## Distribution Agreement

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

Signature:

Jamie Felzer
Date

Prostate Cancer Treatment Patterns in Relation to Risk Category: a Georgia Statewide Analysis By

Jamie Felzer
Master of Public Health

Department of Epidemiology

Michael Goodman
Committee Chair

# Prostate Cancer Treatment Patterns in Relation to Risk Category: a Georgia Statewide 

 Analysis
## By

Jamie Felzer
Bachelor of Science, Psychobiology
University of California, Los Angeles
2010

Thesis Committee Chair: Michael Goodman, MD MPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in the Department of Epidemiology 2012

Abstract<br>Prostate Cancer Treatment Patterns in Relation to Risk Category: a Georgia Statewide Analysis

By Jamie Felzer

Introduction: Prostate cancer is the most common invasive malignancy of men in the United States. In 2011, 240,890 men were estimated to be diagnosed and 33,720 were estimated to die of this disease. Management and control of prostate cancer is complex. Although no single treatment can be considered the standard of care, it is evident that certain subgroups of men may receive better treatment than others. Rural residents, black men, those with low SES or less access to medical care have a worse prognosis. In this population-based study, we seek to determine patterns of prostate cancer treatment in the state of Georgia.
Methods: Data for men with newly diagnosed prostate cancer within a six year (2004-2009) interval were obtained from the recently expanded, statewide Georgia SEER Registry. Criteria for prostate cancer risk classification were based on the 2010 NCCN categories that incorporate disease stage, grade and the pre-diagnosis level of the prostate specific antigen (PSA). The main treatments of interest were surgery, radiation, or "any treatment" (surgery and/or radiation).
Results: Among 37,667 prostate cancer cases diagnosed in Georgia during the study interval, $37,274(99 \%)$ had sufficient data to be classified into a risk category. 23,935 out of 37,274 men, or $64 \%$, received either radiation or surgery. Due to the strong interactions between risk category and the covariates, no overall effect could be calculated. All models were stratified on age, while some still required further stratification. For example, radiation had additional interactions with marital status and county type. Overall, men with low risk disease were 6 - to 11 -fold less likely than high risk men to receive any localized prostatedirected treatment, although the magnitude of this association differed significantly by age. Discussion: Our results clearly demonstrated that risk category plays a critical role in determining which patients receive certain treatments, but the magnitude and direction of the relationship between disease characteristics and therapy receipt varies by age, marital status, race and nature of residential area. The mechanisms by which patient (and perhaps provider) characteristics modify the association with treatment type are not clear, and need to be further explored.

Prostate Cancer Treatment Patterns in Relation to Risk Category: a Georgia Statewide Analysis

## By

Jamie Felzer
Bachelor of Science, Psychobiology
University of California, Los Angeles
2010

Thesis Committee Chair: Michael Goodman, MD MPH

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of

Master of Public Health
in Department of Epidemiology
2012

## TABLE OF CONTENTS

INTRODUCTION ..... 1
METHODS ..... 6
Variable Classification ..... 6
Statistical Analysis ..... 7
RESULTS ..... 9
Unadjusted Analyses and Descriptive Statistics ..... 9
Overview of Multivariable Analyses ..... 10
Multivariable and Stratified Analyses for Any Prostate-Directed Treatment (Surgery and/or Radiation) ..... 10
Multivariable and Stratified Analyses for Radiation Treatment ..... 11
Multivariable and Stratified Analyses for Surgery ..... 12
DISCUSSION ..... 14
Strengths ..... 16
Limitations ..... 16
Conclusions and Future Directions ..... 18
REFERENCES ..... 19
APPENDIX ..... 22
Table 1. Distribution of variables according to NCCN Risk Categories ..... 23
Table 2. Stratified, Adjusted Logistic Regression of Any Treatment ..... 24
Table 3a. Stratified, Adjusted Logistic Regression of Overall Radiation Therapy for Men Under 60 Years Old ..... 25
Table 3b. Stratified, Adjusted Logistic Regression of Overall Radiation Therapy for Men Greater Than or Equal to 60 Years Old ..... 26
Table 4. Adjusted, Stratified Logistic Model for Men of All Ages Receiving Surgery ..... 27

