1,092 (18.4%) | 2,404 (26.1%) | |
| **T Stage** | | | | *0.08* |
| T1 | 6,296 (41.6%) | 2,417 (40.7%) | 3,879 (42.2%) | |
| T2 | 8,832 (58.4%) | 3,515 (59.3%) | 5,317 (57.8%) | |
| **Grade** | | | | *<0.001* |
| Well differentiated, 2-4 | 759 (5.0%) | 333 (5.6%) | 426 (4.6%) | |
| Moderately Differentiated, 5-7 | 13,867 (91.7%) | 5,439 (91.7%) | 8,428 (91.6%) | |
| Missing | 502 (3.3%) | 160 (2.7%) | 342 (3.7%) | |
| **Comorbidities** | | | | *<0.001* |
| 0 | 10,245 (67.7%) | 4,129 (69.6%) | 6,116 (66.5%) | |
| 1 | 3,298 (21.8%) | 1,240 (20.9%) | 2,058 (22.4%) | |
| 2 | 998 (6.6%) | 354 (6.0%) | 644 (7.0%) | |
| 3 or more | 587 (3.9%) | 209 (3.5%) | 378 (4.1%) | |
| **Age, in years** | 73.9 (5.5) | 73.7 (5.5) | 73.9 (5.5) | *0.03* |
| **Race/ethnicity** | | | | *<0.001* |
| Non-Hispanic White | 12,008 (79.4%) | 4,878 (82.2%) | 7,130 (77.5%) | |
| Non-Hispanic Black | 1,175 (7.8%) | 303 (5.1%) | 872 (9.5%) | |
| Hispanic | 925 (6.1%) | 352 (5.9%) | 573 (6.2%) | |
| Other | 550 (3.6%) | 249 (4.2%) | 301 (3.3%) | |
| Missing | 470 (3.1%) | 150 (2.5%) | 320 (3.5%) | |
| **Marital Status** | | | | *0.01* |
| Not Married | 2,767 (18.3%) | 1,022 (17.2%) | 1,745 (19.0%) | |
| Married | 10,231 (67.6%) | 4,086 (68.9%) | 6,145 (66.8%) | |
| Missing | 824 (14.1%) | 5,923 (13.9%) | 9,196 (14.2%) | |

| | | | | |
|---|---|---|---|---|
| **Pre-treatment Primary Care Use** | | | | *0.19* |
| 0-2 visits in prior year | 2,991 (19.8%) | 1,135 (19.1%) | 1,856 (20.2%) | |
| 3-5 visits in prior year | 6,753 (44.6%) | 2,693 (45.4%) | 4.060 (44.1%) | |
| 6 or more visits in prior year | 5,384 (35.6%) | 2,104 (35.5%) | 3,280 (35.7%) | |
| **Primary Care Consultation** | | | | *0.21* |
| No | 7,104 (47.0%) | 2,823 (47.6%) | 4,281 (46.6%) | |
| Yes | 8,024 (53.0%) | 3,109 (52.4%) | 4,915 (53.4%) | |
| **Radiation Oncology Consultation** | | | | *0.008* |
| No | 10,805 (71.4%) | 4,309 (72.6%) | 6,496 (70.6%) | |
| Yes | 4,323 (28.6%) | 1,623 (27.4%) | 2,700 (29.4%) | |
| **Medical Oncology Consultation** | | | | *0.04* |
| No | 14,603 (96.5%) | 5,703 (96.1%) | 8,900 (96.8%) | |
| Yes | 525 (3.5%) | 229 (3.9%) | 296 (3.2%) | |
| **Urology Consultation** | | | | *0.008* |
| No | 156 (1.0%) | 45 (0.8%) | 111 (1.2%) | |
| Yes | 14,972 (99%) | 5,887 (99.2%) | 9,085 (98.8%) | |
| **Rural Residence** | | | | *<0.001* |
| No | 14,835 (98.1%) | 5,768 (97.2%) | 9,067 (98.6%) | |
| Yes | 293 (1.9%) | 164 (2.8%) | 129 (1.4%) | |
| **SEER Region** | | | | *<0.001* |
| Seattle | 751 (5.0%) | 644 (10.9%) | 107 (1.2%) | |
| Connecticut | 1,037 (6.9%) | 477 (8.0%) | 560 (6.1%) | |
| Detroit | 1,270 (8.4%) | 108 (1.8%) | 1,162 (12.6%) | |
| Hawaii | 163 (1.1%) | 105 (1.8%) | 58 (0.6%) | |
| Iowa | 1,133 (7.5%) | 439 (7.4%) | 694 (7.5%) | |
| New Mexico | 368 (2.4%) | 51 (0.9%) | 317 (3.4%) | |
| California | 4,498 (29.7%) | 1,982 (33.4%) | 2,516 (27.4%) | |
| Utah | 678 (4.5%) | 631 (10.6%) | 47 (0.5%) | |
| Georgia | 332 (2.2%) | 27 (0.5%) | 305 (3.3%) | |
| Kentucky | 1,212 (8.0%) | 670 (11.3%) | 542 (5.9)% | |
| Louisiana | 1,233 (8.2%) | 340 (5.7%) | 893 (9.7%) | |
| New Jersey | 2,453 (16.2%) | 458 (7.7%) | 1,995 (21.7%) | |
| **Median Income of Patients' Communities** | | | | *<0.001* |
| $2,506-35,031 | 3,574 (23.6%) | 1,495 (25.2%) | 2,079 (22.6%) | |
| $35,051-46,079 | 3,817 (25.2%) | 1,660 (28.0%) | 2,157 (23.5%) | |
| $46,084-60,668 | 3,563 (23.6%) | 1,351 (22.8%) | 2,212 (24.1%) | |
| $60,669-200,008 | 3,596 (23.8%) | 1,205 (20.3%) | 2,391 (26.0%) | |
| Missing | 578 (3.8%) | 221 (3.7%) | 357 (3.9%) | |

| | | | | |
|---|---|---|---|---|
| **Proportion of Patient's Community w/o High School Education** | | | | *0.002* |
| 0-9.7% | 3,615 (23.9%) | 1,499 (25.3%) | 2,116 (23.0%) | |
| 9.7-15.5% | 3,720 (24.6%) | 1,469 (24.8%) | 2,251 (24.5%) | |
| 15.5%-25.2% | 3,569 (23.6%) | 1,313 (22.1%) | 2,256 (24.5%) | |
| 25.2%-100% | 3,653 (24.1%) | 1,431 (24.1%) | 2,222 (24.2%) | |
| Missing | 571 (3.8%) | 220 (3.7%) | 351 (3.8%) | |

P-values by t-test for continuous variables and chi2 test for binary / categorical variables

**Table 5.2. Characteristics of ADT-Prescribing Urologists**

| | Overall | ADT Reimbursement ≤ to National Average | ADT Reimbursement > National Average | |
|---|---|---|---|---|
| | Mean (Standard Deviation) or % | | | |
| | **N=1800** | **N= 701** | **N= 1,099** | ***p*** |
| **Proportion of Patients in Practice Receiving Primary ADT** | 0.3 (0.3) | 0.3 (0.3) | 0.3 (0.3) | *0.56* |
| **Reimbursement Generosity Index** | 2.9 (73.6) | -37.0 (62.2) | 28.4 (68.9) | *<0.001* |
| **Time in Practice** | | | | *0.42* |
| <20 years | 686 (38.1%) | 259 (36.9%) | 427 (38.9%) | |
| ≥20 years | 1,114 (61.9%) | 442 (63.1%) | 672 (61.1%) | |
| Gender | | | | *0.41* |
| 0 | 1,763 (97.9%) | 689 (98.3%) | 1,074 (97.7%) | |
| 1 | 37 (2.1%) | 12 (1.7%) | 25 (2.3%) | |
| U.S. Trained | | | | *0.29* |
| 0 | 298 (16.6%) | 108 (15.4%) | 190 (17.3%) | |
| 1 | 593 (83.4%) | 593 (84.6%) | 909 (82.7%) | |
| Board Certified | | | | *0.55* |
| 0 | 113 (6.3%) | 41 (5.8%) | 72 (6.6%) | |
| 1 | 1,687 (93.7%) | 660 (94.2%) | 1,027 (93.4%) | |
| Medical School Affiliation | | | | *<0.001* |
| 0 | 903 (50.2%) | 391 (55.8%) | 512 (46.6%) | |
| 1 | 854 (47.4%) | 294 (41.9%) | 560 (51.0%) | |
| 2 | 43 (2.4%) | 16 (2.3%) | 27 (2.5%) | |
| Physician Prostate Panel Size | | | | *0.45* |
| 0-20 prostate patients/year | 1,195 (66.4%) | 474 (67.6%) | 721 (65.6%) | |
| 21-37 prostate patients/year | 454 (25.2%) | 175 (25.0%) | 279 (25.4%) | |
| 38 or more prostate patients/year | 151 (8.4%) | 52 (7.4%) | 99 (9.0%) | |
| Practice Type | | | | *0.03* |
| Group Practice | 1,274 (70.8%) | 471 (67.2%) | 803 (73.1%) | |
| Solo Practice | 442 (24.6%) | 193 (27.5%) | 249 (22.7%) | |
| Missing | 84 (4.7%) | 37 (5.3%) | 47 (4.3%) | |
| Proportion of Patients Minority | | | | *<0.001* |
| 1 | 668 (37.1%) | 295 (42.1%) | 373 (33.9%) | |
| 2 | 522 (29.0%) | 211 (30.1%) | 311 (28.3%) | |
| 3 | 610 (33.9%) | 195 (27.8%) | 415 (37.8%) | |

P-values by t-test for continuous variables and chi2 test for binary / categorical variables

**Table 5.3. Regression Results: Reimbursement Excess, ADT Users Only**

| | | Odds Ratio | 95% Confidence Interval | |
|---|---|---|---|---|
| **Reimbursement Generosity Index** | | 1.00 | 1.00 | 1.00 |
| **Time in Practice** | <20 years | 1.00 | | |
| | ≥20 years | 0.98 | 0.84 | 1.14 |
| **Gender** | Male | 1.00 | | |
| | Female | 1.12 | 0.58 | 2.18 |
| **Training Location** | Foreign Trained | 1.00 | | |
| | US Trained | 1.00 | 0.81 | 1.23 |
| **Board Certification** | None | 1.00 | | |
| | Board Certified | 0.77 | 0.57 | 1.04 |
| **Medical School Affiliation** | None | 1.00 | | |
| | Some | 0.94 | 0.80 | 1.09 |
| | Missing | 2.00 | 1.21 | 3.30 |
| **Practice Type** | Group Practice | 1.00 | | |
| | Solo Practice | 1.27 | 1.07 | 1.52 |
| | Missing | 0.86 | 0.58 | 1.26 |
| **Physician Prostate Panel Size** | <20 prostate patients/year | 1.00 | | |
| | 21-37 prostate patients/year | 0.75 | 0.65 | 0.86 |
| | 38 or more prostate patients/year | 0.81 | 0.68 | 0.96 |
| **Proportion of Patients Minority** | <6.1% | 1.00 | | |
| | 6.2-19.5% | 0.94 | 0.80 | 1.10 |
| | ≥20% | 1.14 | 0.95 | 1.38 |
| **T Stage** | T1 | 1.00 | | |
| | T2 | 1.91 | 1.72 | 2.13 |
| **Grade** | Well differentiated, 2-4 | 1.00 | | |
| | Moderately Differentiated, 5-7 | 2.26 | 1.78 | 2.88 |
| | Missing | 3.50 | 2.50 | 4.91 |
| **Comorbidities** | 0 | 1.00 | | |
| | 1 | 1.40 | 1.24 | 1.57 |
| | 2 | 1.43 | 1.18 | 1.72 |
| | 3 or More | 2.07 | 1.65 | 2.60 |
| **Age, in years** | | 1.78 | 1.38 | 2.30 |
| **Age²** | | 1.00 | 1.00 | 1.00 |

| | | | | |
|---|---|---|---|---|
| **Race/ethnicity** | Non-Hispanic White | 1.00 | | |
| | Non-Hispanic Black | 1.42 | 1.17 | 1.73 |
| | Hispanic | 1.25 | 1.00 | 1.56 |
| | Other | 1.30 | 0.94 | 1.79 |
| | Missing | 1.95 | 1.50 | 2.53 |
| **Marital Status** | Unmarried | 1.00 | | |
| | Married/Living with Partner | 0.79 | 0.70 | 0.90 |
| | Missing | 1.85 | 1.56 | 2.18 |
| **Rural Residence** | Urban | 1.00 | | |
| | Rural | 0.98 | 0.68 | 1.43 |
| **SEER Region** | Seattle | 1.00 | | |
| | Connecticut | 1.76 | 1.14 | 2.73 |
| | Detroit | 0.99 | 0.64 | 1.54 |
| | Hawaii | 1.15 | 0.53 | 2.51 |
| | Iowa | 1.37 | 0.87 | 2.15 |
| | New Mexico | 1.14 | 0.64 | 2.01 |
| | California | 1.03 | 0.71 | 1.50 |
| | Utah | 1.11 | 0.67 | 1.87 |
| | Georgia | 1.16 | 0.67 | 2.01 |
| | Kentucky | 1.00 | 0.65 | 1.55 |
| | Louisiana | 1.52 | 0.99 | 2.34 |
| | New Jersey | 1.79 | 1.22 | 2.63 |
| **Proportion of Patient's Community w/o High School Education** | 0-9.7% | 1.00 | | |
| | 9.7-15.5% | 1.09 | 0.92 | 1.29 |
| | 15.5%-25.2% | 1.19 | 0.97 | 1.45 |
| | 25.2%-100% | 1.16 | 0.91 | 1.48 |
| | Missing | 0.25 | 0.02 | 3.35 |
| **Median Income of Patients' Communities** | $2,506-35,031 | 1.00 | | |
| | $35,051-46,079 | 0.97 | 0.82 | 1.13 |
| | $46,084-60,668 | 0.82 | 0.67 | 1.01 |
| | $60,669-200,008 | 0.81 | 0.62 | 1.04 |
| | Missing | 3.55 | 0.27 | 46.68 |
| **Radiation Oncology Consultation** | No | 1.00 | | |
| | Yes | 0.26 | 0.23 | 0.31 |
| **Medical Oncology Consultation** | No | 1.00 | | |
| | Yes | 0.88 | 0.65 | 1.19 |

| | | | | |
|---|---|---|---|---|
| **Urology Consultation** | No | 1.00 | | |
| | Yes | 5.62 | 3.19 | 9.90 |
| **Primary Care Consultation** | No | 1.00 | | |
| | Yes | 0.41 | 0.36 | 0.46 |
| **Pre-treatment Primary Care Use** | 0-2 visits in prior year | 1.00 | | |
| | 3-5 visits in prior year | 1.58 | 1.36 | 1.83 |
| | 6 or more visits in prior year | 1.89 | 1.60 | 2.22 |
| **Year Treated** | 2000 | 1.00 | | |
| | 2001 | 1.04 | 0.90 | 1.20 |
| | 2002 | 1.10 | 0.95 | 1.27 |
| | 2003 | 0.93 | 0.80 | 1.08 |
| **Constant** | | 0.95 | 0.87 | 1.04 |
| **N=15,128** | | | | |

