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## Multilevel Factors Associated With Overall Mortality for Men Diagnosed With Prostate Cancer in Florida

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## Abstract

To identify individual and contextual factors contributing to overall mortality among men diagnosed with prostate cancer in Florida, a random sample of patients (between October 1, 2001, and December 31, 2007) was taken from the Florida Cancer Data System. Patient's demographic and clinical information were obtained from the Florida Cancer Data System. Comorbidity was computed following the Elixhauser Index method. Census-tract-level socioeconomic status and farm house presence were extracted from Census 2000 and linked to patient data. The ratio of urologists and radiation oncologists to prostate cancer cases at the county level was computed. Multilevel logistic regression was conducted to identify significance of individuals and contextual factors in relation to overall mortality. A total of 18,042 patients were identified, among whom 2,363 died. No racial difference was found in our study. Being older at diagnosis, unmarried, current smoker, uninsured, diagnosed at late stage, with undifferentiated, poorly differentiated, or unknown tumor grade were significantly associated with higher odds of overall mortality. Living in a low-income area was significantly associated with higher odds of mortality (p = .0404). After adjusting for age, stage, and tumor grade, patients who received hormonal, combination of radiation with hormone therapy, and no definitive treatment had higher odds of mortality compared with those who underwent surgery only. A large number of comorbidities were associated with higher odds of mortality. Although disease-specific mortality was not examined, our findings suggest the importance of careful considerations of patient sociodemographic characteristics and their coexisting conditions in treatment decision making, which in turn affects mortality.

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**Declaration of Conflicting Interests** 

#### Keywords

prostate cancer; diagnosis; mortality; comorbidity; multilevel

### Introduction

Prostate cancer is the most common solid malignancy (excluding skin cancer) and the second leading cause of cancer-related death for American men. In the United States, an estimated 238,590 new cases of prostate cancer will be diagnosed in 2013, whereas an estimated 29,720 men will die of this disease (American Cancer Society, 2013). The State of Florida ranks second behind California for both incidence (17,330 estimated new cases) and mortality (2,200 estimated deaths) from prostate cancer in 2013 (American Cancer Society, 2013).

Prostate cancer mortality rate in the United States started declining steadily in the early 1990s. This decline is believed to be partly due to early detection and treatment (Howlader et al., 2012; Sarma & Schottenfeld, 2002). In spite of this decline, striking racial/ethnic differences in incidence and mortality still persist in the United States and the State of Florida. Reasons for the persistence of these racial disparities have been difficult to disentangle. Possible explanations include differences in screening leading to differences in the stage and size of tumors at diagnosis, tumor biology (aggressive disease), inadequate receipt of appropriate prostate cancer treatment, and underlying patient comorbidities and socioeconomic factors (Gilligan, Wang, Levin, Kantoff, & Avorn, 2004; Harlan, Brawley, Pommerenke, Wali, & Kramer, 1995; Haynes & Smedley, 1999; Smedley, Stith, & Nelson, 2003).

Stages at diagnosis and tumor characteristics have been consistently associated with mortality (Johansson, Holmberg, Johansson, Bergström, & Adami, 1997; Jonsson et al., 2006; Taksler, Keating, & Cutler, 2012). Black men tend to be diagnosed at an advanced stage and have a poorer clinical outcome than do Whites. It also has been documented that Black men living in the United States develop prostate cancer at an earlier age and have a higher mortality than do White men of similar clinical staging (American Cancer Society, 2013; DeLancey, Thun, Jemal, & Ward, 2008; Moul et al., 1995; Powell, Bock, Ruterbusch, & Sakr, 2010). However, it is unclear whether racial differences in stage at diagnosis are solely due to biologic factors (Hoffman et al., 2001; Jones et al., 2008).

Underutilization of screening services by Blacks and other minority groups may be a factor contributing to advanced stage at diagnosis (Jones et al., 2008; Ward et al., 2009), and subsequently to greater mortality. Indeed, research on screening reported that Black men were less likely to get prostate-specific antigen (PSA) screening than their White counterparts (Carpenter et al., 2010; Etzioni et al., 2008). Despite this argument, there is an ongoing debate over the extent to which PSA screening contributes to the decline in prostate cancer mortality (Andriole et al., 2009; Barry, 2009; Schröder et al., 2009; Schwartz et al., 2009). For instance, after completing an evidence review, the U.S. Preventive Services Task Force decided to recommend against screening for PSA, concluding that there is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits

(Chou et al., 2011). However, due to notable underrepresentation of Blacks in these recent studies, our understanding of racial differences remains unclear.

Patients of lower socioeconomic status (SES) and with limited health insurance coverage are likely to be diagnosed at later stages and/or have worse mortality outcomes (Dall'Era, Hosang, Konety, Cowan, & Carroll, 2009; Major et al., 2012). Men with private health insurance are, in general, diagnosed with prostate cancer at a more favorable stage than do men who are insured through Medicare or Medicaid, or the uninsured, which allows them to have a more favorable mortality prognosis. Lack of facilities or availability of providers also persist in certain geographic areas, mostly in rural settings (Comer & Mueller, 2008; Joynt, Harris, Orav, & Jha, 2011), which may contribute to late-stage diagnosis and increased mortality in prostate cancer. SES differences explain a large portion of the racial disparity in prostate cancer mortality (Berglund et al., 2012; Taksler et al., 2012).

Studies have suggested that Black men are not receiving optimal treatment for prostate cancer and have also been experiencing delays in treatment (Schwartz et al., 2009; Shavers et al., 2004; Spencer, Fung, Wang, Rubenstein, & Litwin, 2004). Early tumor detection may reduce mortality by increasing the chances of successful curative treatments and decreasing the number of treatment-related complications. Prostate cancer treatments are also influenced by many other factors, some of which have a sound scientific basis, whereas others are based on highly personal opinions of physicians, patient preferences, availability of a broad range of treatment options, and on the type of hospital in which medical practice is conducted (Jayadevappa, Chhatre, Johnson, & Malkowicz, 2011; Pollack, Bekelman, Liao, & Armstrong, 2011; Pollack, Weissman, Bekelman, Liao, & Armstrong, 2012).

