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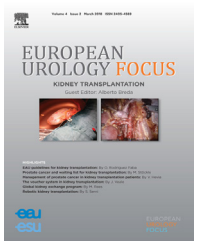

Prostate Cancer

Diet and Health-related Quality of Life Among Men on Active Surveillance for Early-stage Prostate Cancer: The Men's Eating and Living Study (Cancer and Leukemia Group 70807 [Alliance])

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Abstract

Background: Health-related quality of life (HRQoL) among patients with localized prostate cancer (PC) on active surveillance (AS) and whether it may be improved through lifestyle-focused interventions remain underdefined.

Objective: To assess longitudinal changes in HRQoL in patients who received and those who did not receive a behavioral intervention that increased vegetable intake.

Design, setting, and participants: A secondary analysis of participants in the Men's Eating and Living (MEAL) study (Cancer and Leukemia Group 70807 [Alliance]), a randomized trial of vegetable consumption in patients on AS, was conducted.

Outcome measurements and statistical analysis: Patient-reported outcomes (PROs) included the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), the Expanded Prostate Cancer Index Composite 26 (EPIC-26), and the Functional Assessment of Cancer Therapy Scale—Prostate (FACT-P). Areas under the curves (AUCs) were used to summarize serial HRQoL.

Results and limitations: PROs were completed in 87% (n = 387) of the intention-to-collect population. Baseline characteristics of patients completing HRQoL measures did not differ significantly from the entire study population or between groups. Baseline scores were high for all PROs and remained stable over 24 mo, with no significant differences from baseline at any time point. In adjusted analyses, there were no significant differences in summary AUC measures comparing control with intervention for the total

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MAX-PC score (p = 0.173); EPIC-26 domains of urinary incontinence (p = 0.210), urinary obstruction (p = 0.062), bowel health (p = 0.607), sexual health (p = 0.398), and vitality (p = 0.363); and total FACT-P scores (p = 0.471).

Conclusions: Among men with localized PC on AS enrolled in a randomized trial, HRQoL was high across multiple domains at baseline, remained high during follow-up, and did not change in response to a behavioral intervention that increased vegetable intake.

Patient summary: Patients with localized prostate cancer enrolled on active surveillance experience minimal cancer-associated anxiety, suffer low levels of cancer-associated symptoms, and perceive high physical and emotional well-being.

1. Introduction

Most patients with prostate cancer present with early-stage disease. An alternative to radical prostatectomy or radiation for many of these patients is active surveillance, which involves serial monitoring with prostate-specific antigen (PSA), magnetic resonance imaging (MRI), and follow-up prostate biopsies [1–3]. Approximately 30% of active surveillance patients undergo curative treatment within 2 yr of follow-up. Most patients receive treatment because of disease progression. Nevertheless, some data suggest that a substantial proportion of active surveillance patients undergoing treatment—up to 30%—do so from cancer-associated anxiety, rather than due to clinically significant disease [4–6].

These observations suggest opportunities for developing interventions to decrease anxiety and promote health-related quality of life (HRQoL) among prostate cancer patients on active surveillance—particularly because 70% of eligible patients choose active surveillance to avoid treatment-related sides effects. HRQoL-targeted interventions might decrease cancer-associated anxiety and help dissuade patients with nonaggressive disease from pursuing unnecessary curative treatment.

However, HRQoL data in patients on active surveillance remain limited. HRQoL among patients on active surveillance is high compared with those treated with radical prostatectomy or radiation [7,8], and small cross-sectional analyses of active surveillance cohorts suggest a low prevalence of generalized depression and decisional conflict [8], but there is a paucity of longitudinal data using comprehensive HRQoL metrics [9,10]. Further analyses could inform care of these patients.

The Men's Eating and Living (MEAL) study (Cancer and Leukemia Group [CALGB] 70807) was a randomized clinical trial (RCT) of a behavioral intervention to increase vegetable intake among patients with localized prostate cancer on active surveillance. The intervention produced robust and sustained increases in vegetable consumption through 2 yr of follow-up, with cruciferous vegetable intake 29.9 g/d in the intervention versus –0.40 g/d in the control group and lycopene intake 5179 μg/d in the intervention versus –466 μg/d in the control group. However, this change did not reduce significantly the risk of clinical progression compared with control [11].

As part of a preplanned secondary analysis, comprehensive HRQoL data were collected serially in MEAL participants using validated questionnaires. The aims of this study were to measure longitudinal changes in HRQoL among active surveillance patients and to analyze differences in HRQoL between study arms. Our a priori hypothesis was that HRQoL would improve over time in the behavioral intervention group, and remain stable or decrease in the control group.

