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Factors Associated with Time-to-Treatment of Prostate Cancer in Florida

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Prostate cancer is the most commonly diagnosed cancer after skin cancer and the second leading cause of cancer death for American men, behind only lung cancer.[1] The American cancer society estimates that there will be about 238,590 new cases of prostate cancer, and 29,720 men will die from the disease in 2013.[1]

Prostate cancer mortality rate is declining in developed countries, however it is not clear whether this is due to the increasing use of screening procedures based on prostate-specific antigen (PSA) blood test, improved treatment,[2] or combination of these and/or other factors.[3] In spite of declining prostate cancer mortality, striking racial disparities in prostate cancer outcomes exist in the U.S. Compared with Caucasian men, African American are

more likely to be diagnosed at advanced stage disease and die from prostate cancer in the U.S.[1,4]

Studies have shown differences in prostate cancer treatment among patients with various races/ethnicities or socioeconomic backgrounds.[5–8] Existing literature suggests that African American men have not been receiving optimal treatment for prostate cancer and have been experiencing delays in treatment.[9–11] Such differences in treatment must be understood better and explained as they might be one cause of the racial disparities in prostate cancer mortality observed in the U.S. This information is critical for the development of appropriate policy and intervention strategies to eliminate long-term racial/ethnic disparities.

Several factors have been suggested to influence time-to-treatment in cancer patients, including socioeconomic status and other demographic characteristics.[12–15] In breast cancer, for instance, studies have shown that time-to-treatment may be linked to socioeconomic status as well as race. The same studies suggested that delays of greater than three months after an initial diagnosis may decrease breast cancer survival by 12%.[13–16]

Some studies found that men with prostate cancer experience longer wait time for diagnosis and treatment than those observed for other cancers.[17–19] Studies in both the urologic and medical literature have paid increasing attention to the question of overdiagnosis in prostate cancer. As evidence, a study reported overdiagnosis rates of 15% among White men and 37% among Black men.[20] The association between wait time and prognosis of prostate cancer is inconclusive.[21–26] Even though we recognize the current literature's debate on whether or not prostate cancer has been over-treated, the intent of this project was not to make a clinical judgment about this matter. This study intended to investigate factors contributing to time-to-treatment and examine whether there was a difference in wait time or treatment rate between African American and Caucasian men in Florida.

Methods

Population studied

Caucasian and African American men 40 years of age or older diagnosed with prostate cancer between Oct. 2001 and Dec. 2007 in Florida. Other races were excluded due to small numbers in the dataset.

Data sources

The study used data from three sources. First, prostate cancer incidence data between Oct. 2001–Dec. 2007 were obtained from the Florida Cancer Data System (FCDS) that is managed by State of Florida Department of Health and housed at the University of Miami through a contract. The FCDS is the largest population-based, cancer incidence registry in the nation.[27] It contains information on patient demographic characteristics, residence, prostate tumor characteristics, and other information such as tobacco use and primary payer of health insurance.

Second, comorbidity data were obtained from the Florida Agency for Health Care and Administration (AHCA). The AHCA maintains two databases (Hospital Patient Discharge

Data and Ambulatory Outpatient Data) on all patient encounters within hospitals and freestanding ambulatory surgical and radiation therapy centers in Florida. Comorbidity was computed following the Elixhauser Index method[28] based on diagnoses information from AHCA. The study used a total of 45 conditions, including 29 from the Elixhauser Index plus 16 new additional conditions based on clinical characteristics of the study population.

Third, data on demographic and area-level socioeconomic characteristics were extracted at the census tract level from the U.S. Census Bureau public use files (Census 2000, Summary File-3) for the State of Florida. Data obtained from the three sources were merged into a single dataset for analyses.

