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Quality of life in the year after new diagnosis with advanced prostate cancer for Black and White individuals living in the US

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Abstract

Purpose To assess differences in baseline and longitudinal quality of life among Black and White individuals in the US with advanced prostate cancer.

Methods Secondary analysis of data from the International Registry for Men with Advanced Prostate Cancer (IRONMAN) including US participants newly diagnosed with advanced prostate cancer and identifying their race as Black or White from 2017 to 2023. Participants completed the EORTC QLQ-C30 Quality of Life (QoL) Survey at study enrollment and every 3 months thereafter for up to 1 year of follow-up reporting 15 scale scores ranging from 0 to 100 (higher functioning and lower symptom scores represent better quality of life). Linear mixed effects models with race and month of questionnaire completion were fit for each scale, and model coefficients were used to assess differences in baseline and longitudinal QoL by race.

Results Eight hundred and seventy-nine participants were included (20% identifying as Black) at 38 US sites. Compared to White participants at baseline, Black participants had worse constipation (mean 6.3 percentage points higher; 95% CI 2.9–9.8), financial insecurity (5.7 (1.4–10.0)), and pain (5.1 (0.9–9.3)). QoL decreased over time similarly by race; most notably, role functioning decreased by 0.7 percentage points (95% CI −0.8, −0.5) per month.

Conclusion There are notable differences in quality of life at new diagnosis of advanced prostate cancer for Black and White individuals, and quality of life declines similarly in the first year for both groups. Interventions that address specific aspects of quality of life in these patients could meaningfully improve the overall survivorship experience.

Keywords Prostate cancer · Epidemiology · Racial disparities · Quality of life

Introduction

In the US, Black individuals have a 1.7 times higher incidence and 2.1 times higher mortality from prostate cancer compared to White individuals [1]. Patients with advanced disease experience the highest prostate cancer-associated morbidity and mortality, and Black individuals have the highest incidence of advanced disease resulting from cultural factors (e.g., mistrust of the medical system and more stigma around prostate cancer) and economic factors (e.g., poorer access to care and increased financial burden of treatment) driven by institutional racism [2, 3]. There are two major categories of advanced prostate cancer: metastatic hormone-sensitive (mHSPC) and castration-resistant prostate cancer (CRPC), both representing incurable states of disease [4].

Quality of life (QoL) is a multidimensional construct that comprises several aspects of the human experience including health and psychological status, independence, social relationships, environment, and personal beliefs. Integration of patient-reported outcome measures of QoL into routine oncology care represents a potential point for intervention to improve survivorship in prostate cancer populations. In a randomized trial of individuals with metastatic solid tumors, the group assigned to complete electronic patient-reported

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symptom measures with notifications sent to the care team for severe/worsening symptoms had a median overall survival time that was 20% longer than the control group [5]. Further, a 10-point increase in global QoL (on a scale of 0 to 100) on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) was associated with a 17% lower risk of death in a population of 1,097 prostate cancer patients with primarily localized disease [6].

Several population-based studies of racial disparities in QoL in individuals with localized prostate cancer have found poorer QoL in Black patients compared to White patients [7–10]. For example, in 1178 patients newly diagnosed with prostate cancer in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), Black patients had poorer QoL at baseline and slower improvement over time compared to White patients for numerous QoL scales from pain to mental health and physical functioning [7]. Importantly, these studies all focused on individuals with localized disease, neglecting to include those with advanced prostate cancer who face the most severe QoL burdens due to progressed disease and aggressive therapies.

Studies of QoL in advanced prostate cancer suffer from a lack of racial diversity, primarily because most previous studies have focused on the association between a specific disease-directed therapy and QoL in overwhelmingly White randomized controlled trial (RCT) populations [11–14]. Black individuals are underrepresented in RCT populations due to factors such as fewer clinical trials being offered at institutions where they receive care and bias in health professionals in recommending trial enrollment; as such, investigation of racial disparities in QoL is typically not possible in this setting [3].

Observational studies represent a promising means to investigate QoL independent of a specific disease-directed therapy; however, recent observational studies of QoL in populations with advanced prostate cancer have also only focused on White individuals [15, 16]. For example, a study of 280 White patients with advanced prostate cancer across seven countries in 2007 found a steady decline in QoL over the first year after study enrollment [15]. As Black individuals are the population that is most affected by advanced prostate cancer, there is a need to extend this work into understanding QoL into this population. Identifying specific unmet QoL needs in Black individuals with advanced prostate cancer would meaningfully improve the survivorship experience for this population and also has the potential to decrease racial disparities in overall survival with prostate cancer through intervention on specific QoL detriments.

This study used patient-reported measures to examine racial differences in QoL among individuals newly diagnosed with mHSPC or CRPC in the International Registry for Men with Advanced Prostate Cancer (IRONMAN). We assessed differences in baseline and longitudinal QoL at 3-month intervals over the first year after new diagnosis with mHSPC or CRPC using the EORTC QLQ-C30 questionnaire. We described overall group differences in trajectories of functional status and symptom domains of QoL among IRONMAN participants identifying as Black or White in the US.

Patients and methods

Study participants

Study participants included individuals enrolled in the IRONMAN registry (NCT 03151629) between July 21, 2017 and January 23, 2023. Participants are recruited through IRONMAN-affiliated clinicians at approximately 100 study sites in 16 countries, and detailed data are collected at study enrollment (corresponding to those newly diagnosed with mHSPC or CRPC with no more than 90 days of systemic therapy prior to enrollment for patients with CRPC and no more than 90 days of active therapy for patients with mHSPC) and throughout a follow-up period of at least 5 years [17]. Study sites span academic, private practice, and government health centers and are primarily located in urban centers in regions with high prostate cancer mortality. All study participants gave written informed consent prior to study enrollment and were able to withdraw from the study at any time. Because race has different social and historical contexts with different classifications in different global regions, this analysis focuses specifically on participants enrolled in the US (38 study sites located in 21 states).