## INTRODUCTION

Prostate cancer (PC) is the most common invasive malignancy of men in the United States. In 2011, 240,890 men were estimated to be diagnosed and 33,720 were estimated to die of this disease. ${ }^{1}$ Although the lifetime risk of dying from prostate cancer is 1 in 35 , the risk of developing prostate cancer is 1 in $6 .{ }^{2}$ In spite of the decreasing mortality rates, it is the second leading cause of cancer deaths for US men. ${ }^{3}$ Prostate cancer becomes more common with increasing age; $31.6 \%$ of men between 55 and 64 , and $35.5 \%$ of men between 65 and $74,{ }^{2}$ develop PC. Most of the deaths among PC patients occur due to unrelated and co-morbid health conditions, as well as from treatments for the disease itself. ${ }^{4}$ Depending on the stage of disease and the man's life expectancy, treatment is not necessary for many cases of PC; however many more cases are being treated due to widespread screening. Many of the commonly used treatments can increase morbidity when they are over- or inappropriately utilized, especially in asymptomatic cases.

Management and control of prostate cancer is complex due to a multitude of factors that include high prevalence of the disease, uncertain value of the available screening and diagnostic measures, comorbidities and variability of treatment methods. Prostate cancer may progress at differing paces, making specific diagnostic and treatment guidelines difficult to apply uniformly.

Some known risk factors for development of PC are increasing age, race and family history. Other possible risk factors include hormone levels, diet, lifestyle and environment. The risk and survival rates of prostate cancer differ by race, socioeconomic status (SES) and rural/urban settings. The disparities between black and white men are most evident. Black men in the United States have a $72 \%$ higher incidence of PC than white men. ${ }^{5}$ According to
data from the Surveillance Epidemiology and End Results (SEER) program, the average annual incidence rate for men of all races in the US between 2005 and 2009 was 154.8 per 100,000 , with black men having a rate of 236.0 per 100,000 , much higher than the corresponding rate of 146.9 per 100,000 among whites. ${ }^{2}$ The SEER data also indicates disparities in mortality. The 2005-2009 data shows that for whites the PC-specific death rate was 21.7 per 100,000 compared to 53.1 per 100,000 for blacks.

Black men are also more likely to be diagnosed with a more advanced stage of PC and tend to be younger at the time of diagnosis than men of any other race/ethnicity, as well as more likely to die from PC. ${ }^{6-9}$

The PC incidence rates also differ by level of education. One study demonstrated that men with only a high school education experience a $21 \%$ lower PC incidence compared to those with a college education. ${ }^{10}$ This difference could be due to increased screening in more educated men. Similarly, lack of screening and other preventative health services is the likely explanation for lower PC incidence rates among men who are unemployed or unable to work. ${ }^{10}$

Typical screening methods for PC include the prostate specific antigen (PSA) test and the digital rectal examination (DRE). If the results of any screening test are considered positive, the diagnosis is confirmed by conducting a transrectal ultrasound-guided core needle biopsy. The positive predictive value (PPV) of PSA has great variability, ranging from $20 \%$ to $71.4 \%$, depending on the antigen level. ${ }^{11}$ There is no cut-point that clearly defines a level above which cancer is deemed to be present. The DRE has a low specificity and misses $23 \%$ to $45 \%$ of cancers that are subsequently diagnosed. ${ }^{12}$ Cancers that are detected via DRE are often in a more advanced stage than those identified by PSA alone.

The American Urological Association (AUA) and National Comprehensive Cancer Network (NCCN) have both produced PC treatment guidelines. Although these guidelines indicate that no single treatment can be considered definitively superior in all patients, different treatment options may be considered more appropriate based on a patient's life expectancy, likely disease progression and stage of the cancer. The most common forms of PC treatment are active surveillance (AS), radical prostatectomy (RP), androgen deprivation therapy (ADT) or radiation therapy (RT). Both AUA and NCCN recommend AS only for those with low risk PC and a shorter life expectancy because, even though it helps combat over-diagnosis and over-treatment, this conservative approach may be dangerous in patients with aggressive disease. ${ }^{13}$

Both AUA and NCCN recommend that treatment for men with a longer life expectancy should be more aggressive, with intent to cure the disease. Curative treatment for PC typically involves localized prostate-directed treatments, surgery (usually RP) or radiation therapy.