2. Patients and methods

2.1. Study participants

Details of the MEAL study (CALGB 70807 [Alliance for Clinical Trials in Oncology {Alliance}])—including methodology, follow-up data, and primary outcomes—have been described previously [11]. Briefly, the MEAL study was an RCT that enrolled 478 men aged 50–80 yr with early-stage prostate cancer who were on active surveillance at 91 US sites. Patients were randomized 1:1 to a behavioral intervention (n = 237) that promoted daily consumption of targeted seven of more vegetable-fruit servings (emphasizing cruciferous and tomatoes) or a control group (n = 241). Thirty-five patients were deemed ineligible by review of eligibility criteria or centralized pathology of baseline prostate biopsy specimens; therefore, the full analysis set comprised 443 patients: 226 in the behavioral intervention and 217 in the control group.

2.2. Trial design and oversight

The MEAL study was conducted through the Alliance, a Clinical Trials Network group of the National Cancer Institute. All participants signed an institutional review board–approved informed consent document. Data collection was conducted by the Alliance Statistics and Data Management Center (SDMC). Data quality was ensured by the Alliance SDMC and by the study chairperson following Alliance policies [12].

2.3. Patient-reported outcome measures

The patient-reported outcome (PRO) questionnaires Memorial Anxiety Scale for Prostate Cancer (MAX-PC) [13,14], Expanded Prostate Cancer Index Composite 26 (EPIC-26) [15], and Functional Assessment of Cancer Therapy Scale—Prostate (FACT-P) [16,17] were administered at baseline (prior to randomization) and at 6, 12, 18, and 24 mo after baseline. Across the three questionnaires, there were 17 serially measured PROs: the MAX-PC comprised three domains (general prostate anxiety, anxiety related to PSA levels, and fear of recurrence) and a total summary score; the EPIC-26 consisted of five domains, namely, incontinence, obstruction, bowel, sexual, and vitality; and the FACT-P comprised four subscales (physical, social, emotional, and functional), the additional concerns subscale, the Functional Assessment of Cancer Therapy Scale—General total score, the FACT-P total score, and the trial outcome index score. The manual for each questionnaire was used for the corre-

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sponding scoring procedures; however, all PROs were transformed into 0–100 scales, with higher scores representing favorable HRQoL, to facilitate the presentation and interpretation of the PRO results by maintaining the same direction and scale [18].

The intention-to-collect PRO population included patients who consented, were randomized, and were eligible to participate in the PRO data collection [19]. For each of the three questionnaires, the PRO analysis population was confined to patients within the intention-to-collect PRO population who completed the questionnaire at baseline and on at least one occasion after baseline. This definition was considered meaningful for the analysis and was consistent with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use E9 [20,21].

Within each of the three PRO analysis populations, serially measured PROs were not always complete for each patient. To determine whether these missing data were missing completely at random (MCAR), such that many missing data analysis techniques including a complete case analysis approach would lead to a valid inference [22], the MCAR assumption for each PRO (domain and summary score) was evaluated by applying the tests developed by Jamshidian and Jalal [23], which use tests of homoscedasticity that work well for non-normally distributed data. While there was strong evidence of non-normality (all $p < 0.001$) for each PRO, there was insufficient evidence to conclude that any of the PROs were not MCAR (all $p > 0.10$). Moreover, the MCAR assumption was plausible clinically, and consistent with the study design and patient population.

2.4. Statistical analysis

Boxplots were used to depict the sampling distribution of each PRO at each protocol-defined collection time point and by study arm. The sampling distributions of the serial PROs were all left skewed, with many patients reporting perfect scores (ie, 100 on a scale from 0 to 100) across all protocol-defined collection time points. An attempt to approximate a normal distribution by applying a meaningful transformation was unsuccessful because of the preponderance of perfect scores. A simple area under the curve (AUC) summary measure, approximated with the trapezoid method, was used to summarize the sequence of serially measured PROs for each patient to maintain fidelity to the 0–100 scale [23,24]. The AUC summary measure for each patient was calculated based on the scores at baseline and months 6, 12, 18, and 24 using the trapezoidal rule, and scaled according to the number of assessable time points for each patient. Linear interpolation was applied to handle missing data.

The calculated AUC summary measure ranged from 0 to 100, with higher scores representing more favorable health-related quality of life. This analytic approach was easily interpretable, appropriate for the stable PROs reported over time and within each arm, and consistent with the aim to assess clinically significant differences (10-point difference) in average HRQoL between groups [25]. Furthermore, the approach mitigated the inflation of the type I error by reducing the multiple measurements for each patient to a single summary measure.

Although the AUC summary measure and the difference in AUC tend to be approximately normally distributed, even when they are made up of non-normal observations, this was not always the case with all PRO sampling distributions. Therefore, a nonparametric test for stratified continuous response outcomes was applied, which allowed for the adjustment of the three stratification factors used in the randomization algorithm. The AUC summary measure was compared between arms using the nonparametric van Elteren test statistic [19], an extension to the Wilcoxon rank-sum statistics, after adjusting for the three stratification factors in the MEAL RCT: age (<70; ≥70 yr), race (Black/African American; other), and time since diagnostic prostate biopsy (0–12 mo prior to enrollment; >12 and ≤24 mo prior to enrollment) [11]. These covariates were stratification factors at the time of randomization, so these data were available for all patients in the PRO analysis populations. To control the study-wise type I error at 0.05, a Bonferroni correction was applied to the 17 PRO comparisons such that any comparisons associated with $p < 0.0029$ were deemed statistically significant.

