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The Association of Long-term Treatment-related Side Effects With Cancer-specific and General Quality of Life Among Prostate Cancer Survivors

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Abstract

OBJECTIVE—To examine the association between treatment-related side effects and cancer-specific and general quality of life (QOL) among long-term prostate cancer survivors.

MATERIALS AND METHODS—Within the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, we conducted telephone interviews with prostate cancer survivors (N = 518) who were 5–10 years after diagnosis. We assessed demographic and clinical information, sexual, urinary, and bowel treatment-related side effects (Expanded Prostate Cancer Index Composite), cancer-specific QOL (Functional Assessment of Cancer Therapy—total score), and general QOL (the Medical Outcomes Study Short Form 12's physical and mental subscales).

RESULTS—Participants were aged 74.6 years on average, primarily White (88.4%), and married (81.7%). Pearson correlation coefficients between the 3 treatment-related side effect domains (urinary, sexual, and bowel) and QOL ranged between 0.14 and 0.42 ($P < .0001$). Multivariable linear regression analyses revealed that poorer urinary and sexual functioning and greater bowel side effects were independently associated with poorer cancer-specific QOL ($P < .0001$). Bowel and urinary functions were also associated with poorer general QOL on the Medical Outcomes Study Short Form 12's physical component summary and mental component summary ($P < .05$). Bowel side effects demonstrated the strongest association with all QOL outcomes.

CONCLUSION—Treatment-related side effects persisted for up to 10 years after diagnosis and continued to be associated with men's QOL. These results suggest that each of the treatment-related side effects was independently associated with cancer-specific QOL. Compared with the other Expanded Prostate Cancer Index Composite domains, bowel side effects had the strongest association with cancer-specific and general QOL. These associations emphasize the tremendous impact that bowel side effects continue to have for men many years after their initial diagnosis.

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Quality of life (QOL) continues to be of paramount importance for men diagnosed with prostate cancer (PCa), given that most men are diagnosed at an early stage and live for many years after treatment. Both longitudinal and cross-sectional studies have demonstrated that radical prostatectomy is primarily associated with urinary and sexual dysfunction, whereas radiation therapy is more often associated with bowel dysfunction.¹⁻⁴ Although the short- and intermediate-term side effects of treatment on QOL have been well documented⁵⁻⁷; increasingly, the long-term influence of side effects on QOL is being evaluated.⁸⁻¹⁰ In an earlier publication, we reported that patients treated with radiation therapy reported better sexual and urinary functioning but poorer bowel outcomes compared with those treated with radical prostatectomy. These results demonstrated the persistence of clinically significant, long-term treatment-related urinary and sexual side effects up to 10 years after diagnosis among PCa survivors from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial.¹⁰ Similarly, in a recent study of functional outcomes 15 years after diagnosis for localized PCa, men had consistent declines in all functional outcomes.⁹ Given that the treatment-related side effects do not resolve with time, more research is needed to fully understand the association between long-term side effects and QOL for PCa survivors.

As there is currently no gold standard for the treatment of early stage PCa, QOL is an important consideration when physicians and patients review treatment options and make decisions.^{4,11,12} Because men with PCa tend to be older and to have comorbid conditions, age and comorbidities as well as other demographic and clinical factors must also be considered when examining treatment decisions.¹³⁻¹⁷ Some studies have demonstrated that QOL improves with age, although comorbidities negatively impact QOL in men with PCa.^{15,16} Although the association between treatment side effects and QOL has been recognized,¹⁸⁻²⁰ little research has been conducted to address the extent to which side effects are associated with long-term QOL.

Understanding this relationship in long-term survivors is important as it may assist newly diagnosed PCa patients in making their treatment decisions, as well as help survivors cope with long-term side effects that impact their well-being.^{4,21} In the present study, we assessed the extent to which treatment-related side effects were associated with cancer-specific and general QOL in men up to 10 years after diagnosis. Furthermore, we explored whether any one side effect domain was particularly related to subsequent QOL compared with the other domains.

MATERIALS AND METHODS

Overview of the PLCO Trial

From 1993 to 2001, the PLCO trial^{22,23} enrolled 76,705 men aged 55-74 years at 10 screening sites in the United States. PLCO exclusion criteria for male participants were: (1) history of prostate, lung, or colorectal cancer, (2) current cancer treatment, (3) prior surgical removal of the prostate, lung, colon, or rectum, (4) current finasteride use, (5) 1 prostate-specific antigen (PSA) test 3 years ago, (6) colon cancer screening 3 years ago, (7) enrollment in another cancer screening or prevention study, and (8) unwilling or unable to consent.

