Original Article

Survival of African American and Non-Hispanic White Men With Prostate Cancer in an Equal-Access Health Care System

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BACKGROUND: African American (AA) men in the general US population are more than twice as likely to die of prostate cancer (PC) compared with non-Hispanic white (NHW) men. The authors hypothesized that receiving care through the Veterans Affairs (VA) health system, an equal-access medical system, would attenuate this disparity. **METHODS:** A longitudinal, centralized database of >20 million veterans was used to assemble a cohort of 60,035 men (18,201 AA men [30.3%] and 41,834 NHW men [69.7%]) who were diagnosed with PC between 2000 and 2015. **RESULTS:** AA men were more likely to live in regions with a lower median income ($40,871 for AA men vs $48,125 for NHW men; $P < .001$) and lower high school graduation rates (83% for AA men vs 88% for NHW men; $P < .001$). At the time of diagnosis, AA men were younger (median age, 63.0 years vs 66.0 years; $P < .001$) and had a higher prostate-specific antigen level (median, 6.7 ng/mL vs 6.2 ng/mL; $P < .001$), but were less likely to have Gleason score 8 to 10 disease (18.8% among AA men vs 19.7% among NHW men; $P < .001$), a clinical T classification ≥3 (2.2% vs 2.9%; $P < .001$), or distant metastatic disease (2.7% vs 3.1%; $P = 0.01$). The 10-year PC-specific mortality rate was slightly lower for AA men (4.4% vs 5.1%; $P = .005$), which was confirmed in multivariable competing-risk analysis (subdistribution hazard ratio, 0.85; 95% CI, 0.78-0.93; $P < .001$). **CONCLUSIONS:** AA men diagnosed with PC in the VA health system do not appear to present with more advanced disease or experience worse outcomes compared with NHW men, in contrast to national trends, suggesting that access to care is an important determinant of racial equity. ***Cancer* 2020;126:1683-1690**. © *2020 American Cancer Society*.

KEYWORDS: disparities, health services research, prostate cancer, race, veterans.

INTRODUCTION

African American (AA) men in the general US population are more than twice as likely to die of prostate cancer (PC) as non-Hispanic white (NHW) men due to both increased incidence and poorer survival after diagnosis.[1,2] Epidemiological evidence has suggested that genetic and/or biologic[3-6] factors may be an important component of the increased incidence and younger age at diagnosis noted among AA men, but there are numerous studies demonstrating differences in patterns of care and socioeconomic factors that may contribute to the remarkable difference in prostate cancer–specific mortality (PCSM) between AA and NHW men.[7-10] It is interesting to note that the racial gap in general cancer mortality in the United States diminishes after age 65 years, most likely due to near-universal coverage from Medicare.[11] Similarly, reports have demonstrated no observable difference in PC outcomes between NHW and AA men with Medicaid coverage.[12,13]

For these reasons, the Veterans Affairs (VA) health care system, an equal-access system for qualifying members that treats a large, diverse, male population of all adult ages, is an important[14] setting in which to evaluate racial disparities in PCSM. The objective of the current study was to elucidate the contemporary differences in prostate cancer survival outcomes between AA and NHW patients using the VA Informatics and Computing Infrastructure (VINCI), thus benefiting from the large percentage of AA men within the VINCI registry and the availability of socioeconomic, comorbidity, and cancer data. We hypothesized that within this equal-access medical system, we would observe similar severity of disease at the time of presentation, with no difference in PCSM noted between AA and NHW patients.

MATERIALS AND METHODS

Data Source

We used data from patients treated in the US VA health care system, accessed through VINCI, a research platform hosting secured analytical tools for the treatment of these data.[15] These include a broad variety of medical and demographic

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data from >20 million veterans across 152 medical centers including registries and drug/prescription and outpatient and inpatient records, among other data. The cancer registry that was used for the current study specifically is one data set within the VA Corporate Data Warehouse, which aggregates data for VINCI. The current study was reviewed and approved by the VA San Diego Healthcare System. Waivers of consent and authorization were granted by the institutional review board and the Research and Development Committee of the VA San Diego Healthcare System (institutional review board protocol number 150169).