As a secondary analysis, a change from baseline analysis was performed at months 6, 12, 18, and 24 for each PRO (domain and summary score), and was assessed for potential baseline differences for each PRO. For these secondary analyses, between-group comparisons were made using the Wilcoxon rank-sum test [26]. For the MAX-PC (domain and summary score), these secondary analyses were repeated within the subset of Black/African-American patients with the aim of testing the hypothesis that baseline anxiety was higher among Black/African-American patients in both groups, and may have differentially improved on the intervention. No statistical adjustment was made for performing these additional tests. A ≥10-point change from baseline on the 0–100 scale was deemed clinically significant. Owing to the potential for type 1 error due to multiple comparisons, findings from these secondary analyses should be interpreted as exploratory. Although these HRQoL analyses were preplanned, a priori power analyses were not performed. The p values were two sided and reported as continuous quantities. Statistical analyses were conducted using SAS version 9.4 by the Alliance SDMC.

3. Results

3.1. Questionnaire response rates

Of the 443 patients in the intention-to-collect PRO population, 87% contributed to a PRO analysis population for all three questionnaires (Table 1). Baseline characteristics of patients contributing to at least one of the three PRO analysis populations ($N = 387$) were clinically representative of the intention-to-collect population as a whole (Table 2). A total of 201 individuals in the control arm and 186 patients in the treatment arm had both a baseline measurement and at least one follow-up measurement. There were no significant differences in baseline characteristics between groups (Table 3).

3.2. Prostate cancer anxiety: the MAX-PC

The baseline summary score for the MAX-PC was high at baseline and did not differ between the control and intervention groups (median: 80.3 vs 82.2; $p = 0.110$), which indicated low levels of anxiety attributable to prostate cancer. Notably, the lower quartiles at baseline in the control and intervention groups were 73.2 and 70.7, respectively; a summary score of ≤50 on the 0–100 scale (higher is better) would be indicative of being clinically anxious (corresponding to ≥27 on the original 0–54 scale [14]). The distribution of the outcome at each subsequent 6-mo assessment remained stable in both groups during follow-up. A change from baseline analysis did not demonstrate any clinically significant changes from baseline in either group for any of the domains (Table 4).

An AUC summary analysis of longitudinal outcomes showed that general prostate cancer anxiety, PSA-associated anxiety, fear of recurrence, and total prostate cancer anxiety did not differ significantly between the two groups (Fig. 1). Of all subdomains, anxiety related to PSA levels tended to be lowest, with 75% of men reporting no

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Table 1 – Number of patients within each patient-reported outcome (PRO) analysis population

Questionnaire	No. of patients within each PRO analysis population [a]	Intention-to-collect PRO population [b]	% of the intention-to-collect PRO population
MAX-PC	*N* = 387	*N* = 443	87
EPIC-26	*N* = 385	*N* = 443	87
FACT-P	*N* = 387	*N* = 443	87

EPIC-26 = Expanded Prostate Cancer Index Composite 26; FACT-P = Functional Assessment of Cancer Therapy Scale—Prostate; MAX-PC = Memorial Anxiety Scale for Prostate Cancer.
[a] For each questionnaire, the PRO analysis population was defined as those patients within the intention-to-collect PRO population who completed the questionnaire at baseline and on at least one occasion after baseline.
[b] The intention-to-collect PRO population was defined as all patients who consented, were randomized, and were eligible to participate in the PRO data collection.

anxiety related to PSA levels at baseline or throughout the 24-mo period.

3.3. Prostate cancer anxiety: Black/African-American patients

Since prior data have suggested differences in emotional well-being and depression between Black/African-American and White patients with prostate cancer [27], MAX-PC analyses were performed comparing Black/African-American (9.3%) with non-Black/African-American patients [28]. The MAX-PC summary score did not differ significantly between Black/African-American (median: 79.8) and non-Black/African-American (median: 79.3) patients (P = 0.832) at baseline. There were no clinically significant changes from baseline at any time point (data not shown).

3.4. Patient symptoms and satisfaction: the EPIC-26

The baseline summary scores comparing control to intervention in the domains of urinary incontinence (median: 100 vs 100; p = 0.194), urinary obstruction (median: 87.5 vs 90.6; p = 0.022), bowel health (median: 100 vs 100; p = 0.726), sexual health (median: 79.2 vs 75.0; p = 0.999), and vitality (median: 95.0 vs 95.0; p = 0.132) were high and did not differ significantly between groups. The distribution of the scores for each domain was similar over time and between groups. There were no clinically significant changes from baseline in either group for any of the domains (Table 4). For several domains, the median change from baseline was zero in both groups at each time point. Nearly 50% of all patients had perfect scores for urinary incontinence, bowel health, and vitality at baseline and during follow-up.