**Table 5.4. Logistic Regression of Reimbursement Generosity on Primary ADT Overuse among Group Practice Organizations**

| | | Odds Ratio | 95% Confidence Interval | |
|---|---|---|---|---|
| **Reimbursement Generosity Index** | | 1.00 | 1.00 | 1.00 |
| **Group Practice Type** | Urology | 1.00 | | |
| | Multispecialty | 0.79 | 0.64 | 0.97 |
| | Urology-Radiation Oncology | 1.61 | 0.18 | 14.35 |
| **Time in Practice** | <20 years | 1.00 | | |
| | ≥20 years | 0.99 | 0.83 | 1.19 |
| **Gender** | Male | 1.00 | | |
| | Female | 1.52 | 0.80 | 2.89 |
| **Training Location** | Foreign Trained | 1.00 | | |
| | US Trained | 0.74 | 0.54 | 1.01 |
| **Board Certification** | None | 1.00 | | |
| | Board Certified | 0.49 | 0.29 | 0.81 |
| **Medical School Affiliation** | None | 1.00 | | |
| | Some | 0.79 | 0.65 | 0.94 |
| | Missing | 1.83 | 0.89 | 3.78 |
| **Physician Prostate Panel Size** | <20 prostate patients/year | 1.00 | | |
| | 21-37 prostate patients/year | 0.71 | 0.59 | 0.84 |
| | 38 or more prostate patients/year | 0.77 | 0.62 | 0.95 |
| **Proportion of Patients Minority** | <6.1% | 1.00 | | |
| | 6.2-19.5% | 0.94 | 0.78 | 1.13 |
| | ≥20% | 1.26 | 1.00 | 1.58 |
| **Proportion of Patients Medicare** | <25% (reference) | 1.00 | | |
| | ≥25% | 1.49 | 1.09 | 2.04 |
| **T Stage** | T1 | 1.00 | | |
| | T2 | 1.41 | 1.25 | 1.59 |
| **Grade** | Well differentiated, 2-4 | 1.00 | | |
| | Moderately Differentiated, 5-7 | 2.28 | 1.68 | 3.09 |
| | Missing | 4.42 | 2.86 | 6.83 |
| **Comorbidities** | 0 | 1.00 | | |
| | 1 | 1.29 | 1.11 | 1.49 |
| | 2 | 1.36 | 1.07 | 1.72 |
| | 3 or More | 1.64 | 1.20 | 2.24 |

| | | | | |
|---|---|---|---|---|
| **Age, in years** | | 1.35 | 1.00 | 1.82 |
| **Age²** | | 1.00 | 1.00 | 1.00 |
| **Race/ethnicity** | Non-Hispanic White | 1.00 | | |
| | Non-Hispanic Black | 1.31 | 1.04 | 1.65 |
| | Hispanic | 1.61 | 1.19 | 2.18 |
| | Other | 1.33 | 0.89 | 1.99 |
| | Missing | 1.04 | 0.72 | 1.49 |
| **Marital Status** | Unmarried | 1.00 | | |
| | Married/Living with Partner | 0.85 | 0.73 | 0.99 |
| | Missing | 1.17 | 0.95 | 1.45 |
| **Rural Residence** | Urban | 1.00 | | |
| | Rural | 1.30 | 0.84 | 1.99 |
| **SEER Region** | Seattle | 1.00 | | |
| | Connecticut | 1.89 | 1.06 | 3.40 |
| | Detroit | 1.14 | 0.64 | 2.04 |
| | Hawaii | 1.72 | 0.37 | 7.99 |
| | Iowa | 1.50 | 0.83 | 2.69 |
| | New Mexico | 1.49 | 0.67 | 3.29 |
| | California | 1.11 | 0.65 | 1.88 |
| | Utah | 1.05 | 0.50 | 2.19 |
| | Georgia | 1.25 | 0.63 | 2.48 |
| | Kentucky | 1.29 | 0.73 | 2.28 |
| | Louisiana | 2.25 | 1.24 | 4.10 |
| | New Jersey | 2.64 | 1.53 | 4.53 |
| **Proportion of Patient's Community w/o High School Education** | 0-9.7% | 1.00 | | |
| | 9.7-15.5% | 1.05 | 0.88 | 1.26 |
| | 15.5%-25.2% | 0.93 | 0.75 | 1.17 |
| | 25.2%-100% | 1.33 | 0.89 | 1.99 |
| | Missing | 1.04 | 0.72 | 1.49 |
| **Median Income of Patients' Communities** | $2,506-35,031 | 1.00 | | |
| | $35,051-46,079 | 1.01 | 0.82 | 1.24 |
| | $46,084-60,668 | 0.84 | 0.65 | 1.08 |
| | $60,669-200,008 | 0.72 | 0.52 | 0.98 |
| | Missing | 1.61 | 0.11 | 22.96 |

| | | | | |
|---|---|---|---|---|
| **Radiation Oncology Consultation** | No | 1.00 | | |
| | Yes | 2.19 | 1.90 | 2.53 |
| **Medical Oncology Consultation** | No | 1.00 | | |
| | Yes | 1.24 | 0.90 | 1.69 |
| **Primary Care Consultation** | No | 1.00 | | |
| | Yes | 0.62 | 0.54 | 0.72 |
| **Pre-treatment Primary Care Use** | 0-2 visits in prior year | 1.00 | | |
| | 3-5 visits in prior year | 1.48 | 1.23 | 1.77 |
| | 6 or more visits in prior year | 1.84 | 1.50 | 2.24 |
| **Year Treated** | 2000 | 1.00 | | |
| | 2001 | 0.92 | 0.78 | 1.09 |
| | 2002 | 0.97 | 0.81 | 1.16 |
| | 2003 | 0.71 | 0.59 | 0.86 |
| **Constant** | | 0.00 | 0.00 | 0.01 |

N=7,096 patients; n=780 physicians

# CHAPTER 6 EFFECT OF PRE-MMA ANDROGEN DEPRIVATION THERAPY OVERUSE ON POST-MMA QUALITY OF CARE FOR LOCALIZED PROSTATE CANCER

## Introduction

Primary androgen deprivation therapy (PADT) for the treatment of localized prostate cancer has been a growing quality of care problem since the 1990s, especially for African Americans (37, 59, 146, 147). Comparative effectiveness studies (148, 149) and clinical practice guidelines do not support the use of PADT, the use of ADT as the only treatment, in patients with localized prostate cancer (12, 19, 20, 146, 147), and the evidence of its harms—including increased risk for osteoporosis, fractures, heart disease, diabetes, thromboembolic events, and cardiac death—continues to mount (26-28). Medicare reimbursement policy changes associated with the Medicare Modernization Act (MMA) are thought to have brought about a marked decline in the overuse of PADT for the treatment of patients with clinically localized prostate cancer over the last decade. MMA significantly lowered reimbursement paid to physician practices for Part B drugs, including those used for PADT. Use of PADT fell as much as 34% from 2003 to 2005 among men with localized disease (10, 39), an acknowledged improvement in quality of care. However, the full impact of the declining use of PADT on quality of care depends on: 1) the type of care that replaced PADT use; and, 2) the appropriateness of that care based on a patients' prostate cancer recurrence risk.

Contemporaneous with declining PADT use, prostate cancer treatment underwent dramatic changes, in advance of evidence to support guideline changes. Although overall rates of guideline-concordant therapies—radical prostatectomy, radiation therapy, and non-definitive therapy—increased (150, 151), the modalities of these treatments changed. Minimally invasive radical prostatectomy (MIRP) replaced open prostatectomy (151, 152). Intensity modulated

radiation therapy (IMRT) rapidly replaced external beam radiation (EBRT) (40, 153). Although it is unknown whether biopsy-driven surveillance has replaced less intensive surveillance methods, non-definitive therapy has replaced PADT (40).

Although, evidence of the comparative effectiveness and harms of these new modalities is emerging (98, 152, 154-156), not all new modalities are equally endorsed, thus quality of prostate cancer care depends on the modality used. The National Comprehensive Cancer Network (NCCN) guidelines acknowledge that MIRP procedures—laparoscopic radical prostatectomy (and later, robotic prostatectomy)—may have equal outcomes compared to open prostatectomy when performed by "highly experienced" surgeons. Nonetheless, they emphasize the developmental nature of laparoscopic methods and ultimately recommended retropubic and perineal prostatectomy, although most recent guidelines are more accepting of MIRP (12, 21). On the other hand, NCCN guidelines have recommended both radiation modalities, EBRT and IMRT, for almost a decade. Similarly, for a decade NCCN has recommended following men with prostate-specific antigen (PSA) testing and/or digital rectal exams and repeated biopsies at regular intervals to monitor disease progression (22). Further, some research suggests that these new modalities might not be adopted equally in minority populations, creating potential disparities in care.

Not only does guideline concordance depend on the treatment modality chosen, but it is also risk category-specific. NCCN treatment recommendations are based on D'Amico categories, thresholds of tumor stage, Gleason grade, and PSA levels at which biochemical failure is predicted (11, 22). Although PADT (ADT used as the sole treatment) is not recommended for any recurrence risk, other therapies are recommended only for some risk levels. Active surveillance is guideline-concordant care for patients with low- and intermediate-risk disease but not for those with high-risk prostate cancer (12). Such lack of risk group differentiation can mask whether care delivered is guideline-concordant (3, 18). For example, previous studies assessing changes in active surveillance do not consider an individual patients' recurrence risk

(40) and subsequently, the appropriateness of this pattern of care change. In addition, some therapies are concordant when delivered in conjunction with certain therapies: ADT adjuvant to external beam and intensity modulated radiation is guideline-concordant for some, but not all risk groups, but it not guideline-concordant when combined with brachytherapy, another third radiation modality.

Therefore, we risk-stratified prostate cancer patients to examine the association of physicians' pre-MMA PADT use and NCCN guideline-concordant initial treatment among a post-MMA, population-based cohort of men with incident prostate cancer. We hypothesize that higher levels of baseline non-concordant PADT use will be associated with guideline-concordant care in the post-MMA period and that racial differences in quality will be resolved. Nonetheless, we further explore the modalities of treatment currently being delivered to describe how emerging technologies have affected quality of care.

## Methods

We identified the initial prostate cancer treatment provided to a large population-based cohort of elderly prostate cancer patients for retrospective analysis. The study was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

### *Data Sources*

We matched Surveillance, Epidemiology and End Results (SEER)- linked Medicare data to American Medical Association (AMA) physician data (90, 91, 157, 158) for patients diagnosed with prostate cancer from 2005 to 2007 within 17 SEER registries and treated through July 2009.

### *Cohort Definition*

*Patient Selection Criteria.* We identified all men diagnosed with incident adenocarcinoma of the prostate between January 1, 2005 and December 31, 2007. Only patients experiencing their first and only cancer, identified by SEER, were included. We excluded patients whose comorbidities and/or initial treatment could not be ascertained, including those

who were younger than 66 years; diagnosed at autopsy, death certificate, or at a nursing/convalescent facility; not enrolled in fee-for-service (defined as continuous Part A and B coverage and not in a health maintenance organization for at least 18 months post diagnosis; or died within 18 months of diagnosis. The Tumor Node Metastasis (TNM) staging system was used to restrict the cohort to men with clinically localized prostate cancer by excluding men with 1) tumors clinically staged T3b or greater; 2) any evidence of nodal involvement; or, 3) any evidence of metastases.