The existence of one or more comorbidity may have an impact on mortality. For instance, obesity was reported to be associated with an increased risk of cancer mortality (Calle, Rodriguez, Walker-Thurmond, & Thun, 2003; Rodriguez et al., 2007). However, findings of this association are still debatable (Mordukhovich et al., 2011).

To better understand overall mortality among patients diagnosed with prostate cancer, a comprehensive database is essential to capture potential factors at individual and contextual levels and elucidate their role in mortality among prostate cancer patients. To address this question, this study capitalized on a comprehensive database built from several existing data sets. Its objective was to investigate the relationship of multilevel factors with overall mortality among prostate cancer patients. Thus, the results may lead to long-term quantification of the benefits of current strategies for reducing the disproportionate mortality among minorities and the medically underserved in the United States.

#### Method

#### **Population Studied**

A random sample was taken from the data set. This study focused on Black and White men aged 40 or older, diagnosed with invasive prostate cancer in the state of Florida between the dates of October 1, 2001, and December 31, 2007. Other races were excluded from the study due to small population sizes.

#### **Data Sources**

Data for this study were assembled from four different sources. Individual-level prostate cancer incidence data for years 2001 to 2007 were obtained from the Florida Cancer Data System (FCDS) that is managed by the State of Florida Department of Health and operated by the University of Miami. The FCDS is the single largest population- based, cancer incidence registry in the nation.

Prostate cancer cases from FCDS contained information on patient's demographics, type of health insurance at diagnosis, tumor characteristics, the first course of treatment, vital status, and tobacco use history. The patient residential address was geocoded by an independent geocoding firm contracted by the Florida Department of Health. Diagnosis information of all diseases, including prostate cancer, was obtained from the Florida Agency for Health Care and Administration (AHCA). AHCA data consist of two databases, namely, the Hospital Patient Discharge Data and Ambulatory Surgical Data, on all patient encounters within hospitals and freestanding ambulatory surgical and radiation therapy centers in Florida. Comorbidity was computed following the Elixhauser method based on diagnoses information from the AHCA data classified by the International Classification of Diseases, Ninth Revision (ICD-9) codes. ICD-9-CM diagnosis code 185 was used to identify the prostate cancer patient group. Prostate cancer, the outcome disease, was excluded from the comorbidity groups in this study. Elixhauser Index was used because it has been extensively validated and allows more disease states to be considered as comorbid conditions compared with the Charlson Index (Li, Kim, & Doshi, 2010; Mnatzaganian, Ryan, Norman, & Hiller, 2012; Southern, Quan, & Ghali, 2004; Stukenborg, Wagner, & Connors, 2001). The study used a total of 45 comorbidities, which includes 29 from the Elixhauser Comorbidity list and 16 additional comorbidities. None of the comorbidities in the database used for the analysis had frequency lower than 5. Details on the computation of the comorbidity measures are described in a methodology paper (Xiao et al., 2013).

Data from the U.S. Census Bureau (Census 2000), Summary File-3; U.S. Department of Commerce, U.S. Census Bureau, 2002) public files for the State of Florida were used to extract sociodemographic and farm house presence information at the census-tract level. Health providers to case ratios per 1,000 were computed using county-level information obtained from the Florida Department of Health Division of Medical Quality Assurance. Specifically, the number of urologists and radiation oncologists was divided by the number of prostate cancer cases diagnosed within each county during 2001 to 2007. This measure was used to capture provider availability.

Data obtained from the four sources were merged into a single data set by assigning each census-tract or county-level data to the individual cases located within these geographical units. Cases were excluded from the analyses if they could not be linked to census data or provider information.

#### **Statistical Analysis**

Multilevel logistic regression was conducted to assess significance of individual and contextual factors in relation to overall mortality among individuals diagnosed with prostate

cancer. The dependent variable was overall mortality, which is simply referred to as mortality in the subsequent sections of this article. Explanatory variables were available at three levels (individual, census tract, and county). Individual-level characteristics included age, race, marital status, tobacco use history, health insurance, comorbidity, treatment type, tumor stage at diagnosis (early and late-stage), tumor grade, year of diagnosis, and medical facility characteristics. Using the primary payer code each case was allocated to one of the following three health insurance types: public, private, and uninsured. If the patient had more than one health insurance type, the first listed payer was used to derive the insurance type. If the primary payer was Medicare, Medicaid, Department of Defense (tricare), military personnel (military), Veteran Affairs, or Indian/Public health service then health insurance type was defined as public health insurance. Private insurance included managed care, health maintenance organization, preferred provider organization, or fee-for-services. If the patient did not have public insurance or private insurance at the time of diagnosis then this person was categorized as uninsured.

The classification of treatment variables was based on three major types of treatment: surgery, radiation, and hormone therapies. Patients who received surgery were classified into four groups: surgery plus radiation, surgery plus radiation plus hormone, surgery plus hormone therapy, and surgery only. Patients who did not receive surgery were grouped based on whether they received radiation and hormone therapy, radiation and no hormone treatment, hormone treatment only, and no definitive treatment (received neither radiation nor hormone treatment). Details on treatment classification are described in another methodology paper (Xiao et al., 2013). Surveillance Epidemiology and End Results (SEER) summary staging was used to classify prostate cancer stages based on FCDS coding. If the patient was diagnosed with localized prostate cancer, tumor stage was labeled as early-stage, whereas if the patient was diagnosed with regional or distant then tumor stage was labeled as late-stage. At the census-tract level, both median household income (expressed in thousands of dollars) and presence of farm house were included. Last, provider availability was considered at the county level as the ratio of urologists and radiation oncologist to prostate cancer cases.