The AUC summary analysis of longitudinal outcomes showed that scores within the domains of urinary incontinence, urinary obstruction, bowel health, sexual health, and vitality did not differ significantly between the two groups (Fig. 2).

3.5. Functional assessment of cancer therapy: the FACT-P

The baseline summary scores for the FACT-P comparing control with intervention (median: 86.1 vs 86.7; p = 0.113) were high and did not differ significantly between

Table 2 – Baseline characteristics for the patients who contributed and who did not contribute to at least one of the three the patient-reported outcome (PRO) analysis populations

	Contributed to a PRO analysis population (*N* = 387)	Did not contribute to a PRO analysis population (*N* = 56)	Intention-to-collect PRO population (*N* = 443)
Age (yr)			
N	387	56	443
Mean (SD)	64 (6)	64 (7)	64 (7)
Median (min, max)	64 (47, 78)	65 (50, 80)	64 (59, 68)
Age group <70 yr, *n* (%)	317 (81.9)	42 (75.0)	359 (81.0)
Race and ethnicity, *n* (%)			
White	319 (82.4)	38 (67.9)	357 (80.6)
Black/African American	36 (9.3)	14 (25.0)	50 (11.3)
Hispanic or Latino	13 (3.4)	3 (5.4)	16 (3.6)
Asian	14 (3.6)	1 (1.8)	15 (3.4)
More than one race	2 (0.5)	0 (0.0)	2 (0.5)
Native Hawaiian or Pacific Islander	1 (0.3)	0 (0.0)	1 (0.2)
American Indian or Alaska native	1 (0.3)	0 (0.0)	1 (0.2)
Not reported	1 (0.3)	0 (0.0)	1 (0.2)
Prostate biopsy within 12 mo, *n* (%)	324 (83.7)	51 (91.1)	375 (84.7)
Tumor stage, *n* (%)			
cT1a	5 (1.3)	0 (0.0)	5 (1.1)
cT1b	3 (0.8)	0 (0.0)	3 (0.7)
cT1c	332 (86.0)	52 (92.9)	384 (86.9)
cT2a	46 (11.9)	4 (7.1)	50 (11.3)
Missing	1	0	1
Serum PSA, *n* (%)			
0–2.5	48 (12.5)	7 (12.5)	55 (12.5)
>2.5–5	173 (44.9)	24 (42.9)	197 (44.7)
>5	164 (42.6)	25 (44.6)	189 (42.9)
Missing	2	0	2

PSA = prostate-specific antigen; SD = standard deviation.

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Table 3 – Baseline characteristics according to arm (MEAL intervention; control) for the 387 patients who contributed to at least one of the three PRO analysis populations

	MEAL intervention (*N* = 201)	Control (*N* = 186)	Total (*N* = 387)	*p* value [a]
Age (yr)				
N	201	186	387	0.909
Mean (SD)	64 (7)	64 (6)	64 (6)	
Median (min, max)	64 (50, 78)	64 (47, 77)	64 (47, 78)	
Age group <70 yr, *n* (%)	165 (82.1)	152 (81.7)	317 (81.9)	0.925
Race and ethnicity, *n* (%)				
White	168 (83.6)	151 (81.2)	319 (82.4)	0.504
Black/African American	18 (9.0)	18 (9.7)	36 (9.3)	
Hispanic or Latino	8 (4.0)	5 (2.7)	13 (3.4)	
Asian	6 (3.0)	8 (4.3)	14 (3.6)	
More than one race	0 (0.0)	2 (1.1)	2 (0.5)	
Native Hawaiian or Pacific Islander	0 (0.0)	1 (0.5)	1 (0.3)	
American Indian or Alaska native	1 (0.5)	0 (0.0)	1 (0.3)	
Not reported	0 (0.0)	1 (0.5)	1 (0.3)	
Prostate biopsy within 12 mo, *n* (%)	170 (84.6)	154 (82.8)	324 (83.7)	0.635
Tumor stage, *n* (%)				
cT1a	4 (2.0)	1 (0.5)	5 (1.3)	0.511
cT1b	1 (0.5)	2 (1.1)	3 (0.8)	
cT1c	173 (86.5)	159 (85.5)	332 (86.0)	
cT2a	22 (11.0)	24 (12.9)	46 (11.9)	
Missing	1	0	1	
Serum PSA, *n* (%)				
0–2.5	21 (10.6)	27 (14.5)	48 (12.5)	0.438
>2.5–5	89 (44.7)	84 (45.2)	173 (44.9)	
>5	89 (44.7)	75 (40.3)	164 (42.6)	
Missing	2	0	2	

MEAL = Men's Eating and Living study; PRO = patient-reported outcome; PSA = prostate-specific antigen; SD = standard deviation.
Baseline characteristics were balanced between the two groups.
[a] Based on a chi-square test for categorical variables and a two-sample *t* test for continuous variables.

groups. A change from baseline analysis did not demonstrate any clinically significant changes from baseline in either group for any of the domains (Table 4). In the domain of physical well-being, 25% of men reported perfect quality of life scores at all time points.