Patient Selection

We studied patients with PC who were diagnosed between 2000 and 2015 and had no prior malignancies. Initial query of the VINCI registry identified 75,221 patients. We sequentially eliminated 469 patients with unknown stage of disease, 5361 patients for whom the Gleason score was missing, and 1941 patients who were missing zip code–associated income data. We then limited the cohort to NHW and AA patients, eliminating a total of 1267 patients with missing/unknown race and 4263 patients of other races. We then removed 1423 patients with an unknown rate of prostate-specific antigen (PSA) screening (as defined below). Finally, we eliminated 462 patients who received nonguideline radiation modalities that were concerning for comorbid cancer diagnoses. This resulted in a final cohort of 60,035 patients (see Supporting Fig. 1).

Laboratory and Prescription Data

We aggregated primary laboratory data and selected the most recent PSA value before the date of initial therapy as the pretreatment PSA (after logarithmic transformation owing to non-normal distribution[16]). This approach using laboratory-encoded values (rather than registry records) is important because other studies have questioned the accuracy of registry-encoded PSA values.[17] We defined the 5-year PSA screening rate as a ratio of the number of years in which a patient had ≥1 PSA measured divided by 5 or the number of years that the patient was in the VA system prior to diagnosis of PC, whichever was less.

We aggregated all outpatient and inpatient prescriptions within VINCI, and restricted analyses to drugs of interest, including aspirin, statins, nonsteroidal anti-inflammatory drugs, and 5-alpha-reductase inhibitors. The use of these drugs was defined as any treatment received within the year prior to diagnosis. Androgen deprivation therapy (ADT) was defined as any prescription of a gonadotrophin-releasing hormone receptor agonist/antagonist within the 6 months prior to or after the initiation of therapy.

Variable Definitions

Body mass index (BMI) was calculated using height and weight values from the vital signs obtained most recently prior to the date of PC diagnosis, categorized as <18.5 (underweight), ≥18.5 and <25 (normal weight), ≥25 and <30 (overweight), and ≥30 (obese). The Charlson Comorbidity Index was calculated using the National Cancer Institute adaptation of this index, which uses diagnostic codes to tabulate comorbidities and also eliminates the cancer-related diagnoses from the Charlson Comorbidity Index.[18]

For survival analysis, we used the National Death Index from the Department of Defense to identify the date and cause of death (*International Classification of Diseases, Tenth Revision* [ICD-10] death codes). The National Death Index is linked to VA data through social security numbers. Patients who were alive at the date of last follow-up were censored on that date. Survival was measured from the date of diagnosis.

Statistical Analysis

The current study was a retrospective observational analysis of a cohort derived from a large, multicenter, national health care database. The primary endpoint for this analysis was PCSM as defined by any death from PC within the cohort. It is interesting to note that this is distinct from PC mortality, which references the overall mortality from PC within a population, rather than just those with a confirmed PC diagnosis. We modeled competing events of cancer versus noncancer death using Fine-Gray regression and reported subdistribution hazard ratios (SHRs) with 95% CIs. We selected all variables significant at the 0.05 (see Supporting Table 1) level in the univariate analysis for the multivariate analysis (Table 1). Overall survival analysis was performed using Cox regression, again using a univariate screen for variable selection in the multivariate analysis. Competing event rates were visualized using cumulative incidence function curves; other survival analyses were represented using Kaplan-Meier curves.

To elucidate possible mechanisms of improved PCSM among AA patients, we performed a hierarchical regression analysis[19] in which individual or clustered variables were added sequentially to the model, and at each iteration the AA SHR and *P* value were assessed: 1) T, N, and M classifications and American Joint