All participants completed a baseline questionnaire (BQ) regarding demographic characteristics and screening history and were randomly assigned to the usual care or screening arm. Usual care participants were instructed to follow their normal health-care routine. Male screening arm participants received an annual digital rectal examination in years 0–3 and a PSA level test during years 0–5. Participants received the screening results and recommendations for necessary diagnostic examinations with their own physician. All participants completed an annual assessment of health status and new cancer diagnoses.

Disease-related Functioning and QOL Substudy

Participants—Eligibility criteria included: (1) completed BQ, (2) English-speaking, (3) enrolled at 1 of the 5 participating PLCO screening centers (Georgetown University, Henry Ford Health Systems, University of Minnesota, Washington University, and Marshfield Clinic), (4) White or African American (others were excluded because of small samples at these screening centers), (5) no dementia or cognitive difficulties, (6) no hearing impairment, (7) active PLCO participation, (8) diagnosed ≥ 5 and <10 years before the QOL interview (diagnosis dates: July 1998–July 2003), and (9) no other cancer diagnosis, except nonmelanoma skin cancer. Because the primary analyses included treatment modality, we excluded the few men who chose watchful waiting ($N = 9$) or cryotherapy ($N = 2$), resulting in a final sample of 518 cases. We included all disease stages and both screen-detected and interval cancers.

Procedures—We conducted a single telephone interview with participants that required 15–20 minutes and for which participants received a \$10 gift card. Institutional review board approval was covered under the overall PLCO consent form. The readers are referred to the study by Taylor et al¹⁰ for details of the procedures.

Substudy Measures

Demographic and Medical Information: We assessed education level, marital status, employment status, income level, and comorbidities. Regarding comorbidities, participants indicated if they had been diagnosed by a physician with any of the 16 comorbidities. These were categorized into 1 vs 2.

Cancer Treatments and Recurrence: As the PLCO trial collected treatment data from medical records only during the first year after diagnosis, we obtained survivors' self-report of (1) dates and types of all PCa treatments and (2) PCa recurrence (yes or no). Treatment modality was categorized into the following 3 groups: surgery only (RP; $N = 201$), radiation only (RT; $N = 110$: brachytherapy = 65 and external beam = 45), and treatment combinations (TCs; $N = 207$), which included men who had received only hormone therapy (HT), as well as any combination of RP, RT, and HT. Overall, 135 ever had HT, and 32 were receiving HT at the time of the QOL interview. For treatments received within 12-months after diagnosis, agreement between self-report and the PLCO records was 89.6%; an additional 8.3% indicated partial agreement, suggesting high reliability of the subsequent self-reported treatments. Furthermore, self-reported PCa recurrence was significantly associated in the expected direction with medical record information on stage at diagnosis,

Gleason score, PSA level, use of androgen deprivation therapy, and treatment modality (all P values $<.01$).

PCa-specific Functioning: The Expanded Prostate Cancer Index Composite Short-Form (EPIC-26)²⁰ evaluated function in the past 4 weeks on sexual (6 items; $\alpha = 0.89$), urinary (9 items; $\alpha = 0.83$), and bowel domains (6 items; $\alpha = 0.78$). Higher scores indicate better functioning and fewer side effects (range = 0–100).

Cancer-specific QOL: The Functional Assessment of Cancer Therapy—General (FACT-G)²⁴ contains 27 items across 4 QOL domains: physical well-being, social and/or family well-being, emotional well-being, and functional well-being. The functional, physical, and social well-being subscales each contain 7 items with scores ranging from 0 to 28. The emotional well-being subscale contains 6 items with scores ranging from 0 to 24. The FACT-G is a well-validated and widely used measure of cancer-specific QOL. The total score ranges from 0 to 108, with a higher score indicating better QOL ($\alpha = 0.91$).

General QOL: The Medical Outcomes Study Short Form 12 (SF-12) scale contains two subscales, the mental component summary (MCS) and the physical component summary (PCS).²⁵ This scale is widely used among medical patients and in the general population. The 2-week test-retest reliability for the MCS was 0.76 and 0.89 for the PCS.²⁶ Based on normative data, the average score for US men (all ages combined) is 50.7 for the MCS and 51.2 for the PCS.²⁶

Information Obtained From PLCO Records

PLCO Baseline Questionnaire: We obtained date of birth, race, and years since initial diagnosis from the BQ, which was administered by the PLCO upon trial enrollment. All alphas reported are from the current dataset.

