Oncology

Racial or Ethnic and Socioeconomic Disparities in Prostate Cancer Survivors' Prostate-specific Quality of Life

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OBJECTIVE   To conduct a prospective study to examine whether there are pretreatment and post-treatment disparities in urinary, sexual, and bowel quality of life (QOL) by race or ethnicity, education, or income in men with clinically localized prostate cancer (PCa.)

METHODS   Participants (N = 1508; 81% white; 12% black; 7% Hispanic; 50% surgery; 27% radiotherapy; 23% active surveillance) completed the Expanded Prostate Cancer Index Composite measure of PCa-specific QOL prior to treatment, 6 weeks, 6, 12, 18, and 24 months after treatment. We analyzed pretreatment differences in QOL with multivariable linear regression and post-treatment differences with generalized estimating equation models.

RESULTS   Blacks and Hispanics (compared with whites) and men with lower income had worse pretreatment urinary function; poorer and less educated men had worse pretreatment sexual function ($P < .05$). In adjusted models, among men treated surgically, blacks and Hispanics had worse bowel function compared with whites, and men with lower income experienced more sexual bother and slower recovery in urinary function. Not all racial or ethnic differences favored whites; blacks had higher sexual function than whites prior to surgery and improved faster after surgery. Blacks receiving radiotherapy had lower post-treatment bowel bother than whites ($P < .05$).

CONCLUSION   Controlling for baseline QOL, there were some post-treatment disparities in urinary and sexual QOL that suggest the need to investigate whether treatment quality and access to follow-up care is equitable. However, survivorship disparities may, to a greater extent, reflect disadvantages in baseline health that exacerbate QOL issues after treatment.   UROLOGY 112: 132–137, 2018. © 2017 Elsevier Inc.

There are close to 3 million prostate cancer (PCa) survivors in the United States, constituting 43% of all male cancer survivors.[1] Quality of survivorship is a major concern with respect to PCa care as most patients will die with, rather than of their disease, and many live with treatment-related side effects. Estimates of the prevalence of side effects vary considerably. Most men treated surgically experience urinary incontinence and erectile dysfunction, with urinary function improving in the year after surgery and sexual function improving in 2 years.[2] In 1 study, 2 years after surgery, 52% of men with functional erections before treatment had erectile dysfunction.[3] In another large study, 60% of men had erectile dysfunction 18 months post-operatively.[4] Men who receive radiotherapy are most likely to experience erectile dysfunction and bowel side effects that can increase in severity over time.[5] Of concern is whether vulnerable groups, including racial or ethnic minorities and men with low income or educational attainment disproportionately experience decrements in quality of life (QOL) after PCa treatment. Some evidence indicates this may be the case.

There have been a small number of studies of racial or ethnic disparities in PCa QOL during survivorship, including 3 large-scale studies.[3,6-8] Results provide an incomplete and sometimes inconsistent picture of racial or ethnic differences in QOL among PCa survivors, in part because

the studies examine varying stages of survivorship, different populations, and diverse facets of QOL. Data from these studies are also relatively old, collected between 1994 and 2006, and may not reflect the evolution of PCa care.

Findings for African American men are mixed. In the Prostate Cancer Outcomes Study (PCOS), among men treated surgically, African American survivors reported better sexual function at 5 years, although they were also more likely to report sexual bother or perceived problems with function than whites.[6] Blacks also reported better urinary function and lower bother than whites among men treated with radiotherapy. In the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) study, black men had worse urinary function and bother and worse bowel function and bother than whites.[8] More recently (data collected from 2003 to 2006), in the Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment (PROST-QA) study, African American men, 2 years after brachytherapy had better erectile function than whites and other groups. Function did not differ by race or ethnicity among the men treated with either surgery or external beam radiation.[3] Single-institution studies have been reviewed elsewhere[7]: the number of minority participants included in the studies has been small and findings have been mixed. One of the largest, with a sample of 665 men (30.5% African American), indicated that African Americans experienced a greater decrease in urinary function than whites 1 year after treatment regardless of treatment received.[9]

Hispanics have rarely been studied. One exception was PCOS, which reported disparities among Hispanics. Compared with whites, Hispanic men were more likely to report that their sexual function was a problem.[6] Given the widely varying results of past studies and lack of attention to Hispanic men, we sought to update the literature on racial or ethnic differences in QOL.