Outcome measure: Quality of life (EORTC QLQ-C30 version 3)

QoL was measured with the EORTC QLQ-C30 over a period of up to 12 months, with assessments performed at study enrollment and 3, 6, 9, and 12 months afterward. Surveys were self-administered using a web-based platform (TrueNth) or paper questionnaires [18]. The EORTC QLQ-C30 survey consists of 2 questions on global health status (1–7 Likert scale, "very poor" to "excellent"), 15 questions on functional status (1–4 Likert scale, "not at all" to "very much"), and 13 questions on symptom status (1–4 Likert scale, "not at all" to "very much"). The 30 questions are combined and linearly transformed to 15 scale scores with a range of 0–100. The instrument covers five functional scales (physical, role, emotional, cognitive, and social) with higher scale scores representing better functioning in the domain. In addition, nine symptom scales were assessed (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss,

constipation, diarrhea, and financial difficulties) with higher scale scores representing more severe symptoms.

The EORTC QLQ-C30 questionnaire has shown high construct validity and good reliability in a population of cancer patients and a racially diverse population over the age of 50 years with similar factor structures by race [19, 20]. The EORTC recommends using a minimally important difference (MID) of 5–10 points for interpreting both group differences in QLQ-C30 scale scores as well as changes in scores over time [21]; a study of EORTC outcomes in clinical trials of disease-directed therapies validated this estimate in a population of patients with prostate cancer [22]. Prior to February 20, 2020, IRONMAN participants could complete the questionnaire two weeks before or after the target date; this was subsequently adjusted to be ± three months of the target date to improve study feasibility.

Demographic and clinical characteristics

Demographic information (age, highest level of education, employment status, marital status, military status, race, ethnicity) was collected through a patient-reported questionnaire at study enrollment. Clinical variables (disease state at enrollment, Gleason score, prostate-specific antigen (PSA) level, treatment at baseline, metastatic status at baseline, and type of health center) were abstracted from patient medical records and entered by study sites.

Race was self-reported by participants at study enrollment, allowing multiple selection from the following categories: White/Caucasian, African/African American/Black/Black British/Caribbean, Asian/Asian American/Asian British, Native Hawaiian or Other Pacific Islander, American Indian/Alaska Native, Middle Eastern, and other. Ethnicity was self-reported by participants choosing between "Hispanic/Latino" and "not Hispanic/Latino" categories. This study focuses specifically on individuals self-identifying their race as only Black or White regardless of their ethnicity.

Age at study enrollment (years) was included as a continuous variable. Disease state at enrollment was categorized as mHSPC (de novo metastatic disease at diagnosis or progressed to metastasis after localized prostate cancer diagnosis) and m0 or m1 CRPC (progression of disease while on androgen deprivation therapy or with castrate level of testosterone as determined by the investigator).

Statistical analysis

We summarized demographic and clinical participant characteristics, stratified by self-reported race. We calculated the 15 EORTC scale scores described above for each individual at each time point if the questionnaire and all required questions for each scale were complete [23]. Missing individual covariates and EORTC scale scores on completed questionnaires were imputed using multiple imputation by chained equations (MICE) [24] with the data in wide format. Scale scores in which the entire questionnaire was missing were temporarily given a value of − 250 as a numerical, proxy missing indicator to ensure that these scores would not be imputed. MICE was conducted using classification and regression trees with 10 iterations for each of 10 imputations and with the scale scores constrained between 0 and 100 (inclusive of the bounds). Subsequently, scale scores for missing questionnaires were re-marked as missing. Sensitivity analyses were conducted with different values for the missing indicator.

Longitudinal missingness in questionnaires was assessed, and an in-depth description of missing data exploration is included in the Supplementary Methods. As no clear patterns of reasons for missing whole questionnaires arose from these analyses, we fit linear mixed effects models for each of the fifteen scale scores with timepoints clustered within participant who were then clustered within study site. Initial models included only race, month of follow-up questionnaire time point (continuous), and their interaction, assuming a linear relationship between the outcome scale and time. As we were interested in overall differences by self-reported race, adjusted models additionally controlled for time-invariant variables (age at study enrollment and disease state at enrollment). We did not control for variables that may mediate the association between self-reported race and QoL (e.g., employment, marital status, etc.) in the statistical models [25]. Baseline differences and differences in longitudinal trajectories in each scale by race were estimated and pooled using Rubin's Rules [26]. A sensitivity analysis excluding individuals who were censored due to being off-study was conducted. Figures depicting these trajectories by race using model coefficients were created to visualize trends. The longitudinal analyses were additionally stratified by disease state at enrollment to determine differences for participants with mHSPC and CRPC.

Additional methods information can be found in the Supplementary Methods. All analyses were completed using R version 4.1.0 with statistical significance assessed at the 0.05 level.

Patient involvement

A Black advanced prostate cancer survivor and long-time patient of one of the IRONMAN lead investigators with decades of experience as an advocate in his community was involved in setting the research question, study design, interpretation of the research findings, and review of the manuscript. With the goal of increasing the accessibility of this manuscript to patients and individuals outside of

academia, we have included a *glossary of technical terms* in the supplementary material.

