Published in final edited form as:

Med Care. 2014 June ; 52(6): 482–489. doi:10.1097/MLR.000000000000113.

Prostate Cancer Treatment and Survival: Evidence for Men with Prevalent Comorbid Conditions

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Abstract

Background—The absence of evidence-based guidelines for prostate cancer treatment led the Institute of Medicine to include localized prostate cancer treatment among the 25 most important topics for comparative effectiveness research.

Objective—This study compared prostate cancer treatment and survival in men with and without prevalent comorbid conditions.

Research Design—The sample comprised elderly men, aged 66 years and older, extracted from SEER-Medicare data, 2004–2009 (N=73,563). Treatment and survival for men with at least one of four prevalent comorbid conditions were compared to men who did not have any of the 12 Charlson comorbid conditions. The sample was stratified by comorbid condition and low, intermediate, and high risk disease.

Results—Over half of men received some form of cancer-directed treatment, regardless of comorbid condition. Men who have Congestive Heart Failure (CHF) or multiple comorbid conditions were less likely to be treated, whereas men with diabetes were more likely to be treated. With the exception of men with CHF, men with comorbid conditions and low risk disease received no survival benefit from any type of treatment.

Conclusions—Most men received treatment, particularly radiation therapy, regardless of comorbid condition. The evidence suggests more caution should be used when treating men with low risk disease and comorbid conditions as they are at risk for adverse events and additional medical costs, without a survival benefit.

Introduction

The most critical problem facing prostate cancer patients and their physicians is uncertainty about how to manage the disease. The absence of evidence-based guidelines for prostate cancer treatment led the Institute of Medicine to include localized prostate cancer treatment among the 25 most important topics for comparative effectiveness research.¹ The premise of comparative effectiveness research is to “inform health care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options.”² The emphasis on comparative effectiveness in medicine gave rise to patient-centered outcomes research that seeks to tailor care to a patient’s personal characteristics, conditions, and preferences.³ Central to clinical decision making in prostate cancer treatment is whether to screen and to treat men given their life expectancy, presence of comorbid conditions, and potential outcomes.

For the past two decades, a large body of literature has focused on shared decision making in prostate cancer treatment,⁴ overtreatment of men with low risk disease,⁵ and the cost of prostate cancer treatment, contrasted with its tenuous benefits.⁶ At the crux of this research is whether the potential benefits of one type of treatment (e.g., surgery) are greater than the benefits from another type of treatment (e.g., radiation), or if any treatment is better than no treatment since most patients do not die from prostate cancer and instead have other chronic conditions that lead to death. Moreover, it is unclear how other chronic conditions affect the decision to screen or once diagnosed, the selection of treatment options,^{7–9} including the use of newer, expensive forms of radiation treatment versus active surveillance.¹⁰

Prostate cancer treatment may exacerbate comorbid conditions and likewise, some comorbid conditions may worsen prostate cancer treatment outcomes. Androgen deprivation therapy (ADT), for example, has been associated with increased risk of sudden cardiac death in men with coronary artery disease.^{11–14} Men with comorbid conditions have higher all-cause mortality,⁸ but whether mortality is hastened or delayed by prostate cancer treatment is unknown.

Using a population-based sample, we compare prostate cancer treatment in men with and without prevalent comorbid conditions. We examine whether treatment influences all-cause and cancer specific mortality by comparing treated and untreated men with comorbid conditions. The chronic conditions investigated are: diabetes, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), and cerebrovascular disease (CVA). These conditions were selected because of their high prevalence in the population. The study sample comprises men aged 66 years and older. Findings from this study have implications for clinical management of prostate cancer in older men with comorbid conditions and fits within a framework of comparative effectiveness and patient-centered approaches to care.

Methods

Data

We used the linked SEER-Medicare data for 2004 through 2009. The SEER program is funded by the National Cancer Institute and covers approximately 28% of the U.S.

population.¹⁵ Incident cases are available through 2009 with claims through 2010; and survival is reported through December 2011. A total of 172,836 incident prostate cancer cases in men age 66 years and older were in the dataset.

To ensure we identified men that are likely to have favorable survival (and thus have the potential to benefit from treatment) and complete data, we applied the following exclusions to the sample: prior cancer diagnosis (n=6135); unstaged cancer (n=10,006); histology other than adenocarcinoma (n=5043) or metastatic disease (4928); identification through a death certificate or autopsy (n=26); and not enrolled in fee-for-service Medicare Parts A and B (n=15,335) or enrolled in a managed care plan (38,007). Another 970 men were excluded because their month of diagnosis was unknown and therefore, we could not assess their observation period. We excluded patients with Charlson comorbid conditions other than those of interest (n=4889) and 12,950 additional men because they had insufficient information to assign them to a risk category. Following these exclusions, the analytic sample comprised 73,563 men.

