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## Racial Variation in Patient-Reported Outcomes Following Treatment for Localized Prostate Cancer: Results from the CEASAR Study

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## Abstract

**Background**—Relatively little is known about the relationship between race/ethnicity and patient-reported outcomes after contemporary treatments for localized prostate cancer.

**Objective**—To test the hypothesis that treatment-related changes in urinary, bowel, sexual, and hormonal function vary by race/ethnicity.

**Design, setting, and participants**—The Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study is a prospective, population-based, observational study that enrolled 3708 men diagnosed with localized prostate cancer in 2011–2012.

**Outcome measurements and statistical analysis**—Patient-reported disease-specific function was measured using the 26-item Expanded Prostate Index Composite (EPIC) at baseline and 6 and 12 mo after enrollment. Mean treatment differences in function were compared by race using risk-adjusted generalized estimating equations.

**Results and limitations**—While all race/ethnic groups reported considerable declines in scores for urinary incontinence after radical prostatectomy (RP) when compared to active surveillance, African-American men reported a greater difference than white men did (adjusted difference-in-differences 8.4 points, 95% confidence interval 2.0–14.8;  $p = 0.01$ ). No difference in bother scores was noted and the overall proportion of explained variation attributable to race/ethnicity was relatively small in comparison to primary treatment and baseline function. No clinically significant racial variation was noted for the sexual, bowel, irritative voiding, or hormone domains. Limitations include the lack of well-established thresholds for clinical significance using the EPIC instrument.

**Conclusion**—While these data demonstrate that incontinence at 1 yr after RP may be worse for African-American compared to white men, the difference appears to be modest overall. Treatment selection and baseline function explain a much greater proportion of the variation in function after treatment.

**Patient summary**—We observed that the effect of treatment for prostate cancer on patient-reported function did not vary dramatically by race/ethnicity. Compared to white men, African-American men experienced a somewhat more pronounced decline in urinary continence after radical prostatectomy, but the corresponding changes in bother scores were not significantly different between the two groups.

## Keywords

Prostate cancer; Active surveillance; Surgery; Radiation; Comparative effectiveness; Patient-reported function

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## 1. Introduction

Health outcomes for individual men with prostate cancer vary widely and may be influenced by a variety of factors such as race/ethnicity. It is well established, for example, that African-American (AA) patients with prostate cancer exhibit more advanced disease at younger ages and are more likely to die of their disease compared to white men [1,2]. While racial variation in oncologic outcomes after prostate cancer treatment is well studied [3–6], data on how patient-reported changes in urinary, sexual, and bowel function vary after treatment remain sparse [7].

Data from the Prostate Cancer Outcomes Study (PCOS) have previously demonstrated that AA men reported better urinary outcomes compared to white man after radical prostatectomy [8]. However, prostate cancer treatment modalities have undergone substantial technological advances since the inception of PCOS in 1994. Furthermore, the PCOS study did not include patients who underwent active surveillance (AS), which limited the ability to estimate the effects of treatment and, by extension, to formally test the race-treatment interaction. Thus, a contemporary understanding of how race/ethnicity influences the effects of modern management strategies, including AS, on functional outcomes is needed.

In this context, we tested the hypothesis that post-treatment functional outcomes at 12 mo vary across racial/ethnic groups in a contemporary, prospective, population-based prostate cancer inception cohort. On the basis of the previous PCOS study, we hypothesized that AA men would report better functional outcomes at 1 yr after treatment. Characterizing the impact of race/ethnicity on treatment-related functional outcomes is actionable for all racial/ethnic communities, allowing patients, providers, and other stakeholders to make data-driven treatment decisions.