*Physician Inclusion Criteria*. Treating physicians were identified in Medicare claims. After limiting claims to those submitted for prostate cancer treatment and identifying the primary therapy received with an algorithm giving preference to the most definitive therapies, the physician responsible for the most initial primary therapy treatment claims was considered the treating physician.

### *Measures*

***Dependent Variable.*** *Guideline concordance*, a binary outcome, was derived from the 2004 NCCN prostate cancer treatment algorithm (12). Although a guideline update was issued in 2007 (159), NCCN did not change risk stratification or initial treatment recommendations, so this outcome remained stable throughout the study period. The algorithm stratifies patients by stage, grade, PSA, and in some cases, the presence of multiple risk factors. The low-risk group includes men with T1–2a stage, Gleason grade 2–6, and PSA <10 ng/mL. Intermediate risk includes men with T2b or T2c stage, Gleason grade 7, or PSA 10–20 ng/mL. The high-risk group includes men with PSA >20 ng/mL, Gleason >7, or stage T3a. Concordant treatments were assigned for each risk category.

For *initial treatment received*, we used claims to categorize patients into one of five mutually exclusive options: 1) active surveillance; 2) radiation therapy; 3) radical prostatectomy; 4) PADT; and, 5) other less frequently used treatments (See Appendix C for relevant codes). Only the first treatment received within 18 months of diagnosis was considered as the initial

treatment decision, except where ADT was considered adjuvant. Although SEER registry data and Medicare claims are roughly comparable for radiation therapy and surgery (94, 95) and their use in combination ascertains additional treatment, SEER data tend to underestimate use of medical therapies including ADT (37). In addition, registry data may inaccurately represent active surveillance (96). Thus, for consistency, treatment was derived from Medicare claims only. Each treatment was defined as follows:

- *Radiation therapy* was defined as either EBRT (2- or 3-dimensional conformal radiation therapy), IMRT, or brachytherapy, with or without ADT from claims definitions used in prior studies (18, 97, 98) and from search of International Classification of Disease-9 (ICD-9) and Current Procedural Terminology (CPT) dictionaries (99). Other forms of radiation (stereotactic-body radiation and proton therapy) are not guideline-recommended and were considered as "other" therapy.
- *Radical prostatectomy* consisted of 1) guideline-concordant open prostatectomy (retropubic, or perineal radical prostatectomy); and 2) guideline-discordant MIRP, distinguished by CPT code.
- *Primary ADT* was considered ADT use in the absence of other definitive therapy. ADT included either orchiectomy or a GnRH agonist, as neither are guideline-concordant for clinically localized disease (39, 100).
- *Active surveillance* was defined in two ways: 1) guideline-discordant surveillance denoted $\geq$1 claim for PSA or digital rectal examination (DRE), $\geq$2 prostate cancer specialist visits, and the absence of any other definitive prostate therapy within the initial treatment window; 2) guideline-concordant surveillance was defined as $\geq$2 claims for PSA or DRE and $\geq$1 claim for needle biopsy of the prostate, in the absence of other definitive treatment (12). Although DRE claims are rarely coded, some claims did include them, which we counted as a component of surveillance, but neither definition required a DRE claim.

- *Other therapy* included cryosurgery, chemotherapy, and therapy combinations not included in the NCCN guidelines (e.g., radical prostatectomy with adjuvant ADT).

***Explanatory Variables***

*Pre-MMA PADT use* is a provider-level measure based on the 4-year period preceding the first MMA implementation in 2004. It is calculated as each physicians' average annual proportion of patients receiving primary ADT, defined as GnRH agonists claims only, during the pre-MMA years 2000–2003. Orchiectomy is excluded, because MMA did not affect surgical ADT and should not be replaced by other care. *Patient race* is defined from SEER data and measured by five categories: 1) non-Hispanic white; 2) black or African-American; 3) Hispanic; 4) other; or, 5) unknown.

***Control Variables***

We controlled for patient and, physician characteristics associated with prostate treatment selection, quality of care, or responsiveness to incentives.

*Clinical Factors.* We used the SEER Collaborative Staging variables to assign patients to American Joint Committee on Cancer stage categories used for treatment by the NCCN guidelines (12, 20). Both grade and PSA are quantitative variables in SEER records. Although PSA and grade are used to stratify D'Amico risk groups, as described above, we also controlled for them, because earlier studies have suggested that men with higher risk levels are more likely to receive guideline discordant care (135, 160). We included age and the NCI Combined Comorbidity Index (NCICI), which is derived from relevant medical conditions appearing in both hospital and physician claims using uniform weights (107, 123).

*Treatment Support.* We compared men married/living with a partner to those single, widowed, divorced, or missing marital status. We also assessed men's use of consultations in the prostate cancer treatment decision (108). *Primary Care Consultation* was >1 visit to the same primary care physician occurring during 1) the 12 months prior to diagnosis; and, 2) the window between diagnosis and treatment. *Specialist Care Consultation* was three binary variables

indicating presence of >1 prostate-related carrier claim filed by a radiation oncologist, urologist, or medical oncologist between diagnosis and the first treatment date or 18 months, whichever is earlier (108).

*Healthcare access*: We included several geographic indicators: *SEER region*, grouped by state; *rurality* of the community in which the patient resided at diagnosis; and *community deprivation*, defined as median income of the patients' zip code of residence and as proportion of adults residing in the patients' zip code with less than high school education.

*Provider Factors:* Using data from the AMA and SEER-Medicare Hospital files, we controlled for: (1) *physician gender*; (2) *time in practice*, (years between a patient's SEER diagnosis date and the date of a physicians' medical degree (from the AMA) dichotomized as <20 and ≥20 years; *(3) physician specialty* (urology, radiation oncology, medical oncology, primary care, or other); *(4) medical professionalization*, defined by a binary indicator of board certification and a categorical indicator measuring the degree of affiliation with an academic institution (none, some, or missing) (109, 110); and (5) *training location* (U.S. versus non-U.S.). Practice factors included *panel size* (58), measured by quartiles of the number of prostate cancer patients/year/physician; *practice type* (group practice, solo practice, or missing); and *proportion of a practice's Medicare patients that are minority* (quartiles); and quartiles of the *proportion of a practice's Medicare patients that are minority* (111).

### *Statistical Analysis*

We stratified the patient sample by receipt of guideline-concordant care and assessed differences between groups using Pearson's chi-squared tests and t-tests for categorical and continuous variables, respectively. We used a common benchmark (121) to stratify physician guideline concordance, with physicians defined as high-concordance when 80% or more patients received guideline-concordant care, or alternatively defined as low–concordance. Multilevel logistic regression was used to model the association between pre-MMA ADT use and guideline-concordant care post-MMA. Separate multilevel logistic regressions comparing the

effect of pre-MMA use on each emerging modality within multi-modality treatment categories (MIRP in radical prostatectomy; IMRT in radiation therapy; and, NCCN surveillance among all surveillance) were run. Statistical significance was determined at $\alpha$=0.05, and Stata/SE 12.1 was used for all analyses (112).

**Results**

We identified 27,315 men diagnosed with localized prostate cancer from 2005 through 2007 who met our inclusion criteria. Care for these men was provided by 4,104 physicians of all specialties paid under fee-for-service Medicare during the 18-month treatment window (Figure 6.1).

Among elderly prostate cancer patients, 15,876 (58%) received some type of radiation therapy; 5,573 (20%) received either open or laparoscopic radical prostatectomy; 3,420 (13%) received other treatments including ADT, and 2,446 (9%) received some form of active surveillance. Treatment received differed by risk category ($p<0.001$) (Figure 6.2).

After assigning guideline concordance based on D'Amico risk and treatment received, overall NCCN guideline concordance was 60.1% and reached 75.3% overall when considering MIRP and non-biopsy surveillance as concordant therapies. Guideline concordance was higher for men in the high risk category (62.7%) than for men in the low (61.5%) and intermediate risk (56.3%) categories ($p<0.001$) (Figure 6.2). NCCN guideline concordance was also higher among younger men and those with less severe cancer and fewer comorbidities (all at $p<0.001$) (Table 1). Additional unadjusted results (Table 2) showed that of the 4,104 physicians providing care in the post-MMA period, those providing guideline-concordant care had lower average pre-MMA PADT overuse ($p<0.001$).

After controlling for patient and physician characteristics, greater physician pre-MMA PADT use was associated with lower odds of providing guideline-concordant initial treatment in the post-MMA period (OR 0.25, 95% CI 0.19, 0.34). Female physicians had greater odds of providing guideline-concordant care than male physicians (OR 1.32, 95% CI 1.03, 1.69).

Physicians' time in practice was not associated with provision of guideline concordant care (OR 1.06, 95% CI 0.95, 1.20), nor was board certification (OR 1.10, 95% CI, 0.84, 1.42). We found no racial/ethnic differences in receipt of guideline-concordant care, other than for men whose race was missing from the SEER registry (Table 6.3).

Compared to conventional modalities, the odds of receiving all three of the newer modalities (MIRP, IMRT, and NCCN surveillance) increased over time in this cohort (Tables 6.4 and 6.5). Compared to 2005, the odds of a patient receiving MIRP was two times greater in 2006 (OR 2.39; 95% CI 1.75, 3.25) and almost four times greater in 2007 (OR 3.92; 95% CI 2.86, 5.36). Compared to 2005, the odds of a patient receiving IMRT was one and half times greater in 2006 (OR 1.49, 95% CI1.32, 1.69) and two times greater in 2007 (OR 2.15; 95% CI 1.88, 2.46). Thirty-eight percent of patients receiving any radical prostatectomy had MIRP (2,107/5,573). A majority of patients receiving radiation (63%) received IMRT (10,071/15,876). Only 7% of surveillance patients received the level of surveillance recommended by NCCN (171/2,446).

In separate analyses for each treatment category, the modality of treatment used was not associated with pre-MMA PADT overuse. Among the 6,265 men who received some form of radical prostatectomy, their treating physicians' pre-MMA PADT overuse was not associated with use of MIRP rather than open radical prostatectomy (OR 2.63, 95% CI 0.90, 7.67). Among the 15,876 who received radiation, pre-MMA PADT overuse was not associated with use of IMRT over the other radiation modalities (OR 1.15, 95% CI 0.39, 3.44). Too few patients received NCCN-concordant active surveillance to model factors associated with its use. However, descriptive analyses (Table 6.5) suggest that among the 2,446 men receiving surveillance, pre-MMA PADT use was not associated with use of guideline-concordant surveillance over guideline-discordant surveillance (p=0.22).

**Discussion**

To the best of our knowledge, ours is the first study to look at overall guideline concordance for localized prostate cancer in a post-MMA population and identify emerging

patterns of care (161). Contrary to our hypothesis, after adjusting for patient and physician characteristics, high levels of pre-MMA ADT overuse were associated with lower NCCN guideline concordance post-MMA. Physicians who we categorized as overusing ADT pre-MMA were *less* likely to provide NCCN guideline-recommended care in more recent years. There may be several reasons for this. Our sample included all physician groups. Radiation oncologists were less likely to overuse PADT in the pre-MMA period (ADT adjuvant to radiation is guideline concordant; PADT would be prescribed by the diagnosing urologist) and may have maintained these practices into the current period (93). Although the most recently trained urologists were also less likely to overuse ADT (93), and these same urologists also are more likely to adopt new robotic technology (162) despite its lack of strong recommendation by NCCN (12), MIRP has not penetrated the Medicare population as quickly as it may have younger populations of prostate cancer patients. Thus, the net effect of changes due to the training imprint may have yet to be realized.

Further, some physicians appeared to replace PADT use with active surveillance. However, surveillance techniques have not yet reached levels currently endorsed by guidelines and it may be directed to the wrong group of patients. Although levels of *guideline-discordant surveillance* in our study mirror those found in other studies (4), we identified very little *NCCN guideline-concordant surveillance*, that which consisted of a non-diagnostic prostate biopsy and at least two PSA tests or DREs within 18 months of diagnosis. A much larger number of men received some follow-up that included a PSA test. Little is known about the low rates of uptake of biopsy-monitored active surveillance (4), and no studies to date have assessed the degree to which urologists provide the currently recommended level of surveillance intensity. Prior research has generally assessed the absence of definitive therapy, or less often, the confirmed receipt of PSA testing and/or evidence of post-diagnosis medical visits (163). However, standards of active surveillance have intensified over the last decade (4, 12, 20-22), with one component of that approach, prostate biopsy, becoming increasingly important. However,

prostate biopsy is an invasive and painful procedure, and many physicians may perceive that their patients would not consent to it (164, 165). Moreover, risks of infection and other complications are higher among men who undergo repeat biopsies (154, 155), and the contribution of more sophisticated biopsies to patients' prognosis are in doubt (156). Thus, some physicians may be reluctant to offer the procedure as part of surveillance.

Lastly, the use of PADT among high ADT users in the pre-MMA period was still relatively high at 17%. This may be due to the volume response that we observed in an earlier study (93). The majority of urologists studied had either low, stable ADT overuse or decreased their ADT overuse sharply over the 2000s. However, the residual overuse observed may be attributed to the group of *increasing users*, a sizeable group of urologists who increased overuse of ADT coincident with MMA reimbursement changes (93).