Associations between socioeconomic status (SES) and QOL in PCa survivors have been reported infrequently.[10] Assessments of CaPSURE participants 2 years after treatment indicated almost no differences in QOL as a function of income or education. In a study of 204 white, black, and Hispanic PCa survivors assessed within 18 months of starting treatment, Penedo et al found that men with lower income and education had lower general QOL; however they were unable to account for baseline QOL in their analyses.[11]

In the present study we examined whether there are pretreatment and post-treatment differences in urinary, bowel, and sexual function and bother by race or ethnicity, education, and income, including whether there are differences in the temporal trajectory of these dimensions over time. We separately examined QOL in men who received surgery and radiotherapy as their primary treatments, and men who were managed with active surveillance. We hypothesized that we would find a pattern of differences indicating that disadvantaged men—blacks, Hispanics, men with low income, and men with low education—experience worse pretreatment and post-treatment quality of life for multiple dimensions of QOL.

METHODS

Data Source and Procedure
We analyzed data from the Live Well Live Long study in which men with clinically localized PCa were recruited at, or shortly after diagnosis. Men were recruited at 2 comprehensive cancer centers and 3 large group practices between 2010 and 2014. As it was not possible to approach all men as the large group practices had multiple clinic sites, priority was always given to recruiting minority patients in an effort to enrich this subsample. We approached 3337 patients, of whom 2476 were consented, and 2008 completed a baseline survey prior to treatment. We surveyed men again 6 weeks (n = 1679), 6 months (n = 1638), 12 months (1580), 18 months (n = 1394), and 24 months (n = 1184) after surgery. We abstracted clinical information from medical records after treatment (n = 1946). All procedures were institutional review board approved. As the number of men whose race or ethnicity was other than white, black, or Hispanic was too small to analyze separately (n = 25), data from these individuals were excluded. After excluding cases with missing data on predictors and covariates, the final sample included 1508 men.

Measures
As side effect profiles vary by treatment modality, and treatments are received at different rates across race or ethnicity and SES groups, we stratified by treatment type for all analyses of post-treatment data. Men were categorized depending on whether they had been treated with surgery or radiotherapy (external beam radiation, brachytherapy, external beam radiation and brachytherapy, or proton therapy), or managed with active surveillance. The 3 predictors of interest were (1) self-reported race or ethnicity (non-Hispanic white and non-Hispanic black, hereafter referred to as white and black, and Hispanic); (2) educational attainment, a continuous variable ranging from having completed first grade to fourth year of graduate school; and (3) a 9-level income variable ranging from <\$5000 to ≥\$100,000.

Covariates included D'Amico disease risk. Low-risk PCa was defined as clinical stage prostate-specific antigen (PSA) ≤10 ng/mL, Gleason score ≤6, and American Joint Commission of Cancer Staging (AJCC) less than cT2b.[12] Intermediate-risk PCa was defined as PSA >10 and ≤20 ng/mL or Gleason 7 disease or AJCC cT2b. High-risk disease was defined as PSA >20 ng/mL or Gleason 8-10 disease or AJCC cT2c or higher.[12] We also controlled for whether men had received androgen deprivation therapy along with their primary treatment. As comorbid disease may be associated with QOL as well as the predictors, we abstracted information on 23 comorbidities included in the calculation of the Charlson Index. For a given QOL outcome we controlled for any comorbidity that was associated with the outcome at a time point other than