The AUC analysis of longitudinal outcomes showed that physical, social, emotional, and functional outcomes did not differ significantly between treatment groups (Fig. 3).

4. Discussion

HRQoL—as measured by comprehensive, validated, prostate cancer–specific PROs—was high across multiple domains among men with localized prostate cancer on active surveillance enrolled in a randomized trial. HRQoL remained high during 2 yr of follow-up and did not change in response to a behavioral intervention that increased vegetable intake markedly. These results suggest that patients with localized prostate cancer enrolled on active surveillance experience minimal cancer-associated anxiety, suffer low levels of cancer-associated symptoms, and perceive high physical and emotional well-being.

To our knowledge, these data represent the most comprehensive longitudinal assessments of HRQoL to date among patients on active surveillance. They provide assurance that these patients express high levels of satisfaction with prostate cancer–focused HRQoL [7,9]. Demographic characteristics of participants in the MEAL study were consistent with typical patients in clinical practice. They met well-defined and widely accepted clinical criteria for active surveillance, represented a broad swath of geographically diverse academic and community practices in the USA, and included a relatively large (12%) sample of Black/African-American patients [11].

These results confirm that appropriately selected patients who have chosen active surveillance express minimal anxiety and depression about prostate cancer [8,10,29,30]. They do not align with prior observations of cancer-associated anxiety driving treatment decisions [4–6]. Indeed, the incidence of curative treatment during 24-mo of follow-up with radical prostatectomy or radiation in the MEAL study was very low: <2% [11]. Of the patients in the MEAL study, 75% expressed no PSA-associated anxiety at any time point during 2 yr of follow-up despite PSA measurements every 3 mo. There were no significant differences in anxiety between Black/African American and other patients.

Increased vegetable intake was not associated with differential changes in PRO scores in any of the domains compared with the control group, an observation consistent with a small RCT of an intervention combining vegan diet, exercise, and stress management [31]. A likely explanation is that lifestyle-focused interventions, such as diet, will not offer meaningful benefits for prostate cancer–associated HRQoL since these patients already experienced a high sense of well-being.

PROs for each of the domains—urinary function, incontinence, bowel function, sexual function, and vitality—did not change significantly from baseline during follow-up. Almost 50% of these patients maintained perfect PRO scores for several domains throughout the study's duration. These results do not support prior observations of declining sexual function over time among patients on active surveillance (possibly related to serial prostate biopsies) [32–34], but are

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Table 4 – Median scores at baseline and median change from baseline at months 6, 12, 18, and 24 for the domains and summary scores of the MAX-PC, EPIC-26, and FACT-P according to arm

