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Racial Differences in Prostate Cancer Treatment: The Role of Socioeconomic Status

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Objective: This study examines whether socioeconomic status (SES), measured at both the individual and neighborhood levels, is associated with receipt of definitive treatment for localized prostate cancer and whether these associations mediate racial differences in treatment between non-Hispanic White and non-Hispanic Black men.

Design: The Philadelphia Area Prostate Cancer Access Study (P² Access) is a mailed, cross-sectional survey of men sampled from the Pennsylvania Cancer Registry, combined with neighborhood Census data.

Setting: Eight counties in southeastern Pennsylvania.

Participants: 2,386 men with prostate adenocarcinoma.

Main Measures: Receipt of definitive treatment, race, self-reported income, education, employment status, and neighborhood SES.

Results: Overall, Black and White men were equally likely to receive definitive treatment. Men living in neighborhoods with higher SES were more likely to receive definitive treatment (OR 1.57, 95%CI 1.01, 2.42). Among men who received definitive treatment, Black men were significantly less likely to receive radical prostatectomy compared with White men (OR .71, 95% CI .52, .98), as were men with some college education compared with those with a high school education or less (OR .66, 95% CI .47, .94). SES does not mediate racial differences in receipt of definitive treatment or the type of definitive treatment received, and associations with income or employment status were not significant.

Conclusions: These results stress the importance of examining racial disparities within geographic areas and highlight the unique associations that different measures of SES, particularly neighborhood SES and education, may have with prostate cancer treatment. *Ethn Dis*. 2017;27(3):201-208; doi:10.18865/ed.27.3.201.

Keywords: Prostate Cancer; Treatment; Race; Socioeconomic Status

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Introduction

Second only to skin cancer,[1] prostate cancer is one of the most common cancers affecting men in the United States, with an estimated 180,890 men diagnosed in 2016 and approximately 26,120 dying of the disease.[2] Prostate cancer incidence and mortality vary significantly by race and ethnicity. Black men are at least 1.4 times more likely to be diagnosed with prostate cancer[3] and 2.4 times more likely to die from the disease compared with White men.[4,5] Despite higher incidence and mortality,[6,7] Black men remain significantly less likely to receive definitive treatment[4,8,9] and less likely to undergo radical prostatectomy.[4,8,10,11]

The reasons why Black men are less likely to receive definitive treatment and radical prostatectomy are poorly understood and likely multifactorial. Socioeconomic status (SES) is one factor that may play an important role in shaping racial/ethnic differences in treatment. Black men tend to have lower SES than White men across a range of dimensions including education, income, wealth and neighborhood SES.[5,12-14]

Though previous studies have demonstrated that individuals with lower SES are less likely to receive definitive treatment,[5,12-15] they have typically relied on a single measure of SES, whether this be an individual measure

such as income or a neighborhood measure like census tract-level poverty rate.[16-18] Few studies utilize both individual-level and area-level data.[19,20] Yet, research increasingly recognizes that different dimensions of SES are not interchangeable,[21-23] and it is believed that different socioeconomic factors may provide unique information related to health disparities.[21]

Our study aims to shed light on differences in prostate cancer treatment with respect to race and SES. Using a registry-based sample of men with prostate cancer in the Philadelphia area, we examine whether SES—measured at both the individual and census-tract levels—is associated with definitive treatment and formally test whether SES mediates racial differences in prostate cancer treatment.

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Methods

Study Population

The data for our study came from the Philadelphia Area Prostate Cancer Access Study (P^2 Access), which surveyed men diagnosed with localized prostate cancer between January 1, 2012 and December 31, 2014. White and Black men were identified by the Pennsylvania Cancer Registry (PCR); criteria for inclusion (N=2,386) were: 1) having a primary diagnosis of localized cancer of the prostate; 2) adenocarcinoma histology; and 3) being a resident of one of the following eight counties in southeastern Pennsylvania: Berks, Chester, Delaware, Lancaster, Lehigh, Montgomery and Philadelphia.

Men were excluded from the study (N=123) if they: 1) died prior to data collection; 2) did not speak English or Spanish; 3) had unknown surgical and radiation treatment status; or 4) received chemotherapy. We further excluded men with military, Tricare or Veterans Administration insurance, because these plans have different benefit designs that could potentially impact associations with SES. Because we focused on examining disparities in treatment between Black and White men, those who reported their race/ethnicity as Hispanic/Other (n=69) were excluded.

