Brief Report

"Just As I Expected": A Longitudinal Cohort Study of the Impact of Response Expectancies on Side Effect Experiences During Radiotherapy for Prostate Cancer

Elise J. Devlin, PhD, Hayley S. Whitford, PhD, Linley A. Denson, MPsych, PhD, and Andrew E. Potter, BMedSc, MBBS, FRANZCR

School of Psychology (E.J.D., H.S.W., L.A.D.), Faculty of Health and Medical Sciences, The University of Adelaide, Adelaide, South Australia; University of South Australia Cancer Research Institute (H.S.W.), University of South Australia, Adelaide, South Australia; and GenesisCare Radiation Oncology South Australia (A.E.P.), Adelaide, South Australia, Australia

Abstract

Context. Previous research has indicated that pretreatment response expectancies of side effects often predict subsequent toxicity severity. However, this has been largely based on female patients undergoing chemotherapy.

Objectives. We tested whether this association also occurred in a novel cohort, men with prostate cancer undergoing radiotherapy. We investigated these associations throughout treatment (before and after side effects were medically predicted to occur), controlling known and novel variables.

Methods. Homogenous male patients scheduled for radiotherapy ($N = 35$, mean age 71 years) completed baseline (pretreatment) measures; response expectancies of 18 treatment-related side effects; questions about baseline health and hormonal treatment, emotional state, and coping style. Response expectancies of the side effects were again measured two weeks into treatment. The severity of the same 18 toxicities was assessed two and seven weeks into treatment.

Results. Hierarchical multiple linear regressions revealed baseline response expectancies significantly and independently predicted six of 18 toxicities two weeks into radiotherapy, contributing 12%−30% of explained variance ($\beta = 0.39-0.59$). Response expectancies assessed two weeks into treatment significantly and uniquely predicted seven of 17 experienced toxicities at seven weeks, explaining 17%−50% of variance ($\beta = 0.49-0.91$). Sexual toxicity response expectancies revealed the strongest associations with experience throughout treatment ($\beta = 0.46-0.91$), with "inability to reach orgasm" showing the largest effect.

Conclusion. In this older male sample, response expectancies of side effects predicted experiences throughout treatment, including the period before toxicities were medically expected. Response expectancies of sexual side effects were robust, independent predictors of subsequent toxicities across treatment, especially issues with orgasm, warranting focus in practice and future research. J Pain Symptom Manage 2019;57:273−281.

Key Words

Expect, nocebo, oncology, psychology, radiotherapy, sexual dysfunction

Introduction

It is important to understand how to predict and reduce cancer treatment−related side effects (toxicities), which can have adverse physical, psychological, social, and economic outcomes for patients and often persist after treatment.[1−3] Patients' pretreatment response expectancies are one potential nonpharmacological predictor of side effect severity.

Address correspondence to: Elise J. Devlin, PhD, School of Psychology, The University of Adelaide, Level 5, Hughes Building, North Terrace, Adelaide, South Australia 5000, Australia. E-mail: elise.devlin@adelaide.edu.au

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Response expectancies (REs) are individuals' anticipations for how they will automatically respond to treatments, medications, and other stimuli.[4] These specific expectancies are proposed to directly impact subsequent experiences[4] and have been extensively investigated; REs for cancer treatment–related side effects generally demonstrate small-to-moderate associations with subsequent toxicities.[5–7] Accordingly, REs may inform screening tools for patients requiring additional preventative intervention or assistance, particularly when delivering side effect information.[8]

A comparative investigation of REs for cancer treatment toxicities indicated female patients, aged younger than 65 years, and scheduled for chemotherapy form more REs than other groups.[9] This also reflects the profile of the current literature, female chemotherapy patients (average age of 53.4, SD = 5.81), treated for breast cancer.[6,7] Thus, explicit research considering the impact of REs of side effects in other treatment modalities and patient groups is needed, to test the robustness of these associations.

The influence of REs on radiotherapy-induced toxicities has not been measured directly[7]; however, patients undergoing radiotherapy demonstrated associations between REs for nausea and subsequent nausea severity, in a two-day preintervention assessment.[10] Furthermore, REs remain significant predictors of toxicity severity in studies of patients receiving adjuvant chemotherapy and radiotherapy.[11]

Specific investigation of radiotherapy REs is required, given inherent treatment differences. Unlike chemotherapy, a systemic pharmacotherapy targeting cancer cells throughout the body, radiotherapy is localized and targets specific body regions, most commonly causing isolated side effects in the treated area (e.g., skin irritation, organ disruption). Nevertheless, radiotherapy side effects can be severe enough to require reduction in intensity, or premature discontinuation (potentially impacting tumor control[12]), and can induce subjective toxicities (i.e., fatigue[13,14]).

Treatment regularity also differs. Chemotherapy is commonly administered in cycles with recovery periods, whereas radiotherapy is typically continuous—every weekday for approximately 7.5 weeks. It is often observed (clinically) that patients experience nonspecific side effects in the early weeks of radiotherapy, which are not medically expected and can be reduced by reassurance alone.[15] This suggests that REs may be prevalent and influential early in treatment. Repeated experience with a treatment can strengthen future REs for side effects that have occurred[16,17]; thus, radiotherapy protocols may induce increasingly strong REs of side effects throughout treatment.

Other pretreatment variables influence associations between REs of side effects and subsequent experiences.[18] For example, patients may misattribute preexisting symptoms to treatment.[9] Of 1129 patients with mixed cancer diagnoses, 84% reported symptoms before radiotherapy.[14] Furthermore, 30%–60% of patients with prostate cancer experience anxiety[3,19] and/or depression[20] during treatment, and 15 of 20 chemotherapy toxicity REs were associated with anxiously preoccupied coping style.[21]

We investigated associations between REs of side effects and subsequent toxicity experience in a novel and homogenous patient sample (different from typical samples)—older men undergoing radiotherapy for prostate cancer. Based on chemotherapy research, we hypothesized that REs of side effects would independently predict experienced toxicity severity at two follow-ups, controlling for related demographic, health, and psychological variables.

Methods

Patients and Procedures

Consecutive male outpatients diagnosed with Stage I–III prostate cancer were identified. They were scheduled to begin external beam radiation therapy (EBRT) with curative intent, between 74 and 78 Gray (Gy), in two public teaching hospitals in the Australian state of South Australia. Patients' treating radiation oncologist determined eligibility: a clinical nurse mailed out study invitations. Criteria were as follows: aged over 18 years, English fluency, able to consent, chemotherapy, and radiotherapy naïve. Patients receiving neoadjuvant androgen deprivation (hormone) therapy were eligible. Patients were excluded if they had a psychiatric disease or cognitive impairment, previous prostatectomy, or if participating in another study. This study was approved by the Human Research Ethics Committee of the presenting hospital, compliant with the Declaration of Helsinki, and The National Statement on Ethical Conduct in Human Research (Approval #130929).

Owing to slow accrual, inclusion criteria were expanded in June 2014 from patients having EBRT in isolation, to include patients having EBRT at 46–50 Gy, combined with high-dose-rate brachytherapy boost, after a radiation oncologist verified treatment regimens were identical throughout the first five weeks. The initial two assessments were obtained from these additional participants, but they were excluded from T3 follow-up (seven weeks) because treatment schedules diverged. Between March 2014 and July 2015, 48 patients enrolled at the baseline (Fig. 1). Thirteen did not continue to their specified