RP involves surgical removal of the prostate and surrounding tissue, and is usually recommended in men whose disease is confined to the prostate. ${ }^{13}$ The most common side effects of prostatectomy are blood loss, rectal or urethral injury, incontinence and impotence, although all of these conditions may improve over time. ${ }^{11,13}$

External beam radiation therapy (EBRT) utilizes precise high-energy rays or particles to selectively target cancer cells where the dose can be adjusted based on the expected risk level. ${ }^{11,13}$ EBRT consists of up to 41 treatments over 9 weeks. ${ }^{13}$ This is an appropriate treatment for cancer that is confined to the prostate or the surrounding tissues. However, the side effects of radiation can be long lasting and certain effects, such as impotence, may
occur years later whereas with surgery, the risk of impotence decreases over time. ${ }^{11}$ Due to the impact of radiation, EBRT may also affect urinary, bowel and sexual function.

Brachytherapy is another method of delivering radiation by implanting radioactive pellets directly into the prostate. The most significant side effect of brachytherapy is rectal problems, which can be hard to effectively treat. ${ }^{13}$ Although frequent urination sometimes occurs with brachytherapy, impotence is less likely than with EBRT. ${ }^{13}$

Androgen Deprivation Therapy (ADT) blocks the systemic production of a derivative of androgen, testosterone, which can decrease the growth rate of a tumor or even shrink it. ${ }^{13}$ ADT can be used alone when other therapies are not an option because the disease has spread, or it can be used in combination with other treatment modalities. There are significant side effects associated with ADT including reduced libido, impotence, hot flashes, breast tissue growth, and/or osteoporosis. ${ }^{11,13}$

Although no single treatment can be considered the standard of care, it is evident that certain subgroups of men may receive better treatment than others. Rural residents, ${ }^{14}$ black men, ${ }^{9,15}$ those with low SES ${ }^{16}$ or less access to medical care ${ }^{14}$ have a worse prognosis, which may be explained by delayed diagnosis, less effective treatment or both. The likelihood of being diagnosed with advanced stage PC, as well as the probability of fatality, increases with lower SES. ${ }^{16}$ Rural residents often have a worse prognosis because they tend to be financially disadvantaged, less educated, more likely to be uninsured and farther from health care facilities. ${ }^{17}$

In this population-based study, we seek to determine patterns of prostate cancer treatment in the state of Georgia. We will use the Georgia SEER registry, which now includes statewide
data of both urban and rural communities, and racially diverse populations of varying socioeconomic status.

## METHODS

Data
Data were obtained from the recently expanded, statewide Georgia SEER Registry. Emory IRB classified this project as exempt since all the data were de-identified. As cancer is a nationally reportable disease, all cases of prostate cancer are expected to be in the database, although some ancillary data may be missing.

All men in the state of Georgia with newly diagnosed prostate cancer from January 1, 2004 through December 31, 2009 were included in the current study. This resulted in the identification of a total of 37,667 prostate cancer cases during this time period. The line listing of cases obtained from SEER was converted into a SAS data file that was used for all subsequent analyses.

## Variable Classification

Main exposure variable: Criteria for risk classification were based on the 2010 NCCN risk assessment categories. These criteria are considered a standard in the United States and are based on the combination of American Joint Committee on Cancer (AJCC) staging, PSA score and Gleason score. Criteria for classification of "low risk" included a stage of T1 to T2a, a Gleason score less than 6 and a PSA of less than 10. "Intermediate risk" was determined based on a stage of T2b to T2c, or a Gleason score of 7 or a PSA of 10-20. Lastly, "high risk" was classified based on a stage greater than or equal to T3a, or a Gleason score of 8-10 or a PSA greater than 20 .

Main dependent variables: The main treatments of interest were surgery (local or radical prostatectomy) and radiation (EBRT or brachytherapy, or some combination thereof). For purposes of this analysis, radiation of any type was classified into an overall radiation category and not analyzed separately. Those that obtained surgery and/or radiation were classified as obtaining "Any Treatment." Those with missing treatment data were classified as missing and were not assumed, one way or another, to have obtained any type of treatment.

Covariates: The 2003 Metropolitan Statistical Areas (MSA) were used to categorize Georgia counties into those that resided within the Atlanta metropolitan area (and therefore within a reasonable drive of Atlanta medical services), other metropolitan areas throughout the state, and rural areas. Classification of county was used as a measure of available healthcare resources. Race was dichotomized as white or black, while any other races were classified as missing due to low numbers in those categories. Age was classified into three age groups: less than 60 years old, greater than or equal to 60 years old but less than or equal to 70 years old, and greater than 70 years old. Year of diagnosis was a continuous variable for the years 2004 through 2009. Marital status was classified as currently married or not married, which included men that were single, divorced, separated, or widowed.