To account for homogeneity within a county or a census tract and heterogeneity between counties or census tracts, county and census tract random intercepts were added to the logistic model. Therefore, if  $Y_{ijk}$  is the mortality indicator for the *k*th individual in the *j*th census tract from the *i*th county, and  $p_{ijk} = P(Y_{ijk} = 1)$  is the probability that this individual died, the multilevel logistic regression model is written as follows:

$$\ln\left(\frac{p_{ijk}}{1-p_{ijk}}\right) = x_{ijk}^T \beta + u_{ij} + v_i.$$

In the above model,  $x_{ijk}^T$  are the explanatory variables for this person at three levels,  $\beta$  are the regression coefficients,  $v_i$  is the random intercept accounting for homogeneity within each county, and  $u_{ij}$  is the random effect to model homogeneity within each census tract. County and census tract random effects were assumed to be independent. The random

intercepts  $v_i$  and  $u_{ij}$  were assumed to be independent realizations of normal distributions  $N(0, \sigma_v^2)$  and  $N(0, \sigma_u^2)$ , respectively.

Likelihood ratio tests based on Laplace approximation method were used to assess significance of random intercepts. Odds ratios were calculated for explanatory variables. The statistical analyses were conducted using SAS/STAT<sup>®</sup> software, Version 9.3, of the SAS System for Windows.

#### Results

The sample consisted of 18,042 individuals diagnosed with prostate cancer in Florida during October 2001 to December 2007. Their age at diagnosis ranged from 40 to 100 years, with a median of 67 years. The majority of these individuals were White (87.61%), married (78.69%), non–current smoker (83.95%), and had public insurance (59.06%). The majority of these men were diagnosed at early-stage (88.25%) and had a tumor that was well or moderately differentiated (59.26%). In this sample, surgery was the most frequently received treatment (40.91%). Among the patients, 2,363 died (from any cause) during the study period. The study population characteristics are summarized in Table 1.

According to the joint test of random intercepts (p = .0114) individuals were not independent; hence, a logistic regression with independence assumption would not be suitable. The change in -2 log likelihood between model with only census tract random effects and that with both county and census tract random effects was only 0.11, meaning that the county random effects were not necessary if census tract random effects were already in the model. In addition, the estimate and standard error for the county random effects variance also suggest standard error of county variance estimate (0.01176) was relatively large compared with the variance estimate itself (0.003962). Therefore, only census tract random effects were kept in the final model.

The results of multilevel logistic regression are reported in Table 2. The following individual-level factors were significantly associated with higher odds of mortality: older age, unmarried, current smoker, uninsured, diagnosed at late-stage, having poorly or undifferentiated or unknown tumor grade. Cases diagnosed in more recent years had lower odds of mortality compared with those diagnosed in earlier years. Black men were around 18% more likely to die compared with White individuals, although the *p* value for this effect was .15. Compared with patients who received surgery only, those receiving no definitive treatment were about twice more likely to die. People who received hormonal therapy or a combination of radiation and hormone therapy had a higher risk of mortality compared with those who received surgery only. Among census- tract factors, living in a tract with lower median household income was associated with higher odds of mortality. There was not enough evidence to support the association between county-level providers-to-case ratio and mortality among patients who were diagnosed with prostate cancer in Florida.

Several comorbidities were associated with higher odds of mortality. These included congestive heart failure, paralysis, other neurological disorders, chronic pulmonary disease, diabetes, renal failure, liver disease, metastatic cancer, solid tumor without metastasis, fluid

and electrolyte disorders, chronic blood loss anemia, deficiency anemias, alcohol abuse, genitourinary system disease, respiratory disorders, other mental disorders, other anemias, and brain and other neurological disorders. The comorbidities that were not statistically significant according to the multilevel logistic regression are shown in the appendix.

## Discussion

This study examined individual and contextual factors contributing to overall mortality among men diagnosed with prostate cancer in Florida during 2001 to 2007. There was no racial difference found in this study. The higher rate of mortality among Blacks might be explained by the difference of stage, treatment, and insurance. Older patients are reported to be more likely to have advanced stage and thus have a greater risk of mortality than younger patients (Bechis, Carroll, & Cooperberg, 2011). For older men, curative treatment is only indicated for selected patients as comorbidities can play a role in treatment decisions (Heinzer & Steuber, 2009; Scosyrev, Messing, Mohile, Golijanin, & Wu, 2012). The association between marital status and mortality benefit appears to be explained by the fact that married men are thought to have more socioeconomic resources, tend to have less risky behaviors, and benefit from social support, all of which contribute to overall better health practice (Du et al., 2012; Dupre, Beck, & Meadows, 2009). Smoking has been identified as the most preventable cause of prostate cancer morbidity and mortality (Giovannucci et al., 1999; Giovannucci, Liu, Platz, Stampfer, & Willett, 2007; Gong, Agalliu, Lin, Stanford, & Kristal, 2008). Studies on prostate cancer have suggested that patients of lower SES and with limited health insurance coverage may have less access to cancer screening services, subsequently leading to late-stage diagnosis, treatment delay, as well as worse mortality outcomes (Robbins, Whittemore, & Thom, 2000). This may explain the higher odds of mortality among uninsured men.