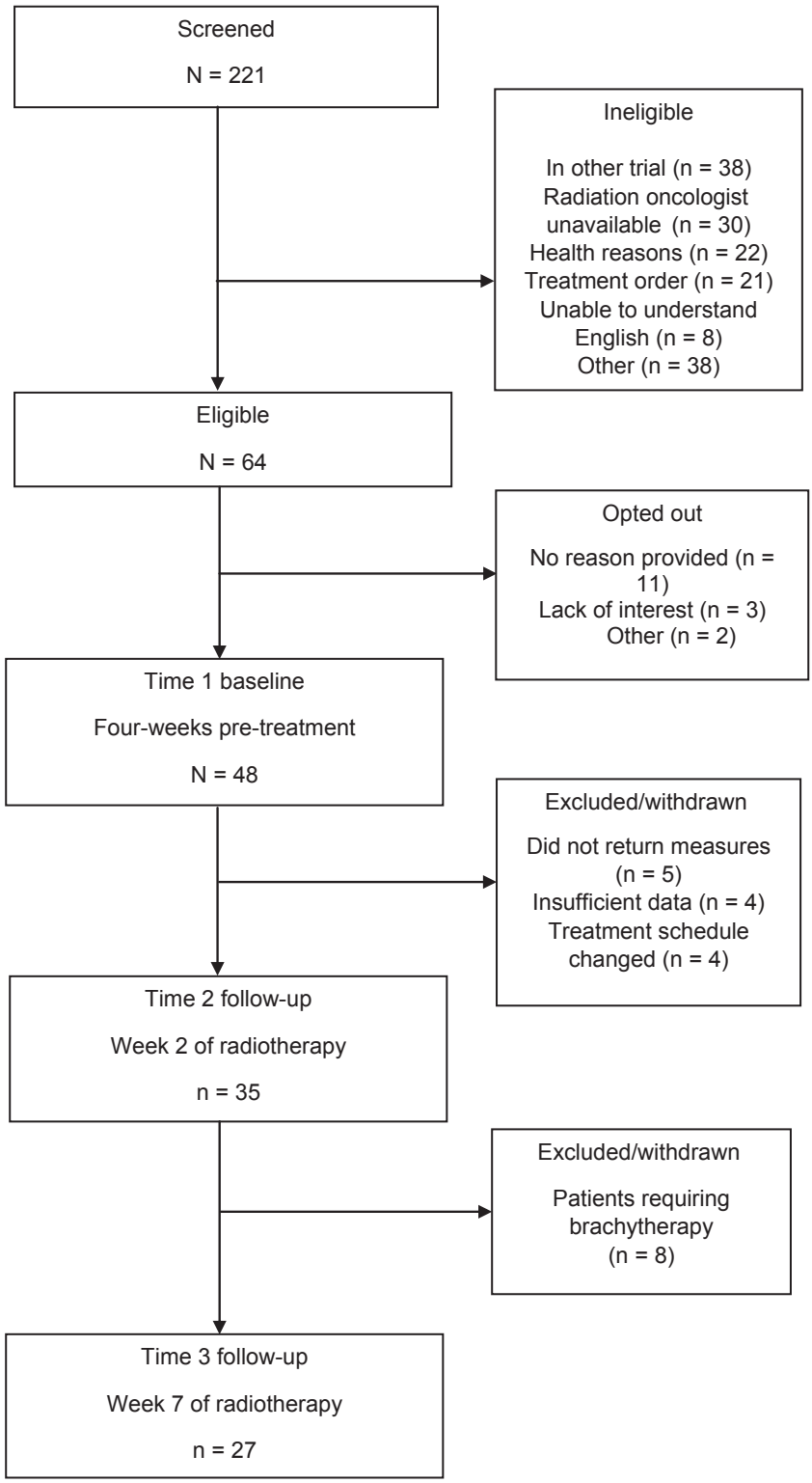

Fig. 1. Participant flowchart throughout the study.

final follow-up, leaving 35 participants (73% retention rate).

Written informed consent and baseline self-report questionnaires were completed immediately after planning scans (approximately four weeks before treatment). If requested, the questionnaire could be taken and returned (within 48 hours), to increase accrual. Baseline measures (T1) included emotional state, cancer coping style, demographic information, and REs of side effects for the initial two weeks of treatment.

T2 follow-up occurred two weeks into EBRT, approximately 6 weeks after the baseline. Patients reported side effect experiences, and those receiving EBRT in isolation again reported their toxicity REs, anticipated during the next 5 weeks of treatment. Patients scheduled for brachytherapy ceased participation at T2. T3 follow-up, 7 weeks into treatment (11 weeks after the baseline), was similar to T2 follow-up but excluded RE assessment. All follow-up sessions occurred in waiting rooms before patients' radiation oncologist appointments, for participants' convenience. Three patients could not complete the scale on their appointment day, instead completing it within the same week.

Measures

The study-specific demographic and health questionnaire comprised 26 questions: basic demographic and health information (including preexisting symptoms) and perceived knowledge of treatment. The Charlson Comorbidity Index[22] measured incidence of comorbidities, based on medical records.

The Depression, Anxiety and Stress Scale 21 (DASS21[23,24]) measures an individual's levels of depressive, anxious, and stress symptomatology, over the preceding week. Twenty-one items produce separate scores for each construct (seven items per scale). DASS21 has good reliability,[24] replicated in our study for stress and depression but not anxiety (Cronbach's $\alpha = 0.86$, 0.87, and 0.62, respectively).

The Mental Adjustment to Cancer scale documents cognitive and behavioral coping responses to cancer diagnoses. Patients self-rate how 40 statements apply to them "at the present moment." Five subscales (Fighting Spirit, Fatalistic, Helpless/Hopeless, Anxious Preoccupation, and Avoidance) each demonstrate adequate reliability, validity, and acceptability to patients.[25] We found similar reliability to original research, except lower reliability for the Fatalistic scale (Cronbach's $\alpha = 0.43$; all others $\alpha = 0.70–0.90$).

Patients rated REs of 18 treatment-related side effects on Visual Analogue Scales. They were asked how severely they believed they would experience each side effect, marking horizontal 100 mm lines, segmented at multiples of 10 and anchored at (0) "do not expect the side effect at all" and (100) "expect the worst possible severity of the side effect." Specific times were used for each assessment, as recommended in previous research.[7] These were as follows: 1) the first two weeks of treatment, 2) the next five weeks of treatment. The list of side effects comprised common known acute toxicities,[26] compiled in conjunction with radiation oncologists and radiotherapy information nurses. Each scale had an additional implausible side effect (loss of head hair) included as quality control for careless responding.[27]

Participants recorded side effect severity on near-identical Visual Analogue Scales, with the same toxicities listed, but anchored by (0) "did not experience the side effect at all" and (100) "experienced the worst possible severity of the side effect." Participants were asked to rate how severe their experience of each side effect was during 1) the first two weeks of treatment and 2) the last five weeks of treatment.

Statistical Analyses

Data were analyzed using IBM SPSS Version 22 (Armonk, NY). Frequencies and descriptive statistics characterized the sample. Univariate correlations identified covariates for multivariate analyses (Supplementary Tables 1 and 2). Hierarchical multiple linear regressions investigated associations between side effect REs and subsequent experiences, above and beyond known and novel predictors. Unique covariates or covariate combinations were simultaneously added to Step 1, and patient REs were added to Step 2, to determine their unique variance.

Two series of regression analyses (T1 to T2, then T2 to T3) assessed associations before and after side effects were medically expected. The first model analyzed the strength of T1 REs to predict experiences at T2, above and beyond covariates that correlated with REs or experience for each side effect at $r \geq 0.35$ (i.e., significant relationships). The second model regressed T2 REs of side effects onto T3 experiences and included covariates that were associated at least $r \geq 0.40$ (a higher association was utilized in line with statistical significance).[28]

A priori power analysis indicated that 39 participants were required for 80% power with an alpha level of 0.05, to observe moderate effects ($r \geq 0.30$) in a within-group design of three repeated measures, using two-tailed tests.[28] Because we accrued slightly fewer patients (due to the homogeneity requirements of the sample/treatment, and lower numbers at T3), effect sizes were reported and discussed alongside exact *P*-values.[29] Correlation coefficients (r), phi coefficients (ϕ), and standardized beta coefficients (β) of 0.10, 0.30, and 0.50, and Cohen's d (d) of 0.20, 0.50, and 0.80 represent small, moderate, and large effects,

Table 1
Significant Differences Between Patients Who Continued to Their Specified Final Follow-Up and Those Who Did Not

Outcome Variable	Continued to Final Follow-Up	*n*	M	SD	*t*	df	*P*	ϕd
T1 urinary urgency	Yes	35	1.7	0.5				
	No	9	2.0	0.0	−4.21	34.00	0.001	0.31
Helpless/hopeless coping style	Yes	34	9.2	2.7				
	No	9	7.5	1.8	2.30	41.00	0.03	0.74
T1 response expectancy of urinary urgency	Yes	34	2.4	2.4				
	No	9	0.9	1.1	2.85	41.00	0.01	0.80
T1 response expectancy of urinary frequency	Yes	33	3.3	2.5				
	No	9	1.0	1.3	3.78	24.99	0.001	1.17
T1 response expectancy of hair loss (pelvis)	Yes	33	1.9	2.1				
	No	9	0.7	1.3	2.21	20.61	0.04	0.72
T1 response expectancy of bowel leakage	Yes	34	1.6	1.9				
	No	9	0.6	1.0	2.15	24.28	0.04	0.67

Phi coefficients (ϕ) represent small (0.10), moderate (0.30), and large (0.50) effects, and Cohen's d (d) represent small (0.20), moderate (0.50), and large (0.80) effects.[28]

respectively.[28] Owing to the sample size and the empirical basis of hypotheses, Bonferroni adjustments were not used, to avoid inflating Type II error which was of greater concern.[30]

Results

Data Screening

Missing data were screened and four cases were removed (Fig. 1). No multicollinearity or homoscedasticity of residuals were observed; however, 12 (of 36) models had one outlier (z-score range = 3.55−5.70; 29). Removal of outliers did not improve normality so scores were retained. Error residuals were normally distributed at T3; however, at T2, eight were normally distributed and 10 were not. Transformations were attempted for skewed data but reduced the sample size considerably and did not improve distributions. Ordinal logistic regression was considered; however, the assumption of parallel lines was not met, and there was insufficient power for covariate analyses.[29] Therefore, we conducted two sets of hierarchical regression analyses of raw data because 1) these analyses were consistent with similar chemotherapy studies[21,31] and 2) violation of normality is not considered to invalidate regression.[29]

Attrition Analyses

No significant differences were found between patients who did or did not continue to their specified final follow-up (T2 for brachytherapy patients and T3 for EBRT patients) for demographic or emotional state data. However, those who did not continue reported significantly higher levels of the Mental Adjustment to Cancer helpless/hopeless coping style (Table 1), lower pretreatment levels of urinary urgency, and higher baseline REs of urinary urgency, urinary frequency, hair loss in the pelvic region, and bowel leakage.