## 2. Patients and methods

### 2.1. Study population

The Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study is a prospective, longitudinal, population-based observational cohort designed to measure the effectiveness and harms of contemporary management strategies for men diagnosed with localized prostate cancer (NCT0136286). Patients were accrued from five Surveillance Epidemiology, and End Results (SEER) registry catchment areas (Louisiana, New Jersey, Utah, Atlanta, and Los Angeles). This data set is augmented with a sample of men enrolled in Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) [9]. A total of 3708 participants were enrolled in CEASAR between 2011 and 2012 (Supplementary Fig. 1). Eligible men were aged  $\geq$  80 yr with clinical stage cT1 or cT2 disease, prostate-specific antigen (PSA)  $<$ 50 ng/dl, and diagnosis within 6 mo of enrollment. Race/ethnicity was classified as non-Hispanic white (white), non-Hispanic AA (AA), and Hispanic, according

to patient-reported data or SEER registry data if patient-reported data were missing (Supplementary Fig. 1). All other races/ethnicities were excluded owing to low sample sizes. The CEASAR methodology, which includes power and sample size calculations, has previously been described [10]. The coordinating site at Vanderbilt, each of the SEER sites, and CaPSURE obtained approval from the relevant local institutional review board.

## 2.2. Survey instruments and medical chart abstraction

Patient-reported disease-specific function was captured using the 26-item Expanded Prostate Index Composite (EPIC) questionnaire. EPIC is a validated survey instrument that evaluates function and bother for urinary, sexual, bowel, and hormone domains as continuous measures on a scale of 0–100, with higher scores indicating better function [11]. To assist in the determination of clinically relevant changes in EPIC domain scores, we used previously published and validated domain score thresholds (Supplementary Table 1) [12]. Participants were also asked to complete the Total Illness Burden Index for Prostate Cancer (TIBI-CaP), a validated patient-reported 84-item comorbidity assessment of 11 health domains modified for patients with prostate cancer [13,14]. CEASAR also captured patient-reported race, income, age, educational attainment, marital status, employment/retirement status, insurance coverage, general health and function, physical function, social support, emotional health, cancer-related anxiety, and depression using the Center for Epidemiologic Studies Depression Scale (CES-D).

Tumor characteristics, treatment selection, PSA levels, and treatment date were obtained via medical record abstraction. For patients without chart information, questionnaires and SEER registry data were used to determine the treatment received. AS was defined as a lack of any curative intent treatment (RP, radiation therapy, and cryoablation) or androgen deprivation therapy at the time of the 1-yr functional status assessment. Patients who underwent both RP and external-beam radiation therapy (EBRT) were categorized on the basis of primary treatment. Patients who received primary androgen deprivation therapy or cryoablation were excluded.

## 2.3. Statistical analysis

Patient baseline demographic and clinical characteristics were compared across racial/ethnic groups using Kruskal-Wallis and  $\chi^2$  tests. To characterize typical changes in patient-reported function over time within each treatment group among each racial/ethnic group, we fitted a longitudinal regression model for each EPIC domain score, which included time since treatment, treatment type, race/ethnicity, and all their interactions as independent variables. In these unadjusted models, responses included all of each patient's scores over time within a particular domain, including the baseline score. Time since beginning treatment (time since baseline survey for AS patients) was modeled as a continuous variable. The relationship between time and mean function was modeled as a restricted cubic spline, permitting nonlinearity. We used generalized estimating equations (GEEs) with an independence working covariance matrix to calculate standard errors for the regression coefficients.

