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# PROSTATE CANCER SURVIVAL OF MEN IDENTIFIED AS 'BLACK' BY PLACE OF BIRTH IN THE UNITED STATES:

# SEER ANALYSIS 1988-2007

By

Koo-Whang Chung

Master of Public Health

Epidemiology

_____

Michael Goodman M.D., MPH

Committee Chair

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Bachelor of Science

University of Florida

2006

Thesis Committee Chair: Michael Goodman M.D., MPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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## Abstract

PROSTATE CANCER SURVIVAL OF MEN IDENTIFIED AS 'BLACK' BY PLACE OF BIRTH IN THE UNITED STATES:

SEER ANALYSIS 1988-2007

By Koo-Whang Chung

**Background:** Prostate cancer is one of the most common malignancies in men but disproportionately affects black men compared to their white counterparts, but these disparities are also present across different subpopulations of African ancestry. The disparities associated with prostate cancer are well documented between US whites and blacks however, no population-based studies have been conducted comparing prostate cancer survival in US blacks by place of birth.

**Methods:** Data from the US Surveillance Epidemiology and End Results (SEER) program were used to compare the clinical and demographic characteristics of prostate cancer in 23,152 US born, 834 Caribbean born and 379 African born men diagnosed between 1988 and 2007. Kaplan-Meier curves and multivariate Cox proportional hazard models were used to assess the effect of place of birth on prostate cancer survival.

**Results:** The unadjusted Kaplan-Meier Curves showed that there is a statistically significant increase in survival among Caribbean and African born cases compared to their US born counterparts (log-rank = 75,64, P-value = <0.0001). After controlling for confounders there was a statistically significant increase in survival for cases born in the Caribbean (HR = 0.68, 95% CI = 0.55, 0.84) and in Africa (HR = 0.46, 95% CI = 0.28, 0.75) compared to cases born on the US (reference group).

**Conclusions:** This is the first population-based study that looks at within-race disparities of prostate cancer in the US including cases born in Africa. Our analyses demonstrated that survival among African-Americans is lower than that of blacks born in the Caribbean and Africa and this variation could represent an underlying difference in genetic, cultural, environmental, and dietary factors.

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To my family, thank you for making me the man I am today.

# Table of Contents

# Introduction

In the United States, prostate cancer accounts for an estimated 28% of all newly diagnosed malignancies and is the second leading cause of estimated cancer deaths among men, accounting for 11% of roughly 300,000 cancer deaths in 2010 (1). Although prostate cancer is one of the most common malignancies, if new cases are diagnosed in local or regional stages, the 5-year relative survival is near 100%. Prostate cancer disproportionately affects black men compared to their white counterparts (1-4). The age-adjusted incidence rates for prostate cancer between 2002-2006 for African Americans was 231.9 compared to 146.3 for Whites, 82.3 for Asian Americans and Pacific Islanders, 82.7 for American Indian and Alaska Natives, and 131.1 for Hispanic/Latinos (1). This racial disparity is also present in the prostate cancer mortality rates. The mortality rate for African Americans is twice that of whites and almost five times the rate for Asian Americans and the 5-year relative survival of prostate cancer is also lower in black men compared to their white counterparts (1).

The disparities associated with prostate cancer are well documented between US whites and blacks, but these disparities are also present across different subpopulations of African ancestry. For example, compared to Nigerians, African American men are more than 10 times likely to develop prostate cancer and 3.5 times more likely to die from the malignancy (5). On the other hand, data indicate that prostate cancer incidence and mortality rates are higher among Caribbean men than among African Americans (2, 6).

