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Development and Preliminary Testing of the Perceived Benefit and Burden Scales for Cancer Clinical Trial Participation

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Keywords

Cancer; Clinical Trials; Symptoms; Psychological Distress; Risks and Benefits

Introduction

Risk-benefit assessment is important for all people who contemplate research participation, but is particularly significant for those diagnosed with life-threatening and potentially life-limiting illnesses, such as cancer. Cancer takes the life of more than 1600 people each day (American Cancer Society, 2016) but very few adult cancer patients participate in cancer clinical trials (less than 5%) (CCTs), and minority communities are particularly underrepresented (Albain, Unger, Crowley, Coltman, & Hershman, 2009; Evens, Antillon, Aschebrook-Kilfoy, & Chiu, 2012; Murthy, Krumholz, & Gross, 2004). Once patient-participants are enrolled, however, retention becomes an important priority to minimize the threat of selection bias and meet specified study outcomes. Some evidence suggests that participation in research is motivated by an expectation and hope of benefit that might include cure, alleviation of symptoms, or other personal short and long-term goals (Ulrich et al., 2012). Altruism or 'giving something back' is also cited as an important participant benefit in both adult and pediatric research (Ulrich et al., 2012; Wendler, Abdoler, Wiener, & Grady, 2012).

We don't, however, fully understand what is beneficial or burdensome about research participation through the lens of cancer patient-participants. We often assume that potential CCT side effects such as nausea, vomiting, lack of taste, peripheral neuropathies or other odious possibilities would deter potential research participants from enrolling, or more likely, result in attrition once enrolled. But we do not know whether patient-participants who perceive research as burdensome are just as likely to tolerate various types of burdens (i.e., physical, psychological and others) and remain on trial as those who perceive it as more beneficial. Is there a balance threshold between the perceived benefit and burden that can be used to identify participants who are more likely to drop out from CCTs?

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Currently, there are no comprehensive tools to simultaneously measure both perceived benefits and burdens of research participation. In the literature, there was one measurement tool for burdens. Using our conceptual work of respondent burden as a guide, Linger and colleagues developed a 17-item perceived burden measure with Alzheimer patients and their caregivers who were participating in research at the University of Pittsburgh Alzheimer Disease Research Center (Lingler, Schmidt, Gentry, Hu, & Terhorst, 2015). However, their scale does not assess benefits, thus it does not simultaneously assess the two aspects of research participation. In addition, the authors used hypothetical scenarios to develop their items based on patients' responses instead of patients' actual experiences of participating in a trial.

Due to the absence of quantitative measures, patients and researchers rely on qualitative assessments to make research participation and retention decisions and often consider only a few elements: some focus more on benefits while others focus more on burdens. In qualitative work by Ulrich, et al., (2012) patient-participants enrolled in cancer clinical trials expressed many positive aspects of participating in clinical trials. However, some also expressed that they ignored, downplayed or overlooked the potential burdens. This partial assessment of benefits and burdens could cause problems in retention, for instance, when treatment results are not congruent with participants' expectations, some participants may consider dropping out or experience decisional regret (remorse for their initial decision to participate). Similarly, some patients could decline to participate because they overlook or underestimate some of the benefits of participation. Better assessment of both anticipated benefits and burdens at the enrollment stage of a clinical trial could lead to improved recruitment and retention strategies and participants' informed decision-making.

To address these problems, a measurement tool that can quantify the benefits and burdens of cancer clinical trial participation is needed. In this study, we report the development of the Benefit and Burden scales to quantify these concepts among cancer clinical trial participants and the preliminary results of its psychometric properties.