Patient Questionnaire

We mailed surveys to all participants between June 1, 2014 and August 21, 2015. Participants received up to two mailings of the survey; the first included an unconditional $2 incentive. Participants were compensated an additional $15 after completing the survey. Follow-up phone calls were made to all individuals who did not respond to the mailed surveys.

Main Outcome Measures

Race/Ethnicity

Race/ethnicity was self-reported in the patient survey and defined as non-Hispanic White (White) or non-Hispanic Black (Black).

Treatment

PCR data were used to define an individual's treatment status, typically within four months of diagnosis. Definitive treatment was a dichotomous variable classified as having received either radical prostatectomy or radiation, including both external beam radiation and seed brachytherapy, or not receiving these treatment modalities.

Socioeconomic Status

Individual measures of SES included self-reported education,[14,15] employment status and annual household income.[15] Neighborhood SES was determined using data from the 2010 US Census.[24] Participants' home addresses were geocoded, with ArcGIS software, and subsequently linked to characteristics of the census tracts in which they resided. These characteristics included: percentage of households with children, not headed by a female; percentage of the >16 year-old male population that was employed; percentage of households not receiving public assistance or food stamps; percentage of households with income exceeding the federal poverty level; median household income; percentage of the >25 year-old population that had achieved a level of education ≥ a high school diploma. Z scores for these six variables were summed,[25] with higher scores corresponding to higher neighborhood SES.[25,26]

Covariates

We included a range of characteristics that have been previously associated with receipt of definitive

treatment, such as marital status,[10,14,27] insurance status,[15] and age.[28,29]

We also included participant's life expectancy, which was estimated using a validated, 10-year mortality index.[30] This index measure accounts for self-reported variables including age, body mass index (BMI), tobacco use, comorbidities (diabetes, chronic lung disease, and heart failure) and functional status. Functional status was ascertained by asking participants whether they had difficulty with bathing or showering, managing their finances, walking several blocks, and pushing or pulling large objects. Based on their life expectancy scores, participants were categorized into four categories: low (<25%), intermediate (25-49%), high (50-74%) and very high (>75%) risk of 10-year mortality.[31]

Individual's cancer characteristics, as ascertained from the PCR, included prostate-specific antigen (PSA) values (<10, 10-20 or >20), tumor grade as defined by Gleason score (<6, 7, or >7), and the American Joint Committee on Cancer (AJCC) tumor stage (I, II or III).[32]

Statistics

The patient cohort was described using chi-squared tests to compare differences in characteristics between White and Black men. To model the association between race and treatment, we first ran an unadjusted logistic regression model with receipt of definitive treatment as the primary outcome. Second, we performed a multivariable logistic regression model adjusted for marital status, age, life expectancy, PSA, Gleason, and stage. We then added the four surrogate measures of SES to the above-mentioned multivariable logistic regression model to evaluate the association between various measures of SES and receipt of definitive treatment for localized prostate cancer.