Medical Record Review: PLCO staff abstracted treatment records to obtain disease stage, PSA level at diagnosis, Gleason score at diagnosis, and PCa treatments received during the first year after diagnosis.

Statistical Analysis—We calculated descriptive statistics for demographic and clinical factors. Next, we examined associations between the FACT-G (total score and the 4 subscales), the SF-12 subscales (PCS and MCS), and 3 EPIC domain scores (sexual, urinary, and bowel). Side effects associated with HT on the EPIC-26 were not examined because of the large amount of overlap with items on the QOL measures. Next, we conducted 3 separate multivariate linear regression analyses using a 2-step approach to determine the factors that were significantly associated with cancer-specific QOL (FACT-G total score) and general QOL (the SF-12 PCS and MCS subscales). We included all significant covariates from bivariate analyses. On step 1, demographic and clinical covariates were entered, and on step 2, the 3 EPIC domains were added. We used SAS 9.2 to conduct all analyses.

Power Calculation: At a significance level of 0.05, a sample size of 500 provides at least 80% power to detect an R^2 of at least 0.02 for the 3 EPIC domain independent variables, while adjusting for demographic and clinical factors that have an R^2 ranging from 0.01 to

0.20. For the pairwise comparisons of the 3 treatment modalities (RP, RT, and TC), we had 80% power to detect mean differences of at least 0.33 standard deviations.

RESULTS

Demographic and Clinical Information

Demographic and clinical characteristics are presented in Table 1. Participants had a mean age of 74.6 years and their average time since initial PCa diagnosis was 7.4 years (with a range from 5.0 to 9.9 years since diagnosis). Participants were mostly White (88.4%), married (81.7%), retired (77.1%), and had at least some college education (71.9%). Regarding clinical information, at diagnosis most men had stage-II disease (87.8%), a Gleason score of 3–6 (68.0%), and a PSA level ≤ 10 (82.2%).

Associations Between Treatment-related Side Effects and QOL

Pearson correlation coefficients between cancer-specific QOL (FACT-G total score and subscale scores) and the 3 EPIC domains were low to moderate ($r = 0.23$ – 0.42 ; Table 2).

Correlations between general QOL (PCS and MCS) and the 3 EPIC domains were also low to moderate ($r = 0.14$ – 0.37 ; Table 2). All correlations were positive and all corresponding tests were statistically significant ($P < .001$); better functioning and fewer side effects on the 3 EPIC domains were associated with better cancer-specific and general QOL. The correlations between bowel side effects and the FACT-G total score and PCS and MCS were all stronger than with the other EPIC domains ($r = 0.29$ – 0.42).

To determine whether the EPIC domains were independently associated with men's cancer-specific QOL, we conducted a multivariate linear regression model analysis, using a 2-step approach with the FACT-G total score as the outcome. Demographic and clinical variables explained 14% of the variance ($R^2 = 0.14$; $P < .001$) on the first step (Table 3). On step 2, the 3 EPIC domains were entered and explained an additional 23% of the variance in the FACT-G total score (total $R^2 = 0.37$; $P < .001$). In the final model, significantly poorer cancer-specific QOL was reported by men with more comorbidities, African Americans, men with less than or equal to a high school education, and younger men. Compared with those who received TC, men who received RP or RT reported significantly better QOL. Regarding the 3 EPIC domains, bowel side effects demonstrated the largest association with the FACT-G total score, such that men with higher scores on the bowel subscale (ie, reported fewer side effects) also reported better cancer-specific QOL (with an expected increase of 0.29 points for the FACT-G total score for a 1-unit increase on the bowel score).

