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Interplay of Race, Socioeconomic Status and Treatment on Survival of Prostate Cancer Patients

Kendra Schwartz, MD, MSPH¹, Isaac J. Powell, MD², Willie Underwood III, MD, MS, MPH^{2,3}, Julie George, MS⁴, Cecilia Yee, MS⁴, and Mousumi Banerjee, PhD⁵

¹ Department of Family Medicine and Public Health Sciences and Barbara Ann Karmanos Institute, Wayne State University School of Medicine, Detroit, Michigan

² Department of Urology and Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, Michigan

³ Barbara Ann Karmanos Cancer Institute, Communication and Behavioral Oncology Program, Wayne State University School of Medicine, Detroit, Michigan

⁴ Barbara Ann Karmanos Cancer Institute, Population Studies and Prevention Program, Wayne State University School of Medicine, Detroit, Michigan

⁵ University of Michigan School of Public Health, Ann Arbor, Michigan

Abstract

Objectives—We compared overall and prostate cancer-specific survival, using Detroit SEER registry data, among 8,679 Detroit-area black and white men with localized or regional stage prostate cancer diagnosed 1988-1992 to determine if racial disparities in survival remained after adjusting for treatment type and socioeconomic status (SES).

Methods—Cases were geocoded to census block-group and SES data obtained from the 1990 U.S. Census. Cox proportional hazards regression was used to estimate the hazard ratio of death from any cause. Median follow-up was 16.5 years.

Results—Among 7770 localized stage cases (22% black, 78% white), and 909 regional cases (24% black, 76% white), black men were more likely to receive non-surgical treatment ($p < 0.001$), and to be of low SES ($p < 0.0001$). Survival analyses were stratified by stage; for both stages, black men had poorer survival than white men in the unadjusted model. Adjustment for age and tumor grade had little effect on survival differences, while adjustment for SES and treatment erased the survival differences.

Conclusions—Low SES and non-surgical treatment were associated with higher risk of death among men with prostate cancer, which explains much of the survival disadvantage for black men with prostate cancer.

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Contact Author: Kendra Schwartz, MD, MSPH Wayne State University 101 E. Alexandrine Detroit, MI 48201 313 577 0880 Fax: 313 577 3070 kensch@med.wayne.edu.

Note: Dr. Underwood is currently affiliated with the Roswell Park Cancer Institute, Buffalo, New York

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Keywords

Prostate carcinoma; treatment; race; survival; socioeconomic status

Introduction

Among men, prostate cancer is the most common malignancy and second leading cause of cancer deaths¹. It also is a cancer associated with racial disparities. Prostate cancer incidence is approximately 1.6 times greater and prostate cancer mortality about 2.4 times greater for black men than for white men². Risk of death in the 11 years after prostate cancer diagnosis is 30% greater for black men³. Furthermore, the national 5-year relative survival for men diagnosed with prostate cancer (all stages combined) in 1990-1992 (similar to the time period reported on here) was 95.3% for white and 85.5% for black men².

One possible explanation for the mortality disparity is racial differences in prostate cancer treatment. Black men, compared to white men, are less likely to receive definitive therapy (radical prostatectomy [RP] or radiotherapy [RT]) for prostate cancers that are locally or regionally invasive⁴⁻⁹ which account for approximately 90% of all prostate cancers². This racial difference in the use of definitive therapy is exacerbated among men with poorly differentiated cancers^{8, 9}. Furthermore, when receiving watchful waiting (non-definitive therapy), black men are monitored less closely than white men⁶. The type of definitive therapy received also varies by race; black men are more likely to receive RT as opposed to RP for localized/regional prostate cancer⁸⁻¹⁰.

In studies of survival among prostate cancer patients, non-RP treatment is associated with poorer survival^{11, 12}. However, factors other than treatment affect survival; among RP-treated men, black men have poorer survival and increased clinical progression^{13, 14}, which may indicate racial differences in cancer biology. Socioeconomic status (SES) also has a strong influence on prostate cancer survival; a single hospital study¹⁵, and a Surveillance, Epidemiology, and End Results (SEER)-Medicare linked study¹¹, indicate that both SES and treatment are associated with survival of prostate cancer patients.

Metropolitan Detroit, with its relatively high black population, high prostate cancer mortality¹⁶ and a population-based cancer registry, is an ideal location to investigate the association between treatment, SES, and prostate cancer survival. Therefore, we conducted a retrospective study of black and white men with long-term follow-up after diagnosis of localized or regional stage prostate cancer to determine the clinical and demographic factors associated with survival.