Among the 4,104 physicians providing care to patients with localized prostate cancer in a national, population-based sample, there is an opportunity to improve the quality of initial treatment delivered. In this study sample, concordance with the then-applicable NCCN consensus guidelines was only 60%. An often used benchmark for guideline-concordance is 80% adherence to quality measures (121), suggesting that improvements in prostate cancer care among the elderly are needed. Even assuming all MIRP to be delivered by high volume surgeons, as recent research indicates (150) and NCCN allows, guideline-concordant care did not reach 80%. However, we did not find racial/ethnic differences in guideline concordance. We only detected lower odds of receipt of high quality care to be associated with men whose racial/ethnic status was not available in the SEER registry. Other studies have found differences in prostate cancer treatments delivered between African Americans and white Americans (166-169), but studies assessing overall guideline concordant care have not identified racial disparities (121, 135). Because prostate cancer offers multiple treatment options for each risk category, racial differences in the specific treatment selected can be present without that care indicating a quality problem. Nonetheless, additional research to ascertain whether the

guideline recommendations themselves are appropriate for men of all racial and ethnic groups may be needed. Additionally, research is needed to determine whether care decisions reflect the preferences of all patients.

Like other studies (40), our analysis found that new technologies are being rapidly adopted. IMRT, although expensive (170) and not well established in terms of comparative effectiveness, is a guideline-recommended option. Therefore, by these standards its use is appropriate. MIRP, which may be comparable to open prostatectomy in outcomes but is not yet guideline-recommended, has not reached the level of penetration of IMRT. It is not known whether this is due to lack of evidence or guideline recommendations, poor reimbursement relative to the technology investment hospitals must make, or clinical applicability to the post-MMA Medicare prostate cancer patient population. However, other studies of MIRP uptake have shown much greater use among all-age populations than we found among the elderly (150, 151). Greater patient age and less differentiated cancers were associated with MIRP use over open prostatectomy. Whether MIRP may be beneficial or superior to open prostatectomy in these situations is unknown, but the comparative effectiveness of MIRP versus open prostatectomy should be monitored among these risk groups.

Our study has several limitations. First, we cannot directly compare guideline concordance pre-MMA to that post-MMA, in part because PSA levels were not recorded in SEER registries prior to 2004. Secondly, there may be questions about the validity of our claims-based approach to detect NCCN-level active surveillance, especially given the low prevalence of prostate biopsy in our cohort. However, our estimates are in line with other recent claims studies identifying prostate biopsy when extrapolating to our cohort (142, 171). Third, NCCN guidelines make guarded recommendations regarding MIRP during the period of our study, conceding that MIRP conducted by an experienced surgeon produces similar outcomes to open prostatectomy. We could not evaluate the technical experience of urologists performing the procedure in our sample. Thus, we may have underestimated the guideline concordance of care

for those receiving MIRP. Fourth, our study is not based on a random sample of physicians or patients and may not be generalizable (63). However the SEER registries represent approximately one quarter of the U.S. population and are similar to the national population in the proportion of minorities and low income residents in the U.S. (91). Further, the median age of prostate cancer diagnosis in the US is 66.0 (1), thus our study results are generalizable to at least half of the prostate cancer patient population. Finally, we relied on registry records for stage, grade and PSA information by which to stratify patients to determine guideline concordance. Missing or incorrect information in the registry may have resulted in patients with metastatic disease or clinically advanced disease being in our sample, and thus we may have underestimated guideline concordance (172, 173).

### *Conclusions*

Although fewer men are exposed to the harms of ADT, declining use of PADT following changes in Medicare reimbursement policy may not have improved the overall quality of care for men with localized prostate cancer. PADT may have been replaced by other care that is discordant with current consensus recommendations. Although we cannot determine whether new treatment modalities replaced PADT, regardless of reimbursement, the quality of prostate cancer treatment does not appear to reach common benchmarks, which provides an opportunity to devise better policy-level interventions that target overuse and improve overall care quality.

**Figure 6.1. Cohort Exclusions**

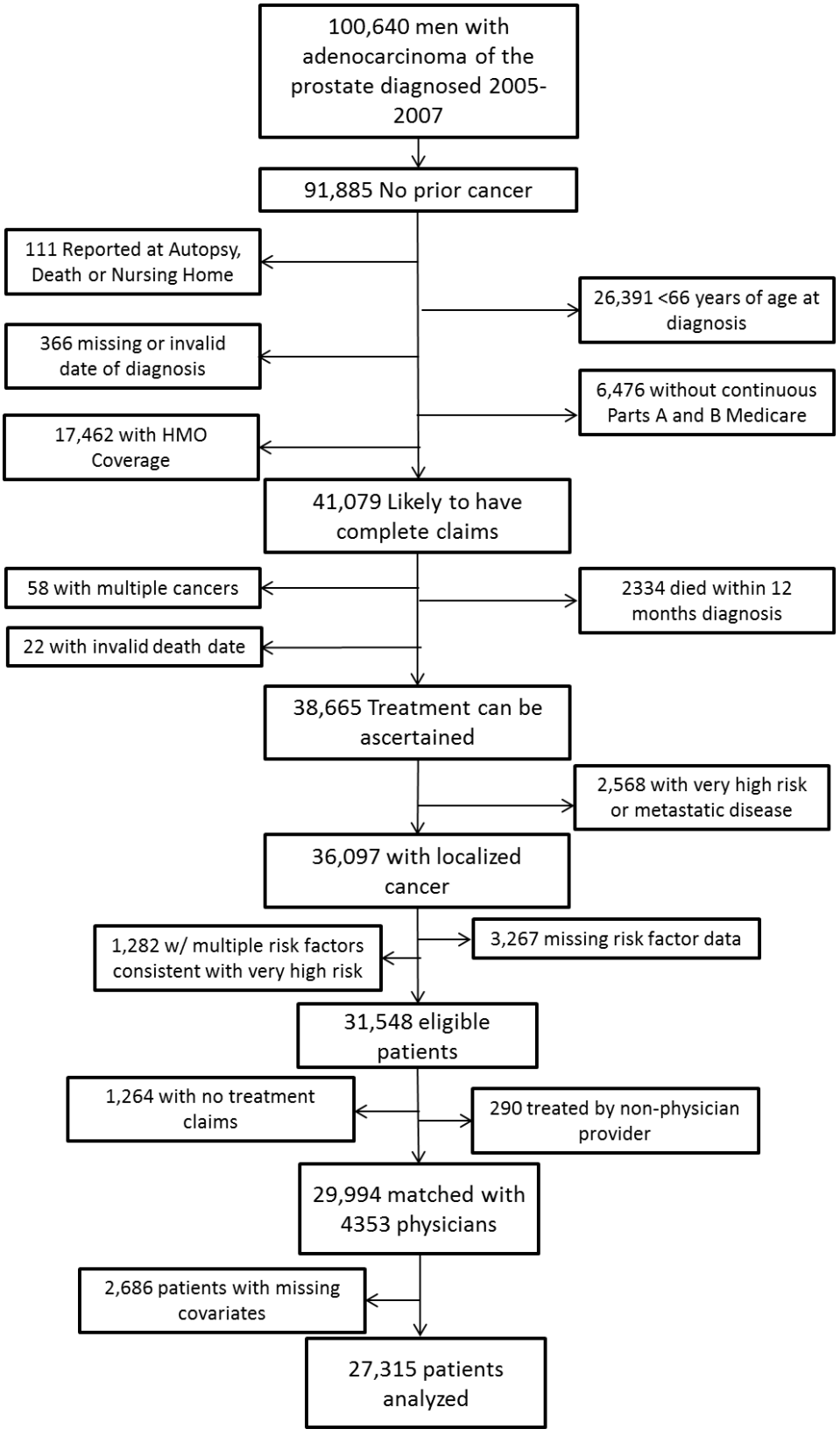
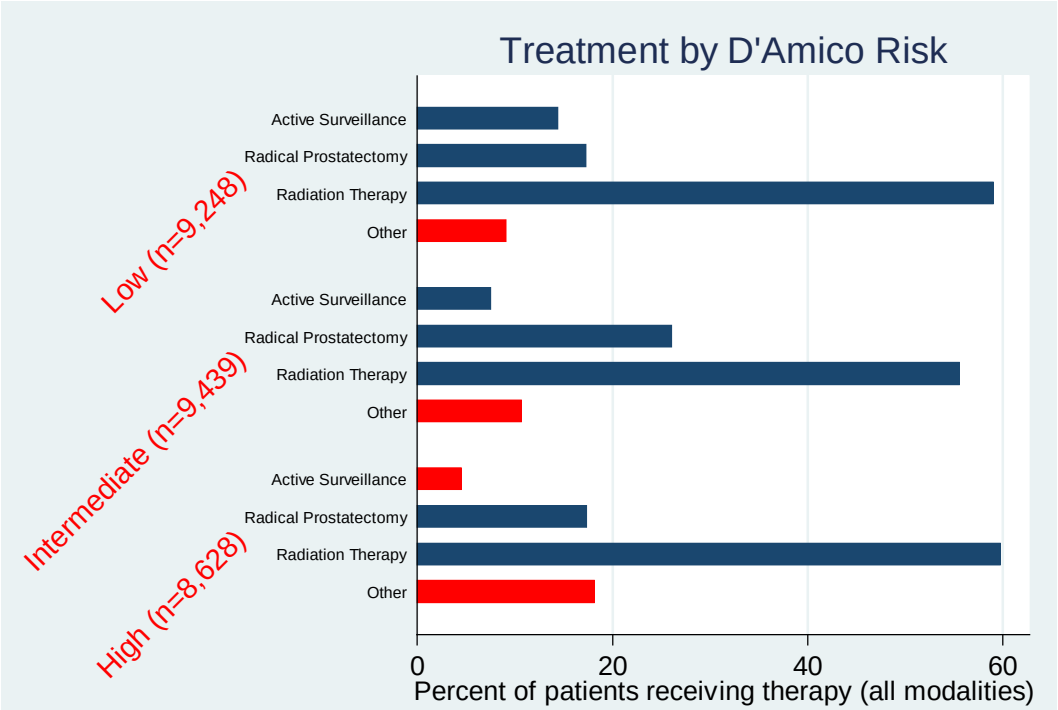


**Figure 6.2. Localized Prostate Cancer Treatment by D'Amico Risk, 2005–2009**




N=27,315, Red denotes guideline-discordant therapy for risk category

p<0.001 for treatment type by D'Amico Risk Category
Active Surveillance includes standard and NCCN surveillance
Radical prostatectomy includes MIRP and open prostatectomy
Radiation Therapy includes IMRT, EBRT and brachytherapy
Other includes ADT, cryosurgery, chemotherapy, and combinations of therapy

**Table 6.1. Patient Characteristics by Receipt of Guideline-Concordant Care**

| | Discordant Care | Concordant Care | |
|---|---|---|---|
| | Mean (Standard Deviation) or N ( %) | | |
| | **N= 10,910** | **N= 16,405** | ***p*** |
| **NCCN Guideline Concordance** | 10,910 (39.9%) | 16,405 (60.1%) | *<0.001* |
| **Year of Diagnosis** | | | *<0.001* |
| 2005 | 3,295 (30.2%) | 5,262 (32.1%) | |
| 2006 | 3,662 (33.6%) | 5,597 (34.1%) | |
| 2007 | 3.953 (36.2%) | 5,546 (33.8%) | |
| **T Stage** | | | *<0.001* |
| T1 | 6,404 (58.7%) | 9,786 (59.7%) | |
| T2 | 4,453 (40.8%) | 6,483 (39.5%) | |
| T3 | 51 (0.5%) | 136 (0.8%) | |
| **Grade** | | | *<0.001* |
| Well differentiated, 2-4 | 77 (0.7%) | 108 (0.7%) | |
| Moderately differentiated 5-7* | 5,313 (48.7%) | 7,560 (46.1%) | |
| Poorly Differentiated, 8-10 | 5,497 (50.4%) | 8,688 (53%) | |
| Undifferentiated | 23 (0.2%) | 49 (0.3%) | |
| **PSA level** | 10.2 (12.7) | 9.3 (10.8) | *<0.001* |
| **Comorbidities** | | | *<0.001* |
| 0 | 7,282 (66.7%) | 10,820 (66.0%) | |
| 1 | 2,311 (21.2%) | 3,782 (23.1%) | |
| 2 | 794 (7.3%) | 1,126 (6.9%) | |
| 3 or more | 523 (4.8%) | 677 (4.1%) | |
| **Age in years** | 74.3 (6.1) | 72.7 (4.8) | *<0.001* |
| **Race/ethnicity** | | | *<0.001* |
| Non-Hispanic white | 8,321 (76.3%) | 12, 935 (78.8%) | |
| Non-Hispanic black | 885 (8.1%) | 1,402 (8.5%) | |
| Hispanic | 659 (6.0%) | 1,047 (6.4%) | |
| Other | 477 (4.4%) | 759 (4.6%) | |
| Missing | 568 (5.2%) | 262 (1.6%) | |
| **Marital Status** | | | *<0.001* |
| Not Married | 2,016 (18.5%) | 3,064 (18.7%) | |
| Married | 7,357 (67.45) | 12,126 (73.9%) | |
| Missing | 1,537 (14.1%) | 1,215 (7.4%) | |
| **Pre-treatment Primary Care Use** | | | *0.22* |
| 0-2 visits in prior year | 1,782 (16.3%) | 2,639 (16.1%) | |
| 3-5 visits in prior year | 4,979 (45.6%) | 7,661 (46.7%) | |
| 6 or more visits in prior year | 4,149 (38.0%) | 6,105 (37.2%) | |