Conceptual Framework and Development of the Benefit and Burden Scales

We used a sequential mixed methods approach to develop and preliminarily test the benefit and burden items. First, the conceptual framework in this study was developed by using a purposive sampling strategy with maximum variation in which we interviewed 32 cancer clinical trial participants about their views on research participation, specifically the benefits and burdens. We purposively included patient-participants from different backgrounds in gender, race and ethnicity, types of cancer (liquid and solid), and diverse types of clinical trials (i.e., Phase I, II, or III and or other types of clinical treatment trials) to capture common patterns across these differences and these characteristics are reported elsewhere (Ulrich et al., 2012). In addition to the themes obtained from these interviews, our theoretical perspective was also shaped by our original conceptualization of respondent burden in clinical research which was adapted from the work of Bradburn in health survey research (Bradburn, 1977). Here, we defined respondent burden as "a subjective phenomenon that describes the perception by the subject of the psychological, physical, and/or economic hardships associated with participation in the research process." This

burden can ultimately influence patient-related and clinical trial outcomes, including but not limited to the recruitment and retention of patient-participants in CCTs. Patient-participants may experience various types of burdens depending on the risk level of the research, the procedures being employed, their current stage of cancer diagnosis and prognosis, and supportive networks available to them. In the model, we proposed that there is a relationship between benefits and burdens and research participation, including both recruitment and retention. We also identify five different indicators of benefits and burdens, including physical, psychological, economic, familial, and social.

Then, using the interview data, the theoretical model, and literature, we developed benefit and burden items with the aim of capturing all domains of the constructs. For the benefit scale, we developed 22 items representing five subscales, physical (7 items), psychological (8 items), economic (3 items), familial (1 item) and social (3 items). For the burden scale, we developed 23 items representing physical burden (8 items), psychological (8 items), economic (2 items), familial (3 items), and social burden (2 items). Each item in the scales has five response categories ranging from strongly disagree to strongly agree (1 to 5). For the benefit scale, higher scores indicate greater perceived benefits; while for the Burden scales, higher scores indicate greater perceived burdens. The concepts and items are summarized in Table 1 and Table 2.

The scales were then reviewed by experts in bioethics, instrument development, and biostatistics for content appropriateness and completeness. Survey methodologists use cognitive interviews to further validate the content domain and the clarity of questionnaire items generated from semi-structured interviews (Willis, 1996; Willis, 2006). We subsequently conducted one cognitive interview each with 8 patient-participants to improve our questionnaire items and explore participants' abilities to interpret questions, their techniques for retrieving information from memory, and their judgment formation on specific questions. Data from cognitive interviews helped guide further modifications of items. All participants in our cognitive interviews reported that the items developed for the benefit-burden measure were relevant to cancer participants' thoughts on perceptions of benefits and burdens of research participation.

Methods

The benefit and burden items were included in a large cross-sectional survey study investigating the relationship between benefit and burden assessment and cancer patients' perceptions of CCT participation and their dropout intention.

Participants

Convenience sampling was used to recruit study participants. Participants were recruited from those actively participating in a CCT at a large northeastern NCI-designated Cancer Center. Sample size for the quantitative survey was determined by statistical power analysis to detect moderate relationships between individual, protocol-related, and system-related factors and cancer research participants' perceptions of benefit and burden and retention in CCTs.

Procedure

The questionnaire included ten different domains, including socio-demographics, symptom burden and psychological mood states, perceived benefits and burdens of research participation, thoughts of dropping out and willingness to remain in the trial, and other areas (which are reported elsewhere) (Ulrich et al., 2012; Ulrich et al., 2016). In this analysis, we report only on the benefit-burden scale, which was embedded in the larger questionnaire. Several open-ended questions were also included in the questionnaire. Informed consent was obtained from all participants and surveys were distributed either face-to-face or through the mail, depending on patient-participants' preferences. An informational letter was included with the mailed survey and addressed all aspects of the research. We received 110 usable surveys from cancer patient-participants who participated in CCTs at a large Northeastern Cancer Center which provided sufficient power (80% power assuming a 5% significance level) for the study with a 77% revised response rate. The Institutional Review Board at the University of Pennsylvania and the participating cancer site approved the study.

Statistical Analyses

Descriptive statistics were used to explore the distribution for all benefit and burden items. Both the benefit scale and burden scale scores were computed as the mean of all items in those with responses on at least 50% of the scale items. To create the benefit-burden difference score, the benefit and burden mean scores were converted to standardized T scores, with mean of 50, and standard deviations of 10, and then the burden score was subtracted from the benefit score. Cronbach's alpha was used to test for internal consistency, principal component analysis (PCA) was used to determine the acceptability of a single underlying latent construct, and item response theory (IRT) graded response models were run to assess the discrimination ability of the individual items within the scale score (Baker & Kim, 2004; Samejima, 1969). Construct validity was assessed using Student's t-tests to compare scale scores between participants who did and did not have thoughts of dropping out (alpha was set at 0.05). StataMP 15 (StataCorp, 2017) was used for all analyses.