To determine whether SES mediated the relationship between race

Table 1. Cohort characteristics

	Total, N=2194	NH White, N=1763	NH Black, N=356[a]	P
	n (%)	n (%)	n (%)	
Treatment				
Definitive	1838 (83.8)	1486 (84.3)	289 (81.2)	.147
Surgery	1153 (55.2)	973 (55.9)	180 (51.9)	.170
Radiation	654 (36.5)	531 (35.5)	123 (41.6)	.046
Education				<.001
≤HS grad	639 (32.5)	463 (28.4)	176 (52.5)	
Some college	423 (21.5)	337 (20.7)	86 (25.7)	
College grad	327 (16.6)	293 (18.0)	34 (10.2)	
>College	577 (29.4)	538 (33.0)	39 (11.6)	
Employment				<.001
Unemployed/other	226 (11.5)	134 (8.2)	92 (27.7)	
Employed	839 (42.7)	740 (45.4)	99 (29.8)	
Retired	898 (45.8)	757 (46.4)	141 (42.5)	
Income				<.001
<35k	376 (20.9)	218 (14.7)	158 (51.1)	
35-50k	200 (11.1)	157 (10.6)	43 (13.9)	
50-75k	304 (16.9)	266 (17.9)	38 (12.3)	
>75k	917 (51.0)	847 (56.9)	70 (22.7)	
NSES				<.001
<25%	502 (24.6)	245 (14.5)	257 (74.1)	
25-50%	494 (24.2)	448 (26.5)	46 (13.3)	
50-75%	534 (26.2)	507 (30.0)	26 (7.5)	
>75%	510 (25.0)	492 (29.1)	18 (5.2)	
PSA				.013
>10	1600 (82.2)	1347 (83.1)	253 (77.9)	
10-20	228 (11.7)	187 (11.5)	41 (12.6)	
>20	119 (6.1)	88 (5.4)	31 (9.5)	
Gleason				.164
<6	842 (41.0)	717 (42.0)	125 (36.4)	
7	843 (41.1)	690 (40.4)	153 (44.6)	
>7	367 (17.9)	302 (17.7)	65 (19.0)	
Clinical stage				.242
I	1522 (72.9)	1254 (72.2)	268 (76.6)	
II	515 (24.7)	440 (25.3)	75 (21.4)	
III	50 (2.4)	43 (2.5)	7 (2.0)	
Marital status				<.001
No	399 (19.1)	262 (15.0)	137 (39.3)	
Yes	1696 (81.0)	1484 (85.0)	212 (60.7)	
10-year mortality risk				<.001
Low	589 (29.5)	501 (30.0)	88 (27.2)	
Intermediate	691 (34.7)	604 (36.2)	87 (26.9)	
High	501 (25.1)	409 (24.5)	92 (28.5)	
Very high	212 (10.6)	156 (9.3)	56 (17.3)	

a. 75 men with missing race/ethnicity data.

Table 2. Multivariable logistic regression models: receipt of definitive treatment

	Unadjusted OR (95% CI)[a]	Adjusted OR (95% CI)[b]	Adjusted OR (95% CI)[c]
Race			
Non-Hispanic White (ref)	1.00	1.00	1.00
Non-Hispanic Black	.80 (.60, 1.08)	.80 (.58, 1.11)	.95 (.65, 1.39)
Education			
≤HS grad (ref)	1.00		1.00
Some college	1.07 (.78, 1.48)		1.02 (.72, 1.45)
College grad	1.24 (.86, 1.80)		1.04 (.68, 1.58)
>College	1.13 (.84, 1.52)		1.04 (.70, 1.53)
Employment			
Unemployed/other (ref)	1.00		1.00
Employed	1.03 (.69, 1.53)		.81 (.50, 1.30)
Retired	.86 (.58, 1.27)		.73 (.45, 1.19)
Household income			
<35k (ref)	1.00		1.00
35-50k	1.04 (.67, 1.62)		.93 (.57, 1.52)
50-75k	1.31 (.88, 1.96)		1.11 (.68, 1.81)
>75k	1.25 (.92, 1.70)		.89 (.55, 1.44)
NSES			
<25% (ref)	1.00		1.00
25-50%	1.24 (.91, 1.70)		1.29 (.88, 1.90)
50-75%	1.44 (1.05, 1.97)		1.49 (.99, 2.22)
>75%	1.49 (1.08, 2.06)		1.57 (1.01, 2.42)

a. Each variable is entered into a separate model where receipt of definitive treatment was the outcome.
b. Adjusted for: marital status, age, life expectancy, PSA, Gleason, stage.
c. Adjusted for: marital status, age, life expectancy, PSA, Gleason, stage, education, employment status, household income, NSES.

and definitive treatment, we conducted multiple logistic regression analyses to evaluate the following hypotheses: 1) Race has a significant effect on SES; 2) SES has a significant effect on definitive treatment; 3) Race has a significant effect on definitive treatment; and 4) The effect of race on definitive treatment is attenuated when SES is added to the model. To support SES as a mediator of the relationship between race and treatment, it was necessary to reject the null for the above-listed four hypotheses. All regression models were adjusted for demographic and tumor characteristics.

In the subgroup of men who received definitive treatment, we performed sequential multivariable logistic regression analyses where the type of treatment (radical prostatectomy or radiation) was the outcome variable. And, we similarly tested the four hypotheses to evaluate SES as a mediator of the association between race and type of definitive treatment.

We accounted for missing data using multiple imputation with chained equations (MICE). Insurance status was highly correlated with employment status and age according to our correlation matrices; for this reason, insurance status was omitted from our multivariable models.