Using the same approach, we conducted 2 multivariate linear regression analyses for the general QOL subscales, PCS, and MCS (Table 4). On step 1 of the analysis predicting PCS, demographic and clinical variables explained 18% of the variance ($R^2 = 0.18$; $P < .001$). On step 2, EPIC domains were entered and explained an additional 9% of the variance (total $R^2 = 0.27$; $P < .001$). In the final model, men with more comorbidities, men with more bowel side effects, and those with poorer urinary function reported significantly poorer QOL on the PCS. Compared with men who received TC, those who received RP or RT reported significantly better QOL. For the MCS, demographic and clinical variables explained 4% of

the variance ($R^2 = 0.04$; $P < .001$). On step 2, the 3 EPIC domains were entered and explained an additional 10% of the variance (total $R^2 = 0.14$; $P < .0001$). In the final model, men with less than or equal to a high school education, men with more bowel side effects, and those with poorer urinary function had significantly poorer QOL on the MCS compared with their counterparts. Similar to the cancer-specific QOL, bowel side effects resulted in the largest association with both the PCS and MCS, such that men with higher scores on the bowel subscale (ie, fewer side effects) reported better general QOL. To further examine the TC group, we conducted similar analyses removing the 32 men who were receiving HT at the time of the QOL interview, and the results remained virtually unchanged.

COMMENT

While most studies on QOL and PCa have focused on the short-term influence of treatment-related side effects, this study examined the long-term (5–10 years after diagnosis) association between PCa-related treatment side effects and cancer-specific and general QOL. The relationships between cancer-specific and general QOL measures and the EPIC domains were similar to those found by Wei et al.²⁰

After adjusting for demographic and clinical variables, our results suggest that the urinary, sexual, and bowel EPIC domains were all independently associated with cancer-specific QOL after adjusting for the other 2 domains. Interestingly, the bowel domain had the strongest association with the FACT-G total score and the PCS and MCS compared with the other 2 EPIC domains. Although we did not hypothesize that any one domain would have a greater impact on QOL than another, results suggest that bowel side effects may have a stronger association with QOL in the long-term. This may indicate that men are particularly disturbed by the negative impact on bowel functioning, especially when concerns do not abate over time. The urinary function domain was also associated with all of the QOL outcomes, whereas the sexual function domain was only associated with the cancer-specific QOL measure. These findings may reflect men's expectation that they will experience some sexual dysfunction, particularly as they reach older age, but they don't expect long-term urinary and bowel side effects and the negative impact on one's usual functioning.

The strong association with the bowel side effects is similar to results from colorectal cancer patients with persistent bowel problems who reported poorer functional, social, and emotional well-being.²⁷ Addressing QOL issues may assist men in being as functional as possible despite their physical limitations. This underscores the importance of doctor-patient discussions on the potential side effects of treatment and the associated long-term impact on QOL. Routine automated monitoring of symptoms or QOL may prove to be an easy and beneficial means of addressing persistent symptoms that negatively impact QOL.²⁸ In a study of PCa survivors, men reported that the automated system was easy to use and that routine assessments of symptoms or QOL would be beneficial for all men after treatment. Such systems allow patients and survivors to play a more active role in their cancer care by systematically bringing their symptoms to the attention of the doctor to facilitate a discussion and create a treatment plan.

Poorer cancer-specific QOL was independently associated with being African American, having less education, more comorbidities, and being in the treatment combination group. Of note was the relationship between being African American and poorer QOL, which has previously been demonstrated.^{13,29} However, these findings differ from those of Halbert et al,¹⁴ who found no racial differences on physical well-being. However, 2–5 months after diagnosis, African American men did report greater emotional well-being compared with White men. The higher levels of emotional well-being parallel findings by Rao et al,²⁹ who found that African American men had more positive emotional responses to treatment compared with their physical response. This latter finding is similar to results of Eton et al,¹³ who found that African American men assessed within months of treatment tended to have greater difficulty coping with the physical effects of treatment compared with their White counterparts. Given the large variability in time since diagnosis across these different studies, further examination of the roles of race, length of follow-up, and other factors are needed in future studies about QOL and PCa survivors. Although there have been some studies that have included a substantial number of African American PCa survivors,^{14,29} it is a limitation of this and other studies to not be able to determine the impact of racial differences on QOL. Therefore, increased efforts to recruit African Americans and other minorities to participate in clinical research studies remains highly important.

The study limitations include the absence of a pretreatment QOL assessment, preventing us from examining the change in QOL over time. Second, the cross-sectional design of the study limited our ability to make causal conclusions about the relationships between the EPIC domains and QOL. Third, generalizability may be limited, although our results were similar to earlier PCa studies suggesting that these results would likely generalize to non-PLCO participants.¹¹

CONCLUSION

In summary, treatment-related side effects persisted up to 10-years after diagnosis and were associated with both cancer-specific and general QOL. These associations were particularly strong for the cancer-specific QOL measure, as evidenced by the larger point estimates and statistical significance of the treatment side effects. The 3 EPIC domains were all independently associated with cancer-specific QOL, with bowel side effects exhibiting the strongest association of the 3 domains. These associations emphasize the persistent association that bowel symptoms have even many years after diagnosis. This study provides further support for the need for providers to discuss treatment-related side effects with men who are evaluating their treatment options and to assess QOL with long-term survivors.³⁰ Additionally, comorbidities, race, education, and treatment modality were also associated with cancer-specific QOL, suggesting their influence on survivors' QOL. More long-term PCa survivorship studies are needed to better understand the experience of survivors, in particular the association between treatment-related side effects and QOL.