TABLE 1. Prostate Cancer–Specific Mortality and OS

Variable	Value	PC-Specific Mortality		OS	
		SHR (95% CI)	P^a	HR (95% CI)	P^a
Race (reference: NHW)	AA	0.85 (0.78-0.93)	**<.001**	0.84 (0.81-0.88)	**<.001**
AJCC stage of disease (reference: I)	II	1.29 (0.97-1.71)	.08	1.39 (1.24-1.55)	**<.001**
	III	1.81 (1.3-2.52)	**<.001**	1.35 (1.16-1.57)	**<.001**
	IV	3.22 (2.3-4.51)	**<.001**	1.8 (1.52-2.14)	**<.001**
Clinical T classification (reference: 1)	2A	1.08 (0.97-1.21)	.179	1.03 (0.98-1.08)	.29
	2B or 2C	1.17 (1.07-1.29)	**<.001**	1.09 (1.04-1.14)	**<.001**
	≥3	1.13 (0.98-1.29)	.085	1.22 (1.11-1.34)	**<.001**
Clinical N classification		1.08 (0.95-1.24)	.239	1.2 (1.07-1.34)	**.001**
Clinical M classification		2.55 (2.13-3.06)	**<.001**	2.19 (1.92-2.49)	**<.001**
Log(PSA)		1.21 (1.18-1.25)	**<.001**	1.11 (1.09-1.13)	**<.001**
Gleason score (reference: ≤6)	7	1.48 (1.31-1.66)	**<.001**	1.14 (1.09-1.2)	**<.001**
	8	2.43 (2.12-2.79)	**<.001**	1.34 (1.26-1.43)	**<.001**
	≥9	4.16 (3.65-4.75)	**<.001**	1.89 (1.78-2.01)	**<.001**
ADT		1.28 (1.18-1.39)	**<.001**	1.14 (1.1-1.19)	**<.001**
Local therapy (reference: none)	Radiotherapy	0.78 (0.71-0.85)	**<.001**	0.72 (0.69-0.74)	**<.001**
	Surgery	0.65 (0.57-0.75)	**<.001**	0.57 (0.54-0.61)	**<.001**
	Combination	0.73 (0.53-1)	.052	0.57 (0.48-0.69)	**<.001**
Age (by year)		1.02 (1.01-1.02)	**<.001**	1.04 (1.04-1.04)	**<.001**
BMI (reference: normal)	Underweight	1.65 (1.45-1.87)	**<.001**	1.69 (1.58-1.81)	**<.001**
	Overweight	0.66 (0.61-0.72)	**<.001**	0.72 (0.69-0.75)	**<.001**
	Obese	0.54 (0.49-0.6)	**<.001**	0.68 (0.65-0.71)	**<.001**
Charlson Comorbidity Index (reference: 0)	1	1.11 (1.01-1.22)	**.029**	1.58 (1.51-1.65)	**<.001**
	≥2	1.14 (1.04-1.26)	**.007**	2.22 (2.13-2.32)	**<.001**
5-alpha-reductase inhibitor		1.11 (1.03-1.2)	**.008**	1.07 (1.03-1.11)	**<.001**
Statin		1.05 (0.97-1.14)	.21	—	—
Aspirin		1.06 (0.98-1.14)	.167	1.19 (1.15-1.24)	**<.001**
NSAID		—	—	1.03 (0.99-1.07)	.129
Tobacco history		1.11 (1.03-1.2)	**.01**	1.27 (1.22-1.32)	**<.001**
Alcohol history		—	—	1.02 (0.98-1.06)	.336
Agent Orange exposure		1.01 (0.88-1.16)	.852	1.07 (1-1.14)	.063
Married		1.07 (0.99-1.15)	.086	0.94 (0.91-0.97)	**<.001**
Employed		0.97 (0.86-1.09)	.565	0.84 (0.79-0.89)	**<.001**
Log(regional income)		—	—	0.92 (0.86-0.98)	**.009**
Regional high school diploma rate		0.66 (0.43-1)	.052	0.75 (0.58-0.97)	**.026**
PSA screening rate		0.92 (0.8-1.05)	.199	0.82 (0.77-0.88)	**<.001**
Year of diagnosis (reference: 2000-2003)	2004-2006	0.84 (0.74-0.96)	**.008**	0.83 (0.78-0.87)	**<.001**
	2007-2009	0.7 (0.62-0.8)	**<.001**	0.63 (0.59-0.66)	**<.001**
	2010-2012	0.58 (0.5-0.66)	**<.001**	0.5 (0.46-0.53)	**<.001**
	2013-2015	0.46 (0.38-0.55)	**<.001**	0.27 (0.24-0.3)	**<.001**
Percentage service connected (reference: not connected)	<50%	0.9 (0.81-0.99)	**.037**	0.9 (0.86-0.95)	**<.001**
	≥50%	0.87 (0.79-0.95)	**.004**	0.8 (0.77-0.84)	**<.001**

Abbreviations: AA, African American; ADT, androgen deprivation therapy; AJCC, American Joint Committee on Cancer; BMI, body mass index; HR, hazard ratio; NHW, non-Hispanic white; NSAID, nonsteroidal anti-inflammatory drug; OS, overall survival; PC, prostate cancer; PSA, prostate-specific antigen; SHR, subdistribution hazard ratio.