Material and Methods

The study included men with a first primary, histologically-confirmed invasive prostate adenocarcinoma diagnosed from 1988 through 1992, identified through the population-based Metropolitan Detroit Cancer Surveillance System (MDCSS), a Surveillance, Epidemiology, and End Results (SEER) registry since 1973. Men with either localized or regional stage disease were included. Localized stage invasive carcinoma is confined to the prostate, without invasion beyond the prostatic capsule. Regional stage is extracapsular extension, either directly or to regional lymph nodes and includes seminal vesicle invasion, but is not found in metastatic sites. In more recent years, the two stages have been combined into one category of localized/regional stage due to inability to determine exact extent of disease in men not surgically treated.

From 1988 through 1992, 10,262 incident cases of invasive prostate cancer were diagnosed. Two cases were excluded for lack of geocodable address. Distant stage cancers (n=1316) were excluded because unadjusted survival was similarly poor for both racial groups in preliminary analyses. Also, hormonal therapy is the most widely accepted therapy for distant stage disease, and SEER has limited capability to capture information on non-surgical hormonal therapy. Patients with multiple definitive therapies were also excluded from analyses: 75 men with localized stage disease, 189 with regional disease.

Measurement of Variables

Clinical (stage and grade) and demographic (age and race) data were obtained by MDCSS on incident prostate cancer cases from all area medical facilities. Using address at diagnosis, the SES Group variable was developed through a geocoding process that first assigned census block-group number, as previously described¹⁷. Aggregate socioeconomic data specific to census block-groups were obtained from 1990 U.S. Census of Population and Housing Summary Tape File 3A (24). Variables used to calculate SES Group for each census block were occupation, poverty status in 1989, educational attainment, and age.

Thirteen occupational categories are used by the 1990 U.S. Census Bureau; 5 were defined as “professional” occupations and 8 as “working class” occupations. Working class block-groups were block-groups in which 66% or more of employed persons reported a working class occupation, such as administrative support or laborers. Professional block-groups contained 34% or more of employed persons with supervisory or executive positions. Poor block-groups had 20% or more of households below poverty level. In Educated block-groups 75% or more of persons age ≥ 25 years had high school education.

Men were initially assigned to one of eight SES Groups, based on occupation, poverty, and education. Due to small numbers in some groups and an effort to create the fewest distinct SES groups, we collapsed cases into three mutually exclusive and exhaustive SES categories: 1) Poor 2) Non-professional/Not poor; and 3) Professional.

Clinical information included registry stage (defined above) and histological tumor grade (categorized as well-differentiated, moderately differentiated, poorly or undifferentiated roughly corresponding to Gleason grades 2-4, 5-7, and 8-10, respectively, and missing). Information on prostate cancer directed therapy was from the SEER “first course of treatment” variable. Treatment categories are based on definitive monotherapy (radical prostatectomy [RP] or radiotherapy [RT]), or no definitive therapy in first 4 months after diagnosis (N). Hormonal therapy was included in the “N” group.

SEER conducts active follow-up of all cases by record linkage to hospital tumor registries, voting records, driver's license records, and death certificates. Overall survival (measured in months) was calculated as the interval between date of diagnosis and date of last follow-up (for censored cases) or death from any cause (for deceased cases). Prostate cancer-specific survival used death from prostate cancer based on death certificate information as the endpoint. Date of last follow-up was November 2008.

Statistical Analysis

Mantel-Haenszel chi-square statistics were used to compare the distributions of demographic and clinical characteristics in the two racial groups. Cox proportional hazards regression was used to estimate the hazard ratio (HR, 95% CI) of death from any cause (overall survival) and death from prostate cancer (cancer-specific survival). Survival analysis was stratified by SEER registry stage (localized or regional stage). For the Cox regression analyses, we fit a series of sequential models with race (black, white), age (≤ 65 years, > 65 years), and tumor grade (well,

moderately, poorly/un-differentiated) entered first, then SES (Poor, Non-professional/Not poor, Professional), then treatment (RP, RT, N). At each step of the modeling process, we calculated adjusted hazard ratio for race (i.e. adjusted for all variables in the model). All two-way interactions were checked in the final model. For interactions that were statistically significant, we do not present the corresponding main effects in the tables, since a significant interaction implies that a simple main effect of one factor varies by the levels of the second factor (i.e. if race by treatment is significant, then the difference in outcome between black and whites varies by treatment group), and presenting the main effect (i.e. difference in outcome between blacks and whites averaged over treatment groups) could be misleading. In such instances, we present the interaction effect in the tables.