baseline at the $P < .05$ level with Bonferroni correction for multiple tests. In sexual function models we controlled for diabetes, coronary artery disease, and hypertension, and in sexual bother models we controlled for diabetes. In bowel function models we controlled for cerebrovascular disease. In bowel bother models we controlled for cerebrovascular disease and diabetes. All models included age at diagnosis, whether men were working or not, and recruitment site, although the latter is not included in the tables as the reference point is arbitrary. Finally, we controlled for baseline QOL scores. Men's corresponding baseline functioning or bother was entered for the outcome of interest (eg, when the outcome was post-treatment urinary function we included pretreatment urinary function in the model).

The outcomes of interest were urinary, bowel, and sexual QOL assessed with the Expanded Prostate Cancer Index Composite (EPIC-50), a 50-item PCa health-related QOL scale ($\alpha \geq 0.82$).[13] EPIC assesses both function (how frequently one has been affected by a treatment-related side effect during the previous 4 weeks) and bother by side effects ("how big a problem" were these side effects). Scores range from 0 to 100, with higher scores representing greater function or bother.

Data Analyses
We explored attrition with bivariate logit models and descriptive statistics, comparing those who were excluded from the multivariable analyses for not completing any follow-up surveys and the original sample of participants who completed the baseline survey. We examined whether there were adjusted differences in pretreatment QOL as a function of race or ethnicity, income, and education using multivariable linear regression. Covariates included associated comorbities, D'Amico risk score, age at diagnosis, education, race or ethnicity, employment status, marital status, income, and site where participants were recruited. We used general estimating equation (GEE) models to test for differences in adjusted QOL averaged across time and QOL trajectories over time by race or ethnicity, education, and income. For each treatment group we tested 4 models: a single main effects model for race or ethnicity, education, income, and time, and 3 interaction effects models that each included an interaction between one of the predictors and time. We repeated this for each of the 6 quality of life dimensions (urinary, bowel, and sexual function and bother). We controlled for baseline QOL, whether men received androgen deprivation therapy along with their primary treatment, and the clinical and demographic covariates described previously. We used GEE to account for nonindependence of predictors and outcomes[14] as time points were nested within participants and participants within sites, although participants were treated at far more facilities than the 5 recruiting sites given that many went on to be treated elsewhere. Gaussian family was specified as the QOL outcomes were continuous. For all multivariable models, we used robust standard errors so that if the nature of the correlation structure was not correctly specified, the standard errors would still be valid.

Table 1. Participant characteristics (N = 1508)

Characteristic	N	% or Mean (SD)
Treatment choice		
Active surveillance	341	22.61
Radiotherapy	408	27.06
Surgery	759	50.33
D'Amico risk		
Low risk	539	35.74
Intermediate risk	718	47.61
High risk	251	16.64
Received hormone therapy	182	12.07
Coronary artery disease	153	10.15
Hypertension	734	48.67
Cerebrovascular disease	22	1.46
Diabetes	203	13.46
Race		
White	1218	80.77
Black	184	12.20
Hispanic	106	7.03
Education		
<12 y	52	3.45
12 y	252	16.71
13-16 y	693	45.95
>16 y	511	33.89
Income		
<$25,000	109	7.23
$25,000-$49,999	191	12.67
$50,000-$74,999	228	15.12
$75,000-$99,999	210	13.93
≥$100,000	770	51.06
Employment status		
Employed	930	61.67
Not employed	578	38.33
Marital status		
Married/cohabitating	1251	82.96
Not married/cohabitating	257	17.04
Age	1508	66.67(7.97)

Percentages may not equal 100% because of rounding. Income and education were continuous variables in the multivariable models.

RESULTS
Participant characteristics are presented in Table 1. A majority of patients had low (35.7%) or intermediate (47.6%), rather than high (16.6%) disease risk. About half of the participants (50.3%) were treated surgically, 27.1% with radiotherapy, and 22.6% with active surveillance. In addition, 12.1% received androgen deprivation therapy along with their primary treatment, of whom (91.7%) received radiotherapy as their primary treatment. Most participants were non-Hispanic white (80.8%), had a median education of college or greater, and a mean income of $75,000-$99,999.