Identification of Comorbid Conditions

We used the Deyo et al.¹⁶ and Klabunde et al.¹⁷ adaptation of the Charlson Comorbidity Index,¹⁸ which has been used to explain the probability and extent of cancer treatment.^{17,19} We used all inpatient, outpatient and physician claims for services rendered in the year prior to diagnosis to identify comorbid conditions (see Appendix for codes). The “healthy” group was conservatively defined as those patients who did not have any of the 12 Charlson comorbid conditions.¹⁸

Identification of Treatment Type

Treatment type was identified from the inpatient, outpatient, and physician claim files. Treatments included the following mutually exclusive groups: radical prostatectomy, radiation (including intensity modulated radiation therapy, brachytherapy, conformal and proton therapies), ADT alone or in combination with radiation, and a single category for combinations of ADT with radical prostatectomy or radical prostatectomy with radiation. Other treatments that are not definitive cancer treatment like suprapubic, retropubic, perineal or transurethral resection of the prostate were not considered as cancer treatments (less than 2% of the sample). We excluded patients who received these treatments from the sample in a sensitivity analysis and found that the results were unchanged. All treatments occurring within one year following diagnosis were considered cancer-directed. Codes used to identify treatments are included in the Appendix.

Survival

Survival time was defined as the number of months from the month of diagnosis to the month of death. The survival time for patients who were still alive was censored and calculated from the month of diagnosis to December 31, 2011. All-cause and cancer specific mortality was used in the survival analysis.

Control Variables

Age was grouped into the following categories: 66 to 74 years, 75 to 79 years, 80 years and older. Race was categorized as white, African-American, other, or unknown. The sample includes 1564 Hispanic men (less than 2% of the sample). Once we stratify the sample by risk, treatment and comorbidity, the Hispanic sample is too small to extract meaningful results and therefore we included these men in the “other” race group. Marital status was defined as married, previously married, not married, and unknown. We also included variables for the SEER region in which men resided and the year of diagnosis. In a separate analysis (results not shown), we controlled for census tract education and median household income. The sample was reduced by 368 observations with missing data. The results were unchanged with the addition of these variables and the loss of observations.

We assigned men a risk level using the National Comprehensive Cancer Network (NCCN) guidelines where high risk is defined as T3–T4 or Gleason score 8–10 or PSA>20, or any T, N1; intermediate risk was defined as T2b–T2c or Gleason score 7 or PSA 10–20; and low risk patients were T1–T2a and Gleason score ≤6 and PSA <10.²⁰

Statistical Analysis

We described patients by comorbidity type. Statistically significant differences in categorical variables were determined by the Pearson chi square test and the t-test was used to determine statistically significant differences between continuous variables. The sample was then stratified by risk level. Separate adjusted logistic regression models were used to measure the relationship between the independent variables and receipt of treatment, by treatment type, and an inclusive category designated as ‘any treatment.’ We reported odds ratios (OR) and 95% confidence intervals (CI), and *P* values. *P* values were derived from likelihood ratio tests and are two-sided. Statistical significance was determined as *p*<.05.

We used a competing risks regression model to estimate survival, controlling for whether the patient received cancer directed treatment. Failure was defined as prostate-cancer mortality and the competing event as non-cancer mortality. Estimates are reported as Hazard Ratios (HR) with 95% CI. If treated men were in better health than those who were not treated, the survival analysis would incorrectly favor treatment. Therefore, a propensity score was estimated using the logistic regression model predicting receipt of treatment.²¹ In addition to demographic variables, we used a wide range of variables to estimate the propensity of receiving a treatment. We included variables for the use of canes or wheelchairs and oxygen tanks using claims from the Durable Medical Equipment file. We calculated the number of inpatient admissions, total charges and length of stays for each patient in the year prior to treatment. We also calculated the number of outpatient visits and their total charges for each patient. We created dummy variables for several conditions that were present prior to treatment that might affect the decision to treat. These conditions include coronary arterial disease, chronic renal disease, chronic hepatitis, depression, psychosis, dementia, obesity, loss of special senses; or conditions that might be related to the tumor like bladder neck obstruction, frequent urination, hematuria, prostatitis, and urine infections. We used all these variables in estimating the propensity scores.