Results

There were 7,770 cases of localized disease (22% black, 78% white), and 909 cases of regional disease (24% black, 76% white) (Table 1). Median follow-up was 16.5 years. Age distribution for both localized and regional stage disease did not differ by race. Greater proportions of black than white men were in the Poor SES group for both localized (62% vs. 7%, $p<0.001$) and regional stage (64% vs. 8%, $p<0.001$). For localized stage, black men had more tumors classified as poorly/undifferentiated (18% vs. 14%, $p<0.001$), while histology was similar for black and white men with regional stage disease. Receipt of RP differed by race: 16% black vs. 26% white ($p<0.001$) for localized stage disease, and 26% black vs. 47% white ($p<0.001$) for regional stage disease.

Among localized patients, the unadjusted hazard ratio (HR) for death due to any cause was greater for black men (1.27, 95% Confidence Interval [CI] 1.19, 1.35) than whites (Table 2). Adjustment for age and tumor grade did not reduce the HR; however further adjustment for SES decreased HR to 1.10 (95% CI 1.02, 1.18). After further adjustment for treatment there was no significant difference between the two races. There was a significant interaction between treatment and age. Older men consistently had poorer survival than younger men, with the most pronounced difference in the subgroup with no definitive therapy. Low SES and poor tumor histology also were significantly associated with poorer survival.

Among localized cancer patients, the unadjusted HR for death from prostate cancer was 1.75 times greater for black men compared to white (Table 3). Adding age and tumor grade to the model did little to change the HR for black men; however when SES was added to model the HR decreased from 1.68 (95% CI 1.47 - 1.93) to 1.35 (1.17 - 1.65). With further adjustment for treatment, we found significant treatment by race and treatment by age interactions. Cancer-specific survival was similar for black and white men receiving RP and RT, but in the subgroup with no definitive treatment, black men had significantly worse survival. Compared to the overall survival endpoint, which showed poorer survival for older men regardless of treatment, for prostate cancer specific-survival, older age was associated with poorer survival only in the no definitive treatment group, which could indicate that comorbidities played a role in the overall survival endpoint.

For regional stage cancers, the unadjusted HR for overall survival was significantly higher for black men (HR 1.37, 95% CI 1.15-1.62) (Table 4). In the final adjusted model, older age, low SES, and poor tumor grade were associated with greater risk of death. Both RT and RP treatment showed improved survival, with RP (HR 0.27, 95% CI 0.22 - 0.33) being significantly better than RT (HR 0.72, 95% CI 0.60 - 0.87) compared to no definitive treatment. The prostate cancer-specific survival analysis yielded similar results with regards to the racial difference in risk of death once age, SES group and tumor grade were included in the model (Table 5). In the final adjusted model, only poor tumor grade was associated with greater risk of death. Only RP was significantly associated with an improved survival (HR 0.20, CI 0.14-0.28).

Comment

In our study population, SES and race were strongly related, with most black men in the lowest SES group. Additionally, race and treatment were significantly associated, with black men less likely to receive RP and more likely to receive no definitive treatment. Higher SES for both localized and regional stage, and receiving RP for regional stage disease were associated with longer overall and cancer-specific survival in this population. Older age and poorly differentiated tumor grade predicted poor survival, but did not explain the racial difference in survival in any of the models. However, adjustment for SES eliminated much if not all of the racial difference in overall and cancer-specific survival among men with localized or regional stage prostate cancer. Adjustment for treatment among regional disease men further decreased the point estimates for risk of all-cause and prostate cancer-specific death among black men, while accounting for age, SES and tumor grade.

We are not the first to report that both SES and treatment are contributing factors to racial differences in prostate cancer survival. In 2005, Tewari et al., reported on a cohort of patients from a single large hospital system in Detroit¹⁵. Among 4,279 men diagnosed with clinically localized prostate cancer between 1980 and 1997, both overall and cancer-specific survival were significantly poorer for black men, compared to white men. The authors estimated that 50% of the racial survival difference was explained by differences in SES (as measured by census block-group income), while 34% was explained by use of surgical treatment. When the authors compared survival among surgically treated black and white patients, they found no difference.