Based on current literature, the incidence and mortality of prostate cancer among men of African ancestry vary across different population groups; however, a large scale

population- based study on men of African descent within the United States has not been conducted. Such population-based studies are possible through the use of the data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). SEER is a population-based cancer registry that covers approximately 28 percent of the United States population including 26 percent of African Americans, 41 percent of Hispanics, 43 percent of American Indians/Alaska Natives, 54 percent of Asians, and 71 percent of Hawaiian/Pacific Islanders. The SEER registry collects data on patient demographics, tumor site, morphology, stage, treatment and follow-up but more importantly, it is the only comprehensive source of population-based information that includes stage of cancer at the time of diagnosis and patient survival information. In this study we aim to examine the survival rates of men identified as 'black' by place of birth to better understand the relative contribution of differences in survival to the reported disparities in mortality.

# Methods

Using SEER data from 17 registries, we selected all eligible prostate cancer cases based on the following inclusion criteria:

- Prostate cancer was the first malignancy diagnosed
- Date of diagnosis between 1/1/1988 and 12/31/2007
- Age greater than 16
- Black race

The data included the main exposure variable, place of birth, along with age, cancer stage, surgery status, radiation type, marital status, and the year of diagnosis. Place of birth was grouped into three categories: US, Caribbean and Africa. The US category encompassed the entire continental US including Alaska and Hawaii. The Caribbean category included Atlantic/Caribbean areas such as Puerto Rico, Cuba, US Virgin Islands, Haiti, Dominican Republic, Jamaica, Bermuda, and the Bahamas. The Africa category encompassed the entire continental Africa including Madagascar. Age was grouped into 4 categories: less than 60, 60-69, 70-79, and over 80 years old. Prostate cancer stage was dichotomized as local/regional versus distant. Treatment variables included radical prostatectomy (yes versus no) and radiation type, which was categorized as none, external beam radiation (EBR) with or without brachytherapy/isotopes and brachytherapy/isotopes alone. Marital status was categorized into married (including common law), not married (single, separated, divorced, and widowed), and unknown groups. Year of diagnosis was grouped into 4 categories: 1988-1992, 1993-1997, 1998-

2002, and 2003-2007. The main outcome variable was prostate cancer-specific deaths as reported by SEER and survival was measured in months.

The difference in survival among the three different categories for place of birth was initially carried out by constructing Kaplan-Meier curves accompanied by a log-rank test. The multivariate analyses testing the association between place of birth and prostate cancer survival after controlling for the covariates were performed using Cox proportional hazards models (7). The proportional hazard assumption was checked for all variables using log (-log) curves. We did not rely on the goodness-of-fit (GOF) tests because in the presence of a very large sample, such as ours, a GOF p-value may be statistically significant even in the absence of meaningful violation of the proportional hazard assumption (7). The results of the Cox proportional hazard models were expressed as adjusted hazard ratios (HR) and 95% confidence intervals (CI).

Collinearity was assessed using cutoff values of 30 and 0.50 for the conditional indices and variance decomposition proportions, respectively. Interaction was assessed for the main exposure variable and each of the covariates of interest in the model. This study did not meet the requirements for Emory University IRB and therefore was excluded from review. All analyses were performed using SAS v. 9.2 (SAS Institute Inc., Carey, NC) and all tests were evaluated at $\alpha = 0.05$ level for statistical significance.

# Results

A total of 24,365 cases met the inclusion criteria. There were 23,152 cases born in the US, 834 cases born in the Caribbean and 379 cases born in Africa. Table 1 displays the clinical and demographic characteristics of the cases by place of birth. Among cases born in Africa, 49% were younger than 60 years old compared to 25% for those born in the US and 31% those born in the Caribbean. African born cases were also more likely to be married (77%) than their Caribbean (67%) and US (55%) counterparts. For both, US and Caribbean born cases, 60% were staged as localized/regional and 40% as distant disease. By contrast, for men born in Africa the disease stage at diagnosis was more evenly distributed (54% localized/regional and 46% distant). Greater proportion of men born in Africa (39%) received surgery compared to those born in the US (25%) and Caribbean (31%).