Attrition
Participants who had at least 1 follow-up data point were included in analyses of follow-up time points. Depending on the amount of missing data for the QOL outcomes, models contained 385-414 fewer participants than completed the baseline survey (see Supplemental Table S1 for a comparison between the baseline sample and smallest GEE sample).

Table 2. Summary or pretreatment and post-treatment differences in quality of life (QOL) by treatment type

	QOL Dimension	Black vs White	Hispanic vs White	Income Gradient	Education Gradient
Urinary	Pretreatment	Disadvantage	Disadvantage	Disadvantage	
	Postsurgery			Disadvantage	
	Postradiotherapy				
Bowel	Pretreatment		Advantage		
	Postsurgery	Disadvantage	Disadvantage		
	Postradiotherapy	Advantage			
Sexual	Pretreatment			Disadvantage	Disadvantage
	Postsurgery	Advantage		Disadvantage	
	Postradiotherapy			Advantage	

Baseline Differences in QOL

Worse baseline pretreatment scores for each QOL domain were associated with worse post-treatment QOL regardless of treatment ($Ps \le .001$; not presented in tables). Men's pretreatment QOL varied by race or ethnicity and SES, with minorities experiencing worse QOL in some domains and poorer and less educated men experiencing disparities in pretreatment QOL in many domains. Blacks (b = −3.07, 95% confidence interval [CI] −5.13 to −1.01, $P = .004$) and Hispanics (b = −2.79, 95% CI −5.48 to −0.11, $P = .041$) had worse pretreatment urinary function than whites. In contrast, Hispanics reported less bowel bother than whites (b = 2.60, 95% CI 0.66-4.53, $P = .009$). Men with lower income had worse urinary function (b = 0.98, 95% CI 0.50-1.47, $P < .001$) and bother (b = 1.09, 95% CI 0.46-1.72, $P < .001$). Lower income was associated with worse sexual function (b = 1.63, 95% CI 0.77-2.48, $P < .001$) and more bowel bother (b = 0.46, 95% CI 0.06-0.86, $P = .025$). Lower education was associated with worse sexual function (b = 0.85, 95% CI 0.40-1.30, $P < .001$) and more sexual bother (b = 1.46, 95% CI 0.84-2.07, $P < .001$). Table 2 summarizes when results indicated disadvantage or advantage for the target groups.

Adjusted Differences in QOL by Race or Ethnicity

Along with potential covariates, adjusted models controlled for baseline function or bother. Table 2 also summarizes the evidence for disadvantages and advantages in post-treatment. QOL among blacks, Hispanics, men with low income, and men with low education. Among men receiving surgery, blacks (−2.55, 95% CI −4.75 to −0.35, $P = .023$) and Hispanics (−3.78 95% CI −6.37 to −1.19, $P = .004$) had worse bowel function after surgery compared with whites. However, the differences were eliminated over time. Bowel function among blacks and Hispanics improved more rapidly than that of whites such that by 2 years after treatment they had the same level of functioning as whites (blacks [1.25, 95% CI 0.36-2.14, $P = .006$]; Hispanics (1.05, 95% CI 0.10-2.01, $P = .03$]). Controlling for pretreatment sexual function, blacks also experienced faster and greater improvement in sexual function over time compared with whites (2.56, 95% CI 0.88-4.24, $P = .003$).

Among men who received radiotherapy, blacks reported less bowel bother compared with whites (3.20, 95% CI 0.59-5.81, $P = .016$). Over time, blacks' bowel bother improved, whereas scores remained relatively steady among whites over time (1.24, 95% CI 0.07-2.41, $P = .038$; Fig. 1).