Questionnaires	Median baseline score (*N*)			Median change from baseline (*N*)											
	Control	Intervention	*p* value	6 mo			12 mo			18 mo			24 mo		
				Control	Intervention	*p* value	Control	Intervention	*p* value	Control	Intervention	*p* value	Control	Intervention	*p* value
MAX-PC															
General prostate anxiety	81.8 (212)	78.8 (224)	0.274	0.0 (171)	0.0 (182)	0.861	3.0 (161)	0.0 (173)	0.589	0.0 (152)	0.0 (150)	0.981	3.0 (140)	3.0 (150)	0.942
Anxiety related to PSA levels	100 (212)	100 (224)	0.547	0.0 (169)	0.0 (182)	0.062	0.0 (161)	0.0 (174)	0.741	0.0 (151)	0.0 (150)	0.126	0.0 (139)	0.0 (150)	0.256
Fear of recurrence	75.0 (212)	66.7 (224)	0.022	0.0 (170)	0.0 (182)	0.234	0.0 (161)	8.3 (174)	0.036	0.0 (152)	8.3 (150)	0.449	0.0 (140)	8.3 (150)	0.065
Total summary score	82.2 (212)	80.3 (224)	0.110	1.8 (171)	1.0 (182)	0.966	2.0 (161)	1.8 (174)	0.582	1.9 (152)	2.8 (150)	0.846	2.8 (140)	2.0 (150)	0.911
EPIC-26															
Incontinence	100 (207)	100 (219)	0.194	0.0 (165)	0.0 (181)	0.900	0.0 (155)	0.0 (173)	0.025	0.0 (144)	0.0 (148)	0.548	0.0 (127)	0.0 (124)	0.706
Obstruction	90.6 (208)	87.5 (224)	0.022	0.0 (172)	0.0 (190)	0.729	0.0 (155)	0.0 (177)	0.962	0.0 (146)	0.0 (153)	0.680	0.0 (129)	0.0 (127)	0.348
Bowel	100 (209)	100 (223)	0.726	0.0 (171)	0.0 (186)	0.505	0.0 (158)	0.0 (178)	0.500	0.0 (146)	0.0 (153)	0.498	0.0 (128)	0.0 (126)	0.673
Sexual	75.0 (200)	79.2 (216)	0.999	0.0 (157)	0.0 (178)	0.534	0.0 (147)	0.0 (172)	0.926	0.0 (138)	0.0 (146)	0.233	0.0 (120)	−4.2 (119)	0.022
Vitality	95.0 (209)	95.0 (222)	0.132	0.0 (170)	0.0 (189)	0.112	0.0 (158)	0.0 (176)	0.330	0.0 (147)	0.0 (152)	0.222	0.0 (128)	0.0 (127)	0.024
FACT-P															
Physical	96.4 (212)	96.4 (224)	0.207	0.0 (168)	0.0 (181)	0.515	0.0 (161)	0.0 (175)	0.274	0.0 (151)	0.0 (150)	0.912	0.0 (140)	0.0 (151)	0.693
Social	85.7 (212)	85.7 (223)	0.786	0.0 (167)	0.0 (179)	0.447	0.0 (161)	0.0 (173)	0.623	0.0 (149)	0.0 (150)	0.991	0.0 (139)	0.0 (150)	0.299
Emotional	87.5 (212)	85.0 (223)	0.106	0.0 (169)	0.0 (180)	0.934	0.0 (161)	4.2 (175)	0.109	0.8 (151)	4.2 (151)	0.736	0.0 (139)	0.0 (149)	0.436
Functional well-being	89.3 (211)	85.7 (223)	0.096	0.0 (168)	0.0 (180)	0.584	0.0 (160)	0.0 (175)	0.152	0.0 (150)	0.0 (151)	0.567	0.0 (139)	0.0 (149)	0.263
FACT-G total score	88.1 (211)	87.2 (223)	0.239	1.2 (167)	1.4 (180)	0.788	1.0 (160)	1.8 (174)	0.226	1.5 (150)	1.3 (150)	0.799	0.9 (139)	1.2 (149)	0.282
Additional concerns	83.3 (212)	81.3 (223)	0.036	0.0 (169)	0.0 (179)	0.755	0.0 (161)	2.1 (172)	0.032	0.0 (151)	0.0 (150)	0.709	0.0 (140)	0.0 (149)	0.217
FACT-P total score	86.7 (212)	86.1 (222)	0.113	0.9 (168)	1.1 (179)	0.650	0.8 (161)	2.1 (173)	0.093	1.3 (151)	1.4 (149)	0.594	0.5 (139)	1.7 (148)	0.126
Trial outcome index score	88.9 (212)	84.2 (224)	0.060	0.5 (169)	0.7 (181)	0.452	0.0 (161)	1.7 (175)	0.043	0.7 (151)	1.1 (151)	0.536	0.2 (140)	0.7 (151)	0.270

EPIC-26 = Expanded Prostate Cancer Index Composite 26; FACT-P = Functional Assessment of Cancer Therapy Scale—Prostate; MAX-PC = Memorial Anxiety Scale for Prostate Cancer; PSA = prostate-specific antigen.
The scores are on a 0–100 scale, with higher scores representing more favorable health-related quality of life (HRQoL). Between-arm comparisons were made using the Wilcoxon rank-sum test. For these secondary analyses, no adjustment was made for performing multiple comparisons. Further, all available HRQoL data self-reported by the patient at baseline and/or after baseline are summarized.

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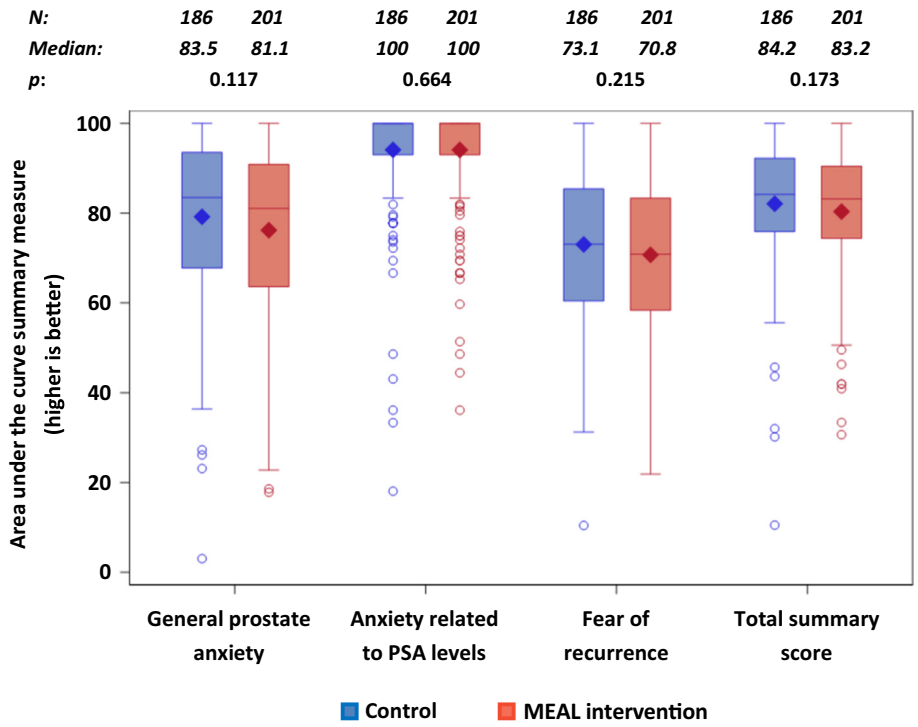