As displayed in the unadjusted Kaplan-Meier Curves (Figure 1) there was is a statistically significant increase in survival among Caribbean and African born cases compared to their US born counterparts (log-rank = 75.64, P-value = <0.0001). The graphical approach for assessing the proportional hazards assumptions was met for every covariate and the final model that was chosen was the no-interaction model with all covariates included. Table 2 shows the results of the multivariate Cox proportional hazard model. After controlling for confounders there was a statistically significant increase in survival for cases born in the Caribbean (HR = 0.68, 95% CI = 0.55, 0.84) and in Africa (HR = 0.46, 95% CI = 0.28, 0.75) compared to cases born on the US (reference group). Compared to men diagnosed at 60 years old or younger (reference group), prostate cancer cases that were diagnosed between ages 60-69 had an HR of 1.17 (95%

CI = 1.07, 1.30), those diagnosed between 70-79 years old observed an HR of 1.56 (95% CI = 1.41, 1.72) and those diagnosed at 80 years old or older had an HR of 2.98 (95% CI = 2.66, 3.33) Prostate cancer stage categorized as distant had a significantly elevated HR of 4.66 (95% CI = 4.31, 5.05) compared to localized/regional disease (reference group). External beam radiation, with or without brachytherapy, had an HR of 0.73 (95% CI = 0.68, 0.79) and brachytherapy had an HR of 0.18 (95% CI = 0.12, 0.27) compared to no radiation treatment (reference group). Cases who received a radical prostatectomy had an HR of 0.34 (95% CI = 0.30, 0.38) compared to those who did not undergo cancer-directed surgery (reference group).

# Discussion

Prostate cancer disproportionately affects African-American men compared to any other group of men. African-American men develop disease at an earlier age, present with disease at a more advanced stage, are more likely to be diagnosed with the disease, may be less likely to respond to treatment for cure, and are more likely to die from the disease (8). However, studies that examine the survival rates of blacks by place of birth are limited. Our population-based analyses demonstrated that survival among African-Americans is lower than that among blacks born in the Caribbean and Africa, indicating presence of within-race disparities exist in the US. This trend remained true even after adjustment for several covariates that have been previously identified in the literature as potential risk factors (2, 4, 5).

The literature on survival differences among Black prostate cancer patients of different origins is limited. One study compared prostate cancer survival among US-born African Americans and Caribbean immigrants residing in Brooklyn and found no discernable difference (2). This is in contrast to our study findings because we show that the survival rates for Caribbean born men are better than African-American men (Figure 1). However, the Brooklyn study differed from ours in a number of aspects. The sample size in the Brooklyn study (N = 6,142) was much smaller than in our study (N = 24,374) and the number of covariates that were included in the multivariable proportional hazard analysis was smaller in the Brooklyn study compared to our study. Our study included all the covariates in the Brooklyn study (place of birth, age of diagnosis, and stage), but also adjusted for additional key demographic and clinical covariates including marital status, tumor grade, radiation treatment, and surgery treatment. Also, the median follow-

up times of US-treated patients in the Brooklyn study (42 months) was slightly shorter than our study (46 months). A major advantage to our analysis compared to the Brooklyn study was the use of a national, population-based sample and the inclusion of cases born in Africa, which have not been studied in previous research which increases the external validity and generalizability of our findings.

One of the main limitations of our analyses was loss of power and possible bias due to missing data, particularly missing data for place of birth. Another limitation of our study that applies to all analyses of SEER data is the inconsistent coding of many variables, in particular, disease stage. To address this problem we had to perform extensive re-categorization of the data to incorporate various coding strategies that were utilized over the years. Another important data concern that should be taken into consideration is the effect of facility-related characteristics. The level of skill of the surgeon performing the surgery or the experience of the oncologist prescribing treatment could impact the survival of the patient however this type of information is not available through SEER.