Descriptive Statistics

Most patients were married, high-school educated, not working, Australian-born, and identified with Western culture (Table 2). Overall, patients reported a normal level of daily activity and moderate knowledge of radiotherapy. Most were not receiving psychological assistance during treatment and felt they had received adequate side effect−related information. At baseline, most patients indicated no intention to participate in alternative or self-management strategies during treatment; but some reported that they would try or continue meditation (n = 8, 22.9%),

Table 2
Baseline Participant Characteristics

Demographics and Health Data	Mean (SD)	Sample Range
Comorbidity	0.4 (0.6)	0−2
Activity	1.3 (0.6)	0−3
Side effect knowledge	3.1 (1.0)	1−5
		n (%)
Country of birth		
Australia		27 (77.1)
Other		8 (22.9)
Culture		
Western		29 (82.8)
Both Eastern and Western		3 (8.6)
Eastern		1 (2.9)
Marital status		
Married/de facto		23 (65.7)
Not married		11 (34.3)
Education		
Secondary		17 (48.6)
Tertiary		9 (25.7)
Primary		7 (20.0)
Work status		
Not working		32 (91.4)
Working		2 (5.8)
Psychological assistance		
No		33 (94.3)
Yes		2 (5.7)
Perception of amount of information received		
Right amount		27 (77.1)
Not enough		7 (20.0)

Table 3
The Prediction of Baseline Response Expectancies on Subsequent Experiences Two Weeks Into EBRT

			Full Model			Unique Contribution of Response Expectancies			
Toxicity	*n*	Covariates	Adjusted R^2	*F*	*P*	R^2 Change	*F* Change	*P*	β
Fatigue	33	[a]	−0.06	0.31	0.82	0.02	0.54	0.47	0.16
Nausea	33	[a,b,c,d,e,f]	0.50	4.93	0.002	0.06	0.05	0.82	0.04
Abdominal cramps	34	[a,b,d,e,f,g]	0.16	1.84	0.13	0.03	1.18	0.29	0.26
Skin irritation	34	[d]	0.01	1.20	0.32	0.06	1.82	0.19	0.26
Urinary frequency	33	[h,i,j]	0.45	7.31	<0.001	0.02	0.95	0.34	0.15
Hair loss (pelvis)	32	[d]	0.06	2.53	0.10	0.06	1.98	0.17	0.27
Pain, burning, or discomfort when urinating	34	[a,c,d,i,j,k]	0.36	3.42	0.01	0.01	0.42	0.52	0.13
Poor urinary stream	34	[e,h,i,j,l]	0.40	4.70	0.003	0.04	2.18	0.15	0.26
Blood in urine	34	[b,d,e,j]	0.22	2.76	0.04	0.22	9.02	0.01	0.63
Urinary urgency	33	[d,e,i,j]	0.24	3.57	0.01	0.07	2.95	0.10	0.42
Urinary incontinence	34	[a,d,j]	0.27	5.28	0.003	0.12	5.31	0.03	0.39
Rectal urgency	33	[a,d,e,n,o]	0.39	4.07	0.01	0.03	1.48	0.24	0.21
Painful bowel movement	34	[a,b,d,e,m]	0.31	3.07	0.02	0.01	0.58	0.45	0.16
Bowel leakage	34	[a,d,m,p]	0.32	3.76	0.01	0.20	8.80	0.01	0.50
Blood in stools	33	[a,b,d,e,p]	0.06	1.31	0.29	0.04	1.26	0.27	0.26
Reduced desire for sex	32	[c,i,p]	0.61	12.99	<0.001	0.29	22.90	<0.001	0.57
Inability to reach orgasm	30	[i,j]	0.38	6.92	0.001	0.30	14.19	0.001	0.59
Inability to have or maintain erection	29	[c,h,i,j]	0.41	8.30	<0.001	0.15	9.67	0.01	0.46

EBRT = external beam radiation therapy.
Included covariates significantly ($r \geq 0.35$) associated with response expectancies or experiences: [a]stage of disease; [b]age; [c]number of comorbidities; [d]highest level of education; [e]helpless/hopeless coping style; [f]stress; [g]anxious preoccupied coping style; [h]culture identification; [i]baseline level of that toxicity; [j]treatment; [k]day-to-day activity level; [l]avoidant coping style; [m]English as a first language; [n]marital status; [o]time since diagnosis; [p]hormone therapy; adjusted R^2 = variance explained by the model predictors, adjusted for the number of predictors; R^2 change = unique variance contributed to the model by expectancies of the side effect; β = standardized regression coefficient (beta), representing small (0.10), moderate (0.30), and large (0.50) effects.[28]

prayer ($n = 4$, 11.4%), or massage, acupuncture, and yoga ($n = 1$, 0.0%).

Patients had an average age of 71 years (SD = 7.5) and few comorbidities[22]: 12 (27.3%) patients had one comorbidity and two (6.7%) had two, well below levels in similar age samples.[32] Most were diagnosed 12 months before participation (range = 2−51 months) and most ($n = 27$, 77.1%) were treated with EBRT in isolation, but eight (22.9%) had additional brachytherapy. Half had received androgen deprivation (hormone therapy; $n = 19$, 54.3%) and most were treated at the presenting hospital ($n = 25$, 71.4%), with 10 (28.6%) treated at the secondary hospital.

Preexisting Side Effects

Preexisting symptoms were measured to ensure toxicities were not long-standing. Baseline symptom levels were generally low ($n = 1$−5, 2.9%−14.3%); however, 12 patients (34.3%) reported urgent urination, 14 (45.7%) reported an inability to reach orgasm, 16 (45.7%) reported reduced desire for sex, and 17 (48.6%) reported erectile inability. Baseline symptoms significantly associated with the relevant side effect REs or experiences were controlled for in regression models.

Associations Between REs of Side Effects and Subsequent Experiences

Hierarchical linear multiple regressions determined the unique contribution of REs on subsequent experiences. Table 3 shows the first regression series for T1 REs (pretreatment baseline) on experiences at T2 (to two weeks into EBRT). The full models (covariates and REs) significantly predicted 13 of 18 T2 side effects, explaining 22%−61% of the variance, according to adjusted R^2 outcomes. T1 REs uniquely and significantly predicted six T2 side effects according to R^2 change values, independently contributing 12%−30% to the variance explained. These were inability to reach orgasm, blood in urine, bowel leakage, and reduced sexual desire (all large effects) and erectile inability and incontinence (moderate effects).

Table 4 shows regressions for T2 REs (two weeks into EBRT) on experiences reported at T3 (seven weeks into EBRT). Models could not be fit for blood in stools at T3 because no men reported this side effect. For blood in urine, no covariates correlated with RE or experience above the cutoff ($r \geq 0.40$), therefore simple regression was used, revealing no significant prediction, $F(1,23) = 0.57$, $P = 0.46$, and a small adjusted R^2 (0.02). For the remaining 16 toxicities, full models significantly predicted 12 side effects. Between 19% and 100% of variance was explained in the significant models. REs uniquely contributed significant variance to seven models, explaining 17%−50% of variance in side effect severity. The unique prediction by REs was large for inability to reach orgasm; erectile inability; reduced sexual desire; pain, burning, or discomfort when urinating; poor urinary stream; and painful bowel movements, and moderate for bowel leakage.

Table 4
The Predictions of Response Expectancies of Toxicities Two Weeks Into EBRT on Subsequent Experiences Seven Weeks Into EBRT

			Full Model			Unique Contribution of Response Expectancies			
Toxicity	*n*	Covariates	Adjusted R^2	*F*	*P*	R^2 Change	*F* Change	*P*	β
Fatigue	25	[a,b,c]	0.06	1.83	0.19	0.15	3.65	0.07	0.44
Nausea	27	[a,d]	0.07	1.61	0.22	0.16	4.20	0.05	0.46
Abdominal cramps	27	[b,e,f,g]	0.40	4.00	0.01	0.00	0.03	0.86	0.03
Skin irritation	27	[f]	0.19	4.00	0.03	0.00	0.00	0.97	0.01
Urinary frequency	27	[h,i,j]	0.32	3.98	0.02	0.03	1.03	0.32	0.21
Hair loss in pelvic region	27	[g,h,k]	0.04	1.26	0.32	0.02	0.54	0.47	0.18
Pain, burning, or discomfort when urinating	27	[i,j,l]	0.62	10.64	<0.001	0.17	10.71	0.004	0.52
Poor urinary stream	27	[i,j]	0.55	11.30	<0.001	0.35	19.57	<0.001	0.77
Urinary urgency	27	[h,i,j]	0.32	3.99	0.02	0.04	1.61	0.22	0.28
Urinary incontinence	26	[h,i]	0.52	9.58	<0.001	0.03	1.24	0.28	0.17
Rectal urgency	27	[h,k]	0.13	2.18	0.12	0.002	0.06	0.82	0.05
Painful bowel movement	27	[i,m]	0.46	7.98	0.001	0.23	10.56	0.004	0.51
Bowel leakage	26	[k]	0.44	10.92	<0.001	0.24	10.76	0.003	0.49
Reduced desire for sex	24	[e,i,n]	0.96	142.62	<0.001	0.40	235.59	<0.001	0.70
Inability to reach orgasm	22	[e,l,o]	1.00	—	—	0.50	—	—	0.91
Inability to have or maintain erection	23	[e,o]	0.77	25.98	<0.001	0.37	36.09	<0.001	0.75