We used nearest neighbor, the kernel, and the caliper methods with and without replacement algorithms to match the treated sample to the non-treated patients. We tested the balance of covariates between the two groups using the standardized differences. The best balance was achieved using the caliper (0.1) method without replacement. All covariates had less than 10% bias between the two groups. We used the matched samples in the survival analysis. However, because this method reduced the sample size to 36,302 observations, we compared the results to two other models; the first used the propensity score as a regressor and the second accounted for the treatment choice by including the inverse probability weights in the regression models. Data management, descriptive statistics, and logistic regression models were conducted using SAS, version 9.3.²² Propensity score matching and competing risk regression models were conducted using STATA12.

Results

Descriptive Statistics

Table 1 reports the sample characteristics by each comorbid condition. Nearly half of the men had one or more of the comorbid conditions of interest (46%). The most common comorbid condition was diabetes mellitus (19%) and a substantial share had multiple comorbid conditions (11%). Men with CHF, CVA, and multiple comorbid conditions were older than men without comorbid conditions whereas men with diabetes were younger. There was a higher proportion of African Americans and unmarried men among those with comorbidities relative to those without comorbid conditions.

Over half of all men received cancer-directed treatment, regardless of comorbid condition. Men with diabetes were more likely to receive cancer-directed treatment than men without comorbidities whereas men with CHF or multiple comorbid conditions were least likely to be treated. Among those treated, men were most likely to receive radiation alone or ADT and radiation together.

About a quarter of the men died during the study period and most deaths were from causes other than prostate cancer. The highest rates of death were among men with CHF or those with multiple comorbid conditions. The median time until death was approximately three years for all-cause mortality whereas the median time until a prostate cancer death was a little more than two years from diagnosis. Across all conditions, men were much more likely to die than men without comorbidities.

Treatment

Table 2 reports the odds ratios from adjusted logistic regressions that predict the likelihood of treatment. Men who had CHF or multiple comorbid conditions were less likely to be treated than men without comorbid conditions (OR=0.77; 95% CI 0.69 to 0.86; OR=0.77; 95% CI 0.73 to 0.82, respectively) whereas men with diabetes were more likely to be treated (OR=1.14; 95% CI 1.09 to 1.20). Men with comorbid conditions were less likely to have a radical prostatectomy as men without comorbidities. In contrast, the likelihood of being treated with radiation alone was higher for men with COPD (OR=1.14; 95% CI 1.07 to 1.22), CVA (OR=1.13; 95% CI 1.03 to 1.24), and diabetes (OR=1.13; 95% CI 1.07 to 1.18)

and across all comorbid conditions (including multiple conditions), men were more likely to have ADT and radiation together than men without these conditions.

When the sample was stratified by risk level, the patterns observed for the full sample remained consistent, but in some cases, lose statistical significance, suggesting that few differences in treatment patterns exist between men with and without comorbid conditions within risk group. Alternatively, statistical significance may be reduced due to sample becoming noticeably smaller in some risk and treatment groups. The likelihood of radical prostatectomy remained lower among men with comorbidities and the likelihood of receiving ADT and radiation was higher among men with comorbid conditions relative to men without comorbid conditions (statistically significant ORs range from 1.14 to 1.38).

Mortality

Figure 1 depicts the percent of deaths that are cancer and non-cancer related by comorbid condition and risk level within three years of diagnosis (N=64,989). Men with high risk prostate cancer have higher rates of death from prostate cancer, although prostate cancer deaths comprise a small proportion of total deaths, even among high risk patients. Very few patients with low risk disease die from prostate cancer or other causes. Men with CHF or multiple conditions have the highest death rates whereas men with diabetes or no comorbid conditions have the lowest death rates.

Table 3 reports the hazard ratios of prostate cancer mortality versus other causes for treated men stratified by risk level and comorbid condition. Across the three methods used to handle propensity scores, hazard ratios (HR) were similar. Among men with low risk disease, treatment offered no survival benefit except for CHF patients (HR=0.24; 95% CI: 0.09, 0.64; caliper matching method). A survival benefit is observed for men with intermediate risk disease and COPD (HR=0.70; 95% CI=0.51, 0.95) and multiple comorbid conditions (HR=0.46; 95% CI=0.35, 0.61) using the matched sample. However, statistically significant differences in survival were observed when we used the propensity score as an inverse probability weight or as a regressor. All men with high risk disease, with or without comorbid conditions, experienced a survival benefit from treatment; with ratios ranged from 0.45 for those with no comorbid conditions to 0.69 for CVA patients ($p<.05$). We note that when we stratify by risk level, the samples become smaller, leading to wider confidence intervals, and possible loss of statistical significance. Overall, the results suggest a survival benefit for men with intermediate and high risk disease, regardless of comorbid conditions.