## Statistical Analysis

SAS ${ }^{\text {TM }}$ version 9.3 (SAS Institute, Cary, NC, USA) was used for all cleaning, categorization and analysis. A series of crude analyses were conducted to compare distributions of covariates across the three risk categories- low, intermediate and high. Cases that could not be classified into a risk category due to insufficient information on clinical stage, PSA or

Gleason scores were excluded from further analysis. Cases that were missing information on the covariates were left in to determine if there were any patterns in the cases with missing ancillary information. All crude comparisons were accompanied by chi-squared tests with a two-sided alpha level of 0.05 .

Three separate logistic models were used to assess the association between risk category and each treatment (defined as surgery, radiation or any treatment). All covariates included in the initial model were selected a priori. All variables were categorical with the exception of year of diagnosis. Normality was checked for year of diagnosis. Collinearity was assessed for all models using the COLIN macro for SAS. Presence of two-way interactions involving the main exposure variable (risk category) was assessed using backwards elimination (BWE) based on a chunk test. Interactions were considered statistically significant based on a twosided alpha level of 0.05 . When interaction was present, a subsequent model was run stratifying on the most pronounced interaction, and then additional testing for interaction was conducted within each stratum-specific model. This was continued until no interaction terms remained, or the strata had odds ratios for the exposure (assessed as overall risk, using high risk as the referent category) that were not meaningfully different.

## RESULTS

## Unadjusted Analyses and Descriptive Statistics

Among 37,667 prostate cancer cases diagnosed in Georgia during the 2004-2009 study interval, $37,274(99 \%)$ had sufficient data to be classified into a risk category based on the 2010 NCCN risk assessment guidelines. $3 \%$ of men fell into the low risk category, $73 \%$ in the intermediate risk category and $23 \%$ in the high risk category. Of those with sufficient data, $52 \%$ were from the greater Atlanta area, while $21 \%$ were from a rural area of Georgia and the remainder from other metro areas of the state [Table 1]. The percentages of cases in the low risk category were fairly evenly distributed between Atlanta, other metro and rural areas $(39 \%, 31 \%, 30 \%$, respectively). The majority ( $65 \%$ ) of men were white. In the high risk category, black men accounted for $38 \%$, a slightly higher amount than their overall percentage of cases.

The majority $(69 \%)$ of men in the low risk category were over the age of 70 . Men in the $60-$ 70 age range accounted for $42 \%$ of the total cases and represented almost the same proportion in the intermediate and high risk categories. The younger and older age groups both accounted for slightly fewer than $30 \%$ of the cases. Most ( $66 \%$ ) of the men were married, while $23 \%$ were unmarried and the remaining $11 \%$ did not include data on marital status.

As shown in Table 1, 23,935 out of 37,274 men, or $64 \%$, received either radiation or surgery. Those that obtained either surgery or radiation had the lowest representation of cases in the
low risk category ( $3 \%$ and $9 \%$, respectively). Less than $3 \%$ of all cases had missing treatment information, and almost half of those were in the low risk category.

## Overview of Multivariable Analyses

In the multivariable analyses there was evidence of strong and statistically significant interaction between risk category and age for all three study outcomes (surgery, radiation and any treatment). For this reason, all models were stratified on age (under 60, 60-70, over 70). For the outcome defined as any treatment, further stratification was necessary in the 60-70 age category by marital status and, additionally, within the stratum "married," into black or white race [Table 2]. In the analyses evaluating the association between risk category and receipt of radiation, among the youngest $(<60)$ and the intermediate ( $60-70$ ) age groups there were additional interactions with marital status and, among married men, there were interactions with county of residence [Tables 3a-3b]. Surgery only had effect modification with age [Table 4].

Multivariable and Stratified Analyses for Any Prostate-Directed Treatment (Surgery and/or Radiation)

In the youngest age group, men in the low risk category were 11 times less likely to receive treatment $(\mathrm{OR}=0.09,95 \% \mathrm{CI}=0.05,0.15)$, whereas those in the intermediate risk group were 1.5 times more likely to receive any treatment than high risk men (OR=1.53, $95 \% \mathrm{CI}$ $=1.33,1.77)$. [Table 2] Black men as compared to white men $(\mathrm{OR}=0.56,95 \% \mathrm{CI}=0.49$,
0.64 ), and men residing in rural counties compared to Atlanta ( $\mathrm{OR}=0.67,95 \% \mathrm{CI}=0.56$, $0.78)$ were significantly less likely to receive any localized tumor directed treatment.