Results

Participant characteristics

This study included 879 participants from IRONMAN self-identifying as White ($N = 704$, 80%) or Black ($N = 175$, 20%) and receiving care at 38 study sites across the US (Fig. 1, Supplementary Table S1). IRONMAN participants enrolled outside of the US ($N = 1979$), missing data on disease state ($N = 7$), and missing race data or identifying with a race that was not Black or White ($N = 227$) were excluded from the analysis to specifically focus on QoL disparities within the US context of race. Demographic and clinical characteristics for the sample, stratified by self-reported race, are shown in Table 1. For the entire cohort, the mean age at enrollment was 69.1 years with a standard deviation of 8.9 years, and most of the participants (65.2%) had mHSPC compared to CRPC (34.8%).

Differences by self-reported race were noted across many of the demographic and clinical characteristics (Table 1). Black participants were diagnosed with advanced prostate cancer at a younger age, reported lower education, were less likely to be married, were more likely to be disabled, had higher first on-study PSA levels, and had a shorter time on study on average compared to White participants. The most commonly received therapies at any point in the first year on study were androgen deprivation therapy (ADT) (88.9%), androgen receptor signaling inhibitors (ARSIs) (61.7%), and chemotherapy (17.5%) (Supplementary Table S2).

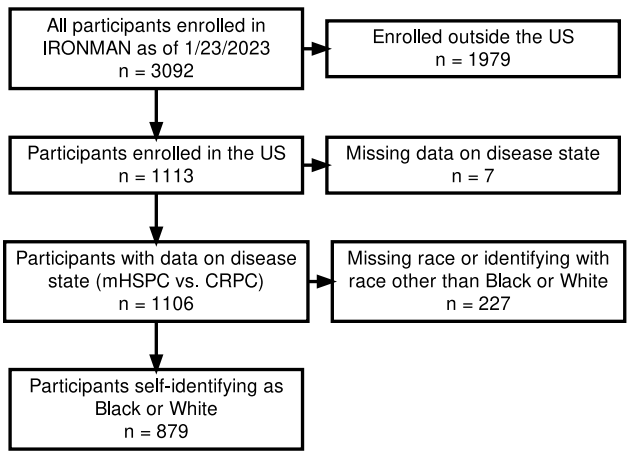

Fig. 1 Selection of study population for analysis of patient-reported outcome measures (IRONMAN, 2017–2023)

Overview of missing data

The proportion of participants completing questionnaires, missing questionnaires, or being off-study is represented in Fig. 2A. Eighty-seven percent of participants completed the baseline questionnaire, declining to 74% completion by individuals on study at month 12.

The longitudinal missing data patterns for full questionnaires are depicted in Fig. 2B. Thirty-nine percent of participants completed questionnaires at all five timepoints. The remainder of study participants exhibited 30 distinct missing non-monotone data patterns. Participants who completed the baseline questionnaire were older, had lower education, were more likely to be retired, and had lower first on-study PSA compared to those who did not complete the baseline questionnaire (Supplementary Table S3). Among participants who were on study at month 12 and reached that timepoint, participants who completed the month 12 questionnaire had higher education, were more likely to be retired, and had lower first on-study PSA compared to those who did not complete the month 12 questionnaire (Supplementary Table S4).

Baseline differences in QoL by race

Baseline results from the longitudinal analyses are shown in Table 2. Overall, participants tended to have high functioning and low symptom burden across each of the scales. White participants had mean functioning scale scores ranging from 80.4 (95% CI 77.7, 83.2) for role functioning to 84.2 (95% CI 82.3, 86.2) for cognitive functioning (on a scale of 0–100; higher score is indicative of higher QoL) at the baseline questionnaire. Symptom burden for White participants was generally low, and the most disruptive symptoms for White participants were sleep problems with a mean scale score of 30.3 (95% CI 27.6, 33.0) and fatigue with a mean scale score of 30.1 (95% CI 27.7, 32.6) (on a scale of 0–100; higher score is indicative of worse QoL).

Compared to White participants, Black participants reported several differences in QoL domains at baseline. Black participants had better emotional functioning (comprising questions about anxious and depressive symptoms) at baseline (increase of mean 4.4 percentage points, 95% CI 1.4, 7.5) compared to White participants. However, Black participants reported worse pain (5.1 point increase, 95% CI 0.9, 9.3) and financial insecurity (7.0 point increase, 95% CI 2.7, 11.4) compared to White participants. Scale scores varied substantially more between participants than between study sites.

Table 1 Cohort demographic and clinical characteristics by self-reported race ($N=879$), 2017–2023

	White ($N=704$)	Black ($N=175$)
Age at study entry, years		
Mean (SD)	69.5 (9.0)	67.2 (8.7)
Hispanic/Latino		
No	657 (97%)	156 (96%)
Yes	22 (3%)	6 (4%)
Missing	$n=25$	$n=13$
Disease state at enrollment		
CRPC	241 (34%)	65 (37%)
mHSPC	463 (66%)	110 (63%)
Highest education level at baseline		
Less than college	29 (14%)	18 (43%)
Some college or bachelor's degree	72 (35%)	13 (31%)
Vocational school/program	2 (1%)	1 (2%)
Graduate degree	101 (49%)	9 (21%)
Other	3 (1%)	1 (2%)
Missing	$n=497$	$n=133$
Marital status at baseline		
Married	545 (78%)	88 (51%)
In a civil partnership	20 (3%)	2 (1%)
Widowed	29 (4%)	12 (7%)
Divorced/separated	76 (11%)	43 (25%)
Never married	28 (4%)	26 (15%)
Missing	$n=6$	$n=4$
Employment status at baseline		
Retired	408 (58%)	82 (48%)
Working full-time	200 (29%)	45 (26%)
Working part-time	58 (8%)	11 (6%)
Unemployed	12 (2%)	16 (9%)
Disabled	22 (3%)	17 (10%)
Missing	$n=4$	$n=4$
Member of national military at baseline		
Yes, currently or previously	182 (33%)	37 (28%)
No, I have never served in the national military	364 (67%)	97 (72%)
Missing	$n=158$	$n=41$
Prostatectomy or biopsy Gleason score		
6 or less	26 (5%)	3 (2%)
7	163 (28%)	45 (34%)
8	106 (18%)	20 (15%)
9–10	278 (49%)	63 (48%)
Missing	$n=131$	$n=44$
First on-study PSA (ng/mL)		
Mean (SD)	88.6 (484.8)	156.9 (396.3)
Missing	$n=33$	$n=8$
Metastases at baseline		
No	65 (9%)	12 (7%)
Yes	639 (91%)	163 (93%)
Type of health center		
Clinic	30 (4%)	7 (4%)
Hospital	125 (18%)	21 (12%)
NCI-designated	535 (76%)	131 (75%)
VA	14 (2%)	16 (9%)
Time on study (months)		
Mean (SD)	28.9 (17.4)	24.8 (17.2)