## 2.4. Adjusted comparisons

To identify racial/ethnic differences in the effect of treatment on functional outcomes at 1 yr after treatment, we fitted a second set of longitudinal models with interactions between race/ethnicity and treatment type and between time since treatment and race, adjusting for the following baseline factors: time since beginning treatment, pretreatment function, patient age, comorbidity tumor characteristics (PSA corrected for 5- $\alpha$  reductase inhibitor use, Gleason score [6, 3 + 4, 4 + 3, or 8], and T stage [T1 or T2]), psychosocial measures (educational attainment, insurance type, employment type, marital status, Short-Form 36 physical function score, social support, CES-D score, and participatory decision-making index), receipt of hormone therapy, and study site. Adjusted models were fitted using the same approach as for the unadjusted models (GEE), but here the baseline score was used as a covariate rather than one of the responses. Treatment effects are characterized by differences in function score at 1 yr after treatment between treatment groups, and racial differences in treatment effects were characterized by the difference between races in these treatment effects. Thus, our estimate of interest is a difference in differences (DID) accompanied by a 95% confidence interval (CI). In a sensitivity analysis, we used propensity score regression adjustment as an alternative means of accounting for systematic pretreatment differences between patients receiving different treatments. We used a multinomial logistic regression model to estimate the log odds of receiving each of the three treatments. The fitted values from this model were then included in a second version of our main analysis model.

Some regression coefficients had missing values; the most often missing contained 5% missing. These values were first imputed using multiple imputation via predictive mean matching to avoid casewise deletion of patient records missing any model covariates [15]. Fifteen cycles of updating imputations were performed to create one final data set used to fit the analysis models. Because AA men were more likely to undergo open RP than robotic RP (and similarly were less likely to receive a nerve-sparing operation and intensity-modulated radiation therapy [IMRT]), we performed a second sensitivity analysis to assess the impact of treatment technique on the results by excluding men who did not have a robotic nerve-sparing operation and those who did not receive IMRT. All analyses were conducted using R version 3.2.2 [16].

## 3. Results

Among the 2338 CEASAR participants in the analytic cohort, 1835 (79%) were white, 324 (14%) were AA, and 179 (8%) were Hispanic. Table 1 presents the distributions of selected demographic, socioeconomic, and clinical characteristics by race/ethnicity. In general, white men had a higher level of educational attainment and were more likely to be married when compared to AA and Hispanic men. Hispanic and AA men were more likely to be uninsured or insured by Medicaid and were more likely to have income of less than \$30 000 per year. AA men were more likely to harbor high-risk disease according to the D'Amico criteria, and were more likely to undergo open rather than robotic RP.

Baseline function also varied significantly by race and ethnicity (Table 2). AA and Hispanic men reported lower EPIC domain scores for sexual function at baseline in comparison to

white men, and Hispanic patients reported lower scores for urinary irritative symptoms and the urinary incontinence domain. No clinically significant differences were noted in the baseline domain scores for bowel function.

### 3.1. Urinary incontinence

Overall, RP was associated with lower adjusted mean scores for urinary incontinence when compared to AS and EBRT at 1 yr after therapy. The adjusted mean score for urinary incontinence at 1 yr was 19.9 points (95% CI 17.2–22.7;  $p < 0.001$ ) lower for RP compared to AS and 21.9 points (95% CI 19.2–24.6;  $p < 0.001$ ) points lower compared to EBRT. While this association between RP and incontinence was observed across all race/ethnic groups, the decline was greater for AA than for white men (adjusted DID 8.4 points, 95% CI 2.0–14.8;  $p = 0.01$ ; Table 3). Despite this result, baseline function and primary treatment appeared to be far more important in predicting post-treatment urinary incontinence than race/ethnicity (Fig. 1).

Because AA men reported a greater decline in urinary incontinence function after RP compared to white men, we tested whether AA men had greater odds of reporting moderate or severe bother secondary to overall urinary function compared to white men after RP (Supplementary Table 2). Notably, there were no apparent between-race differences in the odds of moderate or severe bother by overall urinary function, despite lower scores for the continuous domain ( $p = 0.15$ ).

### 3.2. Sexual, bowel, urinary irritative, and hormone function

There was no evidence of any clinically significant differences by race/ethnicity in the effects of treatment on EPIC scores for sexual, bowel, or hormone function (Table 3) or for bother scores in these domains (Supplementary Table 2). The average difference in effect of RP on urinary irritative symptoms between white and AA men was 4.4 (95% CI 0.8–8.0;  $p = 0.02$ ; Table 3).