| | | | |
|---|---|---|---|
| **Primary Care Consultation** | | | *<0.001* |
| No | 4,330 (39.7%) | 6,920 (42.2%) | |
| Yes | 6,580 (60.3%) | 9.485 (57.8%) | |
| **Radiation Oncology Consultation** | | | *<0.001* |
| No | 6,385 (58.5%) | 3,812 (23.2%) | |
| Yes | 4,525 (41.5%) | 12,593 (76.8%) | |
| **Medical Oncology Consultation** | | | *0.32* |
| No | 10,250 (94.0%) | 15,364 (93.7%) | |
| Yes | 660 (6.0%) | 1,041 (6.3%) | |
| **Urology Consultation** | | | *0.63* |
| No | 243 (2.2%) | 351 (2.1%) | |
| Yes | 10,667 (97.8%) | 16,054 (97.9%) | |
| **Rural Residence** | | | *0.95* |
| No | 10,726 (98.3%) | 16,130 (98.3%) | |
| Yes | 184 (1.7%) | 275 (1.7%) | |
| **State of SEER Registry** | | | *<0.001* |
| Seattle | 690 (6.3%) | 1,030 (6.3%) | |
| Connecticut | 542 (5%) | 1,152 (7.0%) | |
| Detroit | 707 (6.5%) | 1,089 (6.6%) | |
| Hawaii | 152 (1.4%) | 299 (1.8%) | |
| Iowa | 567 (5.2%) | 1,045 (6.4%) | |
| New Mexico | 278 (2.5%) | 400 (2.4%) | |
| California | 3,890 (35.7%) | 5,163 (31.5%) | |
| Utah | 466 (4.3%) | 438 (2.7%) | |
| Georgia | 484 (4.4%) | 591 (3.6%_) | |
| Kentucky | 751 (6.9%) | 1,761 (6.2%) | |
| Louisiana | 884 (8.1%) | 1,184 (7.2%) | |
| New Jersey | 1,499 (13.7%) | 3,004 (18.3%) | |
| **Median Income of Patients' Communities** | | | *0.18* |
| $2,506-35,031 | 2,387 (21.9%) | 3,489 (21.3%) | |
| $35,051-46,079 | 2,545 (23.3%) | 3,790 (23.1%) | |
| $46,084-60,668 | 2,540 (23.3%) | 4,015 (24.5%) | |
| $60,669-200,008 | 2,856 (26.2%) | 4,285 (26.1%) | |
| Missing | 582 (5.3%) | 826 (5.0%) | |
| **Proportion of Patient's Community w/o High School Education** | | | *0.21* |
| 0-9.7% | 2,876 (26.4%) | 4,204 (25.6%) | |
| 9.7-15.5% | 2,607 (23.9%) | 4,069 (24.8%) | |
| 15.5%-25.2% | 2,513 (23.0%) | 3,863 (23.5%) | |
| 25.2%-100% | 2,337 (21.4%) | 3,449 (21%) | |
| Missing | 577 (5.3%) | 820 (5.0%) | |

P-values by t-test for continuous variables and chi2 test for binary / categorical variables

**Table 6.2. Physician Characteristics by High Guideline Concordance**

| | **<80% Concordant** | **≥80% Concordant** | |
|---|---|---|---|
| | Mean (Standard Deviation) or N (%) | | |
| | **N= 2,736** | **N= 1,368** | ***p*** |
| **Average Physician-level ADT Overuse 2000-2003** | 0.2 (0.3) | 0.1 (0.2) | *<0.001* |
| **NCCN Guideline Concordance** | 0.2 (0.3) | 1.0 (0.1) | *<0.001* |
| **Specialty** | | | *<0.001* |
| Urology | 1600 (58.5%) | 416 (30.4%) | |
| Radiation Oncology | 339 (12.4%) | 638 (46.6%) | |
| Medical Oncology | 101 (3.7%) | 23 (1.7%) | |
| Primary Care | 515 (18.8%) | 148 (10.8%) | |
| Other | 181 (6.6%) | 143 (10.5%) | |
| **Time in Practice** | | | *0.04* |
| <20 years | 1,014 (37.1%) | 552 (40.4%) | |
| **≥20 years** | 1,722 (62.9%) | 816 (59.6%) | |
| **Gender** | | | *<0.001* |
| Male | 2,558 (93.5%) | 1,186 (86.7%) | |
| Female | 178 (6.5%) | 182 (13.3%) | |
| **Training** | | | *0.006* |
| Foreign Trained | 413 (15.1%) | 252 (18.4%) | |
| U.S. Trained | 2,323 (84.9%) | 1,116 (81.6%) | |
| **Board Certified** | | | *0.07* |
| No | 214 (7.8%) | 86 (6.3%) | |
| Yes | 2,522 (92.2%) | 1,282 (93.7%) | |
| **Medical School Affiliation** | | | *<0.001* |
| None | 1,212 (44.3%) | 521 (38.1%) | |
| Some | 1,481 (54.1%) | 845 (61.8%) | |
| Missing | 43 (1.6%) | 2 (0.1%) | |
| **Physician Prostate Panel Size** | | | *<0.001* |
| 0-20 prostate patients/year | 1,842 (67.3%) | 1,053 (77.0%) | |
| 21-37 prostate patients/year | 622 (22.7%) | 223 (16.3%) | |
| 38 or more prostate patients/year | 272 (9.9%) | 92 (6.7%) | |
| **Practice Type** | | | *<0.001* |
| Group Practice | 2,069 (75.6%) | 1,052 (76.9%0 | |
| Solo Practice | 494 (18.1%) | 197 (14.4%) | |
| Missing | 173 (6.3%) | 119 (8.7%) | |
| **Proportion of Patients Minority** | | | *0.01* |
| 0-9.7% | 1,139 (41.6%) | 618 (45.2%) | |
| 9.7-15.5% | 707 (25.8%) | 297 (21.7%) | |
| 15.5%-25.2% | 890 (32.5%) | 453 (33.1%) | |

P-values by t-test for continuous variables and chi2 test for binary / categorical variables

| | Odds Ratio | 95% Confidence Interval | |
|---|---|---|---|
| Pre-MMA ADT Use | 0.25 | 0.19 | 0.34 |
| Specialty | | | |
| Urology | 1.00 | | |
| Radiation Oncology | 3.59 | 2.03 | 4.26 |
| Medical Oncology | 0.33 | 0.20 | 0.54 |
| Primary Care | 0.29 | 0.22 | 0.37 |
| Other | 1.09 | 0.83 | 1.44 |
| Time in Practice | | | |
| <20 years | 1.00 | | |
| ≥20 years | 1.07 | 0.95 | 1.20 |
| Gender | | | |
| Male | 1.00 | | |
| Female | 1.32 | 1.03 | 1.69 |
| Training | | | |
| Foreign Trained | 1.00 | | |
| U.S. Trained | 0.83 | 0.70 | 0.99 |
| Board Certified | | | |
| No | 1.00 | | |
| Yes | 1.10 | 0.85 | 1.42 |
| Medical School Affiliation | | | |
| None | 1.00 | | |
| Some | 0.94 | 0.82 | 1.06 |
| Missing | 0.11 | 0.23 | 0.40 |
| Physician Prostate Panel Size | | | |
| <20 prostate patients/year | 1.00 | | |
| 21-37 prostate patients/year | 0.98 | 0.87 | 1.09 |
| ≥38 prostate patients/year | 0.84 | 0.73 | 0.96 |
| Practice Type | | | |
| Group Practice | 1.00 | | |
| Solo Practice | 1.09 | 0.92 | 1.30 |
| Missing | 0.99 | 0.77 | 1.28 |
| Proportion of Patients Minority | | | |
| 0-9.7% | 1.00 | | |
| 9.7-15.5% | 1.00 | 0.89 | 1.12 |
| 15.5%-25.2% | 1.09 | 0.95 | 1.25 |

N=27,158 patients; n=4,104 physicians

**Table 6.3. Regression Results for Pre-MMA Use on Uptake of New Treatment Modalities**

| | Minimally Invasive Radical Prostatectomy | | | Intensity Modulated Radiation Therapy | | |
|---|---|---|---|---|---|---|
| | Odds Ratio | 95% Confidence Interval | | Odds Ratio | 95% Confidence Interval | |
| **Pre-MMA ADT Use** | 2.63 | 0.91 | 7.67 | 1.15 | 0.39 | 3.44 |
| **Specialty** | | | | | | |
| Urology | 1.00 | | | 1.00 | | |
| Radiation Oncology | 15.75 | 2.88 | 86.30 | 28.34 | 18.67 | 43.01 |
| Medical Oncology | 147.34 | 19.45 | 1116.18 | 21.77 | 4.07 | 116.47 |
| Primary Care | 72.91 | 30.18 | 176.15 | 31.44 | 12.54 | 78.79 |
| Other | 6.84 | 2.78 | 16.87 | 6.64 | 3.18 | 13.84 |
| **Time in Practice** | | | | | | |
| <20 years | 1.00 | | | 1.00 | | |
| ≥20 years | 0.53 | 0.34 | 0.84 | 1.03 | 0.81 | 1.32 |
| **Gender** | | | | | | |
| Male | 1.00 | | | 1.00 | | |
| Female | 0.67 | 0.21 | 2.10 | 1.22 | 0.75 | 1.99 |
| **Training** | | | | | | |
| Foreign Trained | 1.00 | | | 1.00 | | |
| U.S. Trained | 1.11 | 0.56 | 2.22 | 0.84 | 0.56 | 1.27 |
| **Board Certified** | | | | | | |
| No | 1.00 | | | 1.00 | | |
| Yes | 1.05 | 0.40 | 2.73 | 1.99 | 0.99 | 4.01 |
| **Medical School Affiliation** | | | | | | |
| None | 1.00 | | | 1.00 | | |
| Some | 2.82 | 1.74 | 4.57 | 1.28 | 0.95 | 1.73 |
| Missing | 0.16 | 0.00 | 128.84 | 6.95 | 0.05 | 938.22 |
| **Physician Prostate Panel Size** | | | | | | |
| <20 prostate patients/year | 1.00 | | | 1.00 | | |
| 21-37 prostate patients/year | 1.76 | 1.18 | 2.64 | 0.89 | 0.72 | 1.10 |
| ≥38 prostate patients/year | 2.65 | 1.60 | 4.38 | 0.86 | 0.67 | 1.11 |
| **Practice Type** | | | | | | |
| Group Practice | 1.00 | | | 1.00 | | |
| Solo Practice | 0.46 | 0.24 | 0.87 | 0.74 | 0.47 | 1.18 |
| Missing | 1.50 | 0.57 | 3.96 | 0.97 | 0.56 | 1.70 |
| **Proportion of Patients Minority** | | | | | | |
| 0-9.7% | 1.00 | | | 1.00 | | |
| 9.7-15.5% | 1.03 | 1.18 | 1.53 | 1.19 | 0.97 | 1.45 |
| 15.5%-25.2% | 0.86 | 0.52 | 1.43 | 1.24 | 0.96 | 1.60 |
| **Year of Diagnosis** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2005 | 1.00 | | | 1.00 | | |
| 2006 | 2.39 | 1.75 | 3.25 | 1.49 | 1.32 | 1.69 |
| 2007 | 3.92 | 2.86 | 5.36 | 2.15 | 1.88 | 2.46 |
| **T Stage** | | | | | | |
| T1 | 1.00 | | | 1.00 | | |
| T2 | 0.76 | 0.60 | 0.97 | 1.14 | 1.02 | 1.26 |
| T3 | 0.16 | 0.05 | 0.54 | 2.55 | 1.34 | 4.82 |
| **Grade** | | | | | | |
| Well differentiated, 2-4 | 1.00 | | | 1.00 | | |
| Moderately differentiated 5-7* | 74.42 | 8.58 | 645.08 | 0.83 | 0.42 | 1.62 |
| Poorly Differentiated, 8-10 | 87.97 | 10.16 | 761.87 | 2.23 | 1.14 | 4.36 |
| Undifferentiated | 3.97 | 0.09 | 174.53 | 1.30 | 0.38 | 4.45 |
| **PSA level** | 0.98 | 0.96 | 0.99 | 1.01 | 1.01 | 1.02 |
| **Comorbidities** | | | | | | |
| 0 | 1.00 | | | 1.00 | | |
| 1 | 0.69 | 0.50 | 0.93 | 1.06 | 0.94 | 1.20 |
| 2 | 0.69 | 0.39 | 1.22 | 1.12 | 0.91 | 1.36 |
| 3 or more | 0.28 | 0.11 | 0.71 | 1.54 | 1.18 | 2.01 |
| **Age in years** | 9.64 | 3.58 | 25.98 | 1.24 | 0.94 | 1.63 |
| **Age²** | 0.98 | 0.98 | 0.99 | 1.00 | 1.00 | 1.00 |
| **Race/ethnicity** | | | | | | |
| Non-Hispanic white | 1.00 | | | 1.00 | | |
| Non-Hispanic black | 1.37 | 0.67 | 2.74 | 1.04 | 0.85 | 1.28 |
| Hispanic | 0.73 | 0.39 | 1.38 | 1.67 | 1.30 | 2.15 |
| Other | 2.92 | 1.33 | 6.39 | 1.39 | 1.03 | 1.87 |
| Missing | 2.31 | 0.59 | 9.11 | 0.81 | 0.52 | 1.27 |
| **RacexPre-MMA Use** | | | | | | |
| Non-Hispanic whitexPre-MMA | 1.00 | | | 1.00 | | |
| Non-Hispanic blackxPre-MMA | 0.12 | 0.01 | 1.76 | 0.38 | 0.04 | 4.07 |
| HispanicxPre-MMA | 0.51 | 0.07 | 3.77 | 5.91 | 0.61 | 57.35 |
| OtherxPre-MMA | 2.92 | 1.33 | 6.39 | 10.30 | 0.68 | 156.59 |
| MissingxPre-MMA | 2.31 | 0.59 | 9.11 | 0.14 | 0.01 | 2.67 |
| **Marital Status** | | | | | | |
| Not Married | 1.00 | | | 1.00 | | |
| Married | 1.20 | 0.86 | 1.68 | 0.98 | 0.86 | 1.12 |
| Missing | 0.86 | 0.43 | 1.75 | 1.17 | 0.91 | 1.51 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Pre-treatment Primary Care Use** | | | | | | |
| 0-2 visits in prior year | 1.00 | | | 1.00 | | |
| 3-5 visits in prior year | 1.51 | 1.02 | 2.23 | 1.14 | 0.97 | 1.35 |
| 6 or more visits in prior year | 1.36 | 0.88 | 2.10 | 1.23 | 1.03 | 1.48 |
| **Primary Care Consultation** | | | | | | |
| No | 1.00 | | | 1.00 | | |
| Yes | 1.33 | 0.98 | 1.80 | 0.84 | 0.74 | 0.95 |
| **Radiation Oncology Consultation** | | | | | | |
| No | 1.00 | | | 1.00 | | |
| Yes | 2.00 | 1.46 | 2.74 | 0.38 | 0.29 | 0.51 |
| **Medical Oncology Consultation** | | | | | | |
| No | 1.00 | | | 1.00 | | |
| Yes | 0.96 | 0.53 | 1.72 | 1.07 | 0.86 | 1.35 |
| **Urology Consultation** | | | | | | |
| No | 1.00 | | | 1.00 | | |
| Yes | 22.46 | 5.68 | 88.81 | 1.30 | 0.93 | 1.81 |
| **Rural Residence** | | | | | | |
| No | 1.00 | | | 1.00 | | |
| Yes | 0.60 | 0.25 | 1.46 | 0.59 | 0.38 | 0.91 |
| **State of SEER Registry** | | | | | | |
| Seattle | 1.00 | | | 1.00 | | |
| Connecticut | 7.49 | 2.08 | 27.01 | 1.14 | 0.54 | 2.40 |
| Detroit | 7.30 | 2.10 | 25.36 | 2.09 | 0.97 | 4.49 |
| Hawaii | 15.06 | 2.05 | 110.54 | 5.27 | 1.69 | 16.39 |
| Iowa | 1.49 | 0.44 | 5.06 | 1.32 | 0.61 | 2.82 |
| New Mexico | 0.81 | 0.16 | 4.25 | 0.93 | 0.38 | 2.28 |
| California | 6.56 | 2.51 | 17.17 | 1.21 | 0.68 | 2.14 |
| Utah | 1.57 | 0.37 | 6.66 | 0.10 | 0.03 | 0.30 |
| Georgia | 2.24 | 0.44 | 11.50 | 0.82 | 0.36 | 1.89 |
| Kentucky | 14.89 | 4.40 | 50.39 | 0.47 | 0.22 | 1.00 |
| Louisiana | 4.84 | 1.36 | 17.29 | 1.26 | 0.57 | 2.77 |
| New Jersey | 8.44 | 2.91 | 24.51 | 1.80 | 0.96 | 3.37 |
| **Median Income of Patients' Communities** | | | | | | |
| $2,506-35,031 | 1.00 | | | 1.00 | | |
| $35,051-46,079 | 0.99 | 0.65 | 1.50 | 1.14 | 0.95 | 1.36 |
| $46,084-60,668 | 0.82 | 0.50 | 1.36 | 1.11 | 0.89 | 1.38 |
| $60,669-200,008 | 1.06 | 0.59 | 1.92 | 1.05 | 0.80 | 1.37 |
| Missing | 1.07 | 0.00 | 2357.77 | 0.41 | 0.03 | 4.92 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Proportion of Patient's Community w/o High School Education** | | | | | | |
| 0-9.7% | 1.00 | | | 1.00 | | |
| 9.7-15.5% | 0.99 | 0.69 | 1.42 | 0.91 | 0.78 | 1.07 |
| 15.5%-25.2% | 0.94 | 0.62 | 1.44 | 0.83 | 0.68 | 1.01 |
| 25.2%-100% | 0.78 | 0.45 | 1.35 | 0.84 | 0.66 | 1.08 |
| Missing | 0.85 | 0.00 | 1916.92 | 2.05 | 0.17 | 24.92 |
| **Constant** | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.15 |
| N=27,158 patients; n=4,104 physicians | | | | | | |