Tabled results were determined based on multivariable Fine-Gray regression and Cox proportional hazards regression. Variables included in the model were selected from a univariate screen (see Supporting Table 1). African American patients who were treated for prostate cancer appeared to have superior survival compared with their white counterparts, even when correcting for younger age at the time of diagnosis.

[a]Bold type indicates statistical significance.

Committee on Cancer stage of disease; log-transformed PSA; and Gleason score; 2) ADT and local therapy; 3) age; BMI; Charlson Comorbidity Index; 5-alpha-reductase inhibitor, statin, aspirin, or nonsteroidal anti-inflammatory drug prescription; tobacco or alcohol history; and agent orange exposure; 4) log-transformed regional income, regional high school graduation rate, and service connection; and 5) year of diagnosis and annualized rate of PSA screening were added cumulatively to a Fine-Gray regression.

We used R statistical software (version 3.5.1) for analyses and figure design, using the "tidyverse," "cmprsk," and "survival" packages for data manipulation and figure design,[20] Fine-Gray regression,[21] and Cox proportional hazards analysis,[22], respectively. All *P* values were 2-sided.

RESULTS

The final cohort included 60,035 men, including 18,201 AA men (30.3%) and 41,834 NHW men (69.7%). The median follow-up was 5.79 years for AA

men and 5.89 years for NHW men ($P = .68$). A total of 8967 men were followed for at least 10 years. AA men were more likely than their NHW counterparts to live in zip codes with a lower median income ($45,069 for AA men vs $51,973 for NHW men; $P < .001$) and lower high school graduation rates (83% for AA men vs 87% for NHW men; $P < .001$), had a higher rate of military service–related disability (50%-100% service connection in 41.5% of AA men vs 34.8% of NHW men; $P < .001$), and had a higher burden of medical comorbidities (Charlson Comorbidity Index ≥2 in 14.4% of AA men vs 12.5% of NHW men; $P < .001$). They also were younger (median age, 63 years for AA men vs 66 years for NHW men; $P < .001$) and had a slightly higher median PSA level at diagnosis (6.7 ng/mL in AA men vs 6.2 ng/mL in NHW men; $P < .001$). Among patients with a known date of biopsy and prediagnostic PSA level (48,463 patients), there was no difference noted between the time from elevated PSA (>4 ng/mL or >2 ng/mL in patients treated with 5-alpha-reductase inhibitors[23]) to biopsy between AA and NHW patients (1.43 years and 1.57 years, respectively; $P = .15$ using the Wilcoxon rank sum test). In addition, AA men were slightly less likely to present with Gleason score 8 to 10 disease (18.8% in AA men vs 19.7% in NHW men; $P < .001$), a clinical T classification of ≥3 (2.2% in AA men vs 2.9% in NHW men; $P < .001$), or distant metastatic disease (2.7% in AA men vs 3.1% in NHW men; $P = .01$) (Table 2).

There were 13,257 deaths, including 3067 from prostate cancer (848 AA men and 2219 NHW men). The 10-year cumulative incidence of death from PC was 5.1% for NHW men and 4.4% for AA men ($P = .005$) (Fig. 1). The 10-year cumulative incidence of noncancer death was 17.4% for NHW men and 13.8% for AA men ($P < .001$) (Fig. 1). The overall survival rate at 10 years was 77.5% for NHW men and 81.8% for AA men ($P < .001$) (Fig. 2).

On multivariable analysis, AA men were found to have improved PCSM (SHR, 0.85; 95% CI, 0.78-0.93 [$P < .001$]) (Table 2), with correction for other variables found to be significantly associated with PCSM, including American Joint Committee on Cancer stage of disease, clinical T and M classifications, log-transformed PSA, Gleason score, receipt of either radiotherapy or surgery, treatment with ADT, age at diagnosis, BMI, Charlson Comorbidity Index, 5-alpha-reductase inhibitor use, smoking, year of diagnosis, and service connection. AA patients also had superior overall survival (hazard ratio, 0.84; 95% CI, 0.81-0.88 [$P < .001$]) (Table 1). For those patients undergoing radical prostatectomy with or without postoperative radiotherapy, the cumulative incidence of PCSM was 1.9% and 3.0%, respectively, for AA men and NHW men ($P < .001$). For those undergoing radiotherapy with or without ADT, the cumulative incidence of PCSM was 3.3% and 4.2%, respectively, for AA men and NHW men ($P < .001$). On multivariable analysis, there was no significant interaction noted between race and treatment ($P = .055$), suggesting that these results are not associated with the specific treatment received.