The recent advances in treatments, screening at earlystage, and receipt of prompt treatment may have contributed to lower the odds of prostate cancer mortality among men who are diagnosed early (Attard & de Bono, 2011; Lu-Yao et al., 2009; Xiao, Tan, & Goovaerts, 2011). Observation period used to be longer in past years, resulting in shorter time to treatment for cases diagnosed in later years. Our finding is consistent with a study that found that men undergoing surgery, specifically radical prostatectomy, had a reduced diseasespecific mortality when compared with men not receiving treatment (Bill-Axelson et al., 2005). To reemphasize, the no definitive treatment category in our study includes active surveillance or treatment deferral for any reason. With regard to deferred treatment, it was suggested to be a reasonable alternative to immediate treatment, allowing for "watchful waiting" in select patients with early and low-risk prostate cancer (Patel et al., 2004). In contrast, active surveillance, a newer and more systematic approach that is usually indicated in men with early and low-risk prostate cancer (Dall'Era et al., 2012; Godtman, Holmberg, Khatami, Stranne, & Hugosson, 2013), allows for an active plan of monitoring disease status and includes predetermined treatment decision points and benchmarks mutually agreed between the patient and provider. Nevertheless, this newer approach also remains controversial, because it is not clear which patients are truly considered to have low-risk prostate cancer and could definitively benefit from this approach. The odds ratio was higher among patients without active treatments than patients with active treatments. We were not

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sure that the patients in our study were really under "active surveillance," or just did not receive any treatment. Further studies are needed to separate patients without any active treatments. Consistent with a published study (Nanda, Chen, Braccioforte, Moran, & D'Amico, 2009), our study demonstrated that a combination of hormonal and radiation therapy for treating prostate cancer was associated with higher odds of mortality in men with moderate to severe comorbidity. These higher odds may be related to older age. Indeed, in our study population the majority of men receiving a combination of hormonal and radiation therapy were 65 years of age and older. Patients receiving combination of radiation and hormonal therapy may have overall poor health condition that does not allow surgical treatment. In a study by Pierorazio and colleagues, most of the men who underwent radical prostatectomy had favorable prostate cancer characteristics and excellent overall health status (Pierorazio, Humphreys, Walsh, Partin, & Han, 2010). Surgical treatment is reserved for patients with localized prostate cancer and who are projected to have a long life expectancy (Aus et al., 2005; Heidenreich et al., 2011; Zincke et al., 1994).

Men who are diagnosed with advanced stage of prostate cancer (Johansson et al., 1997; Jonsson et al., 2006; Taksler et al., 2012) and men with poorly differentiated prostate cancer (Albertsen, Hanley, & Fine, 2005; Schwartz et al., 2009) have a higher odds of mortality. This may be explained by the fact that men with poorly differentiated, undifferentiated, or unknown tumor grades tend to also have a more advanced stage of disease at the time of prostate cancer diagnosis (Enewold et al., 2011; Rapiti et al., 2009).

To disentangle factors associated with overall mortality among patients diagnosed with prostate cancer, area-level information (contextual factors) was included in the model. Patients residing in census tracts with higher median household income had lower odds of mortality. Lower median household income may be associated with limited education and lack of health insurance, which may constitute barriers to health care access (Basler, 2011; Hoffman et al., 2001; Patel et al., 2010).

Of the 45 comorbidities, 19 were significantly associated with higher odds of mortality. This finding is consistent with previous research (Albertsen et al., 2011; Hall, Jani, Ryu, Narayan, & Vijayakumar, 2005) and may have several explanations. First, individuals with comorbidities may not be treated aggressively for prostate cancer based on perceptions about their life expectancy, ability to tolerate therapy, and potential treatment side effects (Bechis et al., 2011; Post, Hansen, Kil, Janssen-Heijnen, & Coebergh, 2002). Second, side effects or complications are likely to cause interruptions in treatment, which may further lead to increased prostate cancer recurrence (Alibhai et al., 2005; D'Ambrosio et al., 2008).

The current study has a number of limitations. First, only cases diagnosed from 2001 through 2007 were analyzed. Thus, the observations made in this analysis may not necessarily reflect the most current trends. Second, mortality obtained from the FCDS database is all-causes mortality instead of prostate cancer–specific mortality. Third, severity data for comorbidities is not available, thus we are not able to suggest how clinicians should consider the presence of these comorbidities in their patients. Fourth, census tract and county-level data on SES were used to compensate for a lack of individual-level information, which would have provided richer information for the analyses. Finally, large

databases like the FCDS are not without limitations. Registry data lack information about events and decisions 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. Current cancer registry data may miss treatments provided by private physician offices. Bias may exist in the collection of information on cancer stage and may affect rates, particularly for unstaged cancers; accuracy of cancer registry data on stage at diagnosis is relatively low compared with other demographic variables. FCDS also fail to include location of treatment and diagnosis in the tumor registry.

Despite these limitations, the study was able to maximize the utility of current information by linking four data sources from different geographical levels and presented a comprehensive picture of patient outcomes. Specifically, patient comorbidity was taken into consideration, which is highly relevant to examining mortality among men diagnosed with prostate cancer.

In conclusion, patient's demographics, tumor characteristics, comorbidity, and treatment received should be considered when studying clinical outcomes among prostate cancer patients. Thus, our findings direct attention to areas in which mortality outcomes differ by sociodemographic characteristics and certain clinical factors. Although certain factors leading to mortality are not adjustable, others such as screening or education imply that strategies can be developed to improve patient final outcomes. These findings have important implications, especially since the reduction of health disparities is recognized as a priority issue by the National Institutes of Health (National Cancer Institute, 2003), whereas Healthy People 2020 calls for the elimination of health disparities among different groups of residents living in the same community (U.S. Department of Health and Human Services, 2011). Future studies are needed to investigate mortality outcome as well as the specific health-system, sociodemographic, and biologic factors that may be responsible for disparities.