All statistical analyses were performed in Stata version 14.[33] This study was approved by the Institutional Review Boards at the University of Pennsylvania and Johns Hopkins University School of Medicine.

Results

Surveys were returned on 2,386 men; after excluding ineligible participants, this resulted in an adjusted response rate of 51.1%. Our final analytic cohort included 2,194 men, of whom 80% (n=1,763) were White, 16% (n=356) were Black, and 75 men did not report their race (Table 1). The mean age was 65.8 for White men and 63.5 for Black men. Approximately 84% of White men received definitive treatment, compared with 81% of Black men. A larger proportion of White men (56%) received surgical treatment by radical prostatectomy compared with Black men (52%). Conversely, 42% of Black men receiving definitive treatment underwent radiation, vs 36% of White men.

Black and White men were statistically significantly different for each of the four measures of SES. White men were more likely to have achieved a college education or higher (51% vs 22%), be employed (45% vs 30%), have an annual household income >$75,000 (57% vs 23%), and live in neighborhoods with higher SES (29% vs 5%).

In our unadjusted model, Black men had 20% decreased odds of receiving definitive treatment compared with White men, although this result was not statistically significant (OR .80, 95%CI .60, 1.08, Table 2). Results were similar when the model was adjusted for demographic and tumor characteristics (OR .80, 95% CI .58, 1.11). In the models that additionally adjusted for measures of SES, the difference in receipt of definitive treatment between Black and White men narrowed (OR .95, 95% CI .65, 1.39). Education, employment, and

annual household income were not significantly associated with receipt of definitive treatment. However, living in a neighborhood with high SES was associated with increased odds of receiving definitive treatment (OR 1.57, 95% CI 1.01, 2.42).

Among the subgroup of men who received definitive treatment, we observed that Black men were significantly less likely than White men to receive radical prostatectomy (OR .71, 95% CI .52, .98) after adjusting for demographic and tumor characteristics (Table 3). After adjusting for the four measures of SES, the point estimate for race did not appreciably change (OR .65, 95% CI .45, .95). In this model, men with some college education were less likely to receive radical prostatectomy than those with a high school education or less (OR .66, 95% CI .47, .94), whereas the other measures of SES were not significantly associated with the type of treatment men received.

In both the full and subgroup analyses, we were unable to reject the null hypotheses for the four multiple logistical regression analyses that comprise the formal mediation analysis. Thus, it was concluded that SES does not mediate the relationship between race and treatment.

Table 3. Subgroup analysis among men who received definitive treatment: receipt of radical prostatectomy (v radiation)

	Unadjusted OR (95% CI)[a]	Adjusted OR (95% CI)[b]	Adjusted OR (95% CI)[c]
Race			
Non-Hispanic White (ref)	1.00	1.00	1.00
Non-Hispanic Black	.80 (0.60, 1.06)	.71 (.52, .98)	.65 (.45, .95)
Education			
≤HS grad (ref)	1.00		1.00
Some college	.86 (.64, 1.17)		.66 (.47, .94)
College grad	1.01 (.72, 1.40)		.71 (.47, 1.06)
>College	1.15 (.87, 1.53)		.86 (.59, 1.26)
Employment			
Unemployed/other (ref)	1.00		1.00
Employed	1.45 (1.00, 2.12)		.92 (.58, 1.45)
Retired	.62 (.43, .88)		1.11 (.69, 1.68)
Household Income			
<35k (ref)	1.00		1.00
35-50k	1.20 (.79, 1.83)		1.16 (.72, 1.88)
50-75k	1.43 (1.00, 2.04)		1.10 (.70, 1.73)
>75k	2.22 (1.66, 2.97)		1.43 (.89, 2.29)
NSES			
<25% (ref)	1.00		1.00
25-50%	.92 (.68, 1.25)		.75 (.51, 1.10)
50-75%	1.16 (.88, 1.58)		.92 (.61, 1.37)
>75%	1.11 (.82, 1.50)		.79 (.51, 1.22)

a. Each variable is entered into a separate model where receipt of radical prostatectomy was the outcome.
b. Adjusted for: marital status, age, life expectancy, PSA, Gleason, stage.
c. Adjusted for: marital status, age, life expectancy, PSA, Gleason, stage, education, employment status, household income, NSES.