A hierarchical regression analysis found that the PCSM SHR for AA men was unperturbed by the addition of tumor, treatment, age and/or comorbidity, demographic and/or SES, or screening variables (SHRs of 0.83 [95% CI, 0.77-0.90], 0.84 [95% CI, 0.77-0.91], 0.86 [95% CI, 0.79-0.94], 0.85 [95% CI, 0.78-0.93], and 0.85 [95% CI, 0.78-0.92], respectively), and remained statistically significant as well (Table 3). In addition, a separate Fine-Gray regression found that interaction between year of diagnosis and AA race was not significant, and an analysis of age at the time of diagnosis by decade of life similarly did not change the significance or SHR estimate for AA race.

DISCUSSION

In the current large and diverse cohort of men diagnosed with PC in an equal-access medical system, several important measures of racial equity were found between AA and NHW men that are distinct from trends in the United States. First, AA men were not found to be more likely to experience delays in diagnosis and care. Second, AA men were not found to be more likely to present with higher grade or metastatic disease. Finally, AA men with PC were not more likely to die of their disease. In fact, there was a very small, but statistically significant, decrease in the rate of death from PC. These favorable outcomes for AA men were noted despite AA men residing in areas with lower SES. Although there likely remain potential differences in biology that affect the frequency and age of onset of the disease in AA men, the current study findings do not support the hypothesis that PC is inherently more aggressive in AA men. Rather, the results herein have suggested that access to high-quality medical care is a major determinant of racial equity among men diagnosed with PC.

The results of the current study add to a growing body of literature supporting the importance of access to high-quality medical care in reducing or eliminating racial disparities. Studies have shown that the disparities in cancer outcomes in patients with prostate cancer (and other cancers) diminish after US patients become eligible

TABLE 2. Patient Demographics

Variable	Value	NHW	AA	P^a
No. (%)		41,834 (69.7)	18,201 (30.3)	—
AJCC 7 stage of disease	I	5686 (13.6)	2507 (13.8)	**<.001**
	II	31,814 (76.0)	14,062 (77.3)	
	III	2286 (5.5)	852 (4.7)	
	IV	2048 (4.9)	780 (4.3)	
Clinical T classification	1	28,371 (67.8)	13,763 (75.6)	**<.001**
	2A	6129 (14.7)	1929 (10.6)	
	2B	1865 (4.5)	629 (3.5)	
	2C	4255 (10.2)	1478 (8.1)	
	≥3	1214 (2.9)	402 (2.2)	
Clinical N classification	1	629 (1.5)	254 (1.4)	.33
Clinical M classification	1	1310 (3.1)	500 (2.7)	**.012**
Median PSA (IQR), ng/mL		6.15 (4.54-9.50)	6.70 (4.82-11.20)	**<.001**
Gleason score	≤6	17,311 (41.4)	6887 (37.8)	**<.001**
	7	16,298 (39.0)	7889 (43.3)	
	8	4337 (10.4)	1968 (10.8)	
	≥9	3888 (9.3)	1457 (8.0)	
Risk group	Low	13,883 (33.2)	5378 (29.5)	**<.001**
	Intermediate	17,797 (42.5)	8176 (44.9)	
	High	10,154 (24.3)	4647 (25.5)	
Local therapy	None	15,690 (37.5)	6615 (36.3)	**<.001**
	Radiotherapy	15,402 (36.8)	7375 (40.5)	
	Surgery	10,141 (24.2)	3973 (21.8)	
	Combination	601 (1.4)	238 (1.3)	
ADT		10,112 (24.2)	4863 (26.7)	**<.001**
Median age at diagnosis (IQR), y		66.0 (62.0-72.0)	63.0 (58.0-69.0)	**<.001**
BMI	Normal	10,293 (24.6)	4988 (27.4)	**<.001**
	Underweight	1051 (2.5)	674 (3.7)	
	Overweight	15,606 (37.3)	6125 (33.7)	
	Obese	14,884 (35.6)	6414 (35.2)	
Charlson Comorbidity Index	0	29,625 (70.8)	12,798 (70.3)	**<.001**
	1	6969 (16.7)	2783 (15.3)	
	≥2	5240 (12.5)	2620 (14.4)	
5-alpha-reductase inhibitor		14,134 (33.8)	6160 (33.8)	.897
Smoking history		26,998 (64.5)	11,359 (62.4)	**<.001**
Alcohol history		21,089 (50.4)	9456 (52.0)	**.001**
Agent Orange exposure		7241 (17.3)	2711 (14.9)	**<.001**
Married		23,216 (55.5)	7521 (41.3)	**<.001**
Employed		7935 (19.0)	3520 (19.3)	.292
Median regional income (IQR), USD		$48,125 ($39,375-$60,380)	$40,817 ($32,187-$53,652)	**<.001**
Median regional diploma rate (IQR)		0.88 (0.83-0.92)	0.83 (0.78-0.89)	**<.001**
Median PSA screening rate (IQR)		0.80 (0.60-1.00)	0.75 (0.40-1.00)	**<.001**
Y of diagnosis	2000-2003	2492 (6.0)	1006 (5.5)	**<.001**
	2004-2006	8516 (20.4)	3218 (17.7)	
	2007-2009	11,454 (27.4)	4656 (25.6)	
	2010-2012	11,502 (27.5)	5487 (30.1)	
	2013-2015	7870 (18.8)	3834 (21.1)	
Service connection	None	20,445 (48.9)	7703 (42.3)	**<.001**
	<50%	6826 (16.3)	2947 (16.2)	
	≥50%	14,563 (34.8)	7551 (41.5)	