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## Appendix

Nonsignificant Comorbidities According to Multilevel Logistic Regression

Variables	Odds Ratio	p Value
Valvular disease	1.242	.2211
Pulmonary circulation disease	2.090	.0984
Peripheral vascular disease	1.349	.1284
Hypothyroidism	0.903	.6635
Peptic ulcer disease excluding bleeding	1.673	.2864

Variables	<b>Odds Ratio</b>	p Value
Acquired immune deficiency syndrome	1.442	.6576
Lymphoma	0.818	.6159
Rheumatoid arthritis/collagen vas	1.818	.1219
Coagulopathy	1.522	.0849
Obesity	0.908	.7188
Weight loss	1.204	.5638
Drug abuse	2.128	.2872
Psychoses	1.665	.1571
Depression	0.893	.6530
Endocrine disorders, nutritional and metabolic, immunity	0.841	.0777
Ischemic heart disease	0.975	.8017
Digestive system disease	0.984	.8757
Injury and poisoning	1.075	.5411
Infection	1.316	.0700
Other circulatory disease	1.034	.8453
Benign neoplasm and in situ cancer	1.046	.7947
Other nervous system and sense organs disorders	0.856	.4123
Skin and subcutaneous tissue disease	1.551	.0702

#### References

Albertsen PC, Hanley JA, Fine J. 20-Year outcomes following conservative management of clinically localized prostate cancer. Journal of the American Medical Association. 2005; 293:2095–2101. [PubMed: 15870412]

0.975

0.997

0.929

.8142

.9954

.3258

- Albertsen PC, Moore DF, Shih W, Lin Y, Li H, Lu-Yao GL. Impact of comorbidity on survival among men with localized prostate cancer. Journal of Clinical Oncology. 2011; 29:1335–1341. [PubMed: 21357791]
- Alibhai SMH, Leach M, Tomlinson G, Krahn MD, Fleshner N, Holowaty E, Naglie G. 30-Day mortality and major complications after radical prostatectomy: Influence of age and comorbidity. Journal of the National Cancer Institute. 2005; 97:1525-1532. [PubMed: 16234566]

American Cancer Society. Cancer facts & figures 2013. Atlanta, GA: Author; 2013.

Andriole GL, Crawford ED, Grubb RL III, Buys SS, Chia D, Church TR, Reding DJ. Mortality results from a randomized prostate-cancer screening trial. New England Journal of Medicine. 2009; 360:1310-1319. [PubMed: 19297565]

Attard G, de Bono JS. Translating scientific advancement into clinical benefit for castration-resistant prostate cancer patients. Clinical Cancer Research. 2011; 17:3867–3875. [PubMed: 21680542]

- Aus G, Abbou C, Bolla M, Heidenreich A, Schmid HP, Van Poppel H, Zattoni F. EAU guidelines on prostate cancer. European Urology. 2005; 48:546–551. [PubMed: 16046052]
- Barry MJ. Screening for prostate cancer-The controversy that refuses to die. New England Journal of Medicine. 2009; 360:1351-1354. [PubMed: 19297564]
- Basler JW. Socioeconomic disparities in prostate cancer mortality. Southern Medical Journal. 2011; 104:560. [PubMed: 21886063]

Congenital anomalies

Musculoskeletal and connective tissue disease

Hypertension (combined uncomplicated and complicated)

- Bechis SK, Carroll PR, Cooperberg MR. Impact of age at diagnosis on prostate cancer treatment and survival. Journal of Clinical Oncology. 2011; 29:235–241. [PubMed: 21135285]
- Berglund A, Garmo H, Robinson D, Tishelman C, Holmberg L, Bratt O, Lambe M. Differences according to socioeconomic status in the management and mortality in men with high risk prostate cancer. European Journal of Cancer. 2012; 48(1):75–84. [PubMed: 21852113]
- Bill-Axelson A, Holmberg L, Ruutu M, Häggman M, Andersson SO, Bratell S, Garmo H. Radical prostatectomy versus watchful waiting in early prostate cancer. New England Journal of Medicine. 2005; 352:1977–1984. [PubMed: 15888698]
- Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of US adults. New England Journal of Medicine. 2003; 348:1625–1638. [PubMed: 12711737]
- Carpenter WR, Howard DL, Taylor YJ, Ross LE, Wobker SE, Godley PA. Racial differences in PSA screening interval and stage at diagnosis. Cancer Causes and Control. 2010; 21:1071–1080. [PubMed: 20333462]
- Chou R, Croswell JM, Dana T, Bougatsos C, Blazina I, Fu R, Maltz A. Screening for prostate cancer: A review of the evidence for the US preventive services task force. Annals of Internal Medicine. 2011; 155:762–224. [PubMed: 21984740]
- Comer J, Mueller K. Access to health care: Urban-Rural comparisons from a Midwestern agricultural state. Journal of Rural Health. 2008; 11:128–136. [PubMed: 10143273]
- Dall'Era MA, Albertsen PC, Bangma C, Carroll PR, Carter HB, Cooperberg MR, Soloway MS. Active surveillance for prostate cancer: A systematic review of the literature. European Urology. 2012; 62:976–983. [PubMed: 22698574]
- Dall'Era MA, Hosang N, Konety B, Cowan JE, Carroll PR. Sociodemographic predictors of prostate cancer risk category at diagnosis: Unique patterns of significant and insignificant disease. Journal of Urology. 2009; 181:1622–1627. [PubMed: 19230923]
- D'Ambrosio DJ, Li T, Horwitz EM, Chen DYT, Pollack A, Buyyounouski MK. Does treatment duration affect outcome after radiotherapy for prostate cancer? International Journal of Radiation Oncology\* Biology\* Physics. 2008; 72:1402–1407.
- DeLancey JOL, Thun MJ, Jemal A, Ward EM. Recent trends in black-white disparities in cancer mortality. Cancer Epidemiology, Biomarkers & Prevention. 2008; 17:2908–2912.
- Du KL, Bae K, Movsas B, Yan Y, Bryan C, Bruner DW. Impact of marital status and race on outcomes of patients enrolled in radiation therapy oncology group prostate cancer trials. Supportive Care in Cancer. 2012; 20:1317–1325. [PubMed: 21720747]
- Dupre ME, Beck AN, Meadows SO. Marital trajectories and mortality among, U.S. adults. American Journal of Epidemiology. 2009; 170:546–555. [PubMed: 19584130]
- Enewold L, Zhou J, McGlynn KA, Devesa SS, Shriver CD, Potter JF, Zhu K. Racial variation in tumor stage at diagnosis among department of defense beneficiaries. Cancer. 2011; 118:1397–1403. [PubMed: 21837685]
- Etzioni R, Tsodikov A, Mariotto A, Szabo A, Falcon S, Wegelin J, Penson DF. Quantifying the ole of PSA screening in the US prostate cancer mortality decline. Cancer Causes and Control. 2008; 19:175–181. [PubMed: 18027095]
- Gilligan T, Wang PS, Levin R, Kantoff PW, Avorn J. Racial differences in screening for prostate cancer in the elderly. Archives of Internal Medicine. 2004; 164:1858–1864. [PubMed: 15451760]
- Giovannucci E, Liu Y, Platz EA, Stampfer MJ, Willett WC. Risk factors for prostate cancer incidence and progression in the health professionals follow-up study. International Journal of Cancer. 2007; 121:1571–1578.
- Giovannucci E, Rimm EB, Ascherio A, Colditz GA, Spiegelman D, Stampfer MJ, Willett WC. Smoking and risk of total and fatal prostate cancer in United States health professionals. Cancer Epidemiology, Biomarkers & Prevention. 1999; 8:277–282.
- Godtman RA, Holmberg E, Khatami A, Stranne J, Hugosson J. Outcome following active surveillance of men with screen-detected prostate cancer: Results from the Goteborg randomised populationbased prostate cancer screening trial. European Urology. 2013; 63(1):101–107. [PubMed: 22980443]