Our findings were similar to the Tewari et al. study for regional stage disease, in that both SES and treatment had an effect on racial disparities in overall and cancer-specific survival. For localized disease, SES had the most effect on the racial disparity in overall survival, and less for cancer-specific survival. Treatment had little effect on racial differences in overall survival for localized disease, while for cancer-specific survival, black men had similar survival as white men when treated with RT or RP, but poorer survival when receiving no definitive treatment.

Using combined SEER-Medicare data, Du et al. also found that SES was a strong predictor of overall and prostate cancer-specific survival among men diagnosed with localized and regional prostate cancer from 1973-1999¹¹. Although black and white men differed in the receipt of treatment, the effect of treatment was minimal in this study. More recently, a study of prostate cancers from 7 state registries also demonstrated an increased risk of all-cause mortality among low SES men¹⁸. Both studies adjusted for age, comorbidity, and stage.

In contrast, a study of prostate cancers in the California Cancer Registry found the primary prognostic factors for prostate cancer-specific survival were stage and treatment, with tumor grade and SES having less effect on survival¹². These investigators also performed sequential adjustment to their survival model, adjusting first for stage and treatment, after age. SES was then grouped with grade and year of diagnosis for the final adjustment, so it is difficult to determine how much of the racial difference in survival might be explained by SES alone in this study.

Low SES also is a predictor of poor outcomes in patients with other cancers. Racial differences in overall and colon cancer-specific survival were significant after adjustment for age, sex, tumor stage, tumor grade, and comorbidity score, with blacks at higher risk of death than whites¹⁹. Adding definitive treatment to the model attenuated the racial difference, while with SES in the final model the racial differences in survival were nearly erased. A study of oral cancer using SEER data, reported that blacks compared to whites had poorer overall survival after adjustment for age and SEER area; SES was associated with the greatest reduction in overall

risk of death.²⁰ Risk of death from breast cancer also was associated with low SES after adjustment for race, stage, age, and treatment²¹. Studies of cancer survival often use multivariable models adjusting for clinical factors, treatment, and SES. However, there is a need to conduct these studies using a sequential approach to adjustment to determine the relative effect of SES on survival. It is likely that SES may be the most significant predictor of survival in many cancers noted for their racially disparate survival outcomes¹⁸.

Along with SES, we found treatment to be an important survival factor among men with regional stage prostate cancer. Significantly smaller proportions of black than white men received RP for treatment of either localized or regional prostate cancer. The racial disparity in use of RP for treatment of localized/regional prostate cancer is well documented^{8, 9, 22, 23}. In our population of men with regional stage cancer, those treated with RP as compared to RT had a 3-times lower hazard of death after adjusting for SES, tumor grade, age and race. Since black men are less likely to receive RP and more likely to receive no definitive treatment, and non-surgical treatment was found to be associated with poorer survival by us and others²⁴, it is not surprising a racial disparity in survival exists. Therefore, our findings support the findings of others^{12, 15} that black-white differences in prostate cancer treatment significantly contribute to the observed racial survival disparity.

It remains unclear how race and SES affect which prostate cancer treatment is received. A study of prostate cancer patients from a single Health Maintenance Organization found that African American men are less likely to be offered treatment with curative intent²⁵. Additionally, poor black men may be given different recommendations than middle-income black men²⁶. A 2006 study of urologists asked to provide treatment recommendations for hypothetical patients found socially vulnerable (low income and widowed) black men were less likely to receive a recommendation of RP than married black men of middle-income.

Although tumor registry data, such as the MDCSS are robust, they are not without limitations. We were unable to adjust for comorbid disease status because it is not consistently available. Consequently, it is difficult to determine if some of the survival differences are due to healthier patients being more likely to undergo surgery than less healthy patients. However, in previously mentioned studies that did consider comorbidities^{15, 18}, that measurement played only a minor role, if any, in the survival outcome. Another limitation of our study is it includes only men from metropolitan Detroit, which limits the generalizability of our findings to other areas of the country. Yet, our findings are similar to those of Du et al.¹¹, which used national SEER-Medicare data, in that we found SES to play a large role in overall survival of men with prostate cancer. In an effort to study long-term survival our cases are from 1988-1992; radiation therapy dosing and technical equipment has improved since that time²⁷, which may account in part for the poorer survival associated with RT. Finally, we stratified our analyses by clinical stage with the limitation that some tumors classified as localized may, in fact, have been regional stage.