### 3.3. Sensitivity analyses

Because there was evidence of differential adoption of modern treatment modalities among minority populations, we performed a sensitivity analysis excluding patients who did not undergo a robotic nerve-sparing operation and those who did not receive IMRT. The results of this analysis were similar to our main analysis with respect to racial differences in treatment effects. There was, however, an even greater decline in the post-RP incontinence domain among AA compared to white men (DID 14.1 points, 95% CI 5.4–22.9;  $p = 0.002$ ). Because this was a nonrandomized clinical trial, we performed a second sensitivity analysis using propensity score adjustment as an alternative method to account for pretreatment differences between patients receiving different treatments. After propensity score adjustment, we did not note any substantial differences from our primary results.

## 4. Discussion

In this prospective, longitudinal, population-based study of functional outcomes after contemporary prostate cancer treatment, we observed that the effect of treatment on patient-



reported function did not vary dramatically by race/ethnicity. Only for the urinary incontinence domain did we find any evidence of a significant interaction between race and prostate cancer treatment. AA men experienced a more pronounced post-RP decline in scores for urinary incontinence compared to white men, but the corresponding changes in bother scores were not significantly different between the races. We also found that race/ethnicity is not nearly as predictive of function at 1 yr as treatment selection and baseline function. These findings are new to the prostate cancer literature and will be leveraged to inform patient-facing, web-based treatment decision aids for men considering treatment for localized prostate cancer.

Only one other study has examined the interaction between race/ethnicity and treatment on functional outcomes after prostate cancer treatment. In PCOS, the authors likewise demonstrated a significant interaction between race/ethnicity and urinary incontinence [8]. However, in that study, AA men reported better domain scores for urinary incontinence after RP compared to white men. By contrast, AA men in the current study reported worse effects of RP with respect to urinary incontinence compared to white men. While the precise reason for this difference between the studies is unknown, we speculate that there may be several plausible explanations. First, compared to the PCOS era, there is now widespread utilization of minimally invasive RP, IMRT, and image-guided radiation therapy. These newer approaches may affect men of different races differently compared to older treatments. This is supported in part by the findings from the sensitivity analysis, which showed that the race-treatment interaction seemed to be even stronger among patients who received robotic surgery or IMRT. Second, it is important to recognize that the original PCOS did not study AS patients. Having an AS cohort allowed us to estimate treatment effects compared to AS within a particular race (eg, the difference in mean EPIC scores between RP and AS among AA men). Subsequently, we are able to formally test the interaction between race and treatment by estimating how the effects of treatment varied by race/ethnicity (eg, the difference in mean EPIC scores between RP and AS among AA men subtracted from the difference in mean EPIC scores between RP and AS among white men, which is the DID). Using this systematic approach, we were able to precisely test the race-treatment interaction for all patient-reported functional outcomes after prostate cancer treatment.

Other studies have examined the racial variation in patient-reported quality-of-life outcomes after prostate cancer treatment, but without testing the interaction between race/ethnicity and treatment. Using the CaPSURE data set, Lubeck et al [17] demonstrated that significant post-treatment differences in functional outcomes existed between AA and white patients at 1 yr. Specifically, AA men reported worse urinary and bowel function with correspondingly worse bother scores at 1 yr after treatment. However, unlike the current analysis, these models did not adjust for baseline function or comorbidity. In a separate prospective, longitudinal multicenter observational cohort, the investigators found that AA men were more likely to report better erectile function compared to white men at 2 yr after brachytherapy [18]. However, this study and many others in this space [19,20] are limited by small sample sizes of minority men, making their estimates less reliable. Furthermore, these studies failed to test or even allow for the interaction between race/ethnicity and treatment; that is, these studies merely report what the post-treatment differences are between races at a single time point. In contradistinction, our study comprises a large cohort of AA and



Hispanic men. Furthermore, because our study uses AS as a comparator, we were able to estimate how the effect of treatment (as compared to AS) varies by race/ethnicity. This approach allows more accurate estimation of the patterns of risk for minority populations.