EBRT = external beam radiation therapy.
Included covariates significantly ($r \geq 0.40$) associated with response expectancies or experiences: [a]age; [b]stage of disease; [c]avoidant coping style; [d]helpless/hopeless coping style; [e]number of comorbidities; [f]anxiety; [g]highest level of education; [h]depression; [i]marital status; [j]treatment; [k]stress; [l]culture identification; [m]English as a first language; [n]hormone therapy; [o]baseline level of that toxicity; adjusted R^2 = variance explained by the model predictors, adjusted for the number of predictors; R^2 change = unique variance contributed to the model by expectancies of the side effect; β = standardized regression coefficient (beta) representing small (0.10), moderate (0.30), and large (0.50) effects.[28]

Discussion

We extrapolated previous research on the influence of REs on experiences to a diagnostically homogenous male radiotherapy sample. Associations were investigated throughout treatment, above and beyond known and novel covariates, specific to each side effect.

By two weeks into EBRT, REs independently explained a significant amount (moderate-to-large variance) of side effect severity for six toxicities. Given side effects are not medically expected at this early stage of treatment, based on low accrued radiation dose,[15] REs might help explain their occurrence. Thus, toxicities at this time may be particularly amenable to expectancy-based interventions such as open-label placebos, information framing, or hypnosis.[10,16,18,33]

By seven weeks of EBRT (near completion), REs (measured two weeks into treatment) uniquely predicted seven side effects, aligning with previous research and theory.[4,7,17] This was not universal; thus, expectancy-based interventions that are specific to individual side effects (or symptom clusters, such as sexual side effects) may be more effective than generally targeting all toxicities.

REs of sexual side effects predicted subsequent experience to a moderate-to-large degree throughout treatment. For "inability to reach orgasm," the full model (including REs, preexistence of this symptom, culture identification, and patient comorbidity) entirely predicted subsequent experience. There is an evidenced lack of association between some sexual toxicities and the strength of radiation dose,[13] suggesting these toxicities may have a large psychological component and thus may be sensitive to intervention. Kirsch[16] highlighted male sexual dysfunction as a gap in RE literature, but minimal investigation has occurred. Male patients warned about potential erectile dysfunction with beta-blockers experienced this more than those who were not told,[34] and significant relationships between REs and "problems with sex" have been reported in male and female patients undergoing chemotherapy.[31,35] A study of 150 male chemotherapy patients (mixed diagnoses) revealed approximately 80% reported receiving no information about sexual side effects from doctors, and of those who did, 24% had directly requested it.[36] Thus, it appears REs of sexual side effects have important clinical implications, requiring effective discussions with patients without heightening REs (and hence experienced severity).

Preexisting levels of symptoms and comorbid conditions were low in our sample and did not account for the ability of REs to predict toxicities: it does not appear that patients were attributing preexisting side effects to treatment. Attrition analyses revealed that participants who withdrew reported significantly higher helpless/hopeless styles of coping and increased REs of four toxicities, indicating potential selection bias toward more healthy and optimistic participants.

Many aspects of this study were novel. Most studies had recruited women (average age 53 years), treated with chemotherapy.[9] Instead, we studied a homogeneous sample of men (average age 71 years), treated with radiotherapy. A previous review revealed that studies including patients with differing cancer diagnoses reported significantly lower effect sizes[6]; thus, we attempted to remove this potential variance. Treatment dosage and schedule and participant demographics were all highly similar, allowing greater control of confounds. Although this reduced sample size, the risk of underpowered analyses (i.e., Type II error) was mitigated by theoretically driven hypotheses, ensuring only variables significantly related to REs or side effects were included in full models. To increase sample size, we broadened inclusion criteria to include patients having EBRT followed by brachytherapy, but they were excluded before T3, thus T3 numbers were too low for repeated-measures analyses.

Some side effect experiences demonstrated skewed error residuals at T2; thus, the models may have been less suited to capturing the full picture of the associations than linear relationships.[29] However, regression analyses are often robust to this assumption.[29] The magnitude of many of the associations and the homogeneity of the sample and treatment support the influence of REs of radiotherapy side effects on subsequent experiences.

Taken together, associations between REs of side effects and experiences were replicated in this novel sample and treatment regimen, although not for all toxicities; hence, interventions should target side effects more strongly predicted by REs. Some toxicities occurred and were predicted by REs before they were medically expected; thus, REs appeared to influence side effects from as early as two weeks into EBRT and may partly explain the experience of nonspecific side effects. Of particular importance, sexual side effects appear to be strongly predicted by pretreatment REs; thus, careful pretreatment discussion is indicated.

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Appendix

Supplementary Table 1

Possible Covariates Correlated $r \geq 0.35$ With Response Expectancies (T1) and Experiences (T2), for Inclusion in Regression Analyses ($n = 23–34$)