mHSPC metastatic hormone-sensitive prostate cancer, *CRPC* castration-resistant prostate cancer, *PSA* prostate-specific antigen

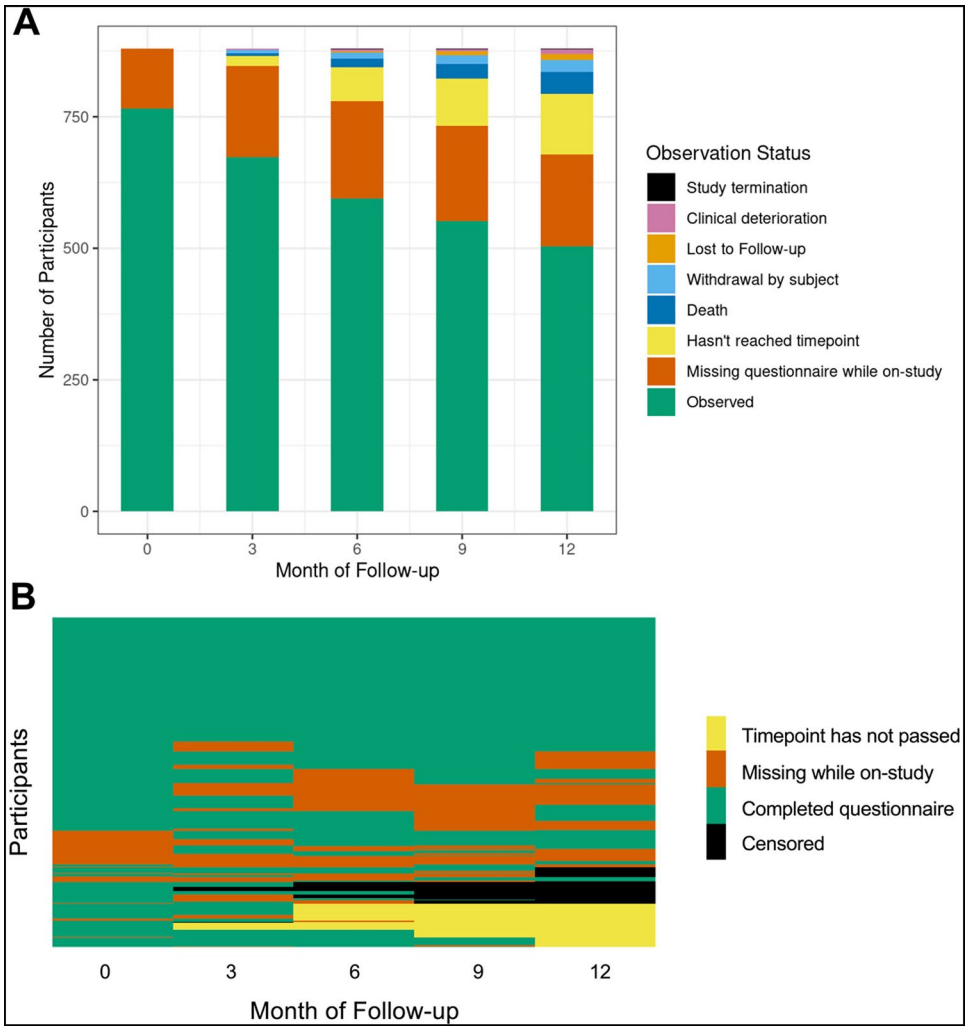

Fig. 2 Overview of longitudinal missing data of cohort in first year of enrollment. **A** Proportion of questionnaire completeness and reasons for incompleteness at each timepoint. **B**: Longitudinal completion of questionnaires for each participant ($N = 897$)

Longitudinal differences in QoL by race

Trajectory results from the longitudinal analyses are provided in Table 3, with a graphical representation provided in Fig. 3. For the majority of scales, White participants showed a decline in QoL over time. Role functioning (the ability to accomplish daily activities) declined most sharply of the functioning scales, with scores for White participants losing 0.7 percentage points on average per month (95% CI − 0.8, − 0.5). Fatigue worsened most sharply of the symptom scales, with scores for White participants gaining 0.6 percentage points on average per month (95% CI 0.5, 0.7).

Black and White participants had similar trajectories in QoL over their first year after enrollment. In a few scales, Black participants had slower decline or faster improvement compared White participants. Most notably, reported financial security for Black participants improved by an additional 0.6 percentage points per month compared to White participants (95% CI − 0.8, − 0.4). The results for both baseline and longitudinal differences in the scale scores were robust to sensitivity analyses with different values for the missing indicator in the MICE procedure (Supplementary Table S5) as well as when individuals who were off-study at any point in the first year were excluded (Supplementary Table S6). When stratified by disease state at study enrollment, results were largely the same across participants with mHSPC and CRPC (Supplementary Tables S7 and S8).