Despite these novel data, several limitations should be acknowledged. First, clinically significant differences in EPIC domain scores are not firmly established. We used published thresholds when interpreting these data [12]. Second, the racial classifications used in this study is almost certainly inadequate for fully describing each person's true racial and ethnic identity, and may not fully capture significant racial, social, and cultural distinctions. Moreover, and more importantly, this racial/ethnic grouping is a fairly arbitrary construct. Our analysis does not acknowledge the variability within each group; the individuals' characteristics may be much more important than race/ethnicity. Third, this is an observational study, and unmeasured confounding, such as differential clinician experience, access to high-quality care, or use of pelvic floor rehabilitation, may give rise to biased effect estimates. To address these concerns, the CEASAR study contains a comprehensive set of patient-level variables, which, in combination with advanced inference model building, should minimize the effects of confounding [21]. We also performed a sensitivity analysis using propensity score adjustment and noted no substantial differences in the model outputs. Fourth, although we present the results of several statistical tests, we have not adjusted for multiple comparisons. While we did not address multiplicity of comparisons, our primary analysis was specified a priori and we have been careful to interpret the results in the context of clinical relevance in addition to statistical significance [22].

Despite these limitations, we believe that our findings provide a valuable framework for a more comprehensive understanding of the effects of treatment and how these effects relate conditionally to race/ethnicity. While our study demonstrated that AA men have a higher risk of incontinence at 1 yr after RP, especially minimally invasive RP, these differences were not observed in the sexual, bowel, urinary irritative, and hormone domains. With longer follow-up, these data will lay a foundation for decision support tools targeting patients and/or providers.

## 5. Conclusions

Unlike oncologic outcomes, the effect of treatment on patient-reported function does not vary dramatically by race/ethnicity. While long-term follow-up is needed to fully characterize how these interactive effects will evolve over time, these data will lay a foundation for decision support tools targeting patients and/or providers.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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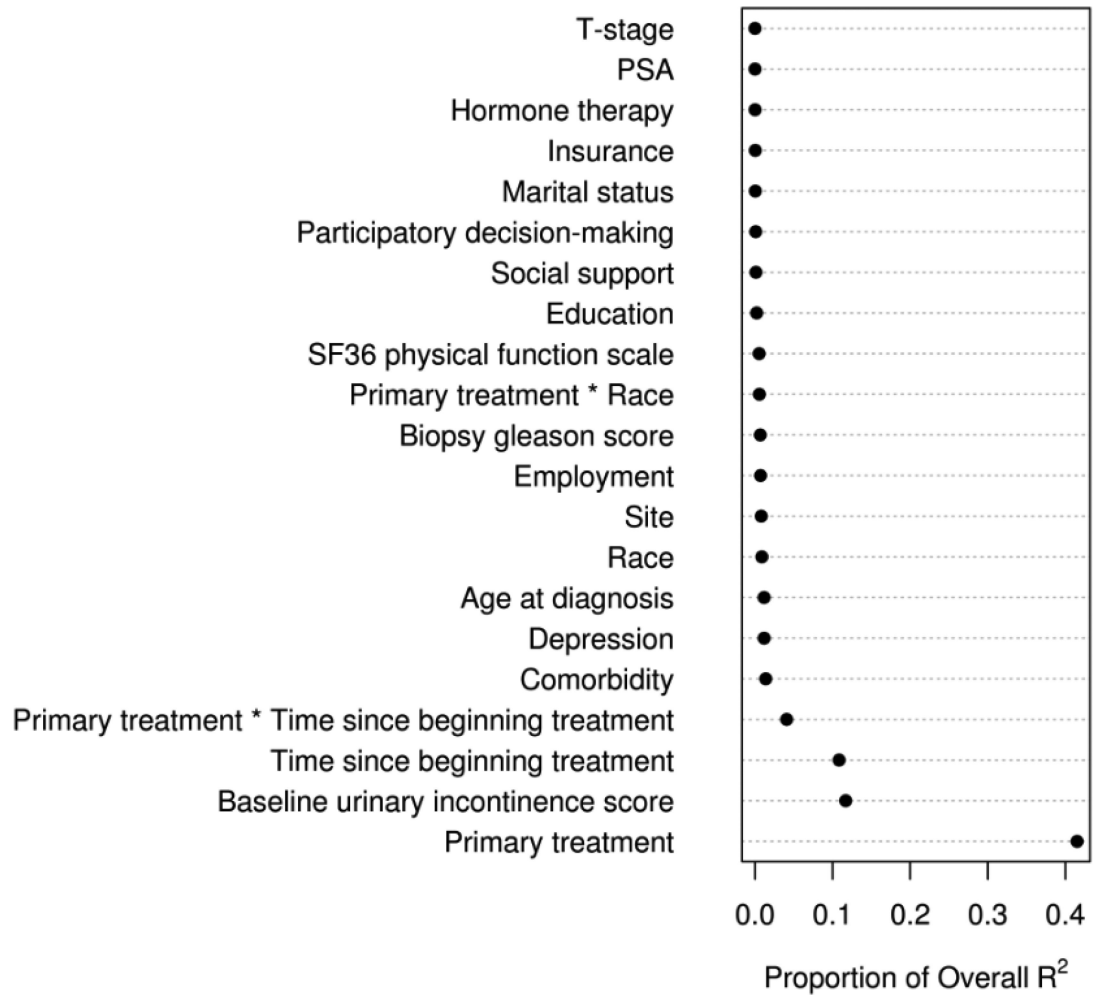
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We observed that the effect of treatment on patient-reported function did not vary dramatically by race/ethnicity. Compared to white men, African-American men experienced a somewhat more pronounced decline in urinary incontinence after radical prostatectomy, but the corresponding changes in bother scores were not significantly different between the two groups.