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Table 1

Demographic and clinical variables among prostate cancer survivors

	Treated Cases		
	(N = 518)		
Variable	Mean	SD	
Age at interview	74.6	5.5	Min/Max
Years since diagnosis	7.4	1.3	5.0/9.9
	Category	N	Percentage
Race	African American	60	11.6
	White	458	88.4
Marital status	Not married	95	18.3
	Married	423	81.7
Education level	High school	146	28.2
	Some college	163	31.5
	College +	209	40.4
Income level	<50,000	237	48.4
	50,000	253	51.6
	Missing	28	
Employment status	Unemployed	398	77.1
	Employed	118	22.9
	Missing	2	
Comorbidities	1	257	49.6
	2	261	50.4
Stage at diagnosis	Stage 2	455	87.8
	Stage 3 and 4	63	12.2
PCA recurrence	No	460	88.8
	Yes	58	11.2
Gleason score	3–6	350	68.0
	7+	165	32.0
	Missing	3	
PSA level at diagnosis	4.0	77	15.9
	4.01–10.0	320	66.3
	10.01	86	17.8
	Missing	35	
Treatment modality	Surgery only	201	38.0
	Radiation only	110	20.8
	Treatment combination	207	39.1

PCA, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation.

Table 2

Correlations between the EPIC domains and general and cancer-specific measures of QOL

QOL Outcome	Mean (SD)	Pearson Correlation Coefficients with EPIC Domains		
		Sexual	Urinary	Bowel
FACT-G	93.6 (11.7)	0.32	0.35	0.42
PWB	25.5 (2.8)	0.26	0.33	0.41
SWB	22.5 (4.4)	0.24	0.23	0.23
EWB	22.1 (2.7)	0.25	0.33	0.38
FWB	23.6 (4.7)	0.29	0.29	0.37
SF-12 PCS	49.3 (8.5)	0.24	0.21	0.37
SF-12 MCS	56.5 (6.0)	0.14 *	0.22	0.29

EPIC, Expanded Prostate Index Composite; EWB, emotional well-being; FACT-G, Functional Assessment of Cancer Therapy General module; FWB, functional well-being; PWB, physical well-being; QOL, Quality of life; SF-12 MCS, Medical Outcomes Study Short Form 12 mental component score; SF-12 PCS, Medical Outcomes Study Short Form 12 physical component score; SWB, social well-being; other abbreviations as in Table 1.

* P value from Pearson correlation coefficients (r) testing: $P = .0022$, all other P values in correlation matrix $< .0001$.

Table 3

Multivariate linear regression model for factors associated with cancer-specific quality of life (FACT-G total score)

Step	Variables	Label	R ²	R ²	Point Estimate	SE	95% CI
1	Study arm	UC (ref: screen)	0.14	0.14	1.50	0.86	-0.22 to 3.22
	Medical comorbidities	1 (ref: 2+)			3.24	0.87	1.50 to 4.98**
	Race	White (ref: A-A)			4.06	1.35	1.36 to 6.76**
	Treatment modality	RP (ref: TC)			3.26	1.06	1.14 to 5.38**
		RT (ref: TC)			3.34	1.20	0.94 to 5.74**
	Education	College+ (ref: HS)			3.06	1.06	0.94 to 5.18**
		Some college (ref: HS)			2.50	1.11	0.28 to 4.72*
	Employment	Unemployed (ref: employed)			1.07	1.05	-1.03 to 3.17
	PCa recurrence	Recurrence (ref: none)			0.42	1.47	-2.52 to 3.36
	Age	Continuous			0.18	0.09	0.00 to 0.36*
2	Bowel bother	Continuous	0.37	0.23	0.29	0.03	0.23 to 0.35***
	Urinary function	Continuous			0.11	0.02	0.07 to 0.15***
	Sexual function	Continuous			0.07	0.01	0.05 to 0.09***

A-A, African American; CI, confidence interval; HS, high school; RP, radical prostatectomy; RT, radiation therapy; SE, standard error; TC, treatment combination; UC, usual care; other abbreviations as in Tables 1 and 2.