Results

Approximately half of the patient-participants were male (52.3%). The mean age of the sample was 58.7 years (SD = 12.0). Most were Caucasian (90.7%) with less than ten percent representing other ethnic and racial groups. More than three-quarters of patient-participants were married (82.6%); more than a third were working full-time (36.1%), another third retired (34.5%), while 29.9% were not employed. On the 109 patient-participants who provided data, 32.1% reported their highest degree was high school with 1.8% not completing high school; 20.2% had some college, and 45.9% were college graduates or beyond. Participants were also involved in a variety of therapeutic clinical trials that included Phases I, I, and III (Ulrich et al., 2016).

All items were assessed for missing values and less than 10% were found to be missing, with no pattern of missingness identified. For the benefit scale, 8 participants (7.3%) had missing items ranging from missing 1 to 11 items. For the burden scale, 9 participants (8.2%) had missing values ranging from missing 1 to 11 items. All items were scored on a

1–5 Likert scale and responses spanned the entire range except for benefit item #2 - “I might help future patients with my cancer (even though my participation might not help me)”. This item only had responses ranging from neutral (3) to strongly agree (5).

Benefit Scale Assessment

Item statistics for benefit questions are summarized in Table 1. The mean benefit item scores range from 1.28 to 4.43. In the category of physical and psychological benefit, a large majority agreed that one of the benefits of participating in research was being treated like a person (90.8%), followed by the benefit of giving them a sense of hope about their cancer (87.2%). Most participants were hoping for a cure (78.9%), and agreed that participation could extend life (76.1%). Less than half of the participants agreed that participation reduced their stress (47.2%) or made them worry less (44.4%). Social and economic benefits included contributing to society (94.4%), helping future patients (94.5%), and helping children or family members in the future (76.1%). Only 43.1% agreed that payment for costs of medications or tests was a benefit; and, 38.0% and 11.2% of patient-participants respectively agreed that insurance coverage for research expenses and receiving money for participating were both perceived benefits. Cronbach’s alpha was 0.90 for the benefit scale. Assessment of individual items showed that the scale alpha could only be marginally improved (0.895 to 0.903) by the removal of item #22 - “I receive money for participating in the clinical trial”. PCA showed a single latent construct that accounted for 35% of the variability, with item #22 having close to a zero weight. IRT models showed significant discrimination ability for all items except #22.

Burden Scale Assessment

The mean burden item scores range from 1.81 to 4.04 (Table 2) and they showed greater variance than the benefit items. Three-quarters of participants indicated that they would be disappointed if they were to receive a placebo (75.5%). About half (50.5%) agreed that participation had made them realize the seriousness of their cancer. Symptom burden was also prevalent with 41.3% experiencing bothersome side effects and slightly more than one in three participants worried about unknown side effects (34.3%). Social and economic burdens included worrying about other family members getting cancer (41.8%), having to re-arrange life in order to participate (38.5%), and economic hardships related to paying out of pocket for research-related activities (25.2%) and limited insurance coverage (23.1%).

Cronbach’s alpha was 0.87 for the burden scale. Assessment of individual items showed that the scale alpha could be slightly improved (0.878 to 0.883) by the removal of item #12 - “I would be very disappointed if I received a placebo (an inactive substance) instead of the treatment”. PCA showed a single latent construct that accounted for 28% of the variability. IRT models showed significant discrimination ability for all items except #12.

Construct validity

Construct validity was supported through hypothesis testing (Nunnally, 1994; Waltz, Strickland, & Lenz, 1991). We hypothesized that perceived benefit and burden are significantly related to thoughts of dropping out. We found that participants who did not have thoughts of dropping out reported higher perceived benefits (3.81 vs. 3.26, $p<0.001$)

and lower perceived burden (2.39 vs. 2.87, p<0.001) than those who had thoughts of dropping out. These results are consistent with our hypothesized directional relationships; supporting the construct validity of both of the scales.