**Fig. 1.** Proportion of overall  $R^2$  explained by different factors and interactions. PSA = prostate-specific antigen; SF36 = Short-Form 36-item questionnaire.

**Table 1**

Pretreatment demographic and clinical characteristics by race/ethnicity

	White (n = 1835)	AA (n = 324)	Hispanic (n = 179)	Combined	p value
Age at diagnosis (yr)	64 (59–70)	63 (55–67)	63 (57–69)	64 (58–69)	<0.001
Body mass index (kg/m <sup>2</sup> )	27 (25–30)	28 (25–31)	28 (26–31)		0.05
Education					<0.001
High school or less	5% (96)	18% (55)	47% (83)	10% (234)	
High school graduate	19% (333)	28% (86)	25% (45)	20% (464)	
Some college	23% (411)	23% (70)	16% (29)	22% (510)	
College graduate	25% (445)	17% (51)	7% (13)	22% (509)	
Graduate/professional	28% (510)	14% (43)	4% (7)	25% (560)	
Marital status					<0.001
Not married	16% (292)	36% (108)	23% (40)	19% (440)	
Married	84% (1498)	64% (196)	77% (136)	81% (1830)	
Insurance					<0.001
Medicaid/None	1% (23)	10% (31)	7% (12)	3% (66)	
VA/military/other	1% (27)	3% (11)	6% (11)	2% (49)	
Medicare	47% (864)	44% (143)	37% (66)	46% (1073)	
Private/HMO	50% (921)	43% (139)	50% (90)	49% (1150)	
Employment					<0.001
Full time	45% (819)	35% (111)	36% (64)	43% (994)	
Part time	8% (153)	7% (21)	5% (9)	8% (183)	
Retired	44% (797)	48% (153)	43% (77)	44% (1027)	
Unemployed	3% (50)	10% (32)	16% (28)	5% (110)	
Annual income					<0.001
\$30 000	13% (215)	40% (116)	56% (92)	20% (423)	
\$30 001–\$50 000	19% (328)	23% (65)	18% (29)	20% (422)	
\$50 001–\$100 000	34% (573)	25% (71)	18% (29)	31% (627)	
\$100 001	34% (578)	12% (36)	8% (13)	29% (627)	
TtBI					<0.001
0–2	27% (483)	26% (81)	46% (81)	28% (645)	