Conclusion

We found that both low SES and non-RP treatment are important in explaining the racial disparity in survival among men with localized and regional prostate cancer in the metropolitan Detroit area. Correcting the historical issues that have contributed to racial differences in SES would take a major societal transformation that is unlikely to be forthcoming; however, equal treatment for equal disease should be attainable and would eliminate one source of the racial disparity in prostate cancer survival.

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Table 1

Characteristics of Men Diagnosed With Prostate Cancer by Stage and Race, Detroit, Michigan 1988 - 1992

	N	Localized Stage		P value	Regional Stage		P value
		Black 1711	White 6059		Black 219	White 690	
Age							
	<= 65 years	27%	25%	0.09	32%	32%	0.95
	>65 years	73%	75%		68%	68%	
SES Group							
	Poor	62%	7%	<0.001	64%	8%	<0.001
	Non-Prof, Not Poor	18%	47%		16%	47%	
	Professional	20%	46%		20%	46%	
Tumor Grade							
	Well	31%	30%	<0.001	10%	7%	0.21
	Moderate	43%	47%		44%	49%	
	Poor or Undifferentiated	18%	14%		37%	37%	
	Missing	8%	9%		10%	7%	
Treatment							
	Radical Prostatectomy (RP)	16%	26%	<0.001	26%	47%	<0.001
	Radiation Therapy (RT)	36%	38%		30%	28%	
	No definitive therapy (N)	48%	36%		44%	24%	

Table 2

Unadjusted and Adjusted Overall Survival Analyses for Localized Stage Prostate Cancers, Detroit, Michigan, 1988 - 1992

	N	7770 Unadjusted			Adjusted		
		HR	CI	HR	CI	HR	CI
Race							
	(Ref) White	1.00		1.00		1.00	
	Black	1.27	1.19, 1.35	1.28	1.21, 1.36	1.10	1.02, 1.18
Age							
	(Ref) <= 65 years	1.00		1.00		1.00	
	> 65 years	2.83	2.64, 3.04	2.80	2.61, 3.01	2.77	2.59, 2.98
SES Group							
	(Ref) Professional	1.00		1.00		1.00	
	Non-Prof, Not Poor	1.16	1.10, 1.23	1.15	1.09, 1.22	1.13	1.06, 1.19
	Poor	1.58	1.48, 1.70	1.43	1.32, 1.55	1.33	1.23, 1.46
Tumor Grade							
	(Ref) Well or Moderate	1.00		1.00		1.00	
	Poor or Undiff.	1.56	1.46, 1.67	1.48	1.39, 1.59	1.48	1.38, 1.58
	Missing	1.35	1.23, 1.47	1.24	1.14, 1.36	1.24	1.13, 1.35
Treatment							
	(Ref) No definitive therapy (N)	1.00		1.00		1.00	
	Radiation therapy (RT)	0.82	0.78, 0.87	0.82		1.48	1.48, 1.71
	Radical prostatectomy (RP)	0.30	0.28, 0.32			1.11	1.02, 1.21
Treatment × Age							
	No definitive therapy						
	(Ref) Age <=65 years	1.00		1.00		1.00	
	Age > 65 years	3.26	2.87, 3.70			1.59	1.48, 1.71
Radiation therapy							
	(Ref) Age <=65 years	1.00		1.00		1.00	
	Age > 65 years	1.77	1.57, 1.98			1.11	1.02, 1.21
Radical prostatectomy							
	(Ref) Age <=65 years	1.00		1.00		1.00	
	Age > 65 years	1.88	1.64, 2.15			1.11	1.02, 1.21

Unadjusted and Adjusted Prostate Ca-Specific Survival Analyses for Localized Stage Prostate Cancers, Detroit, Michigan, 1988 - 1992