Side Effect REs and Experiences	Age	Stage	Comorbidity	Education	Culture	Marital Status	Treatment	Hormone	Time Since Diagnosis	Preexisting Symptoms	English First Language	Activity Level	MAC H/H[a]	MAC AV[a]	MAC Fa[a]	MAC FS[a]	MAC AP[a]	Depression[b]	Anxiety[b]	Stress[b]
Response expectancy	*r (P)*																			
Fatigue	−0.21	0.37	0.01	0.28	0.14	−0.21	−0.10	−0.15	−0.29	−0.05	0.00	−0.22	0.16	0.01	0.05	−0.22	0.08	−0.05	0.18	0.03
	(0.23)	(0.04)	(0.95)	(0.12)	(0.45)	(0.24)	(0.57)	(0.41)	(0.11)	(0.79)	(0.99)	(0.20)	(0.96)	(0.96)	(0.78)	(0.23)	(0.64)	(0.79)	(0.32)	(0.89)
Nausea	−0.40	0.43	0.13	0.49	0.01	−0.17	−0.27	−0.25	−0.16	0.15	0.17	−0.23	0.42	0.21	0.18	−0.01	0.29	0.19	0.34	0.23
	(0.02)	(0.02)	(0.48)	(0.01)	(0.96)	(0.36)	(0.12)	(0.16)	(0.37)	(0.40)	(0.33)	(0.20)	(0.02)	(0.26)	(0.32)	(0.97)	(0.11)	(0.28)	(0.05)	(0.20)
Abdominal cramps	−0.52	0.41	0.25	0.41	−0.03	−0.09	−0.29	−0.10	−0.16	0.14	0.14	−0.20	0.41	0.23	0.06	−0.05	0.39	0.20	0.33	0.29
	(0.001)	(0.02)	(0.1)	(0.02)	(0.86)	(0.62)	(0.09)	(0.57)	(0.36)	(0.42)	(0.44)	(0.26)	(0.02)	(0.20)	(0.74)	(0.78)	(0.02)	(0.25)	(0.06)	(0.09)
Skin irritation	−0.26	0.32	0.12	0.36	0.04	−0.15	−0.17	−0.26	−0.21	—	0.09	−0.30	0.09	−0.11	0.00	−0.17	0.06	0.07	0.17	0.01
	(0.14)	(0.09)	(0.52)	(0.05)	(0.82)	(0.42)	(0.35)	(0.14)	(0.23)		(0.60)	(0.09)	(0.61)	(0.56)	(0.99)	(0.34)	(0.75)	(0.70)	(0.34)	(0.95)
Urinary frequency	−0.20	0.14	−0.08	0.31	0.01	−0.13	−0.33	−0.09	−0.24	−0.38	0.09	−0.04	0.30	0.30	0.22	−0.03	0.30	0.01	0.27	0.12
	(0.26)	(0.46)	(0.65)	(0.09)	(0.97)	(0.48)	(0.06)	(0.61)	(0.19)	(0.03)	(0.63)	(0.82)	(0.09)	(0.10)	(0.23)	(0.89)	(0.09)	(0.97)	(0.13)	(0.49)
Hair loss (pelvis)	−0.26	0.23	−0.00	0.44	−0.04	−0.12	−0.23	−0.21	−0.04	—	0.07	−0.27	0.28	0.14	0.15	0.07	0.32	0.12	0.19	0.10
	(0.15)	(0.24)	(0.98)	(0.01)	(0.83)	(0.52)	(0.07)	(0.24)	(0.90)		(0.71)	(0.13)	(0.13)	(0.46)	(0.43)	(0.70)	(0.08)	(0.51)	(0.11)	(0.57)
Pain, burning, or discomfort when urinating	−0.22	0.28	−0.01	0.44	−0.09	−0.04	−0.39	−0.22	−0.08	−0.44	0.18	−0.22	0.33	0.23	0.22	0.06	0.27	0.15	0.31	0.20
	(0.22)	(0.13)	(0.95)	(0.01)	(0.63)	(0.85)	(0.02)	(0.12)	(0.67)	(0.01)	(0.32)	(0.21)	(0.06)	(0.24)	(0.24)	(0.76)	(0.13)	(0.39)	(0.07)	(0.25)
Poor urinary stream	−0.25	0.23	0.05	0.33	−0.11	−0.04	−0.33	−0.10	−0.12	−0.14	0.09	−0.04	0.37	−0.37	0.25	−0.01	0.33	0.17	0.31	0.17
	(0.16)	(0.23)	(0.80)	(0.06)	(0.55)	(0.84)	(0.06)	(0.59)	(0.52)	(0.44)	(0.60)	(0.83)	(0.03)	(0.04)	(0.17)	(0.95)	(0.03)	(0.35)	(0.08)	(0.35)
Blood in urine	−0.48	0.34	0.04	0.48	0.01	−0.02	−0.36	−0.25	−0.14	0.15	0.04	−0.09	0.37	0.11	0.15	0.01	0.30	0.09	0.29	0.35
	(0.004)	(0.06)	(0.82)	(0.01)	(0.94)	(0.93)	(0.04)	(0.15)	(0.45)	(0.39)	(0.60)	(0.63)	(0.03)	(0.55)	(0.41)	(0.95)	(0.09)	(0.61)	(0.1)	(0.04)
Urinary urgency	−0.23	0.15	−0.05	0.36	−0.08	0.05	−0.25	−0.21	−0.17	−0.77	0.20	−0.04	0.37	0.23	0.33	−0.04	0.20	0.14	0.23	0.19
	(0.20)	(0.43)	(0.78)	(0.04)	(0.64)	(0.76)	(0.16)	(0.23)	(0.35)	(<0.001)	(0.25)	(0.82)	(0.03)	(0.21)	(0.06)	(0.83)	(0.27)	(0.44)	(0.20)	(0.27)
Urinary incontinence	−0.17	0.39	0.06	0.43	−0.12	−0.11	−0.13	−0.34	−0.10	−0.01	0.12	−0.22	−0.30	0.20	0.21	−0.01	0.17	0.21	0.33	0.24
	(0.34)	(0.04)	(0.74)	(0.01)	(0.51)	(0.55)	(0.47)	(0.05)	(0.59)	(0.94)	(0.51)	(0.21)	(0.10)	(0.28)	(0.25)	(0.94)	(0.35)	(0.24)	(0.06)	(0.17)
Rectal urgency	−0.22	0.49	0.17	0.43	−0.12	−0.01	−0.12	−0.29	−0.15	0.23	0.27	−0.23	0.36	0.23	0.24	0.08	0.29	0.13	0.25	0.25
	(0.21)	(0.01)	(0.35)	(0.02)	(0.53)	(0.98)	(0.49)	(0.10)	(0.42)	(0.21)	(0.13)	(0.20)	(0.04)	(0.22)	(0.19)	(0.67)	(0.10)	(0.46)	(0.16)	(0.16)
Painful bowel movement	−0.35	0.36	0.17	0.49	−0.08	−0.11	−0.22	−0.34	−0.11	0.14	0.18	−0.15	0.35	0.10	0.21	0.09	0.33	0.08	0.16	0.13
	(0.05)	(0.05)	(0.35)	(0.004)	(0.66)	(0.54)	(0.21)	(0.05)	(0.54)	(0.42)	(0.32)	(0.39)	(0.05)	(0.57)	(0.25)	(0.61)	(0.06)	(0.67)	(0.36)	(0.46)
Bowel leakage	−0.20	0.38	0.15	0.40	−0.03	−0.12	−0.17	−0.43	−0.10	−0.19	0.47	−0.13	0.19	0.02	0.19	0.14	0.18	0.06	0.17	0.22
	(0.25)	(0.04)	(0.40)	(0.03)	(0.88)	(0.51)	(0.34)	(0.01)	(0.57)	(0.29)	(0.13)	(0.46)	(0.30)	(0.93)	(0.30)	(0.45)	(0.31)	(0.74)	(0.34)	(0.21)
Blood in stools	−0.35	0.35	0.16	0.49	−0.07	−0.12	−0.19	−0.35	−0.14	0.15	0.16	−0.19	0.38	0.15	0.20	0.10	0.34	0.09	0.16	0.18
	(0.05)	(0.06)	(0.37)	(0.01)	(0.70)	(0.51)	(0.29)	(0.04)	(0.46)	(0.42)	(0.38)	(0.30)	(0.03)	(0.42)	(0.27)	(0.60)	(0.06)	(0.61)	(0.36)	(0.32)
Reduced desire for sex	0.01	−0.06	−0.28	0.22	0.01	−0.27	−0.16	−0.26	−0.22	−0.36	0.06	0.09	0.13	0.15	0.35	−0.05	0.10	−0.07	0.14	0.05
	(0.96)	(0.75)	(0.12)	(0.23)	(0.95)	(0.14)	(0.37)	(0.15)	(0.24)	(0.04)	(0.73)	(0.64)	(0.50)	(0.42)	(0.06)	(0.81)	(0.61)	(0.70)	(0.45)	(0.79)
Inability to reach orgasm	−0.03	0.02	−0.15	0.33	0.05	−0.18	−0.36	−0.12	−0.11	−0.24	−0.20	−0.27	0.05	0.00	0.09	0.02	0.09	−0.00	0.27	0.06
	(0.88)	(0.94)	(0.43)	(0.08)	(0.79)	(0.34)	(0.05)	(0.54)	(0.56)	(0.19)	(0.28)	(0.15)	(0.80)	(0.99)	(0.65)	(0.91)	(0.64)	(0.99)	(0.14)	(0.75)
Erectile inability	0.07	−0.10	−0.20	0.21	−0.05	−0.17	−0.36	−0.04	0.10	−0.37	0.07	−0.22	−0.02	0.09	0.10	0.05	0.06	−0.04	0.21	0.21
	(0.71)	(0.61)	(0.27)	(0.27)	(0.78)	(0.36)	(0.04)	(0.85)	(0.60)	(0.04)	(0.70)	(0.22)	(0.91)	(0.63)	(0.59)	(0.79)	(0.77)	(0.83)	(0.26)	(0.26)
Toxicity	*r (P)*																			
Fatigue	−0.21	0.12	0.27	−0.23	0.13	−0.03	−0.04	−0.11	−0.18	−0.10	−0.14	−0.09	−0.17	−0.24	−0.28	−0.28	−0.14	−0.04	0.09	0.18
	(0.24)	(0.53)	(0.13)	(0.21)	(0.47)	(0.85)	(0.81)	(0.53)	(0.32)	(0.56)	(0.42)	(0.60)	(0.35)	(0.19)	(0.11)	(0.12)	(0.43)	(0.81)	(0.62)	(0.62)
Nausea	−0.51	−0.04	0.50	−0.22	−0.02	0.02	−0.30	−0.11	−0.06	0.07	−0.10	0.10	0.21	0.08	−0.02	−0.01	−0.02	0.12	0.22	0.43
	(0.002)	(0.83)	(0.003)	(0.23)	(0.93)	(0.91)	(0.10)	(0.55)	(0.77)	(0.71)	(0.59)	(0.59)	(0.25)	(0.68)	(0.90)	(0.96)	(0.90)	(0.49)	(0.22)	(0.01)
Abdominal cramps	−0.35	0.09	0.27	−0.10	0.09	0.13	−0.25	−0.15	−0.06	0.04	−0.08	0.18	0.20	0.17	0.03	0.08	0.06	0.26	0.25	0.47
	(0.04)	(0.65)	(0.13)	(0.61)	(0.62)	(0.48)	(0.15)	(0.39)	(0.76)	(0.81)	(0.66)	(0.31)	(0.25)	(0.36)	(0.88)	(0.66)	(0.73)	(0.14)	(0.17)	(0.01)
Skin irritation	−0.04	−0.13	0.03	−0.14	−0.10	0.05	−0.03	−0.20	−0.08	—	0.08	0.07	−0.19	−0.19	0.02	−0.03	−0.29	0.06	−0.03	0.10
	(0.84)	(0.49)	(0.86)	(0.45)	(0.58)	(0.77)	(0.88)	(0.24)	(0.65)		(0.64)	(0.69)	(0.29)	(0.29)	(0.93)	(0.85)	(0.10)	(0.73)	(0.86)	(0.59)
Urinary frequency	−0.07	−0.23	−0.22	−0.07	−0.45	0.08	−0.43	0.09	0.17	−0.14	0.33	0.19	−0.03	0.05	0.00	−0.04	0.16	0.00	0.01	−0.07
	(0.71)	(0.22)	(0.20)	(0.69)	(0.01)	(0.65)	(0.01)	(0.61)	(0.34)	(0.42)	(0.06)	(0.27)	(0.85)	(0.77)	(0.99)	(0.85)	(0.36)	(0.99)	(0.97)	(0.69)
Hair loss (pelvis)	−0.14	0.10	−0.16	0.31	−0.03	0.06	−0.30	0.12	−0.09	—	0.13	−0.09	0.22	0.13	−0.01	−0.18	0.13	−0.29	0.12	0.17
	(0.42)	(0.59)	(0.38)	(0.09)	(0.86)	(0.73	(0.09)	(0.48)	(0.63)		(0.48)	(0.62)	(0.21)	(0.47)	(0.94)	(0.33)	(0.48)	(0.10)	(0.50)	(0.33)
Pain, burning, or discomfort when urinating	−0.13	−0.46	0.02	−0.25	0.02	0.02	−0.39	0.15	0.13	−0.06	−0.17	0.35	−0.25	−0.25	−0.12	0.01	0.03	0.16	−0.19	−0.10
	(0.44)	(0.01)	(0.92)	(0.16)	(0.90)	(0.90)	(0.02)	(0.40)	(0.46)	(0.73)	(0.30)	(0.04)	(0.16)	(0.16)	(0.52)	(0.96)	(0.86)	(0.36)	(0.29)	(0.57)