Abbreviations: AA, African American; ADT, androgen deprivation therapy; AJCC 7, American Joint Committee on Cancer seventh edition; BMI, body mass index; IQR, interquartile range.
NHW, non-Hispanic white; PSA, prostate-specific antigen; USD, US dollars.
Continuous variables are shown as the median (IQR) in lieu of count (percentage).
[a]Bold type indicates statistical significance.

for Medicare.[11,13] Furthermore, among patients with PC, there are no apparent disparities by race noted for men with Medicaid insurance.[12] Finally, when AA men receive care as part of randomized controlled trials, they appear to achieve outcomes that are as favorable if not better than those of their NHW counterparts. For example, in the Prostate Cancer Intervention Versus Observation Trial (PIVOT), there was no difference in outcome noted by race and no difference in the benefit of prostatectomy on PCSM between AA and NHW men.[24] A recent meta-analysis of controlled trials reported similar findings within the setting of metastatic PC.[25]

There also are several studies from the US VA health care system or other military medicine settings that have

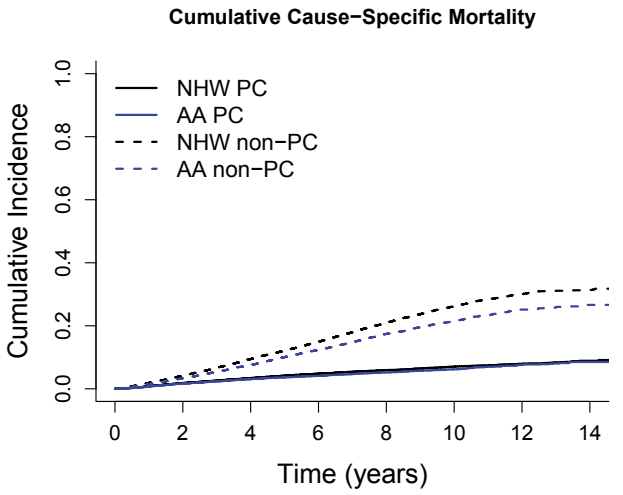

Figure 1. Cumulative incidence of prostate cancer (PC) and non–prostate cancer (non-PC) mortality. Unadjusted cumulative incidence function curves of PC–specific mortality (solid lines) and non-PC death (dashed lines) are shown between African American (AA) and non-Hispanic white (NHW) patients. Although AA patients were found to have statistically significantly improved PC–specific mortality, this effect appeared to be clinically minimal.