Among married men between the ages of 60 and 70, the inverse associations between low (versus high) risk and treatment receipt were strong and statistically significant among both blacks $(\mathrm{OR}=0.17,95 \% \mathrm{CI}=0.08,0.34)$ and whites $(\mathrm{OR}=0.07,95 \% \mathrm{CI}=0.05,0.12) . \mathrm{By}$ contrast, the race-specific associations among married men in this age group were different for intermediate risk men: null for whites ( $\mathrm{OR}=1.10,95 \% \mathrm{CI}=0.93,1.31$ ) and significantly increased for blacks ( $\mathrm{OR}=1.79,95 \% \mathrm{CI}=1.45,2.21$ ). The analyses for unmarried men in the 60-70 age group and for those in the two remaining age groups demonstrated consistent inverse associations between low risk and receipt of treatment, and a moderate increase for intermediate risk groups. There was also evidence that men residing in rural areas (relative to Atlanta), blacks (relative to whites) and unmarried (versus married) were less likely to receive treatment with statistically significant ORs in the 0.56-0.81 range.

## Multivariable and Stratified Analyses for Radiation Treatment

In the under 60-year age group, among married men residing in non-metro Atlanta (rural and other metro counties) those in the low risk category had a roughly 3 -fold higher likelihood of obtaining radiation therapy compared to high risk groups. In the same age group, the corresponding association for married men residing in Atlanta was in the opposite direction, albeit not statistically significant ( $\mathrm{OR}=0.36,95 \% \mathrm{CI}=0.12,1.08$ ). [Table 3a] When the data for the intermediate age category were further stratified on marital status and then by county of residence, the ORs ( $95 \%$ CIs) comparing the lowest to the highest risk
categories were 0.95 ( $0.63-1.69$ ), $0.24(0.09-0.64)$ and 0.14 ( $0.05-0.36$ ) for rural, other metro and Atlanta counties, respectively. Among the non-married 60- to 70- year olds, the OR for the lowest risk category was $0.35(95 \% \mathrm{CI}=0.18,0.68)$ and, among men over the age of 70 , the corresponding OR was $0.11(95 \%=0.07,0.17)$. [Table 3b]

The odds ratios of black men receiving radiation treatment compared to white men were elevated in all analyses, but were the highest in the youngest age group (OR=1.95, $95 \% \mathrm{CI}=$ 1.49-2.55) and the lowest in the oldest age group ( $\mathrm{OR}=1.33,95 \% \mathrm{CI}=1.13-1.57$ ). In the oldest age group (the only category that did not require further stratification in these analyses), residents of rural counties and other metro areas were less likely to receive radiation than their Atlanta counterparts with ORs of $0.73(95 \% \mathrm{CI}=0.66,0.81)$ and 0.68 ( $95 \% \mathrm{CI}=0.61,0.75$ ), respectively.

## Multivariable and Stratified Analyses for Surgery

Prostate cancer patients in the low risk category were significantly less likely to undergo surgery compared to the high-risk men, but the magnitude of association differed by age with ORs $(95 \% \mathrm{CI})$ of 0.07 ( $0.03-0.17$ ) for those under the age of $60,0.11$ ( $0.06-0.21$ ) for the 60 to 70 age group and $0.41(0.23-0.73)$ for men over 70 [Table 4]. Surgery was more likely to be performed in the intermediate (versus high) risk category in the oldest age group ( $\mathrm{OR}=1.28,95 \% \mathrm{CI}=1.11,1.49$ ); however in the youngest and the intermediate age groups the association was inverse. Black men were significantly less likely to undergo surgery, and the difference with whites was most pronounced in the youngest age category ( $O R=0.47$, $95 \% \mathrm{CI}=0.43,0.51$ ). Surgery was significantly less likely to be performed on unmarried
men regardless of age, with ORs ranging from 0.58 to 0.73 and all $95 \%$ CIs excluding unity. Rural residence was associated with a decreased frequency of surgery only in the oldest age group $(\mathrm{OR}=0.81,95 \% \mathrm{CI}=0.68-0.96)$; whereas non-Atlanta metro residents were more likely to undergo surgery relative to Atlanta patients (OR range 1.20-1.56) irrespective of their age. [Table 4]