Poor urinary stream	−0.02 (0.92)	−0.21 (0.26)	−0.18 (0.31)	−0.04 (0.81)	−0.39 (0.03)	0.07 (0.70)	−0.38 (0.03)	−0.03 (0.87)	0.09 (0.62)	−0.60 (<0.001)	0.31 (0.07)	0.16 (0.37)	−0.11 (0.54)	−0.04 (0.85)	0.02 (0.91)	−0.02 (0.93)	0.01 (0.94)	−0.01 (0.95)	−0.04 (0.82)	−0.02 (0.90)
Blood in urine	−0.19 (0.29)	0.02 (0.90)	0.05 (0.80)	−0.21 (0.25)	0.11 (0.56)	0.06 (0.73)	−0.16 (0.36)	−0.23 (0.19)	0.02 (0.90)	0.04 (0.81)	−0.08 (0.67)	0.30 (0.08)	−0.02 (0.91)	−0.08 (0.67)	−0.09 (0.63)	0.03 (0.87)	−0.00 (0.99)	−0.02 (0.93)	0.03 (0.85)	0.27 (0.11)
Urinary urgency	−0.11 (0.55)	−0.04 (0.82)	−0.23 (0.19)	0.07 (0.72)	−0.30 (0.10)	0.19 (0.28)	−0.53 (0.001)	−0.09 (0.63)	0.21 (0.24)	−0.37 (0.03)	0.20 (0.26)	0.15 (0.39)	0.06 (0.74)	−0.07 (0.71)	0.12 (0.53)	0.06 (0.70)	0.15 (0.41)	0.09 (0.60)	0.03 (0.86)	0.07 (0.70)
Urinary incontinence	−0.26 (0.13)	−0.16 (0.40)	−0.14 (0.41)	0.11 (0.56)	−0.12 (0.51)	−0.22 (0.21)	−0.58 (<0.001)	−0.02 (0.93)	0.14 (0.43)	0.07 (0.70)	−0.20 (0.26)	−0.26 (0.14)	−0.05 (0.78)	−0.16 (0.38)	−0.02 (0.93)	−0.04 (0.82)	0.18 (0.32)	0.06 (0.74)	0.05 (0.80)	−0.04 (0.83)
Rectal urgency	0.15 (0.41)	−0.27 (0.15)	−0.18 (0.31)	−0.22 (0.24)	−0.28 (0.12)	0.47 (0.01)	−0.26 (0.14)	0.04 (0.81)	0.63 (<0.001)	0.13 (0.46)	0.11 (0.54)	0.03 (0.87)	−0.08 (0.68)	0.15 (0.41)	−0.00 (0.98)	0.11 (0.55)	0.08 (0.66)	−0.14 (0.43)	−0.16 (0.36)	-0.12 (0.500
Painful bowel movement	0.02 (0.90)	−0.15 (0.43)	−0.10 (0.56)	0.04 (0.81)	0.10 (0.58)	0.29 (0.10)	−0.10 (0.56)	0.09 (0.63)	−0.11 (0.55)	0.05 (0.79)	0.62 (<0.001)	−0.03 (0.87)	−0.03 (0.88)	−0.11 (0.57)	−0.09 (0.63)	0.04 (0.83)	−0.03 (0.86)	−0.05 (0.78)	0.02 (0.94)	−0.04 (0.80)
Bowel leakage	0.27 (0.12)	−0.23 (0.22)	−0.14 (0.42)	−0.17 (0.34)	−0.17 (0.34)	−0.11 (0.52)	−0.13 (0.47)	0.04 (0.84)	−0.15 (0.39)	−0.19 (0.27)	0.40 (0.02)	−0.03 (0.87)	−0.32 (0.07)	0.01 (0.94)	0.15 (0.40)	0.25 (0.16)	−0.29 (0.09)	−0.14 (0.41)	−0.13 (0.46)	−0.07 (0.70)
Blood in stools	−0.36 (0.03)	0.02 (0.93)	0.19 (0.28)	−0.02 (0.93)	0.07 (0.69)	0.15 (0.40)	−0.32 (0.07)	−0.16 (0.37)	−0.04 (0.81)	0.03 (0.87)	−0.05 (0.76)	0.21 (0.22)	0.18 (0.30)	0.05 (0.78)	−0.04 (0.84)	−0.05 (0.78)	0.11 (0.55)	0.08 (0.65)	−0.03 (0.89)	0.30 (0.08)
Reduced desire for sex	0.04 (0.84)	−0.07 (0.73)	−0.35 (0.05)	0.11 (0.58)	−0.25 (0.17)	−0.26 (0.16)	−0.03 (0.85)	−0.39 (0.03)	−0.06 (0.75)	−0.43 (0.01)	0.11 (0.56)	−0.03 (0.89)	0.08 (0.68)	−0.05 (0.80)	0.13 (0.48)	−0.21 (0.27)	−0.05 (0.78)	−0.22 (0.22)	−0.20 (0.27)	−0.21 (0.24)
Inability to reach orgasm	0.16 (0.40)	−0.15 (0.47)	−0.33 (0.07)	0.09 (0.64)	−0.33 (0.08)	−0.17 (0.37)	−0.07 (0.70)	−0.22 (0.23)	−0.01 (0.97)	−0.37 (0.04)	0.10 (0.59)	−0.11 (0.56)	0.06 (0.76)	0.08 (0.68)	0.11 (0.56)	−0.20 (0.30)	−0.09 (0.63)	−0.12 (0.53)	−0.04 (0.84)	−0.14 (0.44)
Erectile inability	0.22 (0.24)	−0.21 (0.29)	−0.39 (0.04)	0.03 (0.88)	−0.43 (0.02)	−0.11 (0.57)	−0.01 (0.94)	−0.25 (0.18)	−0.24 (0.21)	−0.41 (0.02)	0.10 (0.61)	−0.10 (0.59)	0.03 (0.90)	0.06 (0.76)	0.05 (0.79)	−0.21 (0.28)	−0.14 (0.47)	−0.26 (0.17)	−0.20 (0.28)	−0.27 (0.15)

MAC = Mental Adjustment to Cancer; DASS21 = Depression, Anxiety and Stress Scale 21.
All toxicity response expectancies and experiences were measured using Visual Analogue Scale ranging from 0 to 100.
[a]MAC subscales.[25]
[b]DASS21 scales.[24]

Supplementary Table 2

Possible Covariates Correlated $r \geq 0.40$ With Response Expectancies (T2) and Experiences (T3), for Inclusion in Regression Analyses ($n = 23–34$)