- Gong Z, Agalliu I, Lin DW, Stanford JL, Kristal AR. Cigarette smoking and prostate cancer-specific mortality following diagnosis in middle-aged men. Cancer Causes & Control. 2008; 19(1):25–31. [PubMed: 17906959]
- Hall W, Jani A, Ryu J, Narayan S, Vijayakumar S. The impact of age and comorbidity on survival outcomes and treatment patterns in prostate cancer. Prostate Cancer and Prostatic Diseases. 2005; 8(1):22–30. [PubMed: 15700051]
- Harlan L, Brawley O, Pommerenke F, Wali P, Kramer B. Geographic age racial variation in the treatment of local/regional carcinoma of the prostate. Journal of Clinical Oncology. 1995; 13(1): 93–100. [PubMed: 7799048]
- Haynes, MA.; Smedley, BD. The unequal burden of cancer: An assessment of NIH research and programs for ethnic minorities and the medically underserved. Washington, DC: National Academies Press; 1999.
- Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, Wiegel T. EAU guidelines on prostate cancer. Part 1: Screening, diagnosis, and treatment of clinically localised disease. European Urology. 2011; 59(1):61–71. [PubMed: 21056534]
- Heinzer H, Steuber T. Prostate cancer in the elderly. Urologic Oncology: Seminars and Original Investigations. 2009; 27:668–672. [PubMed: 19879477]
- Hoffman RM, Gilliland FD, Eley JW, Harlan LC, Stephenson RA, Stanford JL, Potosky AL. Racial and ethnic differences in advanced-stage prostate cancer: The prostate cancer outcomes study. Journal of the National Cancer Institute. 2001; 93:388–395. [PubMed: 11238701]
- Howlader, N.; Noone, A.; Krapcho, M.; Neyman, N.; Aminou, R.; Altekruse, S.; Cho, H. SEER Cancer Statistics Review, 1975–2009 (Vintage 2009 populations), National Cancer Institute. Bethesda, MD: National Cancer Institute; 2012.
- Jayadevappa R, Chhatre S, Johnson JC, Malkowicz SB. Association between ethnicity and prostate cancer outcomes across hospital and surgeon volume groups. Health Policy. 2011; 99:97–106. [PubMed: 20708815]
- Johansson JE, Holmberg L, Johansson S, Bergström R, Adami HO. Fifteen-year survival in prostate cancer. Journal of the American Medical Association. 1997; 277:467–471. [PubMed: 9020270]
- Jones BA, Liu WL, Araujo AB, Kasl SV, Silvera SN, Soler-Vilá H, Dubrow R. Explaining the race difference in prostate cancer stage at diagnosis. Cancer Epidemiology, Biomarkers & Prevention. 2008; 17:2825–2834.
- Jonsson E, Sigbjarnarson H, Tomasson J, Benediktsdottir K, Tryggvadottir L, Hrafnkelsson J, Jonasson J. Adenocarcinoma of the prostate in Iceland: A population-based study of stage, Gleason grade, treatment and long-term survival in males diagnosed between 1983 and 1987. Scandinavian Journal of Urology and Nephrology. 2006; 40:265–271. [PubMed: 16916765]
- Joynt KE, Harris Y, Orav EJ, Jha AK. Quality of care and patient outcomes in critical access rural hospitals. Journal of the American Medical Association. 2011; 306:45–52. [PubMed: 21730240]
- Li P, Kim M, Doshi J. Comparison of the performance of the CMS hierarchical condition category (CMSHCC) risk adjuster with the Charlson and Elixhauser comorbidity measures in predicting mortality. BMC Health Services Research. 2010; 10(1):245. [PubMed: 20727154]
- Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, Walker-Corkery E. Outcomes of localized prostate cancer following conservative management. Journal of the American Medical Association. 2009; 302:1202–1209. [PubMed: 19755699]
- Major JM, Norman Oliver M, Doubeni CA, Hollenbeck AR, Graubard BI, Sinha R. Socioeconomic status, healthcare density, and risk of prostate cancer among African American and Caucasian men in a large prospective study. Cancer Causes & Control. 2012; 23:1185–1191. [PubMed: 22674292]
- Mnatzaganian G, Ryan P, Norman PE, Hiller JE. Accuracy of hospital morbidity data and the performance of comorbidity scores as predictors of mortality. Journal of Clinical Epidemiology. 2012; 65(1):107–115. [PubMed: 21803545]
- Mordukhovich I, Reiter PL, Backes DM, Family L, McCullough LE, O'Brien KM, Olshan AF. A review of African American-White differences in risk factors for cancer: Prostate cancer. Cancer Causes & Control. 2011; 22:341–357. [PubMed: 21184263]