	White (n = 1835)	AA (n = 324)	Hispanic (n = 179)	Combined	p value
3–5	57% (1024)	53% (162)	44% (78)	55% (1264)	
6–8	13% (236)	17% (53)	10% (17)	13% (306)	
9–15	3% (54)	4% (12)	1% (2)	3% (68)	
D'Amico risk group					<0.001
Low	46% (837)	41% (132)	47% (83)	45% (1052)	
Intermediate	39% (722)	38% (124)	37% (65)	39% (911)	
High	15% (272)	21% (67)	17% (30)	16% (369)	
Clinical T stage					<0.001
T1	75% (1371)	80% (257)	82% (147)	76% (1775)	
T2	25% (457)	20% (66)	18% (32)	24% (555)	
Biopsy Gleason score					<0.001
6	52% (957)	50% (160)	54% (96)	52% (1213)	
3 + 4	28% (521)	31% (100)	21% (37)	28% (658)	
4 + 3	10% (187)	11% (34)	12% (22)	10% (243)	
8	9% (165)	9% (29)	13% (23)	9% (217)	
Prostate-specific antigen					<0.001
<4 ng/ml	22% (402)	19% (62)	16% (28)	21% (492)	
4–9.9 ng/ml	67% (1222)	60% (196)	70% (126)	66% (1544)	
10–19.9 ng/ml	9% (163)	14% (45)	11% (19)	10% (227)	
20–50 ng/ml	3% (48)	6% (21)	3% (6)	3% (75)	
Any hormone therapy in first year					<0.001
No	88% (1619)	81% (264)	82% (146)	87% (2029)	
Yes	12% (216)	19% (60)	18% (33)	13% (309)	
Surgery type					<0.001
Open	20% (203)	31% (42)	24% (23)	22% (268)	
Robot-assisted	78% (794)	67% (90)	74% (70)	77% (954)	
Other	2% (19)	2% (3)	2% (2)	2% (24)	
Nerve-sparing procedure					<0.001
Yes	93% (767)	81% (91)	91% (74)	91% (932)	
No	7% (59)	19% (21)	9% (7)	9% (87)	
IMRT					<0.001



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	White (n = 1835)	AA (n = 324)	Hispanic (n = 179)	Combined	p value
No	78% (1369)	68% (191)	82% (131)	77% (1691)	
Yes	22% (385)	32% (90)	18% (28)	23% (503)	

Data are presented as median (interquartile range) for continuous variables.

AA = African-American; VA = Veterans Association; HMO = Health Maintenance Organization; IMRT = intensity-modulated radiation therapy.

**Table 2**

Pretreatment function quartiles by race/ethnicity.†

	<b>White (n = 1835)</b>	<b>AA (n = 324)</b>	<b>Hispanic (n = 179)</b>	<b>p value</b>
Urinary irritative	88 (75–100)	88 (75–100)	81 (62–94)	0.013
Urinary incontinence	100 (85–100)	100 (73–100)	94 (68–100)	<0.001
Bowel function	100 (96–100)	100 (88–100)	100 (88–100)	0.003
Sexual function	75 (38–90)	67 (22–90)	65 (27–85)	<0.001

Data are presented as median (interquartile range).

AA = African-American.