Among men on active surveillance, Hispanics reported less sexual bother (10.34, 95% CI 1.05-19.63, $P = .029$) than whites.

Differences and Temporal Trends in QOL by Income

Controlling for pretreatment sexual bother, we found that among men who received surgery, men with lower income had greater sexual bother (2.42, 95% CI 0.64-4.20, $P = .008$) than men with higher incomes. They also experienced less improvement in urinary function over time than men with higher incomes (0.30, 95% CI 0.07-0.53, $P = .012$; Fig. 2). However, among men who received radiotherapy, lower income was associated with better sexual function (−1.17, 95% CI −2.16 to −0.18, $P = .021$).

Controlling for baseline QOL, men on active surveillance with lower incomes had worse bowel function (0.63, 95% CI 0.16-1.09, $P = .008$) and more sexual bother (1.99, 95% CI 0.10-3.87, $P = .039$).

Differences and Temporal Trends in QOL by Education

Controlling for pretreatment QOL, the only post-treatment difference as a function of education was in men on active surveillance: less educated men reported better bowel function (−0.26, 95% CI −0.51 to −0.003, $P = .047$) than more educated men.

DISCUSSION

Prior to treatment, minorities, poorer men and men with less education had worse functioning and more bother in several QOL domains. Lower pretreatment QOL among blacks[8,9] and poorer men[15] have been noted previously. This is important because pretreatment deficits (or advantages) in QOL predicted post-treatment QOL and are likely contributing to QOL deficits among disadvantaged men. Disparities in PCa QOL may in part be attributable to health disparities that affect historically disadvantaged populations over their life span. For example, chronic diseases of the circulatory system, diabetes, and some autoimmune disorders that are more common among minorities and people with low SES[16-18] are risk factors for sexual, urinary, and bowel dysfunction.[19-21]

Contrary to our hypotheses, adjusted models revealed few racial or ethnic disparities in QOL indicating that the disparities were rarely uniquely attributable to differential
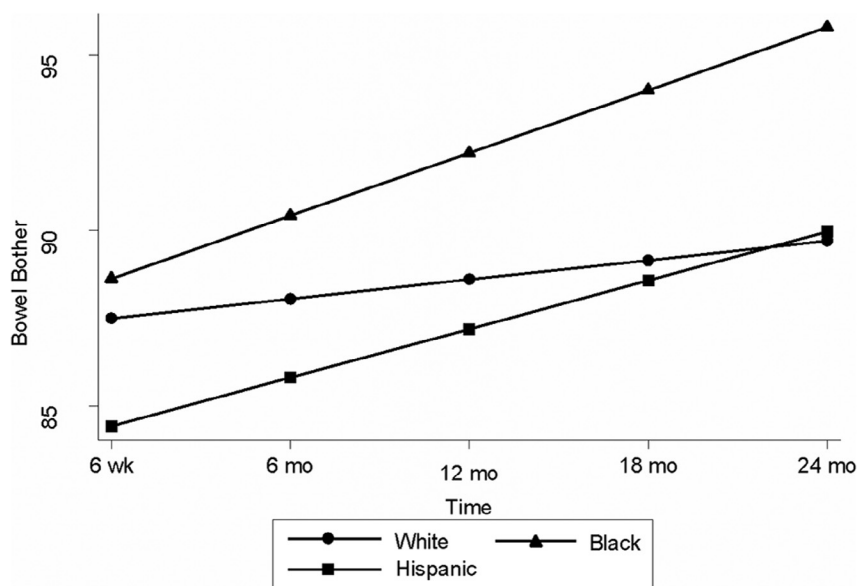
Figure 1. Post-treatment bowel bother over time among men treated with radiotherapy stratified by race or ethnicity. Higher scores indicate lower bother.
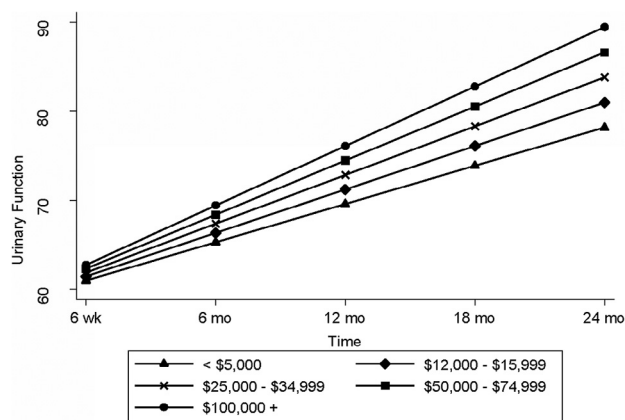