Fig. 1 – Between-arm comparisons of the area under the curve (AUC) summary measure for each MAX-PC domain and the total summary score. The AUC summary measures are on a 0–100 scale, with higher scores representing more favorable health-related quality of life. The AUC was compared between arms using the nonparametric van Elteren test statistics adjusting for the three stratification factors: age (<70; ≥70), race (Black/African American; other), and time since diagnostic prostate biopsy (0–12 mo prior to enrollment; >12 and ≤24 mo prior to enrollment). Based on a Bonferroni correction, comparisons associated with $p < 0.0029$ were deemed statistically significant. MAX-PC = Memorial Anxiety Scale for Prostate Cancer; MEAL = Men's Eating and Living study; PSA = prostate-specific antigen.

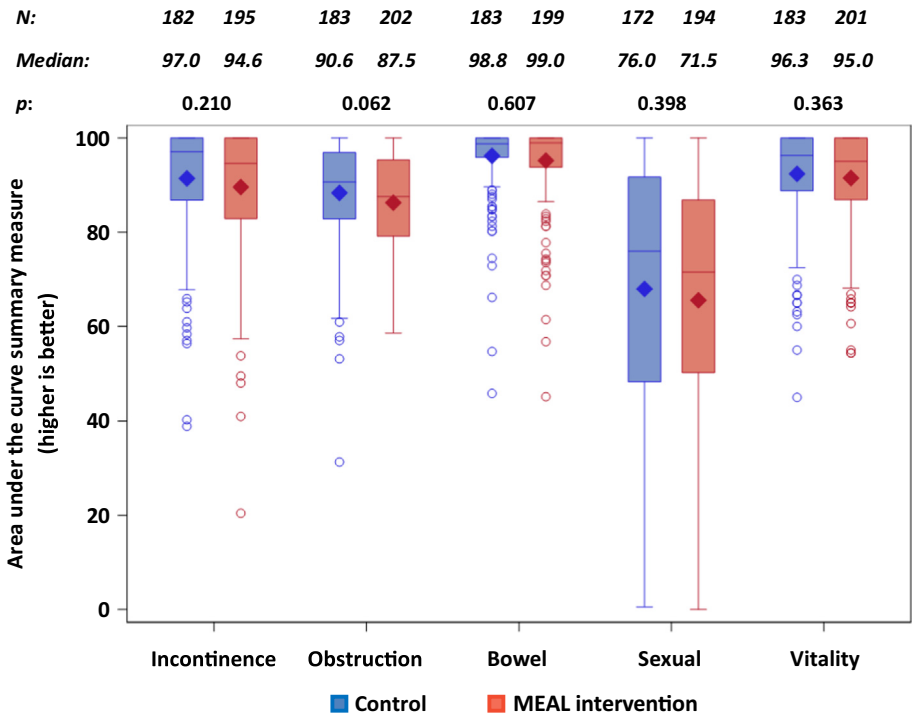

Fig. 2 – Between-arm comparisons of the area under the curve (AUC) summary measure for each EPIC-26 domain. The AUC summary measures are on a 0–100 scale, with higher scores representing more favorable health-related quality of life. The AUC was compared between arms using the nonparametric van Elteren test statistics adjusting for the three stratification factors age (<70; ≥70), race (Black/African American; other), and time since diagnostic prostate biopsy (0–12 mo prior to enrollment; >12 and ≤24 mo prior to enrollment). Based on a Bonferroni correction, comparisons associated with $p < 0.0029$ were deemed statistically significant. EPIC-26 = Expanded Prostate Cancer Index Composite 26; MEAL = Men's Eating and Living study.

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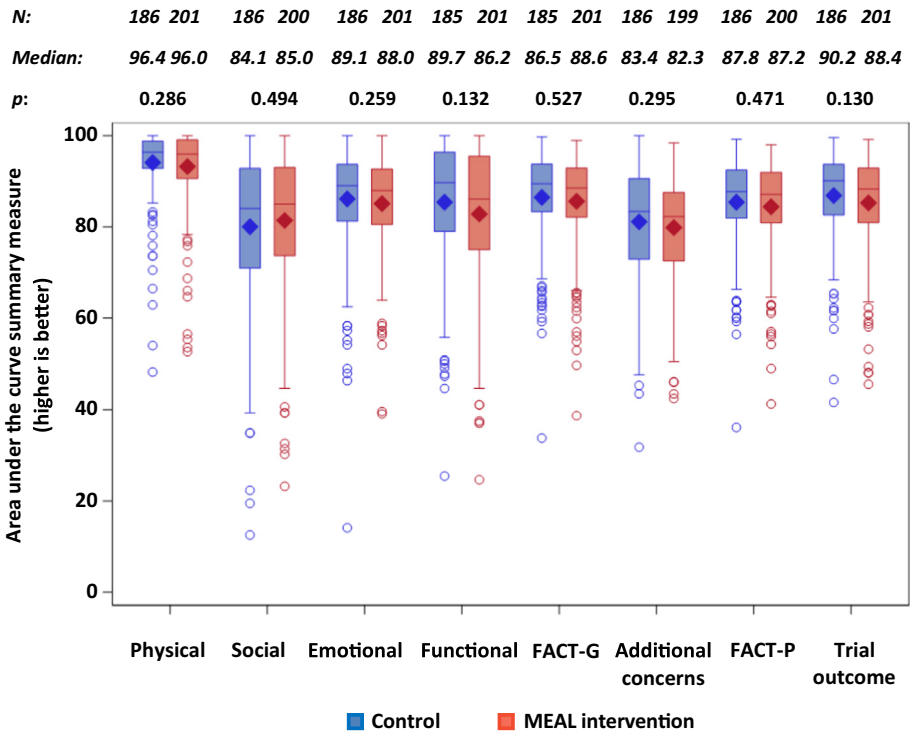