Discussion

In a nationwide sample of 879 individuals with advanced prostate cancer in the US participating in the IRONMAN registry, we found that our study population had better functioning and fewer symptoms at study enrollment compared to the EORTC recurrent/metastatic prostate cancer reference population across all but two scales (diarrhea and financial insecurity) [27]. For example, compared to our study population, the EORTC reference population had poorer global QoL (mean 62.1) and role functioning (mean 67.0) and

Table 2 EORTC QLQ-C30 quality of life scale scores at study enrollment for White and Black participants ($N=879$)

	Score for White participants	Difference for Black participants		Standard deviation of participant random effect	Standard deviation of site random effect
		Mean (95% CI), $N=175$[a]			
	Mean (95% CI), $N=704$	Unadjusted	Adjusted		
Global Quality of Life (QL)[1]	70.9 (68.8, 73.0)	− 0.6 (− 4.0, 2.9)	− 0.7 (− 4.2, 2.8)	15.4	3.3
Functioning Scales[1]					
Physical (PF)	84.1 (81.6, 86.6)	− 1.0 (− 4.3, 2.3)	− 2.0 (− 5.2, 1.2)	15.0	4.9
Emotional (EF)	81.3 (79.3, 83.1)	**4.4 (1.4, 7.5)**	**5.0 (2.0, 8.0)**	13.6	3.0
Social (SF)	80.5 (78.1, 83.0)	0.7 (− 3.1, 4.6)	0.9 (− 3.0, 4.7)	16.3	4.6
Role (RF)	80.4 (77.7, 83.2)	− 0.2 (− 4.6, 4.2)	− 0.5 (− 4.9, 3.9)	18.7	5.0
Cognitive (CF)	84.2 (82.3, 86.2)	0.5 (− 2.5, 3.6)	0.4 (− 2.6, 3.5)	13.8	3.5
Symptom Scales[2]					
Fatigue (FA)	30.1 (27.7, 32.6)	− 1.8 (− 5.7, 2.0)	− 1.8 (− 5.7, 2.1)	17.3	4.5
Nausea/vomiting (NV)	4.1 (3.3, 4.9)	**2.8 (1.0, 4.6)**	**2.4 (0.6, 4.1)**	7.1	0.2
Pain (PA)	19.0 (16.4, 21.6)	**5.1 (0.9, 9.3)**	**4.5 (0.3, 8.6)**	18.3	4.9
Dyspnea (DY)	13.8 (11.7, 15.9)	0.6 (− 3.2, 4.4)	1.2 (− 2.7, 5.0)	17.4	2.9
Sleep (SL)	30.3 (27.6, 33.0)	**− 7.3 (− 11.9, − 2.7)**	**− 7.9 (− 12.5, − 3.3)**	20.0	3.7
Appetite (AP)	10.7 (8.8, 12.6)	2.3 (− 1.1, 5.7)	2.2 (− 1.2, 5.6)	13.9	2.8
Constipation (CO)	12.3 (10.6, 14.0)	**6.0 (2.5, 9.5)**	**6.3 (2.9, 9.8)**	14.5	1.4
Diarrhea (DI)	10.3 (8.5, 12.1)	− 1.4 (− 4.4, 1.6)	− 1.7 (− 4.7, 1.3)	11.4	3.1
Financial insecurity (FI)	16.4 (13.8, 19.0)	**7.0 (2.7, 11.4)**	**5.7 (1.4, 10.0)**	20.2	4.2

Bolded represents statistical significance at the 0.05 level

Unadjusted model includes race as the only covariate. Adjusted model additionally includes age and disease state (mHSPC or CRPC) at study enrollment

All scale scores are rated on a scale of 0–100; [1]a higher score is indicative of higher quality of life for the global and functioning scales, [2]while a lower score is indicative of a higher quality of life for the symptom scales

[a]Interpretation: mean change in EORTC scale score at enrollment for Black participants compared to White participants. For the global and functioning scales, a positive number represents higher quality of life for Black participants compared to White participants. For the symptom scales, a positive number represents lower quality of life for Black participants compared to White participants

worse pain (mean 38.6) and constipation (mean 27.1). These differences are likely due to the EORTC reference population being more diverse and representative of all individuals with advanced prostate cancer (rather than only those receiving care at highly resourced IRONMAN study sites); additionally, the EORTC population only includes individuals who have not yet begun treatment for their prostate cancer, potentially resulting in lower QoL due to higher disease burden at the time of questionnaire completion.

At study enrollment, Black and White participants reported a number of differences in QoL, and the majority of statistically significant differences that we found by race at baseline also reach the 5-point minimally important difference recommended by the EORTC; thus, our findings represent clinically meaningful racial differences as well. Some previous studies in populations with localized prostate cancer suggested that Black individuals have poorer QoL in all domains at baseline compared to White individuals [9, 28], while others reported similar QoL across domains by race [29, 30] or higher QoL in Black individuals [31–33]. Our study suggests that, at the time of new diagnosis with advanced prostate cancer, Black individuals have either similar or worse QoL compared to White individuals. One exception to this is that Black participants reported better baseline emotional functioning than White participants in our study. A 2014 study of 50,856 individuals with prostate cancer in the SEER-Medicare database similarly found that Black individuals had a lower risk of clinically diagnosed mental health disorders compared to White individuals [32]. These findings could be a result of increased stigma around mental health disorders in Black communities leading to underreporting of true symptoms in our study population [34]. Assuming true symptoms were reported, one of many possible explanations for higher emotional functioning in Black participants is higher levels of spirituality leading to better QoL. Numerous studies have shown that spirituality and religiosity are positively associated with well-being in prostate cancer populations often due to increased