Statistical analysis

Time from diagnosis to initial treatment of prostate cancer was calculated. Patients who did not receive any treatment by last recorded follow up, including watchful waiting cases, were censored at time of last follow-up. Descriptive statistics were used to summarize sample characteristics, t-tests and chi-square tests were used for bivariate racial comparisons in Table 1; Kaplan-Meier estimator was applied to generate estimated survival probability curves in figures (probability waiting time is beyond a given time in our case). Wei, Lin and Weissfeld (WLW) survival model[29] was utilized to examine effects of exploratory variables on time-to-treatment while accounting for possible correlation of patients from same census tract. This model choice was supported by the ratio of the robust standard error estimate relative to the model-based estimate that ranged from 0.6 to 1.5, where departure from one indicates improvement while accounting for correlation. Hazard ratios and p-values were calculated. The event of interest in this study was receiving initial treatment instead of death as frequently seen in publications involving time-to-event analysis. Therefore “hazard” in this study is interpreted as treatment rate instead of death rate, and a higher treatment rate corresponds to a shorter waiting time before treatment. Survival probability at any time t in figures is interpreted as the chance that waiting time before initial treatment is longer than time t i.e. chance that patient is still waiting at time t. Statistical analyses were carried out using SAS/STAT® software, Version 9.3 of the SAS System for Windows.

Results

Population characteristics

Characteristics of the study population are summarized in Table 1. A total of 11,284 men diagnosed with prostate cancer in Florida during Oct. 2001–Dec. 2007 were included in the study, among whom 12.61% were diagnosed at late-stage. Patient age in the study ranged from 40 to 99 at diagnosis, with a median diagnosis age of 66 years. The average age at diagnosis was 66.36 years. About 87.57% of the study population was Caucasian and 12.43% was African American. Most patients were married (79.08%). The majority of the sample had public health insurance (56.67%). Public health insurance includes Medicare, Medicaid, Department of Defense (Tricare), military personnel (military), veteran affairs, or Indian/Public Health Service. Since the study only included three months of 2001 data, proportion of 2001 cases was lower than those of later years. Compared with Caucasian men, African American men were diagnosed at a younger age on average, had a lower

percentage of patients treated with radiation only, a lower proportion of married patients, a higher uninsured rate, a lower share of patients with well-moderately differentiated tumor, and a larger fraction of late stage diagnosis.

The observation period ranged from 0 days to 2,408 days (approximately six and a half years). The median time-to-treatment was 47 days, indicating 50% of patients received initial treatment within 47 days after diagnosis. Curves in Figures 1 and 2 dramatically drop down to approximately 90% at around diagnosis time, indicating approximately 10% of patients sought initial treatment shortly after diagnosis. Overall racial comparison of waiting probability for time-to-treatment in Figure 1 and racial comparisons by stage in Figure 2 both indicate that in general African American men had a higher chance to wait a longer time before receiving initial treatment.

Multilevel analysis

The analysis was performed for early-stage and late-stage patients separately. The results are shown in Tables 2 and 3. The comorbidity conditions that were not significant in the analysis were listed separately in Appendix 1 and 2. Among patients diagnosed with early prostate cancer, higher rate of treatment was associated with being diagnosed at for-profit facilities and/or hospitals. Wait time increased for African American patients and those who lived in areas with higher percentages of African American population. These effects did not change over time. For patients diagnosed with early-stage prostate cancer, presence of diabetes without chronic complications was associated with shorter wait time. Two comorbidity conditions were associated with longer waiting time: psychoses, and benign neoplasm and in-situ cancer.

Similar to the association observed among early-stage cases, late-stage patients living in area with higher percentage of African American population had longer waiting time and this effect did not change over time. More comorbidity conditions became significant factors of shorter waiting time for late-stage patients. Specifically, treatment rate was higher among men with liver disease, solid tumor without metastasis, rheumatoid arthritis/collagen vascular disease, deficiency anemias, drug abuse, and genitourinary system disease.

Patients diagnosed in more recent years had lower treatment rate than those diagnosed in early years. This pattern was observed for both early and late stage.

Discussion

Our study differs from other studies investigating time-to-treatment among cancer patients in two major ways: 1) it utilized both the state cancer registry data and patient's diagnosis of other conditions to present a much more complete sickness profile of men with prostate cancer, and 2) early and late-stage prostate cancer cases were analyzed separately.