Figure 2. Post- treatment urinary function over time among men treated surgically stratified by income.

Are QOL Disparities Clinically Significant?

Skolarus et al have identified clinically minimally important differences (MIDs) on the EPIC-26 (highly correlated with EPIC-50[23]) by functional domain.[24] They report that differences in function ranging from 6 to 9 for the incontinence subscale and from 5 to 7 for the irritative or obstructive subscale of the urinary function (we report total urinary function scores), 4-6 for bowel function and 10-12 for sexual function are likely MIDs for clinical significance. Adjusted differences between our poorest and wealthiest participants in baseline functioning were approximately 7.8 and 13.0 points for urinary and sexual function, respectively. These meet or nearly meet MID thresholds. Differences as a function of education were smaller, as were differences by race or ethnicity. However, post-treatment differences in bowel function between minorities and whites approached these criteria. They were 3.6 for blacks and 3.8 for Hispanics.

Limitations

Attrition was a study limitation. Participants excluded from analyses of follow-up time points differed demographically and clinically from the sample that completed the baseline survey but did not differ with respect to QOL. In addition to avoiding attrition, we wished we had been able to recruit a larger sample of minorities, as there may have been disparities that we did not detect because of the small size of the minority groups. Another limitation is generalizability; participants were a convenience sample and findings may not generalize to all PCa survivors. Future work should address the need to explain disparities and advantages. Information about tumor biology, treatment, and follow-up clinical care could help explain the source of disparities and advantages. We also did not collect data on patients' expectations about side effects. It is possible that

consequences of treatment. Also, consistent with results from PCOS,[6] blacks had higher sexual function than whites prior to treatment and also experienced faster improvement after treatment. Black men treated with surgery reported worse bowel QOL than whites, but the reverse was true for men treated with radiotherapy. Poorer men may be at a disadvantage when men are treated surgically; men with lower income experienced more sexual bother and slower recovery in urinary function. Low income men could experience worse side effects from treatment if they receive different levels of follow-up care; for example, some health care plans do not cover treatments for erectile dysfunction. Men may also differ in how proactive they are in seeking treatment for side effects. In the PCa population in general, although to a lesser extent in our sample, access to high-quality initial treatment can also vary.[22]

disappointment due to discrepancies between pretreatment expectations and post-treatment reality[25] could result in lower perceived QOL.

CONCLUSION

The most common side effects of PCa treatment are urinary, sexual, and bowel function related; their impact on QOL can be substantial for many men.[26] As there are treatments and supports for men living with PCa treatment side effects,[27,28] future work should examine whether historically disadvantaged men, in particular poorer men, have access to the same level of post-treatment follow-up care as their more advantaged counterparts. Where there are known inequities such as for access to erectile dysfunction treatment, physicians and hospitals may need to advocate for their patients and for changes to payers' practices. As disparities in survivorship likely also reflect disadvantages in baseline health, primary care providers and even specialists may recognize a PCa diagnosis as a teachable moment for encouraging lifestyle change and better medication management in patients with comorbid chronic disease. Discussion about the role of these diseases in QOL may help to fully inform men about their health.

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APPENDIX

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.urology.2017.08.014.