**Table 6.4. Characteristics of Patients by Receipt of Active Surveillance**

| | No Active Surveillance | Active Surveillance | |
|---|---|---|---|
| | Mean (Standard Deviation) or % | | |
| | **N=2,275** | **N=171** | ***p*** |
| **Year of Diagnosis** | | | *<0.001* |
| 2005 | 31.6 | 20.5 | |
| 2006 | 34.9 | 31.0 | |
| 2007 | 33.5 | 48.5 | |
| **T Stage** | | | *0.20* |
| T1 | 58.2 | 64.9 | |
| T2 | 41.5 | 35.1 | |
| T3 | 0.2 | 0.0 | |
| **Grade** | | | *0.009* |
| Well differentiated, 2-4 | 1.7 | 0.0 | |
| Moderately differentiated 5-7* | 69.7 | 81.3 | |
| Poorly Differentiated, 8-10 | 28.5 | 18.7 | |
| Undifferentiated | 0.1 | 0.0 | |
| **PSA level** | 9.0 (10.6) | 6.1 (4.0) | *<0.001* |
| **Comorbidities** | | | *0.20* |
| 0 | 66.1 | 70.2 | |
| 1 | 21.4 | 22.2 | |
| 2 | 7.5 | 5.8 | |
| 3 or more | 5.1 | 1.8 | |
| **Age in years** | 76.1 (6.0) | 72.9 (4.5) | *<0.001* |
| **Race/ethnicity** | | | *0.17* |
| Non-Hispanic white | 74.2 | 81.3 | |
| Non-Hispanic black | 7.1 | 4.1 | |
| Hispanic | 5.2 | 2.9 | |
| Other | 2.9 | 1.2 | |
| Missing | 10.6 | 10.5 | |
| **Marital Status** | | | *0.02* |
| Not Married | 18.4 | 17.0 | |
| Married | 59.3 | 69.0 | |
| Missing | 22.3 | 14.0 | |
| **Pre-treatment Primary Care Use** | | | *0.69* |
| 0-2 visits in prior year | 16.0 | 17.5 | |
| 3-5 visits in prior year | 45.7 | 47.4 | |
| 6 or more visits in prior year | 38.3 | 35.1 | |

| | | | |
|---|---|---|---|
| **Primary Care Consultation** | | | *<0.001* |
| No | 31.8 | 46.2 | |
| Yes | 68.2 | 53.8 | |
| **Radiation Oncology Consultation** | | | *0.06* |
| No | 77.7 | 71.3 | |
| Yes | 22.3 | 28.7 | |
| **Medical Oncology Consultation** | | | *0.22* |
| No | 92.6 | 90.2 | |
| Yes | 7.4 | 9.9 | |
| **Urology Consultation** | | | *0.49* |
| No | 3.3 | 2.3 | |
| Yes | 96.7 | 97.7 | |
| **Rural Residence** | | | *0.83* |
| No | 98.6 | 98.8 | |
| Yes | 1.4 | 1.2 | |
| **State of SEER Registry** | | | *<0.001* |
| Seattle | 5.4 | 10.5 | |
| Connecticut | 6.1 | 5.3 | |
| Detroit | 6.9 | 7.0 | |
| Hawaii | 0.9 | 0.0 | |
| Iowa | 5.1 | 0.0 | |
| New Mexico | 4.3 | 0.6 | |
| California | 38.5 | 46.2 | |
| Utah | 4.6 | 5.3 | |
| Georgia | 3.1 | 3.5 | |
| Kentucky | 5.9 | 5.8 | |
| Louisiana | 8.0 | 1.2 | |
| New Jersey | 11.3 | 14.6 | |
| **Median Income of Patients' Communities** | | | *<0.001* |
| $2,506-35,031 | 21.1 | 7.0 | |
| $35,051-46,079 | 24.5 | 20.5 | |
| $46,084-60,668 | 23.3 | 25.7 | |
| $60,669-200,008 | 26.2 | 42.1 | |
| Missing | 4.9 | 4.7 | |
| **Proportion of Patient's Community w/o High School Education** | | | *<0.001* |
| 0-9.7% | 27.9 | 45.6 | |
| 9.7-15.5% | 24.3 | 21.1 | |
| 15.5%-25.2% | 24.2 | 17.5 | |
| 25.2%-100% | 18.9 | 11.1 | |
| Missing | 4.8 | 4.7 | |

| | | | |
|---|---|---|---|
| **Time in Practice** | | | *0.19* |
| <20 years | 32.0 | 36.8 | |
| ≥20 years | 68.0 | 63.2 | |
| **Gender** | | | *0.63* |
| Male | 97.0 | 97.7 | |
| Female | 3.0 | 2.3 | |
| **Training** | | | *0.56* |
| Foreign Trained | 12.0 | 13.5 | |
| U.S. Trained | 88.0 | 86.5 | |
| **Board Certified** | | | *<0.001* |
| No | 5.9 | 12.9 | |
| Yes | 94.1 | 87.1 | |
| **Medical School Affiliation** | | | *<0.001* |
| None | 50.4 | 26.9 | |
| Some | 49.1 | 73.1 | |
| Missing | 0.5 | 0.0 | |
| **Physician Prostate Panel Size** | | | *<0.001* |
| 0-20 prostate patients/year | 46.0 | 41.5 | |
| 21-37 prostate patients/year | 35.5 | 26.9 | |
| 38 or more prostate patients/year | 18.5 | 31.6 | |
| **Practice Type** | | | *0.08* |
| Group Practice | 78.8 | 81.9 | |
| Solo Practice | 16.6 | 11.1 | |
| Missing | 4.7 | 7.0 | |
| **Proportion of Patients Minority** | | | *<0.001* |
| 0-9.7% | 38.1 | 37.4 | |
| 9.7-15.5% | 31.0 | 44.4 | |
| 15.5%-25.2% | 30.9 | 18.1 | |

P-values by t-test for continuous variables and chi2 test for binary/categorical variables

# CHAPTER 7 SUMMARY OF FINDINGS AND IMPLICATIONS FOR POLICY, PRACTICE, AND RESEARCH

## Summary of Findings

This dissertation examined factors associated with overuse of medical care, a common and costly problem in healthcare quality which has received little attention, but has emerged as a national priority for improving the U.S. healthcare system. Within this context we studied the declining overuse of Androgen Deprivation Therapy among clinically localized prostate cancer patients in fee-for-service Medicare, a trend which should have improved the quality of care prostate cancer patients receive, since the treatment is not recommended by national consensus guidelines. We assessed reimbursement policy as a lever for not only reducing overuse but also for improving quality of care in situations of overuse. We also explored physician and practice characteristics associated with decreasing overuse, reimbursement responsiveness, and guideline concordance. And, we assessed how changing practice patterns coincident with changing ADT use impacted prostate cancer quality of care.

Economic theory informed our conceptual model and we used economic tools to assess our hypotheses. Our national, population-based sample of prostate cancer patients was drawn from the SEER cancer registries and matched with complete Medicare claims. We identified treating physicians of prostate cancer patients and matched AMA physician and practice data to the enhanced claims. We created three distinct cohorts of localized prostate cancer patients to explore various components of overuse of ADT. Two analyses modeled factors associated with overuse of ADT and one analysis modeled the factors associated with NCCN-guideline concordant care. Our second analysis of ADT overuse used multilevel logistic regression and an innovative reimbursement generosity index which exploited variation among Medicare carriers in reimbursing for ADT during a period of guideline stability. We used multilevel mixed effects

modeling to control for tumor, patient, physician, and practice factors known to be associated with prostate cancer treatment decisions, quality of care, and overuse of healthcare; and to adjust standard errors for clustering of patients within physicians. We conducted multiple sensitivity analyses to assess the robustness of our findings.

Prior to MMA and during a period of guideline stability (2000-2003), we found limited evidence that urologists were responsive to ADT reimbursement differences (OR 1.00, 95% CI, 0.99, 1.00), despite higher ADT overuse in areas of favorable ADT reimbursement observed in unadjusted analysis, and contrary to our expectations. However, we found a small, but negative association between all prostate treatment reimbursement and physicians' overuse of ADT, although the confidence interval rounded to 1 (OR 0.99, 95% CI 0.99, 1.00). Physicians in high reimbursement areas, relative to all treatments, were less likely to overuse ADT, suggesting that physicians with alternative treatment options or alternative reimbursement may have been less likely to overuse ADT. Exploratory analyses among urology group practices demonstrated that physicians in multi-specialty groups, presumably with superior access to more treatment options, were less likely to overuse ADT, compared to single–specialty urology group practices.