Prostate cancer typically tends to grow slowly, which can explain why men diagnosed with late-stage prostate cancer wait less to receive treatment than those diagnosed at early-stage. Significantly shorter wait times were also observed for older patients, which is consistent with a study by Johnston and colleagues[30] and may be partly due to easier access to health

care. Indeed, in the U.S. the elderly are more likely to hold health insurance and, thus interact with health care provider more frequently than younger men. On the other hand, a population-based study in Canada with universal health coverage reported no difference in treatment wait time.[31] Other studies have also suggested that due to rising prevalence of coexisting diseases with age and certain physiologic changes in the elderly, which may reduce their capacity to tolerate therapeutic complications, elderly patients were less likely to undergo treatments for prostate cancer.[32,33]

Another finding of our study is that characteristics of facility where prostate cancer was diagnosed have some impact on time-to-treatment. Men who were diagnosed in hospital settings with early-stage prostate cancer had a shorter wait time compared with those in ambulatory settings. For late-stage patients, treatment rates were comparable among diagnosis facilities. For early-stage disease, men who were diagnosed at for-profit facilities were more likely to wait longer. However, the reasons for this difference are not well understood as we have no data on treatment decision making. It is unclear whether longer time-to-treatment is related to treatment capacity issues, or provider and patient decisions or preferences.

The presence of some comorbidity reduced wait time to prostate cancer treatment. Men with other solid tumors without metastasis received treatment sooner regardless of prostate cancer stage. For men diagnosed with early-stage prostate cancer, having diabetes without chronic complications or other metastatic cancers, was associated with shorter wait time. Since these men are already in the health care system being treated for these co-existing conditions, they should be more likely to be treated early for prostate cancer. It is hard to explain why time-to-treatment of early-stage prostate cancer was lengthened when men had diabetes with other chronic complications and/ or other circulatory diseases. Among men with late-stage prostate cancer, wait time was shorter for those with conditions including but not limited to liver disease, lymphoma, rheumatoid arthritis, deficiency anemia, and drug abuse. This study revealed that AIDS as comorbidity was a deterrent in seeking early treatment for late-stage prostate cancer. Treatments for late-stage prostate cancer tend to be more aggressive, and could adversely affect patients with AIDS due to their weakened immune system. Treatment of both AIDS and cancer can be complex,[34,35] so it is may be necessary for these treatments to be coordinated.

Although our study did not reveal racial differences in time-to-treatment at the individual level, a contextual factor was found to affect treatment rate significantly: the rate was lower in areas with high percentages of African American for analyses of both early-stage and late-stage patients, independent of age at diagnosis, health insurance, and the other factors. In other words, men who resided in predominantly African neighborhoods waited longer to have their prostate cancer treated than did those who lived in less African American-concentrated areas. Such a disparity may be explained in that predominantly African American neighborhoods have poorer health care facilities with less technology and fewer medical specialists, than do Caucasian neighborhoods.[36,37]

African American men have been found to be less likely than Caucasians to receive definitive treatment after being diagnosed with prostate cancer.[38] Since the value of treating

prostate cancer has been questioned, and concrete evidence of benefit from definitive treatment is lacking, it is not clear whether the disproportionate receipt of definitive treatment we observed for African Americans represents inappropriate care. Certain studies have contended that the preferences of African American men may differ from Caucasians or that African American men may weigh the risks of definitive treatment differently.[38] Another view has been expressed that African American men are offered optimal treatment less frequently than their Caucasian counterparts.[8] These are certainly issues worthy of investigation in future studies.

The current study has a number of limitations. First, only cases diagnosed from 2001 through 2007 were analyzed. As a result, the observations made in this analysis may not necessarily reflect the most current trends. Second, census-tract socioeconomic data was used due to lack of individual-level information on socio-economic status which would have provided more accurate information for the analyses. Third, we have no data on treatment decision making to determine whether the wait time is related to physician/patient decision making, or patient preferences. Fourth, cancer registry data are subject to some limitations. Registry data lack information about events leading up to screening. Follow-up information are often limited to vital status, and there are no detailed information on side effects of treatment or treatment compliance. They offer very little information about recurrence of disease.

Despite these limitations, the study was able to maximize the utility of currently available information by linking three data sources and presented a comprehensive picture of patient outcomes. Specifically, patient comorbidity was taken into consideration, which is highly relevant to examining treatment rate among men diagnosed with prostate cancer.