Adjusted mean difference in function at 12 mo between treatment types by race/ethnicity

Table 3

	Adjusted mean difference between treatment types			Differences in treatment effect		
	White (95% CI)	AA (95% CI)	Hispanic (95% CI)	White vs AA DID (95% CI)	White vs Hispanic DID (95% CI)	
<b>Irritative</b>						
EBRT vs AS	1.8 (-0.5 to 4.1)	-1.2 (-5.2 to 2.8)	1.6 (-4.5 to 7.8)	3.0 (-1.0 to 7.0)	0.2 (-5.9 to 6.2)	
RP vs AS	3.8 (1.8 to 5.7) <sup>†</sup>	-0.6 (-4.2 to 2.9)	0.3 (-4.3 to 4.9)	4.4 (0.8 to 8.0) <sup>†</sup>	3.5 (-1.0 to 8.0)	
RP vs EBRT	2.0 (0.2 to 3.7) <sup>†</sup>	0.6 (-2.9 to 4.1)	-1.4 (-6.4 to 3.7)	1.4 (-2.0 to 4.8)	3.3 (-1.8 to 8.5)	
<b>Incontinence</b>						
EBRT vs AS	2.4 (-0.5 to 5.4)	-2.4 (-8.1 to 3.2)	5.9 (-2.5 to 14.3)	4.9 (-0.7 to 10.4)	-3.5 (-11.8, 4.8)	
RP vs AS	-18.6 (-21.4 to -15.8) <sup>*</sup>	-27.0 (-33.4 to -20.6) <sup>*</sup>	-19.8 (-28.0 to -11.6) <sup>*</sup>	8.4 (2.0 to 14.8) <sup>†</sup>	1.3 (-7.0 to 9.5)	
RP vs EBRT	-21.0 (-23.8 to -18.3) <sup>*</sup>	-24.5 (-30.5 to -18.6) <sup>*</sup>	-25.8 (-32.7 to -18.9) <sup>*</sup>	3.5 (-2.5 to 9.5)	4.7 (-2.0 to 11.5)	
<b>Bowel</b>						
EBRT vs AS	-2.9 (-5.1 to -0.8) <sup>*</sup>	-3.6 (-7.8 to 0.7)	-0.7 (-5.4 to 4.0)	0.6 (-3.8 to 5.0)	-2.3 (-6.9 to 2.3)	
RP vs AS	1.3 (-0.3 to 2.9)	1.7 (-2.0 to 5.4)	-0.8 (-5.0 to 3.4)	-0.4 (-4.2 to 3.4)	2.0 (-2.1 to 6.1)	
RP vs EBRT	4.2 (2.5 to 5.9) <sup>†</sup>	5.3 (2.3 to 8.2) <sup>*</sup>	-0.1 (-3.7 to 3.5)	-1.1 (-4.0 to 1.9)	4.3 (0.7 to 7.8) <sup>†</sup>	
<b>Sexual</b>						
EBRT vs AS	-6.8 (-11.0 to -2.6) <sup>*</sup>	-6.0 (-14.0 to 1.9)	-5.0 (-16.0 to 6.0)	-0.8 (-8.8 to 7.1)	-1.9 (-12.7 to 9.0)	
RP vs AS	-28.8 (-32.5 to -25.1) <sup>*</sup>	-28.6 (-36.0 to -21.1) <sup>*</sup>	-26.5 (-36.1 to -17.0) <sup>*</sup>	-0.2 (-7.7 to 7.3)	-2.3 (-11.7 to 7.2)	
RP vs EBRT	-21.9 (-25.4 to -18.5) <sup>*</sup>	-22.5 (-29.0 to -16.0) <sup>*</sup>	-21.5 (-30.8 to -12.3) <sup>*</sup>	-0.6 (-5.9 to 7.1)	-0.4 (-9.6 to 8.8)	

AA = African-American; = difference; CI = confidence interval; DID = difference in difference; EBRT = external-beam radiotherapy; AS = active surveillance; RP = radical prostatectomy.  
<sup>\*</sup>  $p < 0.05$ .