## DISCUSSION

This study was the first state-wide analysis of prostate cancer treatment patterns in Georgia. Because it has sizeable rural and urban populations and a significant number of both rural and urban blacks and whites, Georgia is representative of much of the country. While the goal of this study was to examine the relationship of disease aggressiveness (measured as level of risk) to the type of prostate cancer treatment received, the data indicate that it is impossible to estimate a single measure of association. Rather, the magnitude and direction of the association between risk category and treatment receipt differs in varying population subgroups. The effect is modified first and foremost by age; however even within each age group (except for those that obtained surgery), we found rather complex interactions involving factors such as marital status, area of residence and race.

Overall, men with low risk disease were 6 - to 11 -fold less likely than high risk men to receive any localized prostate-directed treatment, although the magnitude of this association differed by age. Intermediate risk men were more likely than high risk men to receive treatment, however the difference was modest and in our category of white married men in the 60- to 70- year age group had a null result.

In all age groups, low risk men were also significantly less likely than high risk men to obtain surgery. The difference was most pronounced in the youngest age group where the difference was 15 -fold; the difference was 9 -fold in the middle age group and only a 2 -fold in the oldest group. This finding was expected as surgery is not typically recommended for low risk men. ${ }^{13}$

Radiation was the most complex of the treatment outcomes since there was extensive effect modification with marital status and county (for married men only) in both the youngest
$(<60)$ and the middle (60-70) age groups. It is especially interesting that the youngest, low risk men residing outside of Atlanta were about 3 times more likely to receive radiation therapy compared to their high risk counterparts. This trend of receiving radiation in rural and other counties did not hold true for the middle age group, as low risk men were not as likely to receive radiation as those with high risk disease. Instead, intermediate risk men were slightly more likely than high risk men to receive radiation. Previous research in Southwest Georgia also found that men in rural areas were more likely to receive radiation over surgery. ${ }^{18}$

Marital status was a significant factor for every outcome. As demonstrated in previous research ${ }^{19}$ the role of a man's wife in the treatment process can be of major importance. Our results are consistent with these findings, since married men were about twice as likely to obtain treatment of any kind in our data. Our finding that married men were more likely to choose surgery at all ages was also consistent with previous research. ${ }^{20}$ Although young married men in rural and other metro counties with low risk disease had 3-fold higher odds of obtaining radiation therapy compared to high-risk men, this did not hold true for any other radiation subgroup.

Most previously published literature examined the differences between blacks and whites with respect to their receipt of prostate cancer treatment. Our results were largely consistent with previous findings that blacks are less likely to obtain surgery, often choosing radiation. ${ }^{9}$ Previous research demonstrated that black men with localized disease were $10 \%$ less likely to undergo radical prostatectomy compared to white men, and were $21 \%$ less likely to undergo the procedure when the disease was regional. ${ }^{8}$ We observed that black men were much more likely to obtain radiation therapy in all groups, except in the oldest age group where
they were just as likely to obtain radiation as surgery (compared to whites). We are unable to explain why blacks might be more likely to receive surgery at older ages, and believe this observation is interesting and warrants further exploration.

## Strengths

The main strength of these data is the large number of observations and diversity of the patient population. By focusing on interactions, our analyses identified a number of interesting stratum specific associations that otherwise would have been missed. While it was previously known that age, race, county of residence and marital status played a large role in treatment decisions, the extent to which these factors may modify the association between prostate cancer risk categories and various treatment modalities was not known.