Individual-level factors, such as comorbid conditions and sociodemographic characteristics should be considered in prostate cancer treatment. The findings of this study have implications for clinical practice in prostate cancer. They show a difference in the time-to-treatment and also highlight the need for further study to understand treatment decision making for this disease. Further research is needed, especially in the midst of the ongoing debate about possible overdiagnosis and overtreatment of prostate cancer, to investigate the association between time-to-treatment and prostate cancer-specific patient outcomes such as survival and quality of life.

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Appendix 1. NONSIGNIFICANT COMORBIDITIES INCLUDED IN THE MULTIVARIATE ANALYSIS FOR EARLY-STAGE CASES

Variables	Hazard Ratio	95% CI		P-Value
Congestive heart failure	0.922	0.742	1.146	.4649
Valvular disease	0.992	0.852	1.155	.9203
Pulmonary circulation disease	0.718	0.411	1.255	.2452

Variables	Hazard Ratio	95% CI		P-Value
Peripheral vascular disease	0.837	0.697	1.005	.0567
Paralysis	1.178	0.694	2.001	.5440
Other neurological disorders	0.911	0.739	1.123	.3830
Chronic pulmonary disease	1.019	0.942	1.103	.6399
Diabetes w/ chronic complications	0.729	0.515	1.032	.0746
Hypothyroidism	1.040	0.905	1.194	.5802
Renal failure	0.893	0.719	1.109	.3063
Liver disease	0.734	0.527	1.022	.0669
Peptic ulcer Disease excluding bleeding	1.163	0.817	1.657	.4017
Acquired immune deficiency syndrome (AIDS)	1.151	0.568	2.331	.6971
Lymphoma	0.877	0.625	1.231	.4484
Metastatic cancer	1.130	0.952	1.342	.1622
Solid tumor w/out metastasis	1.079	0.957	1.216	.2125
Rheumatoid arthritis/collagen vascular	1.170	0.854	1.604	.3284
Coagulopathy	0.924	0.699	1.221	.5785
Obesity	1.080	0.949	1.230	.2437
Weight loss	0.661	0.407	1.074	.0945
Fluid and electrolyte disorders	1.059	0.926	1.211	.4037
Chronic blood loss anemia	1.032	0.764	1.394	.8376
Deficiency Anemias	1.029	0.896	1.181	.6879
Alcohol abuse	0.877	0.662	1.162	.3595
Drug abuse	1.142	0.533	2.447	.7329
Depression	1.063	0.918	1.231	.4154
Endocrine disorders, nutritional and metabolic, immunity	1.046	0.990	1.105	.1111
Ischemic heart disease	1.015	0.945	1.090	.6862
Digestive system disease	1.037	0.975	1.102	.2461
Genitourinary system disease	1.034	0.977	1.095	.2491
Injury and poisoning	1.052	0.963	1.149	.2651
Respiratory disorders	0.932	0.823	1.055	.2625
Infection	0.962	0.808	1.146	.6658
Other circulatory disease	0.891	0.773	1.026	.1099
Other nervous system and sense organs disorders	0.992	0.870	1.132	.9052
Skin and subcutaneous tissue disease	1.118	0.907	1.378	.2971
Muscularskeletal and connective tissue disease	0.972	0.906	1.043	.4266
Other mental disorders	0.894	0.696	1.147	.3784
Other anemias	1.052	0.820	1.348	.6916
Congenital anomalies	1.117	0.823	1.517	.4781
Brain and other Neurological disorders	0.973	0.779	1.215	.8095
Hypertension	0.965	0.923	1.009	.1166