Fig. 3 – Between-arm comparisons of the area under the curve (AUC) summary measure for each FACT-P domain and summary scores. The AUC summary measures are on a 0–100 scale, with higher scores representing more favorable health-related quality of life. The AUC was compared between arms using the nonparametric van Elteren test statistics adjusting for the three stratification factors age (<70; ≥70), race (Black/African American; other), and time since diagnostic prostate biopsy (0–12 mo prior to enrollment; >12 and ≤24 mo prior to enrollment). Based on a Bonferroni correction, comparisons associated with $p < 0.0029$ were deemed statistically significant. FACT-G = Functional Assessment of Cancer Therapy Scale—General; FACT-P = Functional Assessment of Cancer Therapy Scale—Prostate; MEAL = Men's Eating and Living study.

consistent with others that perceived no significant longitudinal changes [35,36].

This study did not compare active surveillance patients with patients who chose radical prostatectomy, radiation, or androgen deprivation therapy. Further, given that the MEAL study was negative (increased vegetable consumption did not significantly reduce the risk of clinical progression compared with control), the contribution of our HRQoL evaluation to clinical practice in this setting may be considered limited. However, these results are notable because we observed high HRQoL overall among patients on active surveillance, which has not been reported previously. There are at least five additional limitations to this study. First, the MEAL study participants were predominately patients with National Comprehensive Cancer Network (NCCN)-classified very-low- and low-risk disease [11]. All participants volunteered to be in this study, and volunteers have been shown to be healthier than the general population [37]. Thus, these results may not necessarily represent HRQoL among patients on active surveillance with NCCN-classified favorable intermediate-risk disease, which is more aggressive and imparts a higher risk of clinical progression. Still, the MEAL study mirrored current community standards of care; at least one active surveillance cohort with a higher prevalence of intermediate-risk disease reported similarly robust HRQoL scores [34]. Second, longer-term follow-up may have informed better longitudinal assessments of HRQoL by incorporating additional clinical progression and treatment events. However, longer periods of observation would be unlikely to provide further meaningful insight since most progression and treatment events occur within the first 2 yr of follow-up [38]. Third, although the distribution of patient characteristics among those who contributed to the analysis was similar to that of the whole sample, those who did not contribute were more likely to be Black/African-American patients, suggesting the possibility of a selection bias. Fourth, although the percentage of Black/African-American patients who contributed to the analysis was relatively large (9.3%), the number of Black/African-American men was small ($N = 36$) and the study was likely underpowered to determine differences in HRQoL between Black/African Americans and other races. Lastly, the study did not collect patient-level socioeconomic data (eg, income, education level attained, and area deprivation index) or genetic risk factors, information that could have potential implications on the study's findings.

5. Conclusions

In conclusion, among men with localized prostate cancer on active surveillance, HRQoL was high across multiple domains at baseline, remained high during 2 yr of follow-up, and did not change in response to a behavioral intervention that increased vegetable intake markedly.

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***Author contributions*:** David Zahrieh had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Parsons, Zahrieh, Liu, Pierce, Marshall.
Acquisition of data: Parsons, Zahrieh, Liu, Peil.
Analysis and interpretation of data: Parsons, Zahrieh, Patel, Liu, Peil, Pierce, Marshall.
Drafting of the manuscript: Parsons, Zahrieh, Patel, Mohler, Chen, Paskett, Liu, Peil, Rock, Hahn, Taylor, Van Veldhuizen Jr, Small, Morris, Naughton, Pierce, Marshall.
Critical revision of the manuscript for important intellectual content: Parsons, Zahrieh, Patel, Mohler, Chen, Paskett, Liu, Peil, Rock, Hahn, Taylor, Van Veldhuizen Jr, Small, Morris, Naughton, Pierce, Marshall.
Statistical analysis: Zahrieh, Liu, Peil.
Obtaining funding: Parsons, Pierce, Marshall.
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