Additionally, we assessed whether the difference between benefit and burden scale scores could predict retention in CCTs. As shown in table 3, participants with negative benefit-burden difference scores (benefit mean score<burden mean score) were more likely to have thoughts of dropping out than those with positive difference scores (benefit mean score >burden mean score) (−14.75 versus 2.92, p<0.001).

Correlation analysis found a negative and non-significant relationship between the Benefit and Burden scale scores (r=−0.13, p=0.173). Further, a PCA of the combined items showed two latent construct with the benefit items having weights on one and the burden items having weights on the other. These suggest that the benefit and burden scales are relatively independent of each other and represent different concepts.

Discussion

The recent focus on patient-centered care requires researchers to examine more closely the importance of patient preferences that affect outcomes of care, including the meaning and experience of research participation. Our study is one of the first to test a measure of patient-participants' perceived benefits and burdens in cancer clinical trial participation. The scales we developed have preliminary reliability and validity. We found significant associations between perceived benefits and burdens with thoughts of dropping out of research, supporting the construct validity hypothesis that participants who perceive more benefit than burden are less likely to consider dropping out. In addition, the benefit-burden difference score provides important information about the weighting/balancing of the two dimensions that can be used to predict participation and retention as well as provide direction for improving patients' experience in cancer clinical trials.

The National Library of Medicine provides the public with on-line information on the benefits and risks of participating in clinical trials (https://www.nlm.nih.gov/services/ctbenefits.html). They list four possible benefits and risks. Benefits include: "gaining access to new treatments that are not yet available to the public", "obtaining expert medical care at a leading health care facility", "playing an active role in your own health care", and "helping others by contributing to medical research". The possible risks listed are: "there may be unpleasant, serious or even life-threatening side effects from treatment", "treatment may not be effective for some individuals", the study may require a lot of time for traveling to the study site, receiving treatments, or hospital stays", and "health insurance may not cover all the study costs". In our study, we expanded these lists based on patient interview data to include additional domains of psychological, social, and familial benefits and burdens as well as physical and economic. Our preliminary data show that the unique items we developed are relevant indicators with good variability.

We found that for most benefit items, the mean scores were greater than 3 (in a scale from 1–5), indicating that most participants perceive these as beneficial. However, there are two

benefit items with lower mean scores. One of these items “I worry less about my cancer when I participate in research”, (mean 1.28; 44.4% agreed to this statement), suggests that most participants think that research participation does not make them worry less about their cancer. The other item with a low mean score, “I receive money for participating in the clinical trial,” was not perceived by the majority of participants (89%) as beneficial. One reason is that most participants in therapeutic CCTs do not usually receive money for participation. This likely explains why the item was found to be non-discriminatory in the IRT analysis. Future research is needed to determine the role these items play in trial participation decision making for a range of participants. It is plausible that receiving an incentive may be more important to healthy volunteers for example, who have no other reason to participate, than to those who are seriously ill, who likely have other reasons. There is little research about how important a benefit of money might be for research participants with a variety of illnesses. Moreover, research is needed to examine the relationship between the importance of receiving a financial incentive for research participation, the types of trials in which incentives are offered to patient-participants, the amount of incentives in such trials, and socio-demographic characteristics of the population sample.

Two benefit items had limited variance. Almost all participants agreed that both contributing to society and helping future patients were benefits. One reason for this overwhelming perception could be due to our sampling method. All of our participants were already enrolled in CCTs. It is possible that people who do not perceive societal contributions as benefits refused to participate in the CCTs from which we sampled, and thus were not available for inclusion in this study. Future studies with all eligible participants, including those who decide to participate and those who decline participation could help assess how these two items factor into participants’ decision making processes.

The burden items showed greater variance than the benefit items, suggesting that burdens are more individualized. The top three burdens in our study were: 1) disappointment if participants received a placebo, 2) realization of the seriousness of one’s cancer, and 3) having experienced bothersome side effects. Given that our participants are already in CCTs, their perceptions of burdens could be different from people who are considering participation. For instance, the bothersome side effects could directly result from the trial treatment, and not be foreseeable prior to enrollment in their CCT. Yet, providing these items in the scale for eligible participants who are contemplating trial participation could help then make realistic evaluations.