Appendix 2. NONSIGNIFICANT COMORBIDITIES INCLUDED IN THE MULTIVARIATE ANALYSIS FOR LATE-STAGE CASES

Variables	Hazard Ratio	95% CI		P-Value
Congestive heart failure	1.111	0.685	1.803	.6700
Valvular disease	0.740	0.482	1.137	.1693
Pulmonary circulation disease	1.130	0.438	2.912	.8005
Peripheral vascular disease	0.774	0.484	1.237	.2837
Paralysis	1.775	0.919	3.428	.0876
Other neurological disorders	0.763	0.395	1.472	.4195
Chronic pulmonary disease	0.924	0.744	1.146	.4706
Diabetes w/o chronic complications	1.083	0.901	1.302	.3935
Diabetes w/ chronic complications	0.618	0.284	1.347	.2264
Hypothyroidism	1.084	0.820	1.433	.5711
Renal failure	0.683	0.445	1.046	.0797
Peptic ulcer Disease excluding bleeding	0.560	0.222	1.410	.2182
Acquired immune deficiency syndrome (AIDS)	0.227	0.050	1.033	.0551
Lymphoma	1.683	0.748	3.785	.2081
Metastatic cancer	1.144	0.968	1.352	.1147
Coagulopathy	1.184	0.799	1.754	.3997
Obesity	1.075	0.822	1.408	.5968
Weight loss	0.967	0.580	1.612	.8968
Fluid and electrolyte disorders	1.123	0.882	1.430	.3472
Chronic blood loss anemia	1.330	0.867	2.039	.1915
Alcohol abuse	1.044	0.694	1.570	.8366
Psychoses	0.465	0.213	1.016	.0548
Depression	0.817	0.534	1.248	.3495
Endocrine disorders, nutritional and metabolic, immunity	1.016	0.894	1.156	.8037
Ischemic heart disease	0.943	0.779	1.143	.5497
Digestive system disease	1.095	0.946	1.268	.2252
Injury and poisoning	1.186	0.968	1.454	.1002
Respiratory disorders	1.040	0.837	1.292	.7260
Infection	1.074	0.794	1.454	.6422
Other circulatory disease	0.843	0.639	1.112	.2259
Benign neoplasm and in-situ cancer	0.922	0.619	1.374	.6903
Other nervous system and sense organs disorders	1.157	0.873	1.533	.3093
Skin and subcutaneous tissue disease	0.928	0.629	1.368	.7053
Muscularskeletal and connective tissue disease	1.070	0.925	1.239	.3622
Other mental disorders	1.049	0.610	1.803	.8633
Other anemias	0.925	0.570	1.503	.7543
Congenital anomalies	1.112	0.698	1.772	.6542
Brain and other Neurological disorders	0.976	0.687	1.387	.8916
Hypertension	0.983	0.876	1.104	.7775