Table 3 Longitudinal changes in EORTC QLQ-C30 scale per month for White and Black participants during the first month after study enrollment ($N = 879$)

	Change per month for White participants[a]		Additional change for Black participants[b]	
	Mean (95% CI), $N = 704$		Mean (95% CI), $N = 175$	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Global Quality of Life (QL)[1]	**− 0.4 (− 0.5, − 0.2)**	**− 0.4 (− 0.5, − 0.2)**	0.1 (− 0.2, 0.4)	− 0.1 (− 0.2, 0.1)
Functioning Scales[1]				
Physical (PF)	**− 0.6 (− 0.7, − 0.5)**	**− 0.6 (− 0.7, − 0.5)**	0.1 (− 0.1, 0.4)	**− 0.4 (− 0.5, − 0.3)**
Emotional (EF)	− 0.1 (− 0.2, 0)	− 0.1 (− 0.2, 0)	0.1 (− 0.2, 0.4)	**0.3 (0.2, 0.4)**
Social (SF)	**− 0.3 (− 0.4, − 0.1)**	**− 0.3 (− 0.4, − 0.1)**	0.1 (− 0.3, 0.5)	0.1 (− 0.1, 0.2)
Role (RF)	**− 0.7 (− 0.8, − 0.5)**	**− 0.6 (− 0.8, − 0.5)**	0.3 (− 0.1, 0.7)	− 0.1 (− 0.3, 0)
Cognitive (CF)	**− 0.3 (− 0.5, − 0.2)**	**− 0.3 (− 0.5, − 0.2)**	0.3 (0, 0.7)	0 (− 0.1, 0.1)
Symptom Scales[2]				
Fatigue (FA)	**0.6 (0.5, 0.7)**	**0.6 (0.5, 0.7)**	**− 0.5 (− 0.9, − 0.2)**	0 (− 0.1, 0.2)
Nausea/vomiting (NV)	0 (− 0.1, 0.1)	0 (− 0.1, 0.1)	− 0.1 (− 0.3, 0.1)	**− 0.2 (− 0.2, − 0.1)**
Pain (PA)	**0.4 (0.2, 0.6)**	**0.4 (0.2, 0.6)**	− 0.2 (− 0.6, 0.2)	**− 0.3 (− 0.4, − 0.1)**
Dyspnea (DY)	**0.6 (0.4, 0.7)**	**0.6 (0.4, 0.7)**	− 0.1 (− 0.4, 0.3)	0.2 (0, 0.3)
Sleep (SL)	0.1 (− 0.1, 0.3)	0.1 (− 0.1, 0.3)	0.2 (− 0.3, 0.6)	**− 0.3 (− 0.5, − 0.2)**
Appetite (AP)	0.1 (− 0.1, 0.2)	0 (− 0.1, 0.2)	0 (− 0.4, 0.4)	0 (− 0.1, 0.1)
Constipation (CO)	**0.2 (0.1, 0.4)**	**0.2 (0.1, 0.4)**	− 0.3 (− 0.7, 0.1)	0.1 (0, 0.2)
Diarrhea (DI)	0.1 (0, 0.2)	0.1 (− 0.1, 0.2)	− 0.1 (− 0.5, 0.2)	− 0.1 (− 0.2, 0)
Financial insecurity (FI)	− 0.1 (− 0.3, 0.1)	− 0.1 (− 0.3, 0)	− 0.2 (− 0.6, 0.2)	**− 0.6 (− 0.8, − 0.4)**

Bolded represents statistical significance at the 0.05 level

Unadjusted model includes race as the only covariate. Adjusted model additionally includes age and disease state (mHSPC or CRPC) at study enrollment

All scale scores are rated on a scale of 0–100; [1]a higher score is indicative of higher quality of life for the global and functioning scales, [2]while a lower score is indicative of a higher quality of life for the symptom scales

[a]Interpretation: the mean change in EORTC scale score per month for White participants. For the global and functioning scales, a positive number represents an increase in quality of life over time. For the symptom scales, a positive number represents a decrease in quality of life over time

[b]Interpretation: the mean additional change in EORTC scale score per month for Black participants compared to White participants. Adding this number to the change in score per month for White participants gives the change in score per month for Black participants

hopefulness and positivity [35], and this is particularly important for Black populations where spirituality tends to be an integral part of daily life [36]. Health professionals should be supportive of the role that spirituality can play to support overall QoL in Black populations.

Longitudinally, QoL generally declined for both Black and White participants in our study during their first year after enrollment in IRONMAN. A previous study of White individuals with advanced prostate cancer found declines in QoL corresponding to between 3 and 17 points on the EORTC scales over the first 9 months after enrollment [15]. We observed declines in the QoL scales by three to seven points in our study population over the first year, indicating that, while both populations experienced declines in QoL over time, the IRONMAN population exhibited a less steep decline in QoL compared to this previous study. Again, this is likely due to the IRONMAN population most commonly receiving care at highly resourced centers that can provide additional supports for patients when needed. Regardless, a monthly change of approximately 0.4 percentage points per month in our study correlates to the clinically meaningful change of 5 percentage points in a year [22], demonstrating that the majority of statistically significant changes that we find in QoL over time are also clinically meaningful for the participant and their cancer care.