Side Effect REs and Experiences	Age	Stage	Comorbidity	Education	Culture	Marital Status	Treatment	Hormone	Time Since Diagnosis	Preexisting Symptoms	English First Language	Activity Level	MAC H/H	MAC AV	MAC Fa	MAC FS	MAC AP	Depression	Anxiety	Stress
Response expectancy	*r (P)*																			
Fatigue	−0.48 (0.01)	0.24 (0.20)	0.21 (0.24)	0.19 (0.31)	0.11 (0.56)	−0.19 (0.31)	−0.15 (0.40)	−0.14 (0.43)	0.23 (0.19)	−0.10 (0.57)	−0.14 (0.44)	−0.14 (0.45)	0.25 (0.16)	−0.22 (0.23)	0.14 (0.44)	−0.02 (0.91)	0.23 (0.20)	0.09 (0.63)	0.11 (0.53)	0.36 (0.04)
Nausea	−0.41 (0.02)	0.22 (0.24)	0.11 (0.52)	0.35 (0.05)	0.02 (0.93)	0.35 (0.05)	−0.34 (0.05)	−0.10 (0.56)	0.11 (0.54)	0.12 (0.51)	−0.02 (0.90)	−0.15 (0.41)	0.42 (0.02)	0.04 (0.83)	0.21 (0.26)	0.03 (0.88)	0.15 (0.41)	0.09 (0.62)	0.19 (0.30)	0.33 (0.06)
Abdominal cramps	−0.28 (0.12)	0.41 (0.02)	0.03 (0.86)	0.28 (0.12)	−0.01 (0.96)	0.28 (0.12)	−0.24 (0.18)	−0.22 (0.21)	0.08 (0.65)	0.10 (0.58)	0.03 (0.87)	−0.03 (0.88)	0.30 (0.10)	0.10 (0.60)	0.12 (0.50)	−0.02 (0.91)	0.19 (0.30)	0.10 (0.59)	0.26 (0.15)	0.35 (0.04)
Skin irritation	−0.15 (0.42)	0.23 (0.22)	−0.00 (0.99)	0.34 (0.06)	0.08 (0.67)	−0.04 (0.81)	−0.11 (0.53)	−0.29 (0.10)	0.20 (0.25)	—	0.14 (0.44)	−0.07 (0.68)	0.16 (0.37)	−0.05 (0.79)	0.23 (0.21)	−0.01 (0.97)	0.00 (0.99)	0.18 (0.31)	0.11 (0.55)	0.26 (0.15)
Urinary frequency	−0.37 (0.04)	−0.16 (0.40)	−0.21 (0.23)	0.13 (0.48)	0.12 (0.50)	0.00 (0.99	−0.60 (<0.001)	0.10 (0.67)	0.03 (0.88)	−0.16 (0.35)	0.02 (0.92)	0.20 (0.27)	0.12 (0.49)	−0.13 (0.47)	0.16 (0.38)	0.08 (0.67)	0.18 (0.31)	−0.10 (0.57)	−0.01 (0.57)	0.13 (0.46)
Hair loss (pelvis)	−0.22 (0.22)	0.35 (0.06)	0.09 (0.61)	0.42 (0.02)	0.08 (0.66)	−0.19 (0.28)	−0.31 (0.07)	0.02 (0.92)	−0.02 (0.90)	—	−0.14 (0.42)	−0.09 (0.62)	0.30 (0.09)	0.07 (0.70)	0.04 (0.82)	−0.00 (0.98)	0.26 (0.15)	0.44 (0.01)	0.38 (0.03)	0.41 (0.02)
Pain, burning, or discomfort when urinating	−0.29 (0.11)	−0.14 (0.47)	−0.00 (0.99)	0.09 (0.62)	−0.03 (0.86)	0.10 (0.60)	−0.54 (0.001)	0.10 (0.58)	−0.06 (0.74)	−0.18 (0.30)	0.18 (0.32)	0.15 (0.38)	0.09 (0.63)	−0.05 (0.78)	0.07 (0.69)	0.20 (0.28)	0.22 (0.21)	−0.07 (0.68)	−0.05 (0.78)	0.09 (0.61)
Poor urinary stream	−0.26 (0.14)	0.10 (0.59)	−0.14 (0.42)	0.22 (0.23)	0.06 (0.77)	0.08 (0.65)	0.60 (<0.001)	0.04 (0.80)	−0.03 (0.87)	−0.36 (0.04)	0.05 (0.78)	0.10 (0.58)	0.09 (0.63)	−0.10 (0.58)	0.10 (0.61)	0.10 (0.60)	0.17 (0.34)	−0.11 (0.52)	−0.03 (0.86)	0.07 (0.71)
Blood in urine	−0.18 (0.32)	0.34 (0.07)	−0.07 (0.72)	0.32 (0.08)	0.08 (0.65)	−0.28 (0.12)	−0.26 (0.14)	−0.09 (0.61)	0.14 (0.43)	0.12 (0.52)	−0.05 (0.78)	−0.04 (0.83)	0.14 (0.45)	−0.13 (0.48)	0.02 (0.91)	0.07 (0.70)	0.25 (0.17)	0.18 (0.32)	0.26 (0.14)	0.27 (0.21)
Urinary urgency	−0.39 (0.02)	−0.11 (0.57)	−0.19 (0.28)	0.10 (0.59)	0.14 (0.45)	0.03 (0.86)	−0.65 (<0.001)	−0.10 (0.97)	−0.06 (0.75)	−0.39 (0.02)	−0.08 (0.64)	0.25 (0.15)	0.10 (0.57)	−0.18 (0.31)	0.17 (0.35)	0.12 (0.51)	0.24 (0.17)	−0.16 (0.38)	−0.04 (0.81)	0.05 (0.77)
Urinary incontinence	−0.15 (0.41)	0.29 (0.13)	−0.27 (0.35)	0.35 (0.05)	0.14 (0.45)	−0.32 (0.05)	−0.31 (0.07)	−0.12 (0.50)	0.07 (0.68)	0.12 (0.51)	−0.12 (0.51)	−0.05 (0.78)	0.12 (0.53)	−0.14 (0.43)	0.08 (0.68)	0.09 (0.64)	0.24 (0.19	0.14 (0.43)	0.27 (0.13)	0.17 (0.33)
Rectal urgency	−0.06 (0.73)	0.33 (0.09)	−0.13 (0.46)	0.19 (0.30)	−0.14 (0.44)	−0.03 (0.89)	−0.19 (0.30)	−0.15 (0.41)	−0.17 (0.35)	0.10 (0.60)	−0.01 (0.97)	0.06 (0.73)	0.01 (0.95)	0.03 (0.86)	−0.08 (0.66)	0.11 (0.57)	0.17 (0.35)	−0.13 (0.47)	0.17 (0.33)	0.11 (0.53)
Painful bowel movement	−0.09 (0.63)	0.18 (0.33)	−0.11 (0.54)	0.28 (0.13)	−0.04 (0.83)	−0.03 (0.87)	−0.17 (0.34)	−0.08 (0.65)	0.14 (0.43)	0.10 (0.57)	0.31 (0.07)	−0.15 (0.39)	0.13 (0.47)	0.01 (0.97)	0.05 (0.79)	0.04 (0.84)	0.10 (0.60)	−0.06 (0.75)	0.19 (0.29)	0.12 (0.51)
Bowel leakage	−0.04 (0.83)	−0.17 (0.38)	−0.17 (0.33)	0.25 (0.18)	−0.13 (0.48)	−0.10 (0.57)	−0.20 (0.26)	−0.30 (0.08)	−0.04 (0.82)	−0.22 (0.21)	0.08 (0.67)	−0.03 (0.84)	0.02 (0.93)	−0.10 (0.60)	0.07 (0.70)	0.09 (0.63)	0.13 (0.48)	−0.18 (0.31)	0.08 (0.66)	0.10 (0.59)
Blood in stools	−0.35 (0.04)	−0.20 (0.31)	0.08 (0.66)	0.27 (0.13)	0.11 (0.54)	−0.24 (0.18)	−0.38 (0.03)	−0.05 (0.78)	0.08 (0.65)	0.09 (0.60)	−0.09 (0.60)	−0.14 (0.43)	0.25 (0.16)	−0.11 (0.54)	0.16 (0.39)	0.12 (0.51)	0.05 (0.78)	−0.11 (0.53)	0.08 (0.65)	0.17 (0.33)
Reduced desire for sex	0.11 (0.57)	−0.17 (0.38)	−0.31 (0.08)	0.07 (0.72)	−0.09 (0.64)	−0.21 (0.25)	−0.26 (0.15)	−0.22 (0.22)	0.06 (0.74)	−0.36 (0.04)	0.06 (0.74)	−0.03 (0.88)	0.01 (0.95)	−0.19 (0.32)	0.17 (0.38)	0.01 (0.94)	−0.08 (0.69)	−0.24 (0.20)	−0.11 (0.54)	−0.04 (0.82)
Inability to reach orgasm	0.09 (0.63)	−0.20 (0.31)	−0.24 (0.19)	0.18 (0.35)	−0.17 (0.37)	−0.14 (0.44)	−0.29 (0.10)	−0.10 (0.58)	0.12 (0.51)	−0.45 (0.01)	0.03 (0.89)	−0.17 (0.37)	0.02 (0.91)	−0.09 (0.63)	0.12 (0.53)	0.03 (0.86)	−0.15 (0.41)	−0.27 (0.13)	−0.04 (0.81)	−0.10 (0.95)
Inability to have or maintain erection	0.08 (0.65)	−0.17 (0.34)	−0.22 (0.24)	0.19 (0.30)	−0.18 (0.35)	−0.15 (0.42)	−0.25 (0.16)	−0.13 (0.47)	0.11 (0.54)	−0.51 (0.003)	0.03 (0.88)	−0.20 (0.38)	0.04 (0.81)	−0.16 (0.39)	0.11 (0.55)	0.00 (0.99)	−0.07 (0.72)	−0.26 (0.16)	−0.06 (0.77)	0.00 (0.99)
Toxicity	*r (P)*																			
Fatigue	0.02 (0.93)	0.41 (0.06)	0.30 (0.14)	−0.07 (0.77)	0.07 (0.74)	0.01 (0.97)	0.21 (0.30)	−0.37 (0.07)	0.15 (0.49)	−0.36 (0.08)	−0.02 (0.91)	−0.09 (0.66)	−0.38 (0.07)	−0.49 (0.02)	−0.16 (0.48)	−0.07 (0.77)	−0.25 (0.25)	0.22 (0.29)	0.16 (0.45)	0.39 (0.05)
Nausea	0.10 (0.63)	0.34 (0.10)	0.06 (0.79)	−0.02 (0.93)	−0.04 (0.86)	0.14 (0.49)	0.07 (0.75)	0.06 (0.76)	−0.00 (0.99)	0.07 (0.75)	0.15 (0.47)	0.02 (0.94)	0.08 (0.71)	0.05 (0.83)	0.09 (0.68)	0.09 (0.68)	0.07 (0.74)	0.01 (0.96)	0.15 (0.47)	0.38 (0.05)
Abdominal cramps	−0.17 (0.40)	0.16 (0.46)	0.54 (0.004)	−0.46 (0.02)	−0.14 (0.52)	−0.17 (0.42)	0.06 (0.77)	−0.25 (0.21)	−0.31 (0.12)	0.06 (0.77)	−0.11 (0.70)	0.09 (0.67)	0.30 (0.10)	−0.37 (0.07)	−0.16 (0.44)	−0.08 (0.71)	−0.27 (0.18)	0.26 (0.19)	0.60 (0.001)	0.35 (0.08)
Skin irritation	−0.06 (0.78)	0.14 (0.50)	0.28 (0.15)	−0.19 (0.35)	−0.14 (0.51)	0.25 (0.21)	0.09 (0.65)	−0.15 (0.46)	−0.08 (0.69)	—	0.33 (0.09)	−0.10 (0.61)	−0.15 (0.45)	−0.05 (0.83)	0.04 (0.85)	0.10 (0.62)	0.06 (0.76)	0.22 (0.28)	0.51 (0.01)	0.25 (0.20)
Urinary frequency	0.02 (0.92)	0.02 (0.92)	0.13 (0.51)	−0.05 (0.81)	−0.29 (0.17)	−0.47 (0.02)	−0.26 (0.19)	−0.29 (0.14)	−0.11 (0.59)	−0.26 (0.19)	0.01 (0.95)	0.05 (0.80)	−0.19 (0.36)	−0.23 (0.28)	−0.03 (0.89)	−0.11 (0.59)	−0.20 (0.33)	0.44 (0.02)	0.30 (0.14)	0.23 (0.25)
Hair loss (pelvis)	0.02 (0.91)	0.18 (0.39)	0.01 (0.95)	0.28 (0.17)	0.09 (0.66)	−0.06 (0.79)	0.06 (0.75)	−0.03 (0.87)	0.08 (0.68)	—	−0.04 (0.84)	−0.12 (0.57)	0.08 (0.71)	−0.12 (0.58)	0.13 (0.54)	−0.01 (0.97)	0.21 (0.32)	−0.04 (0.84)	−0.06 (0.76)	0.21 (0.30)
Pain, burning, or discomfort when urinating	−0.07 (0.73)	−0.15 (0.48)	0.17 (0.41)	0.07 (0.76)	−0.40 (0.05)	−0.46 (0.02)	−0.31 (0.12)	−0.18 (0.38)	−0.11 (0.57)	−0.12 (0.55)	0.10 (0.62)	0.03 (0.90)	−0.03 (0.87)	−0.17 (0.42)	−0.01 (0.96)	−0.03 (0.91)	0.07 (0.72)	0.30 (0.13)	0.10 (0.64)	0.04 (0.85)
Poor urinary stream	0.02 (0.94)	0.01 (0.95)	0.23 (0.25)	0.05 (0.82)	−0.30 (0.15)	−0.47 (0.02)	−0.30 (0.13)	−0.11 (0.58)	−0.06 (0.78)	−0.43 (0.03)	0.03 (0.89)	−0.01 (0.97)	−0.12 (0.58)	−0.22 (0.30)	0.02 (0.94)	0.06 (0.77)	0.00 (0.99)	0.38 (0.05)	0.25 (0.23)	0.27 (0.17)
Blood in urine	0.04 (0.84)	0.04 (0.86)	0.26 (0.18)	−0.19 (0.36)	−0.39 (0.06)	−0.25 (0.22)	0.06 (0.76)	0.06 (0.77)	−0.23 (0.25)	0.06 (0.76)	−0.11 (0.58)	0.08 (0.70)	−0.17 0.41)	−0.14 (0.51)	−0.04 (0.86)	−0.09 (0.66)	−0.20 (0.34)	0.01 (0.96)	−0.04 (0.84)	0.13 (0.53)