The unknown and possible serious side effects that participants face in clinical research was also a significant worry. Consent forms are required to include a statement saying that there could be possible, unknown side effects. It is interesting that more than 30% of our participants worry about this possibility. Future studies are needed to investigate the percentage of CCTs that have encountered unforeseeable life-threatening side effects and the characteristics of these CCTs. In addition, continued discussions are needed on symptom management strategies and the role of palliative care interventions to alleviate or mitigate symptoms in clinical research. Symptom management studies in cancer should address these concerns. There were only two items where less than 10% of participants judged to be a

burden, including the feeling of being a guinea pig (7.3%) and others perceiving the participant as a guinea pig (4.5%). Past historical abuses and more recent research misconduct continue to raise public concerns about being used as “guinea pigs.” Available evidence suggests that persons who volunteer for research rarely feel like guinea pigs and are instead proud to be research participants (Wendler et al., 2012; Wendler, Krohmal, Emanuel, Grady, & ESPIRIT Group, 2008). Another item with a low mean was “I worry that it is difficult for my family to see me take part in a research study for my cancer” (M=1.96); only 11% of participants agreed this is a burden. Future studies are needed to determine whether these items should remain in the scale. Our study participants were predominantly Caucasian and we were not able to tease out any variation on these views based on race and ethnicity.

Although both the benefit and the burden scales have excellent internal consistency, further psychometric testing is needed to test the structure of the scales using confirmative factor analysis. Also, based on the data, we suspect that the benefit and burden scales might function more like indexes than scales because when one looks at the benefits, for example, not all benefits are related. For example, the economic benefits of participating in the clinical trial might not be related to other benefit items, nor the benefit subscale score.

Similarly, perceiving as benefits extending one’s life or the societal contributions of research participation may not be relevant to having one’s cancer watched closely. Yet, they may all be valid benefits for participating in a clinical trial. According to Janda (2015), although a scale and an index function similarly, an index usually combines observations without concern about their intercorrelations. Further studies with large samples are needed to evaluate the structure of the benefit and burden measures to determine if they are more appropriately conceptualized as scales or indexes.

Several limitations of our study merit discussion. First, the sample size did not allow us to analyze the items to determine the presence of dimensions or subscales based on our conceptual model. Second, because of the exploratory nature of our work in understanding how patient-participants view the benefits and burdens of research participation and the intent to develop a psychometrically sound empirical measure, we chose to focus on those individuals who were actively participating in CCTs. In doing so, however, those who chose not to participate or drop out of their trials may perceive the benefits and burdens differently. Because this study only included CCT patient-participants, it is possible that we overestimate the benefits and underestimate the burdens of participation. Third, our sample was somewhat homogenous in terms of certain socio-demographics characteristics (e.g., education, race, employment). We are currently collecting data for a larger study where we will examine the data for variable clustering to determine dimensional patterns. This future analysis will also allow us to evaluate the structure of the benefit and burden constructs to determine whether they should be considered scales or indexes. In addition, this larger study will allow us to look more closely at how sociodemographic factors may influence benefit-burden perceptions and dropout intentions; and, identify whether there are differences in perceptions based on those who withdraw from CCTs.

Finally, our study fills a methodological void in empirical bioethics by providing researchers and patients with a tool to conceptualize, as well as quantify the benefits and burdens of CCT participation important to individual patients. This comprehensive tool that lists multiple benefits and burdens has the potential to help clinicians work with patients so they can deliberately consider and weigh the full array of possible risks and burdens associated with trial participation. This will add an aspect of objectivity to decision-making. This work has implications for how we recruit, enroll, and retain patients in research.

Educational Implications

A reliable and valid measure of the benefits and burdens of research participation is applicable to diverse patients with cancer and is essential to developing communication strategies that help to better educate, inform, and empower patient-participants to get the information they need to make decisions related to their goals of care. Helping patient-participants discuss the benefits and burdens of their decision-making in CCTs may diminish decisional regret or remorse when treatment results are not congruent with patients' expectations.