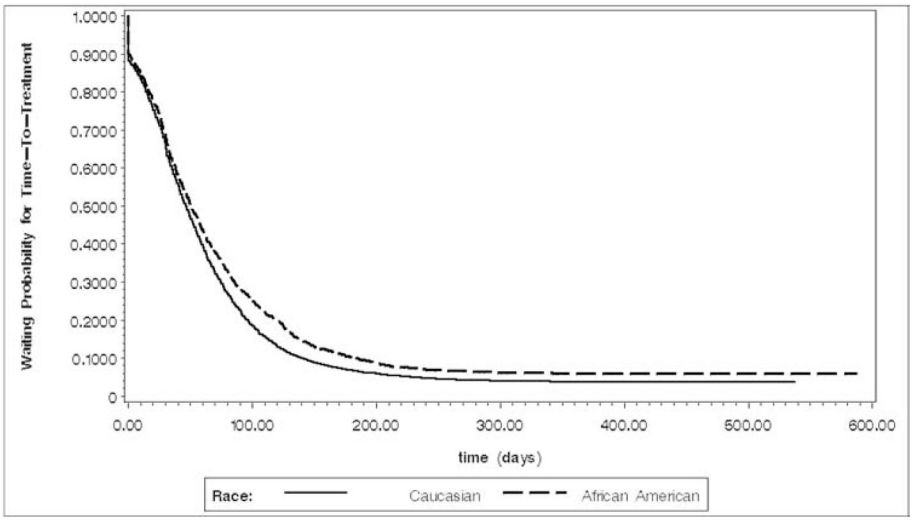
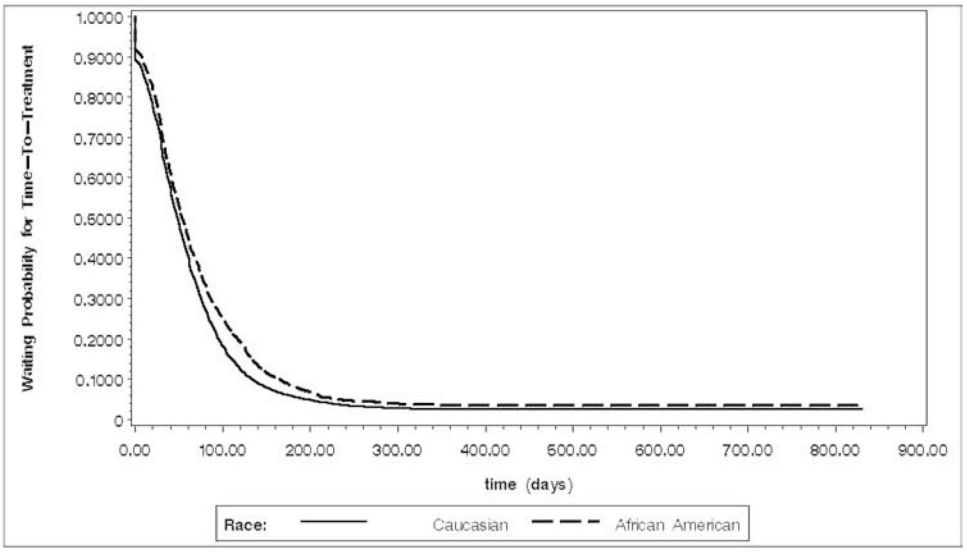
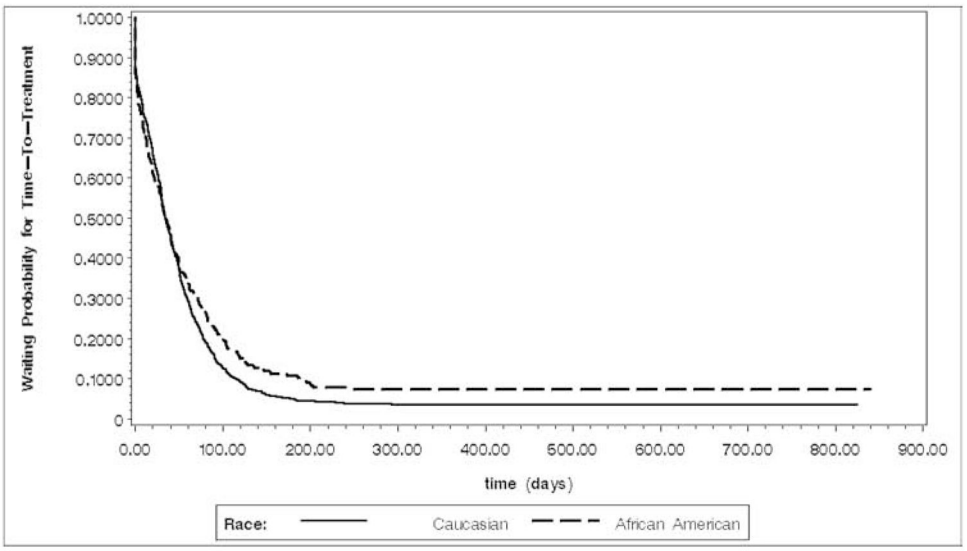


Figure 1.
Waiting probability estimates by race (early follow-up period)



(a) Early stage



(b) Late stage

Figure 2.
Waiting probability estimates for early and late stage by race (early follow-up period)

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Table 1

CHARACTERISTICS OF THE STUDY POPULATION (N =11,284)

Variable		n	Mean(SD) or %[a]	Caucasian[a,c]	African American[a,c]	P-Value
Age		11284	66.36 (8.98)	66.84 (8.90)	62.97 (8.84)	<.0001
Treatment	Active surveillance	883	7.84	7.70	8.77	.0003
	Surgery + radiation	224	1.99	2.00	1.93	
	Surgery + hormone	351	3.11	2.94	4.35	
	Radiation only	2617	23.22	23.73	19.69	
	Hormone only	493	4.37	4.19	5.71	
	Radiation + hormone	1512	13.42	13.34	13.98	
	Surgery only	5189	46.05	46.11	45.58	
Year of dx	2001[b]	579	5.13	5.13	5.13	.1664
	2002	2213	19.61	19.91	17.53	
	2003	1538	13.63	13.54	14.26	
	2004	1605	14.22	14.20	14.40	
	2005	1616	14.32	14.16	15.47	
	2006	1804	15.99	16.17	14.68	
	2007	1929	17.10	16.89	18.53	
Race	Caucasian	9881	87.57			
	African American	1403	12.43			
Marital status	Married	8923	79.08	80.74	67.36	<.0001
	Unmarried	2361	20.92	19.26	32.6	
Insurance	Publicly insured	6395	56.67	58.47	46.68	<.0001
	Privately insured	4684	41.51	40.01	49.28	
	Uninsured	205	1.82	1.52	4.05	
Tumor grade	Well-moderately diff	7078	62.73	63.24	59.09	.0015
	Poorly differentiated	3508	31.09	30.82	33.00	
	Undiff or unknown	698	6.19	5.94	7.91	
Stage	Early (localized)	9861	87.39	87.94	83.54	<.0001
	Late (regional & distant)	1423	12.61	12.06	16.46	