Discussion

In a large cohort of men diagnosed with localized prostate cancer, we did not observe racial differences in receipt of definitive treatment after adjusting for demographic and tumor characteristics; however, men living in neighborhoods with higher SES were more likely to receive definitive treatment compared with individuals living in less advantaged neighborhoods. Among the group of men who received treatment, Black men and men who attended but did not complete college were significantly less likely to receive radical prostatectomy. These results contribute to our understanding of the intersection of racial and SES differences in prostate cancer care by showing the potential for both race and different measures of SES to be linked with treatment.

In our sample, race was not statistically significantly associated with receipt of definitive treatment. This finding differs from previous studies, many of which use SEER-Medicare data,[4,8] that have demonstrated racial differences in receipt of definitive treatment. It is likely that this difference results from our in-depth focus on a single region. This underscores the potential for national data to mask important heterogeneity in disparities within and across regions.[34] The overall rate of definitive treatment was lower in our sample compared to other studies,[11,35] and this could have also impacted our finding.

One strength of our study is that we considered multiple measures of SES, including both individual- and area-level indicators. This is an important contribution to the literature, because few existing studies of the association between race and treat-

Table 4. Characteristics of responders and non-responders overall and by patient race

Characteristic	Responders	Non-responders	P	Non-Hispanic White Responders	Non-Hispanic White non-responders	P	Non-Hispanic Black Responders	Non-Hispanic Black non-responders	P
	N=2386	N=2286		N=1850	N=1405		N=391	N=691	
	N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Age, yrs			.044			.654			.039
<60	704 (29.5)	712 (31.2)		524 (28.3)	401 (28.5)		150 (38.4)	250 (36.2)	
60-64	511 (21.4)	492 (21.5)		388 (21.0)	306 (21.8)		93 (23.8)	159 (23.0)	
65-69	559 (23.4)	464 (20.3)		459 (24.8)	318 (22.6)		73 (18.7)	114 (16.5)	
70-74	349 (14.6)	323 (14.1)		272 (14.7)	210 (14.9)		49 (12.5)	79 (11.4)	
≥75	263 (11.0)	294 (12.9)		207 (11.2)	170 (12.1)		26 6.6)	88 (12.7)	
Missing	0 (0)	1 (0.0)		0 (0)	0 (0)		0 (0)	1 (.1)	
Race/ethnicity			<.001						
NH White	1850 (77.5)	1405 (61.5)							
NH Black	391 (16.4)	691 (30.2)							
Hispanic	32 (1.3)	88 (3.9)							
NH Other	0 (0.0)	0 (0.0)							
Missing	113 (4.7)	102 (4.5)							
Insurance			.058			.524 (F)			.689 (F)
Private	1310 (54.9)	1198 (52.4)		1048 (56.6)	768 (54.7)		196 (50.1)	339 (49.1)	
Medicaid	73 (3.1)	102 (4.5)		22 (1.2)	23 (1.6)		44 (11.3)	68 (9.8)	
Medicare	958 (40.2)	921 (40.3)		748 (40.4)	584 (41.6)		141 (36.1)	257 (37.2)	
None/Other	19 (.8)	20 (0.9)		12 (.6)	11 (.8)		5 (1.3)	5 (.7)	
Missing	26 (1.1)	45 (2.0)		20 (1.1)	19 (1.4)		5 (1.3)	22 (3.2)	
Gleason score			.317			.212			.588
<7	944 (39.6)	901 (39.4)		764 (41.3)	575 (40.9)		135 (34.5)	255 (36.9)	
7	953 (39.9)	896 (39.2)		705 (38.1)	527 (37.5)		170 (43.5)	291 (42.1)	
>7	414 (17.4)	348 (15.2)		323 (17.5)	204 (14.5)		70 (17.9)	110 (15.9)	
Missing	75 (3.1)	141 (6.2)		58 (3.1)	99 (7.0)		16 (4.1)	35 (5.1)	
Clinical tumor stage			.446			.971			.376
Stage 1	1706 (71.5)	1649 (72.1)		1305 (70.5)	981 (69.8)		296 (75.7)	544 (78.7)	
Stage 2	574 (24.1)	514 (22.5)		461 (24.9)	353 (25.1)		74 (18.9)	108 (15.6)	
Stage 3	58 (2.4)	62 (2.7)		46 (2.5)	34 (2.4)		12 (3.1)	23 (3.3)	
Missing	48 (2.0)	61 (2.7)		38 (2.1)	37 (2.6)		9 (2.3)	16 (2.3)	
Active Treatment			<.001			<.001			<.001
No	393 (16.5)	567 (24.8)		304 (16.4)	325 (23.1)		73 (18.7)	216 (31.3)	
Yes	1897 (79.5)	1620 (70.9)		1464 (79.1)	1022 (72.7)		310 (79.3)	445 (64.4)	
Missing	96 (4.0)	99 (4.3)		82 (4.4)	58 (4.1)		8 (2.0)	30 (4.3)	
NSES			<.001			<.001			.233
<25% (ref)	403 (16.9)	712 (31.1)		121 (6.5)	152 (10.8)		257 (65.7)	484 (70.0)	
25-50%	600 (25.1)	519 (22.7)		496 (26.8)	381 (27.1)		71 (18.2)	102 (14.8)	
50-75%	628 (26.3)	485 (21.2)		563 (30.4)	393 (28.0)		31 (7.9)	56 (8.1)	
>75%	664 (27.8)	448 (19.6)		602 (32.5)	399 (28.4)		21 (5.4)	25 (3.6)	
Missing	91 (3.8)	122 (5.3)		68 (3.7)	80 (5.7)		11 (2.8)	24 (3.5)	