- Moul JW, Sesterhenn IA, Connelly RR, Douglas T, Srivastava S, Mostofi FK, McLeod DG. Prostatespecific antigen values at the time of prostate cancer diagnosis in African-American men. Journal of the American Medical Association. 1995; 274:1277–1281. [PubMed: 7563532]
- Nanda A, Chen MH, Braccioforte MH, Moran BJ, D'Amico AV. Hormonal therapy use for prostate cancer and mortality in men with coronary artery disease–induced congestive heart failure or myocardial infarction. Journal of the American Medical Association. 2009; 302:866–873. [PubMed: 19706860]
- National Cancer Institute. The nation's investment in cancer research: A plan and budget proposal for fiscal year 2004. Bethesda, MD: National Institutes of Health; 2003.
- Patel K, Kenerson D, Wang H, Brown B, Pinkerton H, Burress M, Hargreaves M. Factors influencing prostate cancer screening in low-income African Americans in Tennessee. Journal of Health Care for the Poor and Underserved. 2010; 21(1A):114–126. [PubMed: 20173288]
- Patel MI, DeConcini DT, Lopez-Corona E, Ohori M, Wheeler T, Scardino PT. An analysis of men with clinically localized prostate cancer who deferred definitive therapy. Journal of Urology. 2004; 171:1520–1524. [PubMed: 15017211]
- Pierorazio PM, Humphreys E, Walsh PC, Partin AW, Han M. Radical prostatectomy in older men: Survival outcomes in septuagenarians and octogenarians. BJU International. 2010; 106:791–795. [PubMed: 20201836]
- Pollack CE, Bekelman JE, Liao K, Armstrong K. Hospital racial composition and the treatment of localized prostate cancer. 2011; 117:5569–5578. [PubMed: 21692067]
- Pollack CE, Weissman G, Bekelman J, Liao K, Armstrong K. Physician social networks and variation in prostate cancer treatment in three cities. Health Services Research. 2012; 47(1 Pt 2):380–403. [PubMed: 22092259]
- Post P, Hansen B, Kil P, Janssen-Heijnen M, Coebergh J. The independent prognostic value of comorbidity among men aged<75 years with localized prostate cancer: A population-based study. BJU International. 2002; 87:821–826. [PubMed: 11412219]
- Powell IJ, Bock CH, Ruterbusch JJ, Sakr W. Evidence supports a faster growth rate and/or earlier transformation to clinically significant prostate cancer in black than in white American men influences racial progression and mortality disparity. Journal of Urology. 2010; 183:1792–1796. [PubMed: 20299055]
- Rapiti E, Fioretta G, Schaffar R, Neyroud-Caspar I, Verkooijen HM, Schmidlin F, Bouchardy C. Impact of socioeconomic status on prostate cancer diagnosis, treatment, and prognosis. Cancer. 2009; 115:5556–5565. [PubMed: 19787636]
- Robbins AS, Whittemore AS, Thom DH. Differences in socioeconomic status and survival among white and black men with prostate cancer. American Journal of Epidemiology. 2000; 151:409– 416. [PubMed: 10695600]
- Rodriguez C, Freedland SJ, Deka A, Jacobs EJ, McCullough ML, Patel AV, Calle EE. Body mass index, weight change, and risk of prostate cancer in the cancer prevention study II nutrition cohort. Cancer Epidemiology, Biomarkers & Prevention. 2007; 16:63–69.
- Sarma AV, Schottenfeld D. Prostate cancer incidence, mortality, and survival trends in the United States: 1981–2001. Seminars in Urologic Oncology. 2002; 20(1):3–9. [PubMed: 11828352]
- Schröder FH, Hugosson J, Roobol MJ, Tammela TLJ, Ciatto S, Nelen V, Zappa M. Screening and prostate-cancer mortality in a randomized European study. New England Journal of Medicine. 2009; 360:1320–1328. [PubMed: 19297566]
- Schwartz K, Powell IJ, Underwood W, George J, Yee C, Banerjee M. Interplay of race, socioeconomic status, and treatment on survival of patients with prostate cancer. Urology. 2009; 74:1296–1302. [PubMed: 19962532]
- Scosyrev E, Messing EM, Mohile S, Golijanin D, Wu G. Prostate cancer in the elderly. Cancer. 2012; 118:3062–3070. [PubMed: 22006014]
- Shavers VL, Brown M, Klabunde CN, Potosky AL, Davis W, Moul J, Fahey A. Race/ethnicity and the intensity of medical monitoring under "watchful waiting" for prostate cancer. Medical Care. 2004; 42:239–250. [PubMed: 15076823]