Conclusions

Prostate cancer is the most common form of non-skin cancer in men in the United States. Annually, an estimated 200,000 men will be diagnosed with prostate cancer and approximately 30,000 will die from the disease.²³ The Agency for Healthcare Research and Quality, Department of Health and Human Services, and others have joined the Institute of Medicine's call for comparative effectiveness research of prostate cancer treatments.^{1,23-24} Our study provides evidence about the role of prevalent comorbid conditions in treatment decisions and subsequent survival for a population-based sample of men diagnosed with

prostate cancer. This evidence can be used in comparative effectiveness studies, patient-centered decision making for screening and treatment.

Although nearly half of the sample had at least one of the conditions of interest, the evidence suggests that comorbid conditions do not appear to enter the decision about whether to treat unless the patient is diagnosed with CHF or has multiple comorbid conditions in which case treatment is less likely. Similar findings have been reported in a sample of men aged 75 years and older with low risk disease.³¹ Moreover, men with diabetes are more likely to be treated than men without comorbid conditions. Radiation alone or ADT in addition to radiation are the predominant treatments for men with comorbid conditions. Other research, in addition to our own, established that comorbidities lead to higher mortality in cancer patients.^{8, 25–30} Patients with diabetes, especially those with low risk disease, are just as unlikely to benefit from treatment as men with other comorbid conditions, a fact that may be underappreciated by physicians.

Our analysis of data from a population-based sample finds no survival benefit for men with low risk disease and comorbid conditions with the exception of men with CHF. Taken together, the evidence suggests caution when recommending treatment for men with prostate cancer and comorbid conditions, particularly those with low risk disease. As many as 20% to 30% of older men nationwide have prevalent comorbidities severe enough to influence modification of cancer treatment.³² Consideration to comorbid conditions could also enter into the prostate cancer screening decision so that men with these conditions are not screened and potentially exposed to harm arising from the diagnosis and treatment of low risk disease.

The decision to treat men with comorbidities may be driven by the perception that radiation, with or without androgen deprivation, is safer than radical prostatectomy, and thus may be more appropriate to offer to men who are not surgical candidates. However, the evidence suggests otherwise. Recent publications indicate that comorbid conditions, such as diabetes and coronary artery disease, make it less likely that men will benefit from radiation therapy.^{33,34} As this information becomes disseminated throughout the radiation oncology community, it is hoped that fewer men with these comorbidities will be unnecessarily treated. Men may also benefit from participation in multidisciplinary clinics where active surveillance is recommended more often for low risk patients.³⁵

The study has five limitations. First, detailed clinical information such as biochemical progression or performance status is not included in SEER-Medicare data. Nonetheless, SEER-Medicare data remain the best and largest, population-based data available for assessing treatment and survival for men with prostate cancer and is ideal for comparative effectiveness analyses that consider conditions specific to the patient in general practice settings. Second, SEER-Medicare data are specific men age 65 years and older and the fee-for-service population. Therefore, the findings may not be generalized to younger men or to men who are enrolled in managed care insurance plans. Third, prostate cancer as the cause of death may be under-reported. Newschaffer et al³⁶ reported that men treated initially with surgery or radiation were more likely to have death attributed to other cancers than men treated less aggressively. Older age at diagnosis also correlates inversely with the likelihood

of attributing cause of death to prostate cancer.^{36,37} Fourth, the length of follow-up in this patient population is relatively short. Prostate cancer, even in its high grade form, generally is a disease with a long natural history. Thus, with additional follow-up, it may be shown that certain populations of patients will benefit from treatment. Finally, where we stratify by comorbid condition and risk level, the sample sizes become smaller, which may affect the statistical significance of coefficients.