Best Practices

Tulsky and colleagues (2017) stress the importance of having an open dialogue with patients and their families, allowing time to understand and discuss the preferences and goals of those who are seriously ill and feeling comfortable with the expression of both positive and negative emotions that might arise in the course of these discussions. Taking the time to assess patients' understanding of the benefits and burdens of research participation or answering questions related to any aspect of the research process engages patient-participants and their families in shared decision-making, facilitates mutual trust and respect, and conveys caring attitudes (Tulsky, 2017).

Research Agenda

As indicated above, sound methodological instruments in bioethics are critical to operationalizing complex phenomena. There are many opportunities to use the benefit-burden research participation scales to assess outcomes of cancer care as well as to examine relationships between patient-participants' perceptions of the benefits and burdens of research participation and recruitment and retention. In addition, a psychometrically rigorous benefit and burden measure will allow us to identify differences that might exist based on gender, age, race, and ethnicity and other important individual and clinical variables. Given the fact that cancer is currently the second leading cause of death in the United States (American Cancer Society, 2016) and a 45% increase in cancer incidence is expected by 2030—particularly in the elderly (The Institute of Medicine, 2013) — reliable and valid patient-centered benefit and burden measures have broad implications for cancer research as well as for the quality of care delivered to all seriously ill patients who contemplate research as one of their treatment options.

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Table 1

Theoretical concepts, measurement items and item-statistics for the benefit scale

Items	Concepts and Questions	Mean (SD)	Agree / strongly agree (%)	IRT p-value[#]
*	**Physical and Psychological benefits**			
Benefit4	I am treated like a person and not a number by my research team	4.43 (0.72)	90.8%	<.001
Benefit13	It gives me a sense of hope about my cancer	4.20 (0.74)	87.2%	<.001
Benefit18	It is a way for me to actively treat the cancer	4.13 (0.93)	81.5%	<.001
Benefit14	I am hoping for a cure	4.17 (0.99)	78.9%	0.001
Benefit12	I am able to extend my life	4.02 (0.90)	76.1%	<.001
Benefit21	I trust my researcher knows what is best for me	4.07 (0.88)	73.1%	<.001
Benefit16	I have access to drugs and other medicine/tests that are not available to me otherwise	3.90 (1.14)	71.3%	0.001
Benefit3	My cancer is watched more closely than it would otherwise be	3.93 (1.05)	68.8%	<.001
Benefit10	I feel more informed about my specific type of cancer and the treatments	3.72 (1.06)	64.2%	<.001
Benefit9	It gives me information about my disease that it would not otherwise have	3.60 (1.12)	56.9%	<.001
Benefit11	It helps me know what to expect about my specific type of cancer	3.58 (1.09)	56.9%	<.001
Benefit7	It allows me to have some control over my cancer	3.42 (1.19)	54.6%	<.001
Benefit6	It lessens my stress associated with my cancer	1.28 (1.24)	47.2%	<.001
Benefit5	I worry less about my cancer when I participate in research	3.25 (1.24)	44.4%	<.001
Benefit20	It may reduce my risk of cancer in the future	3.25 (1.17)	40.7%	<.001
	Social and Economic Benefits			
Benefit2	I might help future patients with my cancer (even though my participation might not help me)	4.51 (0.60), 3–5	94.5%	0.023
Benefit1	I am providing a valuable contribution to society	4.38 (0.67)	94.4%	0.003
Benefit8	It may help my children or other family members in the future	4.10 (0.98)	76.1%	<.001
Benefit19	It does not interfere with my other life responsibilities	3.66 (1.16)	63.3%	0.001
Benefit15	It helps me pay for the costs of drugs, medications, and/or tests that I might not otherwise been able to afford	3.25 (1.28)	43.1%	<.001
Benefit17	My insurance will likely cover all of my research expenses	3.15 (1.13)	38.0%	0.002
Benefit22	I receive money for participating in the clinical trial	1.94 (1.19)	11.2%	0.719
Total	Scale Mean Score	3.73 (0.58), 2.09–4.82		

[*] The number is the sequential order of the item in the actual scale.

[#] p-value from IRT graded response model discrimination.