The point estimates, standard errors, and confidence intervals are all from the final model that includes all covariates. For categorical variables, the point estimate is the adjusted mean difference between the groups of interest, whereas for the continuous variables it is the adjusted mean change in the outcomes measure for a 1-unit increase in the predictor variable.

Step 1: model without EPIC domains, $F = 8.01$, and $df = 10$; step 2: model with EPIC domains, $F = 22.01$, and $df = 13$.

There was no significant difference when comparing those who received RP to those who received RT (estimate = -0.08, 95% CI = -2.52 to 2.36).

* $P < .05$;

** $P < .01$;

*** $P < .0001$

Table 4

Multivariate linear regression model for factors associated with the general quality of life (SF-12)

SF-12 Domain	Step	Variables	Label	R ²	R ²	Point Estimate	SE	95% CI
PCS	1	Study arm	Screen (ref: UC)	0.18	0.18	0.48	0.67	-0.86 to 1.82
		Medical comorbidities	1 (ref: 2+)			3.40	0.68	2.04 to 4.76***
		Race	White (ref: A-A)			0.83	1.06	-1.29 to 2.95
		Treatment	RP (ref: TC)			2.63	0.83	0.97 to 4.29**
		Education	RT (ref: TC)			2.84	0.94	0.96 to 4.72**
			College+ (ref: HS)			1.50	0.83	-0.16 to 3.16
			Some college (ref: HS)			0.70	0.87	-1.04 to 2.44
		Employment	Unemployed (ref: Employed)			1.13	0.82	-0.51 to 2.77
		PCa recurrence	Recurrence (ref: None)			-1.60	1.15	-3.90 to 0.70
		Age	Continuous			-0.12	0.07	-0.26 to 0.02
MCS	2	Bowel bother	Continuous	0.27	0.09	0.17	0.03	0.11 to 0.23***
		Urinary function	Continuous			0.04	0.01	0.02 to 0.06*
		Sexual function	Continuous			0.02	0.01	0.00 to 0.04
		Study arm	Screen (ref: UC)	0.04	0.04	0.75	0.51	-0.27 to 1.77
	1	Medical comorbidities	1 (ref: 2+)			0.62	0.52	-0.42 to 1.66
		Race	White (ref: A-A)			1.17	0.8	-0.43 to 2.77
		Treatment	RP (ref: TC)			0.67	0.63	-0.59 to 1.93
			RT (ref: TC)			0.66	0.71	-0.76 to 2.08
		Education	College+ (ref: HS)			1.28	0.63	0.02 to 2.54*
			Some college (ref: HS)			1.46	0.66	0.14 to 2.78*
		Employment	Unemployed (ref: Employed)			-0.67	0.62	-1.91 to 0.57
		PCa recurrence	Recurrence (ref: None)			0.49	0.87	-1.25 to 2.23
		Age	Continuous			0.08	0.05	-0.02 to 0.18
	2	Bowel bother	Continuous	0.14	0.1	0.12	0.02	0.08 to 0.16***
		Urinary function	Continuous			0.04	0.01	0.02 to 0.06**
		Sexual function	Continuous			0.01	0.01	-0.01 to 0.03

MCS, mental component score; PCS, physical component score; other abbreviations as in Tables 1-3.

The point estimates, standard errors, and confidence intervals are all from the final model that includes all covariates. For categorical variables, the point estimate is the adjusted mean difference between the groups of interest, whereas for the continuous variables it is the adjusted mean change in the outcomes measure for a 1-unit increase in the predictor variable.

PCS-12: step 1: model without EPIC domains, $F = 10.82$, and $df = 10$; step 2: model with EPIC domains, $F = 13.84$, and $df = 13$.

There was no significant difference when comparing those who received RP to those who received RT (estimate = -0.21 , 95% CI = -2.13 to 1.71).

MCS-12: Step 1: model without EPIC domains, $F = 1.95$, and $df = 10$; step 2: model with EPIC domains, $F = 6.31$, and $df = 13$.

There was no significant difference when comparing those who received RP to men who received RT (estimate = 0.01 , 95% CI = -1.43 to 1.45).

* $P < .05$;

** $P < .01$;

*** $P < .0001$