In conclusion, our study demonstrates that prostate cancer survival among US men identified as 'black' differs by place of birth. African-Americans had the worst survival rates followed by Caribbean and African born men. Previous studies have indicated that the incidences of prostate cancer vary among different groups of black men and our study indicated that this difference is also observed in prostate cancer survival (2, 4, 9). This heterogeneity may have underlying differences that may be an important influence in genetic, cultural, environmental, and dietary factors as well as issues

regarding health literacy, access to healthcare and under utilization of healthcare in an already potentially genetically susceptible population (2, 4, 10).

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# Tables and Figures

**Table 1. Distribution of Clinical and Demographic Prostate Cancer Patient Characteristics by Place of Birth**

| Patient Characteristics | All Cases | US Born (23152 cases) | | Born in Caribbean (834 cases) | | Born in the Africa (379 cases) | |
|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % |
| Age (yrs) | | | | | | | |
| <60 | 6148 | 5707 | 25% | 255 | 31% | 186 | 49% |
| 60-69 | 9161 | 8695 | 38% | 346 | 41% | 120 | 32% |
| 70-79 | 6695 | 6431 | 28% | 198 | 24% | 66 | 17% |
| 80+ | 2361 | 2319 | 10% | 35 | 4% | 7 | 2% |
| Marital status | | | | | | | |
| Married | 13647 | 12799 | 55% | 555 | 67% | 293 | 77% |
| Not married | 9504 | 9208 | 40% | 230 | 28% | 66 | 17% |
| Unknown | 1214 | 1145 | 5% | 49 | 6% | 20 | 5% |
| Stage | | | | | | | |
| Localized/Regional | 14690 | 13983 | 60% | 503 | 60% | 204 | 54% |
| Distant | 9675 | 9169 | 40% | 331 | 40% | 175 | 46% |
| Grade | | | | | | | |
| I-II | 14592 | 13849 | 60% | 509 | 61% | 234 | 62% |
| III-IV | 7909 | 7498 | 32% | 284 | 34% | 127 | 34% |
| Unknown | 1864 | 1805 | 8% | 41 | 5% | 18 | 5% |
| Vital Status | | | | | | | |
| Alive | 13837 | 12845 | 76% | 648 | 88% | 344 | 96% |
| Dead | 4214 | 4106 | 24% | 92 | 12% | 16 | 4% |
| Year of Diagnosis | | | | | | | |
| 1988-1992 | 2955 | 2888 | 12% | 63 | 8% | 4 | 1% |
| 1993-1997 | 5068 | 4921 | 21% | 122 | 15% | 25 | 7% |
| 1998-2002 | 8652 | 8177 | 35% | 322 | 39% | 153 | 40% |
| 2003-2007 | 7690 | 7166 | 31% | 327 | 39% | 197 | 52% |
| Radiation | | | | | | | |
| None | 15811 | 15102 | 65% | 471 | 56% | 238 | 63% |
| External beam radiation* | 7347 | 6931 | 30% | 295 | 35% | 121 | 32% |
| Brachytherapy alone | 1207 | 1119 | 5% | 68 | 8% | 20 | 5% |
| Radical prostatectomy | | | | | | | |
| Yes | 6268 | 5871 | 25% | 245 | 31% | 150 | 39% |
| No | 18097 | 16093 | 75% | 542 | 69% | 221 | 61% |