Many factors can mediate the association between race and QoL in patients with prostate cancer and are worth investigating in future studies as potential points of intervention. One such potential mediator is therapy received, especially because Black individuals with advanced prostate cancer are less likely to receive aggressive treatments compared to White individuals [37]. The majority of participants in our study population received ADT and/or ARSIs in their first year on study. Multiple randomized controlled trials in advanced prostate cancer populations have shown changes in QoL after treatment with various combinations of ADT and ARSIs with and without other treatment options including chemotherapy and radiotherapy for advanced prostate cancer

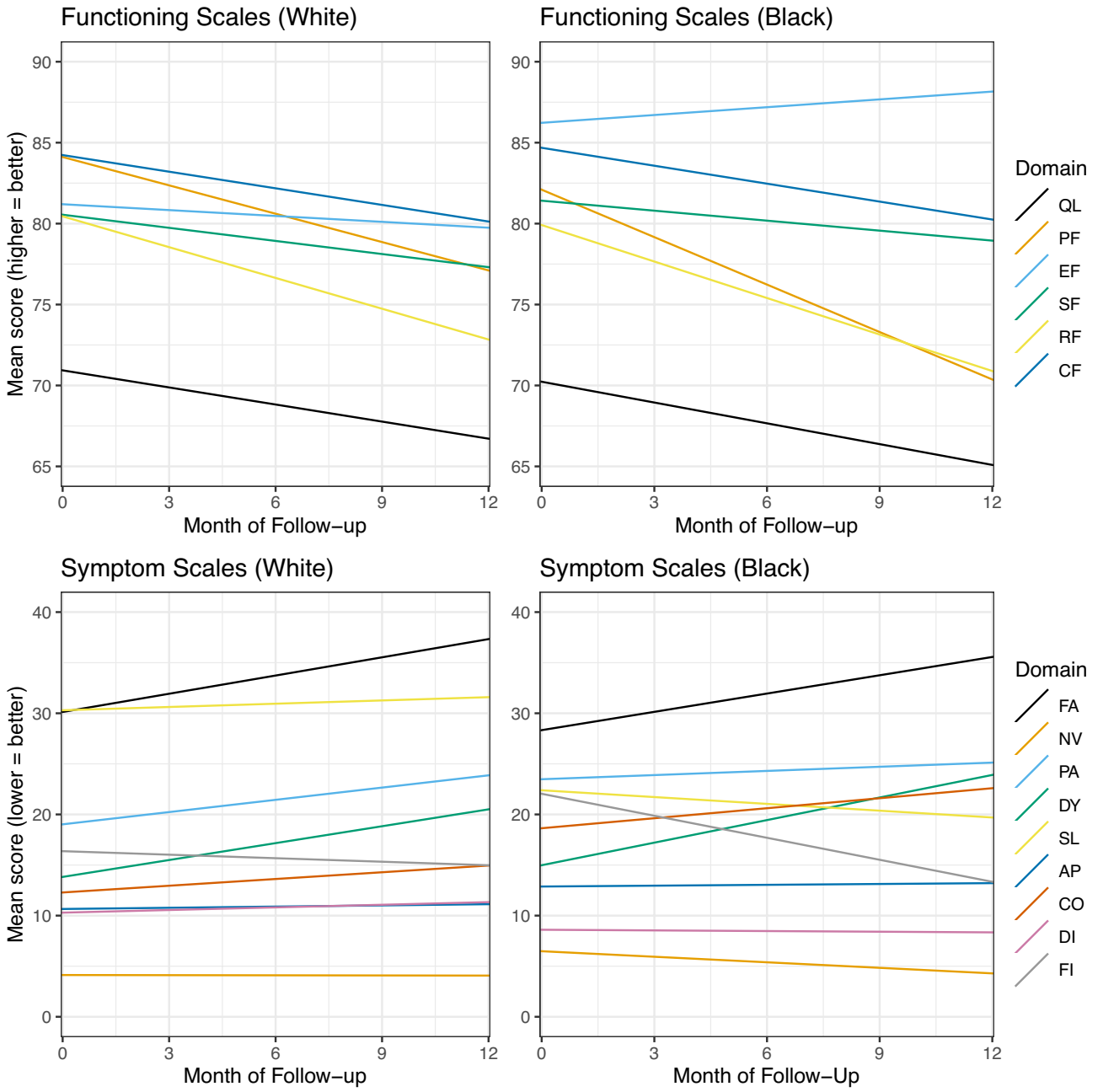

Fig. 3 Longitudinal trajectories in EORTC QLQ-C30 scale scores. **A** Trajectories of functioning scales for White participants. **B** Trajectories of functioning scales for Black participants. **C**: Trajectories of symptom scales for White participants. **D** Trajectories of symptom scales for Black participants. QL = global quality of life, PF = physical functioning, EF = emotional functioning, SF = social functioning, RF = role functioning, CF = cognitive function, FA = fatigue, NV = nausea/vomiting, PA = pain, DY = dyspnea, SL = sleep, AP = appetite, CO = constipation, DI = diarrhea, FI = financial insecurity

[38–41]. These therapies have the ability to improve QoL by decreasing disease burden; however, these therapies are also known to have side effect profiles that can worsen QoL including increased risk of inflammatory rheumatic diseases and back pain [42, 43]. Health professionals should monitor treatment side effects and adjust regimens accordingly to ensure that QoL is negatively impacted as little as possible.

Other potential mediators are social factors that differ by race such as access to social determinants of health resources that support a nutritious diet, physical activity and dietary supplements, quiet living spaces to support high

quality sleep, and access to healthcare resources to decrease treatment side effects, among others [44]. Health institutions should strive to support their patients' socioeconomic needs outside the hospital as much as possible as these are fundamental for improving QoL and overall health. Our study lays the foundation for future studies to investigate the mechanisms underlying differences in QoL seen here and determine the impact of specific interventions on QoL and overall survival.