Comorbid conditions were prevalent in the sample of men with prostate cancer. Overall, men with comorbid conditions, with the exception of CHF or multiple conditions, were as likely or more likely to receive cancer-directed treatment for prostate cancer as men without comorbid conditions. Men with comorbid conditions were more likely to be treated with radiation alone or in combination with ADT. Survival benefits are questionable in most men with low risk disease. In a patient-centered approach to care, men and their treating physicians need a better understanding of treatment outcomes given the presence of comorbid conditions. With this information, harms and benefits associated with treatment can be better weighed, along with the initial decision to screen, in the context of the patient's overall health.

Acknowledgments

Research was supported by NCI grant number P30CA016059, Massey Cancer Center Core Grant, Gordon D. Ginder, M.D., Principal Investigator. The authors wish to thank Umaporn Siangphoe for programming and data analysis support.

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Appendix

Diagnosis and procedure codes used to identify treatment types				
Treatment	ICD-9	CPT	HCPCS	Remarks
Radical prostatectomy	60.5	55810, 55812, 55815, 55840, 55842, 55845, 55866	-	RP only if IP ICD9=60.5 or OP ICD9=60.5
External beam radiation		77413–77417, 77336	-	
Brachytherapy		77326, 77327, 77328	-	
Intensity modulated radiation therapy		77418, 77301 77421, 4165F		
ADT: GnRH agonist		4164F 96402	J1950, J3315, J9155, J9202, J9217, J9218, J9219, J9225, J9226	J codes in carrier file only, 96402 for drug administration Only if within ± 4 months of radiation or surgery ADT and RA or ADT and OP
ADT: Orchiectomy	62.3, 62.4, 62.41, 62.42	54520, 54522		
Radiation			77334, 77014, 77413–77417, 77336, 77427, 76965, 76873, 77328, 77470, 77370, 77778, 55875, 77787, 77263, 77290, 77295, 77326, 77327, 77328, 77750, 77761, 77762, 77763, 77776, 77777, 77778, 77785, 77786, 77787, 77789, 77790, 77300, 77301, 55860, 55862, 55865, 55876, 55920, 76950, 77418, 77421, 4165F, 54521, 54535	

Codes used to identify comorbid conditions

Condition	International Classification of Disease Code, version 9
Congestive heart failure	428, 428.0–428.9
Chronic obstructive pulmonary disease	490–496, 500–505, 506.4
Cerebrovascular disease	430–438, ICD-9 procedure codes 3812, 3842; Healthcare Common Procedure Coding System (HCPCS): 35301, 35001, 35002, 35005, 35501, 35508, 35509, 35515, 35642, 35645, 35691, 3569
Diabetes, no complications	250, 250.0–250.3
Diabetes, with complications	250.4, 250.5, 250.6, 250.7, 250.8, 250.9

Figure 1.
Deaths from prostate cancer and other causes by comorbid condition within 3 years of prostate diagnosis, N=64,989
CHF=Congestive heart failure; COPD=Chronic Obstructive Pulmonary Disease;
CVA=Cerebrovascular Disease; DM=Diabetes mellitus. 8574 patients with less than 3 year follow-up were excluded.

Table 1

Prostate cancer sample characteristics, reported as percentages, by comorbid condition, N=73,563

Characteristic	CHF	COPD	CVA	Diabetes	Multiple Comorbidities	No comorbid condition
N	1,986	6,887	3,288	13,647	8,046	52,659
Age	***	***	***	***	***	
65-74	40.36	58.30	47.00	61.58	48.85	63.47
75-79	24.85	23.59	27.95	23.18	26.14	21.70
80 year and older	34.79	18.11	25.05	15.24	25.01	14.83
Race/ethnicity	***	**		***	***	
White	81.33	82.69	84.55	76.00	75.99	83.95
African American	12.97	10.81	10.07	14.81	16.15	9.88
Other	5.70	6.49	5.38	9.19	7.86	6.17
Marital Status	***	***	***	***	***	
Married	60.79	65.42	67.32	69.10	60.49	70.83
Never married	7.21	7.17	6.40	6.42	7.91	6.70
Previously married	18.42	15.53	12.54	13.13	17.87	12.50
Unknown	13.58	11.88	13.74	11.35	13.74	9.97
Gleason Score	***	*	**	***	***	
2-6	29.45	35.56	35.22	34.29	31.40	37.36
7	40.85	42.52	43.18	43.48	42.63	42.98
8-10	26.67	19.62	19.12	20.01	23.47	17.49
Missing	3.03	2.30	2.47	2.23	2.50	2.17
Prostate Specific Antigen	***	***	***	***	***	
< 10.0	49.39	58.66	59.11	63.52	54.07	63.57
10.0-20.0	20.67	19.41	19.37	17.50	19.22	17.22
> 20	14.42	11.65	10.58	9.09	12.88	10.69
Missing	15.52	10.27	10.94	9.89	13.83	8.51
Tumor stage	***	***	***	***	***	
T1-T2a	13.19	10.86	11.37	10.73	12.93	10.24
T1c	43.05	44.18	44.13	44.88	45.03	41.95
T2_NOS	23.21	24.09	23.60	21.43	22.91	21.55