ment adjust for multiple measures of SES.[8,11,35] We did not find an association between education, employment status, or annual household income and receipt of definitive treatment. However, higher neighborhood SES was associated with increased odds of receiving definitive treatment. An important next step might involve investigating specific neighborhood factors, like the physical and social environment and access to care, that possibly influence treatment patterns.[36] Additionally, education status was linked with type of definitive treatment, and

this calls for a deeper investigation of the relationship between education and choice of treatment for localized prostate cancer. Many studies that use SEER-Medicare data rely on readily available neighborhood SES measures as a proxy for individual-level SES. However, the disparate performance of SES measures contributes weight to the argument that individual- and area-level SES indicators are distinct.[22, 23]

It is important to consider limitations that might have impacted the results of this study. First is the potential for non-response bias (Table 4). White men were more likely than Black men to respond to the P^2 Access survey, as were men who received definitive treatment. We further examined non-response and found generally similar patterns within racial groups; however, there was differential non-response among White men according to their neighborhood SES. Differential non-response by characteristics associated with patient race may bias our findings. Second, there was a high level of missing data for our SES measures[22]; this is consistent with previous studies and likely due to the sensitive nature of SES information. To help account for this missing information, we used multiple imputation with chained equations. Third, though multiple measures of SES is a strength of this study, there are other dimensions of SES that were not evaluated, including occupational status or wealth, each of which have been shown to systematically vary between Black and White men.[22,23] Compared with occupational status, employment status does not capture varying prestige associated with different jobs among men who are employed.[37] Fourth, income was collected and analyzed in categories, which allows for non-linear associations but does not allow for a finer grain investigation. Fifth, although the sample size is large for a cohort study, it is smaller than many analyses that use large claim datasets; this may limit our statistical power to observe significant associations. To examine potential issues of small cell size, we re-ran our models combining stage 2 and 3 disease and performed stepwise selection, omitting variables with P>.10, observing highly similar associations to our main model. Finally, although the Philadelphia area is racially diverse and includes 5.2 million residents living in both urban and rural areas, the generalizability of the study may be limited by its geographic scope.

…men living in neighborhoods with higher SES were more likely to receive definitive treatment compared with individuals living in less advantaged neighborhoods.

Conclusion

Although we found no evidence of racial differences in receipt of definitive treatment among a large cohort of men diagnosed with localized prostate cancer, we found that men living in higher SES neighborhoods were more likely to receive definitive treatment. Among men who received definitive treatment, Black men had decreased odds of receiving surgery than White men. These results underscore the importance of examining disparities within different geographic contexts, including multiple measures of SES, and studying multiple steps of the prostate cancer decision-making process, to best understand the link between race and cancer care.

Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Watson, Grande, Radhakrishnan, Pollack; Acquisition of data: Grande, Pollack; Data analysis and interpretation: Watson, Grande, Mitra, Ward, Pollack; Manuscript draft: Watson, Grande, Radhakrishnan, Mitra, Ward; Statistical expertise: Watson, Mitra; Acquisition of funding: Grande; Administrative: Watson, Grande, Radhakrishnan, Ward; Supervision: Grande, Pollack

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