## Limitations

The limitations of this study fall into two categories: those related to the underlying data and those specific to the current analysis. While SEER data on surgery and radiation are reasonably complete, the information pertaining to systemic treatment such as hormonal therapy is usually missing and is not included in the public use files. Hormone therapy is typically recommended for men with intermediate or high risk cancer. ${ }^{13}$ According to our analysis, only $2 / 3$ of cases received prostate-directed treatment, and for this reason it is vital to know if the other $1 / 3$ of men were receiving hormone therapy. A study by Butler et al also demonstrated that about $30 \%$ of rural prostate cancer patients used complementary and alternative treatment. ${ }^{21}$ In accordance with national observations, patients utilizing Complementary and Alternative Medicine (CAM) in Georgia tended to be younger and more highly educated. Because none of these alternative treatment options are captured in SEER data, it is hard to know if CAM is used by some of the patients as an alternative to standard
therapy. Information on whether men utilized active surveillance is also not captured in SEER data and these men may show up as not obtaining treatment, when they are in fact, actively monitoring their disease progression. Another limitation of the current analysis is failure to take into consideration area based measures of socioeconomic status. In theory it would be possible to perform geocoding of all patients' residential addresses to assign them to one of the census tracts. This information could then be linked to the US census data to determine neighborhood-based socioeconomic characteristics for each patient. Previous research has shown that those who reside in higher SES census tracts have a better probability of survival after a diagnosis of prostate cancer, ${ }^{16}$ likely as a result of obtaining treatment, among other factors. Other important factors that could not be considered in our analyses due to limitations of the SEER data include patients' levels of education, income, and type of health insurance.

In the current analysis we combined brachytherapy and EBRT into a single category. These treatments could have very different predictors; EBRT entails of daily treatment trips for nine weeks, which often requires having a driver to and from each appointment, while brachytherapy is one-time procedure. Categorizing EBRT and brachytherapy into one radiation therapy outcome may have masked further effect modification.

Treatment decisions are not just determined by the disease characteristics and the patient's preferences, but are also impacted by the biases of the physician since many have their own inclinations on how to best treat prostate cancer. For example, in the South, $54 \%$ of radiation oncologists indicated they would recommend androgen deprivation therapy when the PSA rose to $3.0 \mathrm{ng} / \mathrm{mL}$ after surgery, while $68 \%$ of urologists said they would recommend ADT at that time. ${ }^{22}$ Not only do recommended treatment practices vary by
physician specialty and metropolitan statistical area, but they also differ by geographic region. ${ }^{22}$

## Conclusions and Future Directions

This study demonstrated the complex interrelation of factors that determine treatment decisions among men diagnosed with prostate cancer. A recent study ${ }^{23}$ used a conceptual model describing how external, psychological and clinical parameters, as well as attitudes, influence a man's treatment decision; however, their qualitative study was small and based solely in an urban setting. Future studies detailing demographic, socioeconomic and behavioral factors across various population sub-groups are needed to assist in understanding the reasoning behind various prostate cancer treatment decisions to best tailor future recommendations. Although previous research ${ }^{24}$ found that prostate cancer treatment choices in black men were influenced primarily by social networks of family and friends, little is known about the extent to which different communities can influence a man's treatment decision. Future studies could also investigate the relation between reimbursement patterns (i.e. presence and type of insurance) and procurement of treatment.

In summary, our results clearly demonstrated that prostate cancer risk category (as measured by stage, grade and PSA) plays a critical role in determining which patients receive certain treatments, but the magnitude and direction of the relationship between disease characteristics and therapy receipt varies by age, marital status, race and nature of residential area. The mechanisms by which patient (and perhaps provider) characteristics modify this association are not clear, and need to be further explored.