There are several potential limitations of this study. First, this study focuses specifically on participants self-identifying their race as either Black or White; it is important to expand this research among more diverse populations. Second, the EORTC QLQ-C30 questionnaire has not specifically been validated in this study population; however, the majority of scales have shown high reliability in a racially diverse population over the age of 50 years with similar factor structures in Black and White individuals that reflect our study population [45, 46]. Finally, these results may not be generalizable to individuals who choose not to participate in IRONMAN or individuals receiving care at other health centers within or outside of the US. Centers participating in IRONMAN tend to be highly resourced and located in urban environments; individuals living in more rural areas of the US or receiving care at urban centers with less clinical trial infrastructure could have different distributions and trajectories of QoL.

Our study expands QoL research into a more racially diverse population of individuals diagnosed with advanced prostate cancer. We found that Black participants tended to report poorer QoL at diagnosis compared to White participants, and QoL decreased similarly over time for both groups. We identified clinically meaningful increased pain, constipation, and financial insecurity for Black participants; health professionals shouldask about and address these symptoms as needed with clinical treatments and support navigating healthcare costs to improve QoL for this population. As QoL decreased over the first year on study for both Black and White participants, there is a need for health professionals to monitor QoL longitudinally and adjust support as needed to improve survivorship. Our study additionally highlights opportunities for deeper investigation into QoL interventions to improve the prostate cancer survivorship experience and potentially improve overall survival for this patient population, particularly for Black individuals who face the greatest burden of advanced prostate cancer.

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Data availability Raw data was provided by the Prostate Cancer Clinical Trials Consortium (PCCTC), and investigators are not approved to share raw data with others directly. Researchers interested in working with the IRONMAN data can submit a study proposal to PCCTC to obtain access.

Declarations

Competing interest AM consults for Astellas, AstraZeneca, AAA, Bayer, Dendreon, Exelixis, Janssen, Pfizer, Myovant, Novartis, Myriad Genetics, Lantheus, Telix, Sanofi and receives research funding from Astellas, Bayer, Pfizer, Myovant, Sanofi, SeaGen. PB consults for Astellas, AVEO Oncology, Bayer, BMS, Dendreon, Eisai, Exelixis, Janssen, EMD Serono, Guardant Health, Pfizer, Seattle Genetics; receives research support from AstraZeneca, AVEO Oncology, BlueEarth Diagnostics, Merck, Natera, Caris Life Sciences; and is part of the speaker's bureau for Bayer, Caris Life Sciences, Pfizer, Myovant, Natera. HHC receives institutional research support from Astellas, Clovis Oncology, Color Genomics, Janssen, Medivation, Promontory Therapeutics, Sanofi; consults for AstraZeneca; and receives royalties from UpToDate. RD consults for Astellas, Aveo, Bayer, Exelixis, Gilead, Hinova, Janssen, Merck, Pfizer, Sanofi Genzyme, Tavanta. EH consults for Astellas Pharma, Bayer, Janssen Research & Development LLC, Sanofi; receives paid travel from Astellas Pharma, Caris Life Sciences, Sanofi, Seattle Genetics; receives research funding from Astellas Pharma, Arvinas, AstraZeneca, BioXcel Therapeutics, Bristol-Myers Squibb, Calibr, Calithera Biosciences Inc, Caris Life Sciences, Corcept Therapeutics, Corvis Pharmaceuticals, Daiichi Sankyo Inc, Eisai Inc, Exelixis, Five Prime Therapeutics, Fortis Therapeutics, GlaxoSmithKline, Gilead Sciences Inc, Harpoon Therapeutics, Hoffman-La Roche, Infinity Pharmaceuticals, iTeos Therapeutics, Janssen Research & Development LLC, Merck Sharp & Dohme Merck, Mirati Therapeutics, Modra Pharmaceuticals, Oncolys BioPharma, Peloton Therapeutics Inc, Pfizer, Pharmacyclics LLC, POINT Biopharma, Seattle Genetics; and receives honoraria from Bayer, Sanofi, and Seattle Genetics. RRM consults for Aveo, AstraZeneca, Bayer, BMS, Calithera, Caris, Dendreon, Exelixis, JNJ, Lilly, Myovant, Merck, Novartis, Pfizer, Sanofi, Sorrento Therapeutics, Telix, Tempus; receives research funding from Bayer, Tempus, AstraZeneca, Oncternal Therapeutics. DR receives institutional research support from Janssen, Bayer, AstraZeneca, Genentech, BMS/Celgene, Taiho, Promontory; serves on the board for Janssen, AstraZeneca, Bayer, Myovant, Genentech, Promontory, BMS/Celgene. ST receives institutional research support from Sanofi, Medivation, Astellas, Janssen, Amgen, Progenics, Dendreon, Lilly, Genentech, Newlink, BMS, Inovio, AstraZeneca, Immunomedics, Aveo, Rexahn, Atlab, Boehringer Ingelheim, Millennium, Bayer, Merck, Abbvie, Karyopharm, Endocyte, Clovis, Seattle Genetics, Novartis, Gilead, POINT Biopharma, Ambrx; consults for Sanofi, Medivation/Astellas, Dendreon, Janssen, Genentech, Bayer, Endocyte, Eisai, Immunomedics, Karyopharm, Abbvie, Tolmar, Seattle Genetics,

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Ethical approval The original project underwent ethics review and was approved by the Institutional Review Board of the Harvard T. H. Chan School of Public Health. Informed consent was obtained from all participants in the IRONMAN Registry and included consent to access their personal demographic and health information in addition to use of their de-identified data for analyses using IRONMAN Registry data. The authors received access to de-identified IRONMAN registry data for the analyses presented here through an arrangement between the Harvard T. H. Chan School of Public Health and the Prostate Cancer Clinical Trials Consortium (the Clinical and Data Coordination Center for the IRONMAN Registry).

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