Table 3

	N	7770 Unadjusted			Adjusted		
		HR	CI		HR	CI	
Race							
	(Ref) White	1.00			1.00		
	Black	1.75	1.53, 2.01		1.68	1.47, 1.93	1.17 1.65
Age							
	(Ref) <= 65 years	1.00			1.00		
	> 65 years	2.17	1.85, 2.55		2.09	1.78, 2.46	1.75, 2.42
SES Group							
	(Ref) Professional	1.00			1.00		
	Non-Prof, Not Poor	1.12	0.97, 1.29		1.10	0.95, 1.27	0.93, 1.24
	Poor	2.01	1.72, 2.36		1.55	1.28, 1.88	1.14, 1.69
Tumor Grade							
	(Ref) Well or Moderate	1.00			1.00		
	Poor or Undiff.	3.81	3.33, 4.37		3.59	3.14, 4.12	3.30, 4.34
	Missing	1.74	1.40, 2.16		1.65	1.33, 2.06	1.17, 1.81
Treatment							
	(Ref) No definitive therapy (N)	1.00			1.00		
	Radiation therapy (RT)	1.04	0.91, 1.19		3.58	3.13, 4.11	3.30, 4.34
	Radical prostatectomy (RP)	0.26	0.21, 0.32		1.64	1.32, 2.05	1.17, 1.81
	Treatment × Race						
No definitive therapy	(Ref) White	1.00			1.00		
	Black	1.75	1.39, 2.21				
Radiation therapy	(Ref) White	1.00			1.00		
	Black	0.97	0.76, 1.23				
Radical prostatectomy	(Ref) White	1.00			1.00		
	Black	1.03	0.62, 1.70				
	Treatment × Age						
No definitive therapy	(Ref) Age <=65	1.00			1.00		
	Age> 65	3.28	2.34, 4.60				
Radiation therapy	(Ref) Age <=65	1.00			1.00		
	Age> 65	0.98	0.78, 1.23				
Radical prostatectomy	(Ref) Age <=65	1.00			1.00		
	Age> 65	1.28	0.88, 1.87				

Unadjusted and Adjusted Overall Survival Analyses for Regional Stage Prostate Cancers, Detroit, Michigan, 1988 - 1992

Table 4

	N	909 Unadjusted		Adjusted			
		HR	CI	HR	CI	HR	CI
Race							
	(Ref) White	1.00		1.00		1.00	
	Black	1.37	1.15, 1.62	1.35	1.14, 1.60	1.09	0.88, 1.36
Age							
	(Ref) <= 65 years	1.00		1.00		1.00	
	> 65 years	2.02	1.70, 2.40	1.97	1.66, 2.34	1.94	1.64, 2.31
SES Group							
	(Ref) Professional	1.00		1.00		1.00	
	Non-Prof. Not Poor	1.20	1.01, 1.42	1.19		1.13	0.95, 1.34
	Poor	1.74	1.43, 2.11	1.57		1.35	1.05, 1.72
Tumor Grade							
	(Ref) Well or Moderate	1.00		1.00		1.00	
	Poor or Undiff.	1.41	1.20, 1.65	1.39	1.19, 1.63	1.27	1.08, 1.49
	Missing	1.80	1.36, 2.37	1.56	1.18, 2.06	1.07	0.80, 1.42
Treatment							
	(Ref) No definitive therapy (N)	1.00				1.00	
	Radiation Therapy (RT)	0.69	0.58, 0.83			0.72	0.60, 0.87
	Radical prostatectomy (RP)	0.23	0.19, 0.28			0.27	0.22, 0.33

Table 5

Unadjusted and Adjusted Prostate Ca-Specific Survival Analyses for Regional Stage Prostate Cancers, Detroit, Michigan, 1988 - 1992

	N	909 Unadjusted		Adjusted			
		HR	CI	HR	CI	HR	CI
Race							
	(Ref) White	1.00		1.00		1.00	
	Black	1.37	1.04, 1.81	1.35	1.03, 1.78	1.02	0.71, 1.47
Age							
	(Ref) <= 65 years	1.00		1.00		1.00	
	> 65 years	1.57	1.20, 2.06	1.50	1.15, 1.97	1.48	1.13, 1.94
SES Group							
	(Ref) Professional	1.00		1.00		1.00	
	Non-Prof. Not Poor	1.02	0.77, 1.36	1.03		0.96	0.72, 1.27
	Poor	1.67	1.22, 2.29	1.62	1.09, 2.40	1.37	0.91, 2.04
Tumor Grade							
	(Ref) Well or Moderate	1.00		1.00		1.00	
	Poor or Undiff.	2.06	1.59, 2.67	2.05	1.59, 2.66	1.81	1.40, 2.35
	Missing	2.54	1.64, 3.93	2.29	1.47, 3.55	1.52	0.98, 2.38
Treatment							
	(Ref) No definitive therapy (N)	1.00				1.00	
	Radiation therapy (RT)	0.73	0.56, 0.97			0.79	0.60, 1.05
	Radical prostatectomy (RP)	0.17	0.12, 0.24			0.20	0.14, 0.28