[a] May not sum to 100% due to rounding

[b] The study used partial data for the year 2001 (October 1, 2001–December 31, 2001)

[c] Mean (SD) or Column percentages

Table 2

MULTIVARIATE ANALYSIS FOR EARLY-STAGE CASES (N = 9,861)

Variables	Hazard Ratio	95% CI		P-Value
African American vs. Caucasian	0.921	0.857	0.990	.0260*
Age	1.003	1.000	1.007	.0565
Married vs. unmarried	1.013	0.959	1.071	.6396
Uninsured vs. private insurance	0.862	0.724	1.027	.0964
Public insurance vs. private insurance	1.008	0.958	1.062	.7472
Current smoker vs. non-current smoker	0.992	0.936	1.052	.7905
Ambulatory vs. hospital	0.441	0.369	0.527	<.0001*
For-profit vs. not-for-profit	1.199	1.137	1.264	<.0001*
Percentage of African American	0.998	0.997	0.999	.0045*
Comorbidity				
Diabetes w/o chronic complications	1.092	1.017	1.171	.0146*
Psychoses	0.617	0.406	0.939	.0242*
Benign neoplasm and in-situ cancer	0.859	0.750	0.983	.0272*
Year of Diagnosis				
2007 vs. 2001	0.815	0.730	0.910	.0003*
2006 vs. 2001	0.903	0.808	1.009	.0724
2005 vs. 2001	0.876	0.783	0.980	.0207*
2004 vs. 2001	0.993	0.887	1.113	.9081
2003 vs. 2001	0.996	0.889	1.117	.9469
2002 vs. 2001	0.964	0.864	1.077	.5197

* significant at 5% level

Table 3

MULTIVARIATE ANALYSIS FOR LATE-STAGE CASES (N = 1,423)

Variables	Hazard Ratio	95% CI		P-Value
African American vs. Caucasian	0.995	0.817	1.211	.9589
Age	1.004	0.995	1.013	.3882
Married vs. unmarried	0.999	0.873	1.142	.9838
Uninsured vs. private insurance	0.953	0.726	1.252	.7315
Public insurance vs. private insurance	1.002	0.879	1.142	.9749
Current smoker vs. non-current smoker	0.918	0.799	1.054	.2244
Ambulatory vs. hospital	0.640	0.203	2.021	.4467
For-profit vs. not-for-profit	1.032	0.889	1.198	.6815
Percentage of African American	0.996	0.993	1.000	.0285*
Comorbidity				
Liver disease	2.096	1.350	3.255	.0010*
Solid tumor w/out metastasis	1.619	1.133	2.315	.0082*
Rheumatoid arthritis/collagen vascular	1.851	1.005	3.409	.0482*
Deficiency Anemias	1.243	1.003	1.541	.0465*
Drug abuse	2.369	1.231	4.557	.0098*
Genitourinary system disease	1.272	1.099	1.472	.0013*
Year of Diagnosis				
2007 vs. 2001	0.710	0.549	0.917	.0087*
2006 vs. 2001	0.752	0.580	0.975	.0313*
2005 vs. 2001	0.637	0.489	0.831	.0009*
2004 vs. 2001	0.702	0.537	0.919	.0100*
2003 vs. 2001	0.961	0.728	1.269	.7815
2002 vs. 2001	0.800	0.617	1.037	.0923

* significant at 5% level