- Smedley, BD.; Stith, AY.; Nelson, AR. Unequal treatment: Confronting racial and ethnic disparities in healthcare (Committee on Understanding and Eliminating Racial and Ethnic Disparities in Health Care). Washington DC: Institute of Medicine, National Academies Press; 2003.
- Southern DA, Quan H, Ghali WA. Comparison of the Elixhauser and Charlson/Deyo methods of comorbidity measurement in administrative data. Medical Care. 2004; 42:355–360. [PubMed: 15076812]
- Spencer BA, Fung CH, Wang M, Rubenstein LV, Litwin MS. Geographic variation across Veterans Affairs medical centers in the treatment of early stage prostate cancer. Journal of Urology. 2004; 172:2362–2365. [PubMed: 15538268]
- Stukenborg GJ, Wagner DP, Connors AF Jr. Comparison of the performance of two comorbidity measures, with and without information from prior hospitalizations. Medical Care. 2001; 39:727– 739. [PubMed: 11458137]
- Taksler GB, Keating NL, Cutler DM. Explaining racial differences in prostate cancer mortality. Cancer. 2012; 118:4280–4289. [PubMed: 22246942]
- U.S. Census Bureau. Census 2000 summary file 3 technical documentation. Washington, DC: Author; 2002.
- U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. Healthy people 2020. 2011. Retrieved from http://www.healthypeople.gov/2020/ topicsobjectives2020/overview.aspx?topicid=8
- Ward E, Halpern M, Schrag N, Cokkinides V, DeSantis C, Bandi P, Jemal A. Association of insurance with cancer care utilization and outcomes. CA: A Cancer Journal for Clinicians. 2009; 58(1):9–31. [PubMed: 18096863]
- Xiao H, Tan F, Goovaerts G, Ali AA, Adunlin G, Huang Y, Gwede CK. Construction of comorbidity index for prostate cancer patients linking state cancer registry with inpatient and outpatient data. Submitted for publication to the Journal of Registry Management. 2013
- Xiao H, Tan F, Goovaerts G, Adunlin G, Ali AA, Gwede CK, Huang Y. Use of treatment information from a state central cancer registry in prostate cancer research. Journal of Registry Management. 2013; 40:127–130. [PubMed: 24643215]
- Xiao H, Tan F, Goovaerts P. Racial and geographic disparities in late-stage prostate cancer diagnosis in Florida. Journal of Health Care for the Poor and Underserved. 2011; 22:187–199. [PubMed: 22102314]
- Zincke H, Bergstralh EJ, Blute ML, Myers RP, Barrett DM, Lieber MM, Oesterling JE. Radical prostatectomy for clinically localized prostate cancer: Long-term results of 1,143 patients from a single institution. Journal of Clinical Oncology. 1994; 12:2254–2263. [PubMed: 7964940]

Table 1

Characteristics of the Study Population (N = 18,042).

Variable	u	Mean (SD)	Percentage	Variable	u	Percentage
Age		67.1 (9.2)		Insurance		
Mortality				Privately insured	6,960	39.17
Alive	15,679		86.90	Publicly insured	10,494	59.06
Dead	2,363		13.10	Uninsured	313	1.76
Race				Year of diagnosis		
White	15,448		87.61	2001 <sup>a</sup>	901	4.99
Black	2,184		12.39	2002	3,435	19.04
Marital status				2003	2,493	13.82
Unmarried	3,737		21.31	2004	2,589	14.35
Married	13,799		78.69	2005	2,646	14.67
Smoking				2006	2,847	15.78
Non-current smokers	12,434		83.95	2007	3,131	17.35
Current smokers	2,377		16.05	Treatment combination		
Stage				No definitive treatment	2,393	13.31
Early	14,688		88.25	Surgery	7,353	40.91
Late	1,956		11.75	Radiation	4,210	23.42
Grade				Hormone	806	4.48
Well-moderately differentiated	10,691		59.26	Surgery + radiation	188	1.05
Poorly differentiated	5,444		30.17	Surgery + radiation + hormone	114	0.63
Undifferentiated/unknown	1,907		10.57	Surgery + hormone	497	2.77
				Radiation + hormone	2.412	13.42

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 $^{d}\mathrm{The}$  study used partial data for the year 2001 (October 1, 2001, to December 31, 2001).

#### Table 2

Adjusted Odds Ratios of Major Factors to Overall Mortality Among 11,657 Prostate Cancer Patients, Florida, 2001–2007.

Variables	Odds ratio	p Value
Patient demographics		
Age40	1.083	<.0001**
Black vs. White	1.182	.1489
Married vs. unmarried	0.641	<.0001**
Current smoker vs. non-current smoker	1.651	<.0001**
Publicly insured vs. privately insured	1.081	.4087
Uninsured vs. privately insured	2.188	.0016**
Types of treatment and tumor characteristics		
No definitive treatment vs. surgery only	1.975	<.0001**
Surgery + radiation + no hormone vs. surgery only	0.729	.3739
Surgery + radiation + hormone vs. surgery only	1.166	.6234
Surgery + hormone vs. surgery only	1.402	.0695
Radiation vs. surgery only	1.222	.0533
Hormone vs. surgery only	2.668	<.0001**
Radiation + hormone vs. surgery only	1.395	.0027**
Late-stage vs. early-stage	2.092	<.0001**
Undifferentiated/unknown vs. well or moderately differentiated	1.48	.0022**
Poorly differentiated vs. well or moderately differentiated	1.462	.0001**
Year of diagnosis		
Year 2007 vs. 2001	0.093	<.0001**
Year 2006 vs. 2001	0.189	<.0001**
Year 2005 vs. 2001	0.28	<.0001**
Year 2004 vs. 2001	0.474	<.0001**
Year 2003 vs. 2001	0.487	<.0001**
Year 2002 vs. 2001	0.801	.1019
Type of medical facility		
For-profit vs. non-for-profit	1.046	.5867
Ambulatory vs. hospital	1.008	.9707
Census tract and county-level factors		
Median income 1,000	0.995	.0404*
Farmhouse presence	0.945	.5814
Radiologist/urologist-to-case ratio	0.038	.5758
Comorbidities		
Congestive heart failure	2.431	<.0001**
Paralysis	3.412	.0015**

Variables	Odds ratio	p Value
Other neurological disorders	2.154	.0012**
Chronic pulmonary disease	1.854	<.0001**
Diabetes without chronic complications	1.355	.0043**
Diabetes with chronic complications	2.235	.0132*
Renal failure	1.846	.0012**
Liver disease	2.225	.0201*
Metastatic cancer	2.546	<.0001**
Solid tumor without metastasis	2.583	<.0001**
Fluid and electrolyte disorders	1.517	.0014**
Chronic blood loss anemia	2.276	.0041**
Deficiency anemias	1.782	<.0001**
Alcohol abuse	1.669	.0463*
Genitourinary system disease	1.256	.0045**
Respiratory disorders	1.492	.0048**
Other mental disorders	1.962	.0053**
Other anemias	2.376	.0002**
Brain and other neurological disorders	2.552	.0037**

\*\* Significant at .01 level.

\* Significant at .05 level.