Characteristic	CHF	COPD	CVA	Diabetes	Multiple Comorbidities	No comorbid condition
T2b-T2c	14.60	15.57	15.85	16.94	14.21	19.09
T3_NOS	1.11	0.58	0.61	0.66	0.77	0.71
T3a	1.86	2.66	2.16	2.84	1.49	3.63
T3b-T4	1.51	1.55	1.67	1.96	1.76	2.45
Missing	1.46	0.51	0.61	0.56	0.91	0.39
NCCN risk level	***	**			***	
Low Risk	17.09	21.30	22.06	21.58	19.35	22.25
Intermediate Risk	45.45	48.44	48.82	49.21	47.09	49.07
High Risk	37.45	30.26	29.12	29.21	33.55	28.68
Treatments						
Any treatment	54.00***	67.32**	65.21***	70.74***	57.89***	68.71
Radical prostatectomy	6.00***	12.52***	10.83***	14.53***	6.56***	18.68
Radiation only	19.03***	25.16***	24.54	25.48***	21.11***	23.56
ADT only	2.30*	1.86	1.96	1.82	1.95	1.68
ADT plus radiation	26.06***	26.80***	27.34***	27.76***	27.91***	23.27
Other combination	0.48***	0.91***	0.47***	1.07***	0.36	1.40
Mortality						
All cause mortality (%)	41.64***	27.84***	24.75***	19.81***	40.23***	15.52
Median years to death	2.55***	3.03	3.06	3.11	2.65	3.34
Cancer mortality (%)	7.03***	5.89***	4.80***	3.80***	6.07***	3.91
Median years to cancer death	1.71	2.20	2.12	2.24	1.67	2.28

Notes: Statistics reported as percentages unless otherwise noted. COPD=Chronic Obstructive Pulmonary Disease; CVA=Cerebrovascular Disease; RP=radical prostatectomy; ADT=Androgen Deprivation Therapy; NOS=Not otherwise specified; NCCN=National Comprehensive Cancer Network; Other combination=ADT with RP or RP with radiation. Statistically significant differences are determined between 'no comorbid conditions' and each comorbidity.

p<0.01,

**

p<0.05.

Table 2

Adjusted likelihood of treatment within 1 year of diagnosis by treatment type, OR (95% CI), N=73,563