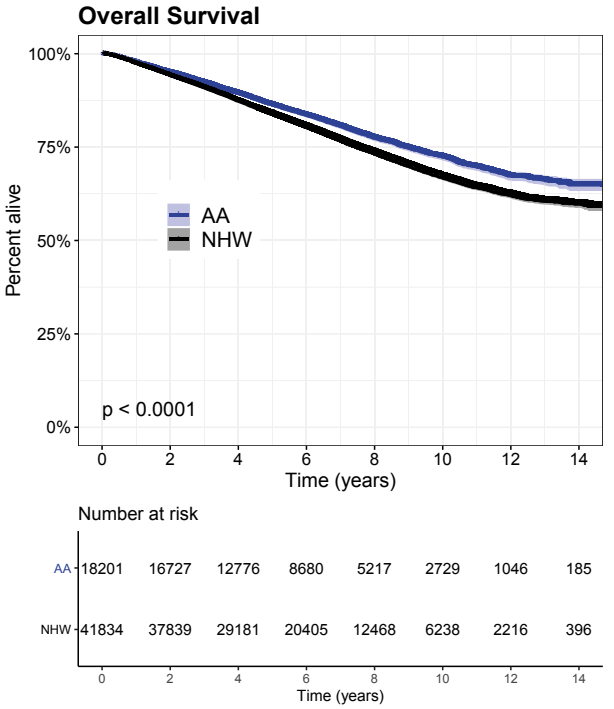

Figure 2. Unadjusted Kaplan-Meier overall survival (OS) curves and 95% CIs are shown between African American (AA) and non-Hispanic white (NHW) patients. AA patients were found to have significantly improved OS compared with their white counterparts. This effect was persistent in adjusted Cox proportional hazards model.

demonstrated reduced or eliminated disparities in men with PC. A study from 1995 found that despite a younger age and higher stage of disease at presentation, AA men had the same distribution of stage-specific treatment modalities as their NHW counterparts, an equivalent time to treatment, and equal PCSM.[26] AA men undergoing radical prostatectomy in studied VA centers have been reported to have very similar pathologic features,[27] recurrence rates, and PCSM[28] compared with their NHW peers. Finally, a multicohort study of NHW and AA men with PC in the Surveillance, Epidemiology, and End Results (SEER) database and 4 clinical trials, as well as a limited sample of men treated with radical prostatectomy in 5 VA hospitals, found that the men treated in the VA had PCSM similar to that of NHW men, unlike the SEER cohort.[29] However, by limiting the analysis to those patients who were treated with radical prostatectomy, this analysis could not study differences in presentation with lymph node–positive or metastatic disease (which would not be treated surgically), which is a major driver of survival disparities. Nonetheless, taken together, these findings suggest that although racial disparities in the incidence of PC within the VA mirror national trends, access to appropriate diagnosis and treatment may attenuate the survival differences.

The current study has several important strengths. First, the VA is a nationwide, equal-access health system

TABLE 3. Hierarchical Regression Analysis

Model	Variables	AA SHR (95% CI)	P^a
Model 1	AA race	0.89 (0.83-0.97)	**.005**
Model 2	Model 1 variables plus tumor characteristics	0.83 (0.77-0.9)	**<.001**
Model 3	Model 2 variables plus cancer treatment	0.84 (0.77-0.91)	**<.001**
Model 4	Model 2 variables plus age/comorbidity	0.86 (0.79-0.94)	**<.001**
Model 5	Model 2 variables plus demographic/SES	0.85 (0.78-0.93)	**<.001**
Model 6	Model 2 variables plus screening	0.85 (0.78-0.92)	**<.001**

Abbreviations: AA, African American; SES, socioeconomic status; SHR, subdistribution hazard ratio.

Table depicts the effect of adding variable clusters on the AA SHR of prostate cancer–specific mortality. Specifically: 1) T classification, log(prostate-specific antigen), and Gleason score; 2) androgen deprivation therapy and local therapy; 3) age; body mass index; Charlson Comorbidity Index; 5-alpha-reductase inhibitor, statin, aspirin, or nonsteroidal anti-inflammatory drug prescription; tobacco or alcohol history; and agent Orange exposure; 4) log-transformed regional income, regional high school graduation rate, and service connection; and 5) annualized rate of prostate-specific antigen screening and year of diagnosis were added cumulatively in order to a Fine-Gray regression. These data suggest that the AA survival advantage is relatively independent of all of these variables because the SHRs were unperturbed at each iteration of correction.

[a]Bold type indicates statistical significance.

allowing for a large cohort with a high percentage of AA men (30%) and relatively long follow-up. By building a cohort that included all patients regardless of their treatment modality (or observation), we were able to: 1) study PCSM across all stages of disease; and 2) evaluate the performance of the VA system nationwide and not just in centers participating in research consortiums. In addition, the central electronic medical record provides a robust and detailed repository of important variables such as PSA, screening rate, disease stage, income level, and educational attainment.