*with or without brachytherapy

**Figure 1. Kaplan-Meier Curves for Prostate Cancer Deaths by Place of Birth**

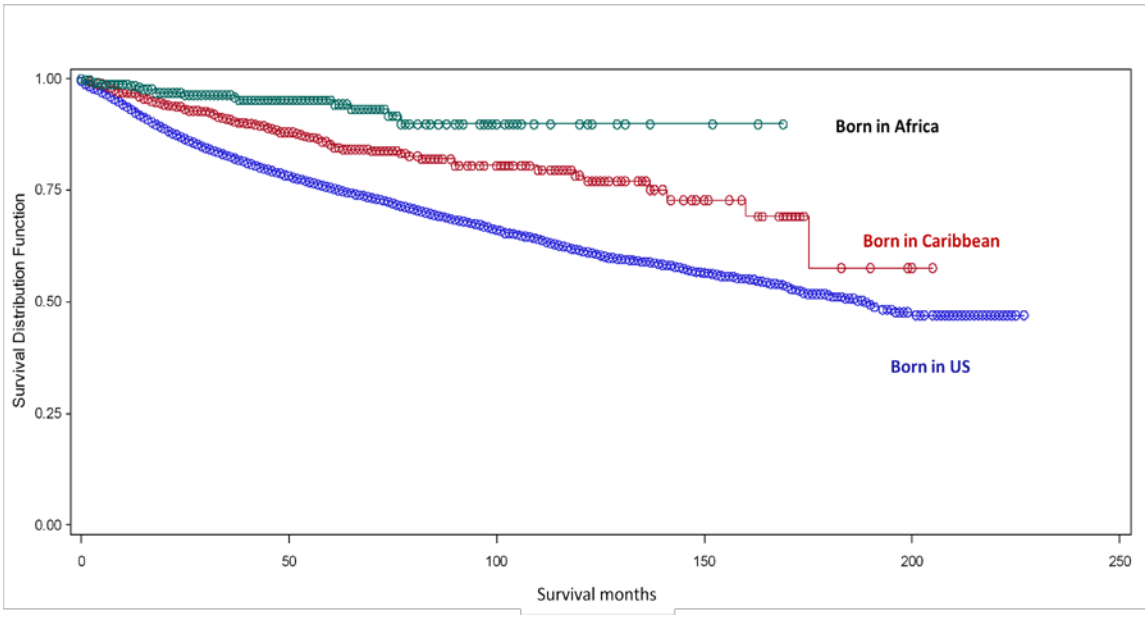

**Table 2. Multivariate Analyses of the Association between Patient Characteristics and Prostate Cancer Mortality**

| Patient Characteristics | | Prostate Cancer Deaths | Hazard Ratio | 95% Confidence Interval |
|---|---|---|---|---|
| Place of birth | | | | |
| | US | 4106 | 1.0 (ref) | |
| | Caribbean | 92 | 0.68 | 0.55, 0.84 |
| | Africa | 16 | 0.46 | 0.28, 0.75 |
| Age (yrs) | | | | |
| | <60 | 792 | 1.0 (ref) | |
| | 60-69 | 1694 | 1.17 | 1.07, 1.30 |
| | 70-79 | 1745 | 1.56 | 1.41, 1.72 |
| | 80+ | 897 | 2.98 | 2.66, 3.33 |
| Marital status | | | | |
| | Married | 2546 | 1.0 (ref) | |
| | Not married | 2220 | 1.30 | 1.22, 1.38 |
| | Unknown | 362 | 1.39 | 1.23, 1.58 |
| Stage | | | | |
| | Localized/Regional | 1684 | 1.0 (ref) | |
| | Distant | 3444 | 4.66 | 4.31, 5.05 |
| Grade | | | | |
| | I-II | 1629 | 1.0 (ref) | |
| | III-IV | 2521 | 2.37 | 2.20, 2.56 |
| | Unknown | 978 | 3.35 | 3.05, 3.68 |
| Year of Diagnosis | | | | |
| | 1988-1992 | 1387 | 1.0 (ref) | |
| | 1993-1997 | 1517 | 0.74 | 0.68, 0.80 |
| | 1998-2002 | 1583 | 0.71 | 0.65, 0.78 |
| | 2003-2007 | 641 | 0.29 | 0.26, 0.33 |
| Radiation | | | | |
| | None | 3798 | 1.0 (ref) | |
| | External beam radiation* | 1302 | 0.73 | 0.68, 0.79 |
| | Brachytherapy alone | 28 | 0.18 | 0.12, 0.27 |
| Radical prostatectomy | | | | |
| | No | 4537 | 1.0 (ref) | |
| | Yes | 444 | 0.34 | 0.30, 0.38 |

* with or without brachytherapy