Looking at changes in ADT overuse across the entire period of MMA's implementation of reimbursement cuts (2000-2007), we observed three patterns of ADT use. A large group of urologists (n=1,478) maintained low and consistent ADT overuse among localized prostate cancer patients throughout the period. However, coincident with the ADT reimbursement reductions, we identified two other groups of urologists who changed their patterns of ADT overuse. The larger of these two groups (n=394) decreased overuse and adopted patterns of overuse similar to the static users by the end of the 2007 treatment window. A smaller but substantial group of urologists (n=276) increased overuse of ADT coincident with reductions in reimbursement and achieved the highest levels of overuse observed in the study. Among this group of physicians ADT overuse was 32.6% among the 2,817 patients they treated over the study period, suggesting a potential quality problem. We could not distinguish increasing users

from decreasing users based on urologists' characteristics, but the patients of these two groups of physicians differed. Increasing users' patients were older, had more comorbid conditions, and were more likely to be non-Hispanic black or "other" race. They also lived in communities of fewer resources. Although there is no guideline recommendation that patients with these characteristics should receive PADT, other research suggests they often do. Thus, it is possible that rather than responding to reimbursement by intensifying the discounted service, as economic theory and empirical work have shown, these providers may have been responding to the changing clinical characteristics of their patient panel.

Nonetheless, overall ADT overuse in our T1 and T2 well- and moderately differentiated prostate cancer cohort remained 13.6% post-MMA. Rates were even higher in the full cohort of localized prostate cancer patients and evidence increasingly supports that PADT's harms outweigh its benefits, so understanding determinants of overuse is especially important. Our analysis of physician characteristics associated with ADT overuse throughout the MMA implementation period used multilevel logistic regression to examine the association of time in practice with ADT overuse. Physicians' time in practice was not associated with ADT overuse (OR 0.89; 95% CI 0.75 -1.05) throughout the era. However, solo practice type (OR 1.65; 95% CI 1.34-2.02) and lack of medical school affiliation (OR 0.65; 95% CI 0.55-0.77) were, suggesting that interventions to address overuse may be hard to deliver.

Although we found that ADT overuse persisted, overall changes in ADT overuse could have improved quality of care. Therefore, our third analysis assessed the effect of pre-MMA ADT overuse on the concordance of post-MMA care with National Comprehensive Cancer Network (NCCN) guidelines among clinically localized prostate cancer patients of varying risk of disease progression. We used multilevel logistic regression to test the association between guideline concordance and prior ADT overuse and, in individual models, the association between prior ADT overuse and use of new treatment modalities. Our study showed that physicians' pre-MMA ADT overuse was associated with delivering guideline-concordant care post-MMA (OR 0.25,

95% CI 0.18, 0.34). However, contrary to our expectations, physicians who were high users of ADT in the earlier period were more likely to overuse ADT and provide guideline-discordant care among their localized cancer patients in the contemporary period. Nevertheless, after stratifying patients according to risk for disease progression and assigning care received as guideline-concordant or -discordant, we found no racial differences in the quality of care delivered.

We also assessed the changing modalities of other prostate cancer treatment options, expecting that changes in ADT overuse may have been driven uptake of emerging modalities among other prostate cancer treatment options. However, in separate analyses for each treatment category, the modality of treatment was not associated with pre-MMA PADT overuse. Among the 6,265 men who received some form of radical prostatectomy, their treating physicians' pre-MMA PADT overuse was not associated with use of MIRP rather than open radical prostatectomy (OR 2.63, 95% CI 0.90, 7.67). Among the 15,876 who received radiation, pre-MMA PADT overuse was not associated with use of IMRT over the other radiation modalities (OR 1.15, 95% CI 0.39, 3.44). Too few patients received NCCN-concordant active surveillance to model factors associated with its use. However, descriptive analyses (Table 6.5) suggest that among the 2,446 men receiving surveillance, pre-MMA ADT use was not associated with use of NCCN-concordant surveillance over non-biopsy surveillance ($p=0.22$).

## Implications for policy, practice, and research

### *Policy*

Current efforts to reduce Medicare spending include limiting across-the-board increases for physician reimbursement (174). However, the effect of reimbursement change on care delivery is contextual and multiple responses are possible. Several economic studies suggest that physicians will actually intensify utilization of discounted services, known as the volume response. However, this effect has not been universal among all specialists or procedures (136). Our study suggests that among urologists treating prostate cancer this type of strategy may not

have the intended effect on decreasing costs. Urologists boast treating the widest variety of conditions with the greatest number of different procedures among specialists. Moreover the treatment of prostate cancer has a number of treatment options, each with multiple modalities. Therefore it is essential that reimbursement policy should not be expected to reduce overuse uniformly especially in situations where there are multiple treatment options. Some physicians may have resources to substitute services, but others may not. Policy makers should consider more targeted, nuanced reimbursement policy strategies, such as value-based reimbursement, which take into account the treatment options, specialty providing the service and alternatives to the discounted care.

In addition, even in situations of overuse, reimbursement reductions may not improve quality of care. Quality of prostate cancer care, as measured by NCCN guideline concordance, allows for multiple treatment options. Even if reimbursement differentials may motivate some physicians' treatment selection, patients may not consent to, or be candidates for, that treatment. Thus, reimbursement policies should not be expected to necessarily improve quality, unless there are guideline-concordant treatment alternatives that patients are willing to accept. Reimbursement policies should carefully consider unintended consequences of change, even in situations of overuse, where common sense suggests that reducing reimbursement should reduce overuse.

Finally, clinical policy, codified in clinical practice guidelines, should make efforts to clarify treatment of older and more vulnerable patients. Research, including these studies, consistently suggest that older patients are more likely to receive ADT, even when there is no benefit and the potential for harm. Even for patients with potentially limited life expectancy, the acute side effects of ADT may not be detrimental enough to quality of life to dissuade its use. Earlier NCCN guidelines allowed for men with less than 5 years life expectancy to receive ADT. However, this recommendation changed in 2004. To date, physicians appear not to have

changed their care of older patients to meet the new recommendations. A clearer policy message should be developed to help physicians struggling to find options for their oldest patients.

***Practice***

The results of this work also suggest several changes to clinical, quality improvement, and implementation practice. First, although the majority of urologists are not overusing ADT, some urologists and other providers still do. Physicians may need support and tools to better manage localized prostate cancer patients so that they do not have to fall back on ADT as a treatment strategy. In addition, our results suggest that Active Surveillance may be an underused therapy in low- and intermediate-risk prostate cancer, but overused among men with high-risk disease. Careful stratification of patients may help remedy this misuse of ADT. Treatment calculators or pocket tools to simplify stratification for physicians may be helpful. Patient decision support tools may need to be improved to better present individual patients' competing risks so that active surveillance is more likely to be chosen by patients who may benefit from that option.

Secondly, our findings suggest a roadmap for quality improvement practice. Although some studies suggest that physicians nearing the end of their career are less likely to change practice, our longitudinal study in fee-for-service Medicare did not find this to be the case. Quality improvement interventions for localized prostate cancer treatment should not focus on physicians with the greatest time in practice, even though they may maintain practice beyond traditional retirement age. Instead, they may more effective by instituting programs for solo practitioners and by devising strategies to reach physicians unaffiliated with academic institutions.

Third, implementation practice should note that interventions designed to encourage uptake of new technology and practices may not work equally well in situations of overuse. Efforts to modify implementation efforts to focus on the determinants of overuse in a particular

setting may be helpful. Moreover, efforts to help physicians evaluate and prioritize emerging evidence around new technologies as they are considering their adoption.

***Research***

A number of research questions are engendered by this research, but at least five issues should be prioritized. First, ADT overuse remains expensive (135), but few studies have assessed the effect of ADT reductions on total prostate cancer care costs. The changes in prostate cancer treatments over the decade seen here and in other studies (40) may have substantially increased overall prostate cancer costs. Assessments of the full financial impact of reductions in ADT overuse on prostate cancer treatment costs are needed. Secondly, our research identified a potential clinical explanation for the volume response. To support and fully inform economic theory, claims-based analyses of factors associated with increasing overuse should be repeated in studies using medical record abstraction. Next, as we further efforts to reduce overuse of medical treatments, strategies to reach isolated healthcare providers will be needed. Identifying the financial pressures, quality improvement infrastructure, and quality improvement motivations of solo practitioners and those without medical school affiliation are important. Although urology practices have undergone consolidation over the last decades, urology still has the highest rate of solo practitioners among all specialties. Most research translation and quality improvement strategies are focused on medical school or large community networks which may miss the providers most likely to need help. Fourth, the comparative effectiveness of localized prostate cancer treatments is incomplete and the guidelines may need to be revised based on better data. In particular, the comparative effectiveness of different modalities of treatment has not been well established. Although guidelines promote biopsy-driven active surveillance, no studies suggest the intensive method is superior to PSA-monitored active surveillance, or even the less intensive watchful waiting approach. Patients and some physicians may be resistant to this therapy and be persuaded to undergo more definitive treatment that can have complications that seriously impact quality of

life. Additional guidance on this strategy may prevent these poor outcomes. Finally, we need better measures of physicians, patient panels, and practices. Available claims data are informative, but coarse, whereas clinical practice is much more nuanced. Demographics are important confounders, but they themselves are confounded by other aspects of training. In addition, information regarding when physicians change practices, how the practices are organized by specialty, compensation structure, payer distributions, and quality improvement programs are important confounders which need to be accounted for. Moreover, data on the infrastructure within solo practices, especially those in urology would be important to have.

**Conclusion**

ADT overuse declined significantly after MMA implementation, but rates of overuse remain high among some urologists who may be professionally isolated and difficult to reach. These urologists may treat more vulnerable populations, which may explain health disparities in prostate cancer treatment quality. Clarifying treatment guidelines for vulnerable patients may improve quality of care. Further, in a pre-MMA period of stable guideline recommendations and exogenous variation in physician reimbursement, we detected no association between ADT overuse and reimbursement greater than the national average. Thus, reducing reimbursement through policy changes such as the MMA may not have the intended effect on limiting overuse when other treatment options are available. However, we did detect a small response to reimbursement when we considered ADT reimbursement relative to all treatment. While reimbursement policy still may not have the intended effect, more nuanced and target policies should be developed. Finally, we observed that decreases in ADT overuse coincident with MMA were not replaced with other guideline-concordant care. Thus quality of prostate cancer care may not have improved. Reimbursement reductions may not be an effective lever to improve quality, unless physicians have access to guideline-concordant alternatives.

## APPENDIX A. TREATMENT CLAIMS

| Treatment | ICD-9 Codes | CPT/HCPCS Codes |
|---|---|---|
| Androgen Deprivation Therapy (GnRH agonist) | | J0128, J1950, J9202, J9217, J9218, J9219, J9225, J9226, J3315, C9216, C9430, or S0165 |
| Non-surveillance Prostate Treatment Codes | 60, 60.1, 60.21, 60.29, 60.3, 60.4, 60.5, 60.61-60.69, 62.3, 62.4, 62.41, 62.42, 92.2, 92.21, 92.22, 92.23, 92.24, 92.25, 92.26, 92.27, 92.28, 92.29, 99.25, V58.0, V58.1x, V66.1, V66.2, V67.1, V67.2 | 00865, 54520, 54522, 54530, 54535, 54690, 55801, 55810, 55812, 55815, 55821, 55831, 55840, 55842, 55845, 55860, 55866, 55873, 55875, 55876, 76873, 77301, 77305, 77310, 77315, 77321, 77326, 77327, 77328, 77338, 77371, 77372, 77373, 77380, 77381, 77402, 77403, 77404, 77406, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416, 77418, 77423, 77432, 77435, 77520, 77522, 77523, 77525, 77750-77760, 77761, 77762, 77763, 77774, 77775, 77776, 77777, 77778, 77779, 77780, 77781, 77782, 77783, 77784, 77785, 77786, 77787, 77789, 77790, 77791- 77798, 77799, G0356, J1675, J9000-J9164, 0073T, 0082T, 0083T, 0182T, 4164F, A9527, C1715, C1716, C1717, C1719, C1728, C2634, C2635, C2636, C2637, C2638, C2639, C2640, C2641, C2642, C2643, C2698, C2699, C9725, G0174, G0178, G0251, G0339, G0340, J1050, J1051, J9165, J9166-J9201, J9203-J9216, J9220-J9224, J9227- J9998, J9999, Q0083-Q0085, Q3001, S0175, S9560, C2616 |
| Abbreviations: ICD-9: International Classification of Diseases, 9th Revision; CPT: Current Procedural Terminology; HCPCS: Healthcare Common Procedure Coding System; GnRH: Gonadotropin-Releasing Hormone. | | |

## APPENDIX B. REIMBURSEMENT GENEROSITY CALCULATION

The reimbursement generosity index was calculated as:

$$R_{it} = \frac{\sum_{g \in g(i,t)} (P_{itg} - P_{tg}) W_{tg}}{\sum_{g \in g(i,t)} W_{tg}}$$

where $P_{itg}$ is the average reimbursement for patients receiving GnRH agonist $g$ prescribed by provider $i$ in year $t$, and $P_{tg}$ is the SEER average reimbursement of GnRH agonist $g$ in year $t$. $W_{tg}$, the weight for GnRH agonist $g$, is the ratio of SEER-wide spending on that regimen to total spending on all GnRH agonists. Each medical ADT regimen was dose-standardized by converting each instance of GnRH agonist in use on separate days to a monthly dosing regimen. Intended duration was determined from the unit designation of the "carrier miles/time/units/serv count" field in carrier claims or the "revenue center unit count" field in outpatient claims. Claims for 12-month implant were assumed to represent 12 months of therapy regardless of unit designation.