## REFERENCES

1. Estimated New Cancer Cases and Deaths for 2011. 2011;
http://seer.cancer.gov/csr/1975 2008/results single/sect 01 table.01.pdf. Accessed 11/19/2011.
2. SEER Stat Fact Sheets: Prostate. http://seer.cancer.gov/statfacts/html/prost.html. Accessed 4/17/2012.
3. Cancer Statistics 2011. A Presentation from the American Cancer Society: American Cancer Society; 2011:43.
4. Beydoun HA, Mohan R, Beydoun MA, Davis J, Lance R, Schellhammer P. Development of a scale to assess patient misperceptions about treatment choices for localized prostate cancer. BJU Int. Aug 2010;106(3):334-341.
5. Cancer Incidence in Five Continents In: D.M. Parkin SLW, J. Ferlay, L. Teppo and D.B. Thomas, ed. Vol 8. Lyon, France: IARC Scientific Publication No. 155; 2002: http://www.iarc.fr/en/publications/pdfs-online/epi/sp155/ci5v8-tabasr\&cr.pdf.
6. Mullins CD, Onukwugha E, Bikov K, Seal B, Hussain A. Health Disparities in Staging of SEER-Medicare Prostate Cancer Patients in the United States. Urology. Sep 2010;76(3):566-572.
7. Carson AP, Howard DL, Carpenter WR, et al. Trends and Racial Differences in the Use of Androgen Deprivation Therapy for Metastatic Prostate Cancer. Journal of Pain and Symptom Management. May 2010;39(5):872-881.
8. DiIorio C, Steenland K, Goodman M, Butler S, Liff J, Roberts P. Differences in Treatment-Based Beliefs and Coping Between African American and White Men with Prostate Cancer. J. Community Health. Aug 2011;36(4):505-512.
9. Swords K, Wallen EM, Pruthi RS. The impact of race on prostate cancer detection and choice of treatment in men undergoing a contemporary extended biopsy approach. Urol. Oncol.-Semin. Orig. Investig. May-Jun 2010;28(3):280-284.
10. Clegg LX, Reichman ME, Miller BA, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. Cancer Causes Control. May 2009;20(4):417-435.
11. Kane C CP, Presti, Jr J , Shinohara K. Neoplasms of the Prostate Gland. Smith's General Urology. Vol 17th ed. New York: McGraw-Hill; 2008.
12. William G. Nelson HBC, Theodore L. DeWeese, Mario A. Eisenberger. Prostate Cancer. Abeloff's Clinical Oncology. 4th ed: Churchill Livingstone, An Imprint of Elsevier; 2008:1653-1699.
13. NCCN Guidelines for Patients. In: Network NCC, ed. Prostate Cancer ed.
14. Engelman KK, Perpich DL, Peterson SL, Hall MA, Ellerbeck EF, Stanton AL. Cancer information needs in rural areas. Journal of Health Communication. Apr-May 2005;10(3):199-208.
15. Evans S, Metcalfe C, Ibrahim F, Persad R, Ben-Shlomo Y. Investigating Black-White differences in prostate cancer prognosis: A systematic review and meta-analysis. International Journal of Cancer. Jul 2008;123(2):430-435.
16. Freeman VL, Ricardo AC, Campbell RT, Barrett RE, Warnecke RB. Association of Census Tract-Level Socioeconomic Status with Disparities in Prostate Cancer-Specific Survival. Cancer Epidemiol. Biomarkers Prev. Oct 2011;20(10):2150-2159.
17. Goodman M, Almon L, Bayakly R, et al. Cancer Outcomes Research in a Rural Area: A Multi-Institution Partnership Model. J. Community Health. Feb 2009;34(1):23-32.
18. Steenland K, Goodman M, Liff J, et al. The Effect of Race and Rural Residence on Prostate Cancer Treatment Choice Among Men in Georgia. Urology. Mar 2011;77(3):581-587.
19. Jones R. Exploring cancer support needs for older African-American men with prostate cancer. Support Care Cancer. 2011;19(9):1411-1419.
20. Sidana A, Hernandez DJ, Feng ZY, et al. Treatment decision-making for localized prostate cancer: What younger men choose and why. Prostate. Jan 2012;72(1):58-64.
21. Butler S, Owen-Smith A, DiIorio C, Goodman M, Liff J, Steenland K. Use of Complementary and Alternative Medicine Among Men with Prostate Cancer in a Rural Setting. J. Community Health. Dec 2011;36(6):1004-1010.
22. Collins MM, Barry MJ, Zietman A, et al. United States radiation oncologists' and urologists' opinions about screening and treatment of prostate cancer vary by region. Urology. Oct 2002;60(4):628-633.
23. Xu JP, Dailey RK, Eggly S, Neale AV, Schwartz KL. Men's Perspectives on Selecting Their Prostate Cancer Treatment. Journal of the National Medical Association. Jun 2011;103(6):468-478.
24. Wagner SE, Drake BF, Elder K, Hebert JR. Social and clinical predictors of prostate cancer treatment decisions among men in South Carolina. Cancer Causes Control. Nov 2011;22(11):1597-1606.

APPENDIX

Table 1. Distribution of variables according to NCCN Risk Categories


Table 2. Stratified, Adjusted Logistic Regression of Any Treatment


Table 3a. Stratified, Adjusted Logistic Regression of Overall Radiation Therapy for Men Under 60 Years Old


[^0]Table 3b. Stratified, Adjusted Logistic Regression of Overall Radiation Therapy for Men Greater Than or Equal to 60 Years Old

*All models also adjusted for year of diagnosis

Table 4. Adjusted, Stratified Logistic Model for Men of All Ages Receiving Surgery

*All models also adjusted for year of diagnosis


[^0]:    *All models also adjusted for year of diagnosis