Items were measured on a Likert scale from 1 (Strongly Disagree) to 5 (Strongly Agree)
Alpha=0.895 for the total scale (number of items=22)
The mean scale score is normally distributed (skewness=−0.19, SE=0.23; Kurtosis=−0.22, SE=0.46)

Table 2

Theoretical concepts, measurement items and item-statistics for the burden scale

Items	Concepts and Questions	Mean (SD)	Agree / Strongly agree	IRT p-value[#]
*	**Physical and Psychological Burdens**			
Burden12	I would be very disappointed if I received a placebo (an inactive substance) instead of the treatment	4.04 (1.12)	75.5%	0.970
Burden4	It has made me realize the seriousness of my cancer	3.23 (1.34)	50.5%	<.001
Burden6	I have experienced bothersome side effects	2.91 (1.32)	41.3%	<.001
Burden5	There are unknown side effects that are potentially life threatening	2.95 (1.04)	34.3%	<.001
Burden11	It might not benefit me	2.69 (1.17)	31.5%	0.006
Burden20	I am uncertain if the research is helping or hurting me	2.64 (1.11)	24.5%	<.001
Burden16	I have to rely on others for my needs (financial, personal care, support)	2.29 (1.20)	21.8%	<.001
Burden2	It has added stress to managing my cancer (for example, trying to coordinate services for my care in seeing different doctors, bills, paperwork, traveling with X-rays and MRIs etc.)	2.38 (1.11)	19.3%	<.001
Burden22	I am tired because of my research participation		18.2%	<.001
Burden7	My quality of life is less	2.33 (1.08)	16.7%	<.001
Burden10	I am not learning anything more about my cancer from being in a research study	2.29 (1.05)	12.0%	<.001
Burden14	The amount of information that I needed to understand (to be in the study) is overwhelming	2.18 (0.93)	10.9%	<.001
Burden21	I often wonder if the researcher is not telling me everything about my treatment	2.05 (0.96)	10.0%	<.001
Burden15	I worry that I did not understand everything about the research and what it meant when I agreed to be in the study	2.06 (0.90)	9.1%	<.001
Burden19	I sometimes feel like a guinea pig	1.81 (0.91)	7.3%	<.001
Burden18	Others perceive me as a guinea pig	1.82 (0.90)	4.5%	<.001
	Social and Economic Burdens			
Burden13	It makes me worry about other family members who could be at risk for cancer	3.12 (1.19)	41.8%	<.001
Burden3	I have had to rearrange my life in order to take part in research (for example, travel time, being out of work, meeting scheduled appointments)	2.78 (1.32)	38.5%	<.001
Burden23	It is costing me money out of pocket	2.45 (1.22)	25.2%	<.001
Burden17	My insurance does not cover all the costs of being in the study	2.47 (1.22)	23.1%	<.001
Burden1	I have additional personal responsibilities that I did not expect	2.33 (1.05)	14.7%	<.001
Burden8	I find it difficult to balance my family needs with my own needs for treatment	2.04 (1.02)	12.0%	<.001
Burden9	I worry that it is difficult for my family (including children) to see me take part in a research study for my cancer	1.96 (1.04)	11.0%	<.001
Total	Scale Mean Score	2.48 (0.58), 1.00–3.82		

[*] The number is the sequential order of the item in the actual scale.

[#] p-value from IRT graded response model discrimination.

Items were measured on a Likert scale from 1 (Strongly Disagree) to 5 (Strongly Agree)
Alpha=0.873 for the total scale (number of items=23)
The distribution of burden mean scale score is normal (skewness=−0.17, SE=0.23, kurtosis=−0.05, SE=0.46)

Table 3

Hypothesis testing: Relationship between thoughts of dropout and benefit and burden scores

		Thoughts of Dropping Out		Hedges g	t-test
	Entire Sample	**Yes**	**No**		**p-value**
Benefit score, Mean (SD)	3.73 (0.58)	3.26 (0.60)	3.81 (0.55)	0.99	0.001
Burden score, Mean (SD)	2.48 (0.58)	2.87 (0.42)	2.39 (0.57)	0.87	0.001
Benefit Burden difference score, Mean (SD)	0 (15.00)	−14.75 (11.77)	2.92 (14.24)	1.27	<.001