## APPENDIX C. TREATMENT CLAIMS

| Treatment | ICD-9 / Revenue Center Codes | CPT/HCPCS Codes |
|---|---|---|
| Active Surveillance-Standard | | [84152-84154, G0103 (PSA) OR G0102 (DRE)] + 99201-99215 (E&M) |
| Active Surveillance-NCCN | 60.1, 60.11 | [84152-84154, G0103 (PSA) OR G0102 (DRE) OR + 99201-99215 (E&M)] + 55700, 55705, 55706, 76942, 10021, 10022, 88172, 88173, C1710, G0416, G0417, G0418, or G0419 (Biopsy) |
| Radical Prostatectomy | 60, 60.4, 60.5, 60.60, 60.61, 60.62, 60.63, 60.64, 60.65, 60.66, 60.67, 60.68, 60.69 | 55801, 55821, 55831, 55810, 55812, 55815, 55840, 55842, 55845, 00865 |
| Minimally Invasive Radical Prostatectomy | | 55866 |
| Other prostatectomy | 60.21, 60.29 | |
| Radiation Planning and Management | | 77261, 77262, 77263, 77299, 77431, 77499 |
| Conformal Radiation Planning | | 77310, 77315, 77321 |
| Conformal Radiation | 0330, 0333, 0339 | 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416 |
| Brachytherapy planning | | 76873, 77326, 77327, 77328 |
| Brachytherapy | 92.20, 92.27, 92.28 | 55860, 55875, 55876, 77761, 77762, 77763, 77776, 77777, 77778, 77781, 77782, 77783, 77784, 77785, 77786, 77787, 77789, 77790, 77799, Q3001, A9527, C1715, C1716, C1717, C1719, C1728, C2616, C2634, C2635, C2636, C2637, C2638, C2639, C2640, C2641, C2642, C2643, C2698, C2699, C9725, 0182T |
| IMRT Planning | | 77301, 77338 |
| IMRT | | 77418, 0073T, G0174, G0178 |
| Stereotactic radiation | | |
| Proton Therapy | 92.24, 92.26 | 77380, 77381, 77520, 77522, 77523, 77525 |
| Androgen Deprivation Therapy (GnRH agonist) | | J9202, J1950, J9217, J9218, J9219, J3315, J9225, J9226 or J1675<br>J1050, J1051, J9165, |
| Orchiectomy | 62.3, 62.4, 62.41, 62.42 | 54520, 54522, 54530, 54535, 54690 |
| Chemotherapy | 99.25, V58.11-V58.19, V66.2, V67.2 | Q0083, Q0084, Q0085, J9000, J9000, J9001, J9002, J9003, J9004, J9005, J9006, J9007, J9008, J9009, J9010, J9011, J9012, J9013, J9014, J9015, J9016, J9017, J9018, J9019, J9020, J9021, J9022, J9023, J9024, J9025, J9026, J9027, J9028, J9029, J9030, J9031, J9032, J9033, |

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| | | J9034, J9035, J9036, J9037, J9038, J9039, J9040, J9041, J9042, J9043, J9044, J9045, J9046, J9047, J9048, J9049, J9050, J9051, J9052, J9053, J9054, J9055, J9056, J9057, J9058, J9059, J9060, J9061, J9062, J9063, J9064, J9065, J9066, J9067, J9068, J9069, J9070, J9071, J9072, J9073, J9074, J9075, J9076, J9077, J9078, J9079, J9080, J9081, J9082, J9083, J9084, J9085, J9086, J9087, J9088, J9089, J9090, J9091, J9092, J9093, J9094, J9095, J9096, J9097, J9098, J9099, J9100, J9101, J9102, J9103, J9104, J9105, J9106, J9107, J9108, J9109, J9110, J9111, J9112, J9113, J9114, J9115, J9116, J9117, J9118, J9119, J9120, J9121, J9122, J9123, J9124, J9125, J9126, J9127, J9128, J9129, J9130, J9131, J9132, J9133, J9134, J9135, J9136, J9137, J9138, J9139, J9140, J9141, J9142, J9143, J9144, J9145, J9146, J9147, J9148, J9149, J9150, J9151, J9152, J9153, J9154, J9155, J9156, J9157, J9158, J9159, J9160, J9161, J9162, J9163, J9164, J9166, J9167, J9168, J9169, J9170, J9171, J9172, J9173, J9174, J9175, J9176, J9177, J9178, J9179, J9180, J9181, J9182, J9183, J9184, J9185, J9186, J9187, J9188, J9189, J9190, J9191, J9192, J9193, J9194, J9195, J9196, J9197, J9198, J9199, J9200, J9201, J9203, J9204, J9205, J9206, J9207, J9208, J9209, J9210, J9211, J9212, J9213, J9214, J9215, J9216, J9220, J9221, J9222, J9223, J9224, J9227, J9228, J9229, J9230, J9231, J9232, J9233, J9234, J9235, J9236, J9237, J9238, J9239, J9240, J9241, J9242, J9243, J9244, J9245, J9246, J9247, J9248, J9249, J9250, J9251, J9252, J9253, J9254, J9255, J9256, J9257, J9258, J9259, J9260, J9261, J9262, J9263, J9264, J9265, J9266, J9267, J9268, J9269, J9270, J9271, J9272, J9273, J9274, J9275, J9276, J9277, J9278, J9279, J9280, J9281, J9282, J9283, J9284, J9285, J9286, J9287, J9288, J9289, J9290, J9291, J9292, J9293, J9294, J9295, J9296, J9297, J9298, J9299, J9300, J9301, J9302, J9303, J9304, J9305, J9306, J9307, J9308, J9309, J9310, J9311, J9312, J9313, J9314, J9315, J9316, J9317, J9318, J9319, J9320, J9321, J9322, J9323, J9324, J9325, J9326, J9327, J9328, J9329, J9330, J9331, J9332, J9333, J9334, J9335, J9336, J9337, J9338, J9339, J9340, J9341, J9342, J9343, J9344, J9345, J9346, J9347, J9348, J9349, J9350, J9351, J9352, J9353, J9354, J9355, J9356, J9357, J9358, J9359, J9360, J9361, J9362, J9363, J9364, J9365, J9366, J9367, J9368, J9369, J9370, J9371, J9372, J9373, J9374, J9375, J9376, J9377, J9378, J9379, J9380, J9381, J9382, J9383, J9384, J9385, J9386, J9387, J9388, J9389, J9390, J9391, J9392, J9393, J9394, J9395, J9396, J9397, J9398, J9399, J9400, J9401, J9402, J9403, J9404, J9405, J9406, J9407, J9408, J9409, J9410, J9411, J9412, J9413, J9414, J9415, J9416, J9417, J9418, J9419, J9420, J9421, J9422, J9423, J9424, J9425, J9426, J9427, J9428, J9429, J9430, J9431, J9432, J9433, J9434, J9435, J9436, J9437, J9438, J9439, J9440, J9441, J9442, J9443, J9444, J9445, J9446, J9447, J9448, J9449, J9450, J9451, J9452, J9453, J9454, J9455, J9456, J9457, J9458, J9459, J9460, J9461, J9462, J9463, J9464, J9465, J9466, J9467, J9468, J9469, J9470, J9471, J9472, J9473, J9474, J9475, J9476, J9477, J9478, J9479, J9480, J9481, J9482, J9483, J9484, J9485, J9486, J9487, |

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| | | J9488, J9489, J9490, J9491, J9492, J9493, J9494, J9495, J9496, J9497, J9498, J9499, J9500, J9501, J9502, J9503, J9504, J9505, J9506, J9507, J9508, J9509, J9510, J9511, J9512, J9513, J9514, J9515, J9516, J9517, J9518, J9519, J9520, J9521, J9522, J9523, J9524, J9525, J9526, J9527, J9528, J9529, J9530, J9531, J9532, J9533, J9534, J9535, J9536, J9537, J9538, J9539, J9540, J9541, J9542, J9543, J9544, J9545, J9546, J9547, J9548, J9549, J9550, J9551, J9552, J9553, J9554, J9555, J9556, J9557, J9558, J9559, J9560, J9561, J9562, J9563, J9564, J9565, J9566, J9567, J9568, J9569, J9570, J9571, J9572, J9573, J9574, J9575, J9576, J9577, J9578, J9579, J9580, J9581, J9582, J9583, J9584, J9585, J9586, J9587, J9588, J9589, J9590, J9591, J9592, J9593, J9594, J9595, J9596, J9597, J9598, J9599, J9600, J9601, J9602, J9603, J9604, J9605, J9606, J9607, J9608, J9609, J9610, J9611, J9612, J9613, J9614, J9615, J9616, J9617, J9618, J9619, J9620, J9621, J9622, J9623, J9624, J9625, J9626, J9627, J9628, J9629, J9630, J9631, J9632, J9633, J9634, J9635, J9636, J9637, J9638, J9639, J9640, J9641, J9642, J9643, J9644, J9645, J9646, J9647, J9648, J9649, J9650, J9651, J9652, J9653, J9654, J9655, J9656, J9657, J9658, J9659, J9660, J9661, J9662, J9663, J9664, J9665, J9666, J9667, J9668, J9669, J9670, J9671, J9672, J9673, J9674, J9675, J9676, J9677, J9678, J9679, J9680, J9681, J9682, J9683, J9684, J9685, J9686, J9687, J9688, J9689, J9690, J9691, J9692, J9693, J9694, J9695, J9696, J9697, J9698, J9699, J9700, J9701, J9702, J9703, J9704, J9705, J9706, J9707, J9708, J9709, J9710, J9711, J9712, J9713, J9714, J9715, J9716, J9717, J9718, J9719, J9720, J9721, J9722, J9723, J9724, J9725, J9726, J9727, J9728, J9729, J9730, J9731, J9732, J9733, J9734, J9735, J9736, J9737, J9738, J9739, J9740, J9741, J9742, J9743, J9744, J9745, J9746, J9747, J9748, J9749, J9750, J9751, J9752, J9753, J9754, J9755, J9756, J9757, J9758, J9759, J9760, J9761, J9762, J9763, J9764, J9765, J9766, J9767, J9768, J9769, J9770, J9771, J9772, J9773, J9774, J9775, J9776, J9777, J9778, J9779, J9780, J9781, J9782, J9783, J9784, J9785, J9786, J9787, J9788, J9789, J9790, J9791, J9792, J9793, J9794, J9795, J9796, J9797, J9798, J9799, J9800, J9801, J9802, J9803, J9804, J9805, J9806, J9807, J9808, J9809, J9810, J9811, J9812, J9813, J9814, J9815, J9816, J9817, J9818, J9819, J9820, J9821, J9822, J9823, J9824, J9825, J9826, J9827, J9828, J9829, J9830, J9831, J9832, J9833, J9834, J9835, J9836, J9837, J9838, J9839, J9840, J9841, J9842, J9843, J9844, J9845, J9846, J9847, J9848, J9849, J9850, J9851, J9852, J9853, J9854, J9855, J9856, J9857, J9858, J9859, J9860, J9861, J9862, J9863, J9864, J9865, J9866, J9867, J9868, J9869, J9870, J9871, J9872, J9873, J9874, J9875, J9876, J9877, J9878, J9879, J9880, J9881, J9882, J9883, J9884, J9885, J9886, J9887, J9888, J9889, J9890, J9891, J9892, J9893, J9894, J9895, J9896, J9897, J9898, J9899, J9900, J9901, J9902, J9903, J9904, J9905, J9906, J9907, J9908, J9909, J9910, J9911, J9912, J9913, J9914, J9915, J9916, J9917, J9918, J9919, J9920, J9921, J9922, J9923, J9924, J9925, J9926, J9927, J9928, J9929, J9930, J9931, J9932, J9933, J9934, |

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| | | J9935, J9936, J9937, J9938, J9939, J9940, J9941, J9942, J9943, J9944, J9945, J9946, J9947, J9948, J9949, J9950, J9951, J9952, J9953, J9954, J9955, J9956, J9957, J9958, J9959, J9960, J9961, J9962, J9963, J9964, J9965, J9966, J9967, J9968, J9969, J9970, J9971, J9972, J9973, J9974, J9975, J9976, J9977, J9978, J9979, J9980, J9981, J9982, J9983, J9984, J9985, J9986, J9987, J9988, J9989, J9990, J9991, J9992, J9993, J9994, J9995, J9996, J9997, J9998 |
| Other | | 55873 (cryosurgery); 77371, 77372, 77373, 77432, 77435, 0082T, 0083T, G0251 (stereotactic radiation); J9165, J1050, J1051, G0356, s0175, S9560, 4164F, J1675 (other hormones); J9999 (unspecified drug) |
| Abbreviations: ICD-9: International Classification of Diseases , 9th Revision; CPT: Current Procedural Terminology; HCPCS: Healthcare Common Procedure Coding System; PSA: Prostate-specific Antigen; E&M: Evaluation and Management | | |

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