	Any treatment	Radical Prostatectomy only	Radiation only	ADT only	ADT + Radiation
N Treated	49639	11675	17435	1297	18308
CHF	0.77 (0.69, 0.86)***	0.40 (0.32, 0.49)***	0.98 (0.86, 1.12)	1.13 (0.81, 1.57)	1.14 (1.02, 1.28)**
COPD	1.03 (0.97, 1.10)	0.68 (0.62, 0.74)***	1.14 (1.07, 1.22)***	1.06 (0.86, 1.30)	1.19 (1.12, 1.27)***
CVA	1.08 (0.99, 1.18)	0.70 (0.61, 0.80)***	1.13 (1.03, 1.24)**	1.06 (0.80, 1.40)	1.25 (1.14, 1.37)***
Diabetes	1.14 (1.09, 1.20)***	0.77 (0.72, 0.81)***	1.13 (1.07, 1.18)***	1.07 (0.92, 1.25)	1.25 (1.20, 1.32)***
Multiple conditions	0.77 (0.73, 0.82)***	0.38 (0.34, 0.42)***	0.99 (0.92, 1.05)	1.03 (0.85, 1.25)	1.23 (1.16, 1.31)***
No comorbid conditions	Referent	Referent	Referent	Referent	Referent
Low	Referent	Referent	Referent	Referent	Referent
Intermediate	1.56 (1.49, 1.63)***	7.37 (6.78, 8.00)***	0.41 (0.39, 0.42)***	0.95 (0.82, 1.15)	1.82 (1.74, 1.92)***
High	1.44 (1.37, 1.51)***	6.43 (5.89, 7.02)***	0.12 (0.18, 0.13)***	1.52 (1.29, 1.78)***	3.23 (3.07, 3.41)***
Low risk (N=28902)					
N Treated	10530	682	7085	236	2519
CHF	0.90 (0.70, 1.17)	0.65 (0.32, 1.33)	0.86 (0.67, 1.10)	0.88 (0.32, 2.40)	1.27 (0.92, 1.74)
COPD	1.09 (0.95, 1.24)	0.79 (0.57, 1.07)	1.17 (1.03, 1.32)**	0.85 (0.51, 1.43)	0.95 (0.80, 1.13)
CVA	1.35 (1.12, 1.63)***	0.66 (0.39, 1.10)	1.25 (1.05, 1.47)**	0.31 (0.10, 0.98)**	1.29 (1.04, 1.61)**
Diabetes	1.21 (1.09, 1.34)***	0.59 (0.46, 0.76)***	1.12 (1.02, 1.22)**	1.1 (0.77, 1.58)	1.25 (1.11, 1.41)***
Multiple conditions	0.87 (0.77, 0.99)**	0.35 (0.22, 0.56)***	0.89 (0.79, 1.01)	1.12 (0.71, 1.76)	1.19 (1.01, 1.39)**
No comorbid conditions	Referent	Referent	Referent	Referent	Referent
Intermediate Risk (N=35877)					
N Treated	25192	7514	8534	524	8405
CHF	0.8 (0.68, 0.95)***	0.37 (0.28, 0.49)***	1.07 (0.90, 1.28)	1.62 (1.00, 2.63)	1.2 (1.01, 1.42)**
COPD	0.97 (0.89, 1.07)	0.68 (0.61, 0.76)***	1.09 (0.99, 1.20)	1.13 (0.82, 1.56)	1.22 (1.11, 1.34)***
CVA	0.9 (0.80, 1.03)	0.69 (0.58, 0.81)***	1.04 (0.91, 1.19)	1.3 (0.87, 1.96)	1.15 (1.01, 1.32)**
Diabetes	1.05 (0.98, 1.13)	0.75 (0.69, 0.81)***	1.1 (1.03, 1.18)***	1.09 (0.85, 1.39)	1.24 (1.16, 1.33)***
Multiple conditions	0.74 (0.68, 0.80)***	0.37 (0.32, 0.42)***	1.05 (0.96, 1.15)	1.1 (0.81, 1.49)	1.24 (1.13, 1.35)***

	Any treatment		Radical Prostatectomy only		Radiation only		ADT only		ADT + Radiation	
	Referent		Referent		Referent		Referent		Referent	
No comorbid conditions										
High Risk (N=21734)										
N Treated	13917		3479		1816		537		7384	
CHF	0.69 (0.58, 0.83) ***		0.40 (0.27, 0.58) ***		0.89 (0.63, 1.25)		0.86 (0.51, 1.43)		1.05 (0.88, 1.26)	
COPD	1.07 (0.95, 1.20)		0.64 (0.54, 0.75) ***		1.26 (1.06, 1.50) ***		1.08 (0.79, 1.48)		1.28 (1.15, 1.42) ***	
CVA	1.23 (1.04, 1.45) **		0.73 (0.57, 0.94) **		1.23 (0.95, 1.58)		1.16 (0.77, 1.77)		1.38 (1.19, 1.61) ***	
Diabetes	1.25 (1.14, 1.37) ***		0.85 (0.76, 0.95) ***		1.22 (1.07, 1.39) ***		1.04 (0.81, 1.33)		1.26 (1.16, 1.37) ***	
Multiple conditions	0.75 (0.68, 0.83) ***		0.42 (0.35, 0.50) ***		0.96 (0.80, 1.14)		0.93 (0.70, 1.24)		1.23 (1.12, 1.36) ***	
No comorbid conditions	Referent		Referent		Referent		Referent		Referent	

Notes: Adjusted logistic regression; OR=Odds ratio; CI=Confidence Interval; CHF=Congestive heart failure; COPD=Chronic Obstructive Pulmonary Disease; CVA=Cerebrovascular Disease; RP=radical prostatectomy; ADT=Androgen Deprivation Therapy. All estimations are adjusted for age (65 to 79, 80+), race/ethnicity (white, African American, other), marital status (married, never married, previously married, unknown), SEER region (California, Connecticut, Detroit, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, Seattle, Utah, Georgia), year of diagnosis (2004–2009). The samples for radical prostatectomy, radiation only, ADT plus radiation do not sum to the sample size reported for 'any treatment' due to the omission of men who received RP with ADT or RP with radiation. There were 34, 461, and 462 men in low, intermediate, and high risk categories, respectively, that received these treatments.