Urinary urgency	0.14	0.03	0.10	0.04	−0.31	−0.46	−0.26	−0.20	−0.06	−0.16	−0.01	0.11	−0.13	−0.18	−0.13	−0.27	−0.29	−0.43	0.21	0.20
	(0.49)	(0.91)	(0.62)	(0.84)	(0.13)	(0.02)	(0.18)	(0.32)	(0.79)	(0.44)	(0.95)	(0.58)	(0.51)	(0.39)	(0.55)	(0.19)	(0.16)	(0.02)	(0.31)	(0.32)
Urinary incontinence	−0.05	0.04	0.17	0.30	−0.32	−0.44	−0.11	−0.08	−0.11	−0.20	−0.09	0.06	0.21	0.04	0.25	−0.04	−0.06	0.65	0.28	0.34
	(0.81)	(0.85)	(0.40)	(0.16)	(0.12)	(0.03)	(0.59)	(0.69)	(0.58)	(0.33)	(0.67)	(0.79)	(0.32)	(0.87)	(0.25)	(0.86)	(0.78)	(<.001)	(0.18)	(0.09)
Rectal urgency	0.32	0.09	0.17	−0.01	−0.01	−0.18	0.03	0.19	0.20	0.12	0.17	0.00	−0.14	−0.01	−0.00	0.31	−0.11	0.48	0.23	0.41
	(0.11)	(0.67)	(0.41)	(0.97)	(0.97)	(0.37)	(0.88)	(0.34)	(0.31)	(0.54)	(0.40)	(0.99)	(0.49)	(0.95)	(0.99)	(0.13)	(0.60)	(0.01)	(0.26)	(0.04)
Painful bowel movement	0.24	0.19	−0.10	0.19	0.11	0.43	−0.17	0.10	0.29	0.10	0.47	−0.02	−0.04	−0.11	−0.00	0.17	−0.10	−0.10	0.00	0.01
	(0.24)	(0.37)	(0.63)	(0.36)	(0.59)	(0.03)	(0.40)	(0.63)	(0.14)	(0.62)	(0.01)	(0.93)	(0.86)	(0.61)	(0.98)	(0.42)	(0.98)	(0.63)	(0.98)	(0.96)
Bowel leakage	0.09	0.34	0.05	0.09	0.06	−0.03	−0.12	−0.03	0.07	−0.17	0.08	−0.06	0.08	−0.12	0.15	0.24	0.10	0.33	0.26	0.50
	(0.67)	(0.10)	(0.79)	(0.66)	(0.79)	(0.89)	(0.56)	(0.90)	(0.74)	(0.40)	(0.71)	(0.77)	(0.69)	(0.57)	(0.47)	(0.24)	(0.63)	(0.09)	(0.20)	(0.01)
Blood in stools	Model could not be achieved (no score on outcome variable)																			
Reduced desire for sex	0.18	−0.24	−0.45	0.08	−0.34	−0.41	−0.20	−0.45	−0.22	−0.36	0.04	−0.02	−0.01	−0.14	0.14	−0.16	−0.13	−0.27	−0.26	−0.29
	(0.40)	(0.28)	(0.02)	(0.73)	(0.11)	(0.05)	(0.33)	(0.02)	(0.29)	(0.08)	(0.85)	(0.94)	(0.98)	(0.52)	(0.52)	(0.46)	(0.55)	(0.20)	(0.20)	(0.16)
Inability to reach orgasm	0.37	−0.25	−0.49	0.06	−0.41	−0.28	−0.21	−0.28	−0.24	−0.32	−0.24	−0.15	−0.06	−0.03	0.07	−0.24	−0.24	−0.25	−0.09	−0.19
	(0.08)	(0.27)	(0.01)	(0.79)	(0.05)	(0.20)	(0.33)	(0.19)	(0.25)	(0.13)	(0.25)	(0.48)	(0.79)	(0.91)	(0.77)	(0.28)	(0.26)	(0.23)	(0.66)	(0.37)
Inability to have or maintain erection	0.41	−0.20	−0.46	0.09	−0.36	−0.31	−0.16	−0.36	−0.22	−0.41	0.04	0.09	−0.18	−0.36	−0.06	−0.16	−0.02	−0.35	−0.22	−0.24
	(0.06)	(0.38)	(0.02)	(0.68)	(0.09)	(0.15)	(0.45)	(0.09)	(0.31)	(0.05)	(0.87)	(0.69)	(0.40)	(0.09)	(0.80)	(0.47)	(0.95)	(0.87)	(0.30)	(0.27)

MAC = Mental Adjustment to Cancer; DASS21 = Depression, Anxiety and Stress Scale 21.
All toxicity response expectancies and experiences were measured using Visual Analogue Scale ranging from 0 to 100.
[a]MAC subscales.[25]
[b]DASS21 scales.[24]