The current study also has important limitations. First, because this was a retrospective, observational study, we were unable to draw firm conclusions regarding causation. In addition, because the cohort included only men diagnosed with PC, we did not evaluate differences in PC incidence between AA and NHW men. Thus, the overall PC mortality across the VA remains an area for future investigation. Similarly, the cohort selection could not account for differences in rates among AA versus NHW men using non-VA health care (which is likely an option for many of these men who are Medicare eligible or who are eligible for employment-based coverage). Because the VA treats a predominantly male, racially diverse population, providers may be using PC screening protocols focused on AA patients,[30] based on the data demonstrating a younger age at diagnosis and higher incidence in these men. This could bias the final cohort of patients with PC in the VA. The exclusion of patients due to missing data also is a potential source of bias (although these data did not appear to be missing in a systematic pattern with relation to race) (see Supporting Fig. 1). Separately, the improved overall survival (after correction for age) in AA men compared with NHW men may suggest that some degree of unmeasured comorbidity or self-care may contribute to the observed PC outcomes between AA and NHW men. However, AA men were overrepresented in the cohort relative to their population in the VA in the years studied,[31] and this was approximately proportionate (1.8-fold) to national differences in PC incidence between AA and NHW men. This, in addition to the above findings, suggests that the improved PCSM observed in AA men may represent a true reduction in PC mortality disparities between AA and NHW patients in the VA, rather than a consequence of overdiagnosis due to differences in the rate of PSA screening use. Finally, we did not study intermediate clinical endpoints such as PSA recurrence-free survival or metastasis-free survival, in part because the validity of such outcomes has been called into question in various database studies.[32] However, due to the high observed event rate and the large size of the current study cohort, we were able to detect statistically significant differences in PCSM, despite having a median follow-up of <6 years.

Overall, the results of the current study found that AA men in the VA do not present with more advanced disease, nor do they demonstrate delays in diagnosis or care, compared with the general population. Given that in the general US population AA men aged <65 years are reported to demonstrate delays in diagnosis compared with NHW men, a disparity that seems to disappear after the age of Medicare eligibility,[13] and that there is no observable difference in PC outcomes between NHW and AA men aged <65 years who have Medicaid coverage,[12] it is plausible that equal-access health care coverage plays an important role in outcomes for these patients. To our knowledge, it is unclear whether the improved PCSM among AA men noted in the current study cohort is due to access to care[33] (ie, testing and other active interventions to minimize disparities[14]) or more aggressive PC screening,[34] treatment, and follow-up, or if other unmeasured self-care factors are driving this phenomenon. In addition, veterans often benefit from social support programs from the VA itself, as well as other governmental and nonprofit organizations, which also may have contributed to the findings observed herein. In the coming years, studies should continue to track longitudinal patterns in PCSM to identify systems-level changes to address racial disparities, especially as VA care begins to involve more private sector alternatives with programs such as the Veterans Choice Program,[30] as the long-term effects of Medicaid expansion on PC outcomes begin to manifest,[12] and as PC screening guidelines continue to evolve.[35]

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CONFLICT OF INTEREST DISCLOSURES

Paul Riviere has acted as a paid consultant with a previous salary from Peptide Logic LLC for work performed outside of the current study. Abhishek Kumar has received consulting fees from and has an ownership stake in Sympto Health for work performed outside of the current study. Reith R. Sarkar has received consulting fees from Boston Consulting Group for work performed outside of the current study. Alex K. Bryant has received consulting fees from Boston Consulting Group for work performed outside of the current study. James D. Murphy has acted as a paid consultant for Boston Consulting Group and has an ownership stake in Sympto Health for work performed outside of the current study. The other authors made no disclosures.

AUTHOR CONTRIBUTIONS

Data collection and processing: **Paul Riviere**, **Abhishek Kumar**, **Lucas K. Vitzthum**, **Reith R. Sarkar**, and **Alex K. Bryant**. Data analysis and figure design: **Paul Riviere** and **Abhishek Kumar**. Conception and study design: **Paul Riviere**, **Abhishek Kumar**, **Andrew Bruggeman**, **John P. Einck**, **James D. Murphy**, **María Elena Martínez**, and **Brent S. Rose**. Article draft writing: **Paul Riviere**, **Elaine Luterstein**, **Abhishek Kumar**, **James D. Murphy**, **María Elena Martínez**, and **Brent S. Rose**. Article editing and final approval: **All authors**.

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