*** p<0.01,

** p<0.05.

Table 3

Competing risks regression analysis, Hazard ratios (95% CI), Propensity scores included as a control variable, N=73,563

Conditions and risk level	N	Censored	Cancer death	Non- Cancer Death	Percent treated	Propensity score inverse probability weight ^a	Propensity as regressor ^b	Matched sample ^c
Low risk								
CHF	282	209	9	64	59.9	0.18 (0.04, 0.90) **	0.11 (0.01, 1.44)	0.24 (0.09, 0.64) ***
COPD	1,223	990	38	195	66.9	0.69 (0.35, 1.33)	0.91 (0.41, 2.04)	1.16 (0.69, 1.93)
CVA	607	507	20	80	68.7	1.41 (0.47, 4.19)	1.75 (0.53, 5.85)	1.99 (0.95, 4.13)
DM	2,492	2,178	44	270	69.7	1.16 (0.57, 2.33)	1.19 (0.54, 2.62)	1.49 (0.86, 2.56)
Multiple conditions	1,292	914	42	336	59.8	0.53 (0.26, 1.07)	0.63 (0.29, 1.35)	0.74 (0.48, 1.15)
No comorbid conditions	10,056	9,133	173	750	65.8	0.56 (0.40, 0.78) ***	0.72 (0.52, 1.00)	0.96 (0.72, 1.29)
Intermediate risk								
CHF	750	463	32	255	59.1	0.58 (0.27, 1.23)	0.61 (0.24, 1.53)	0.68 (0.39, 1.17)
COPD	2,782	2,069	145	568	69.8	0.55 (0.38, 0.79) ***	0.62 (0.42, 0.92) **	0.70 (0.51, 0.95) **
CVA	1,343	1,042	45	256	64.9	0.38 (0.18, 0.79) ***	0.48 (0.23, 0.99) **	0.79 (0.46, 1.37)
DM	5,684	4,680	145	859	72.2	0.54 (0.36, 0.83) ***	0.75 (0.51, 1.09)	0.94 (0.67, 1.33)
Multiple conditions	3,144	1,963	146	1,035	60.8	0.50 (0.35, 0.72) ***	0.50 (0.33, 0.77) ***	0.46 (0.35, 0.61) ***
No comorbid conditions	22,174	19,214	605	2,355	71.8	0.61 (0.51, 0.74) ***	0.73 (0.60, 0.88) ***	0.91 (0.78, 1.06)
High risk								
CHF	618	291	75	252	45.1	0.39 (0.21, 0.70) ***	0.43 (0.23, 0.81) ***	0.64 (0.45, 0.91) **
COPD	1,738	1,085	155	498	63.6	0.50 (0.35, 0.71) ***	0.51 (0.35, 0.75) ***	0.52 (0.40, 0.68) ***
CVA	801	521	67	213	63.2	0.44 (0.25, 0.77) ***	0.46 (0.24, 0.87) **	0.69 (0.49, 0.98) **
DM	3,374	2,404	250	720	69.1	0.40 (0.3, 0.53) ***	0.39 (0.28, 0.53) ***	0.47 (0.38, 0.59) ***
Multiple conditions	2,240	1,113	217	910	52.6	0.58 (0.43, 0.79) ***	0.64 (0.46, 0.90) **	0.61 (0.50, 0.75) ***
No comorbid conditions	12,963	9,830	988	2,145	65.7	0.36 (0.31, 0.42) ***	0.37 (0.32, 0.43) ***	0.45 (0.40, 0.50) ***

Notes: Models estimated using competing risk hazard models; failure defined as prostate-specific mortality and competing risk non-prostate cancer mortality. CHF=Congestive Heart Failure; COPD=Chronic Obstructive Pulmonary Disease; CVA=Cerebrovascular Disease; DM=Diabetes Mellitus with complications; CI=Confidence interval; 95% CI are shown in parentheses. Models predicting survival include all controls as in Table 2.

a controlled for inverse probability weight to account for the likelihood of being treated.

b controlled for propensity score to account for the likelihood of being treated.

c sample size of the matched sample: 36,302 with 50% treated.(or 1:1 matching ratio of treated to not treated). Coefficients for these variables are not reported.

*** <0.01,

** p<0.05.