

# Dispositional Optimism and Therapeutic Expectations in Early-Phase Oncology Trials

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**BACKGROUND:** Prior research has identified unrealistic optimism as a bias that might impair informed consent among patient-subjects in early-phase oncology trials. However, optimism is not a unitary construct; it also can be defined as a general disposition, or what is called dispositional optimism. The authors assessed whether dispositional optimism would be related to high expectations for personal therapeutic benefit reported by patient-subjects in these trials but not to the therapeutic misconception. The authors also assessed how dispositional optimism related to unrealistic optimism. **METHODS:** Patient-subjects completed questionnaires designed to measure expectations for therapeutic benefit, dispositional optimism, unrealistic optimism, and the therapeutic misconception. **RESULTS:** Dispositional optimism was found to be significantly associated with higher expectations for personal therapeutic benefit (Spearman rank correlation coefficient [ $r$ ], 0.333;  $P < .0001$ ), but was not associated with the therapeutic misconception (Spearman  $r$ , -0.075;  $P = .329$ ). Dispositional optimism was found to be weakly associated with unrealistic optimism (Spearman  $r$ , 0.215;  $P = .005$ ). On multivariate analysis, both dispositional optimism ( $P = .02$ ) and unrealistic optimism ( $P < .0001$ ) were found to be independently associated with high expectations for personal therapeutic benefit. Unrealistic optimism ( $P = .0001$ ), but not dispositional optimism, was found to be independently associated with the therapeutic misconception. **CONCLUSIONS:** High expectations for therapeutic benefit among patient-subjects in early-phase oncology trials should not be assumed to result from misunderstanding of specific information regarding the trials. The data from the current study indicate that these expectations are associated with either a dispositionally positive outlook on life or biased expectations concerning specific aspects of trial participation. Not all manifestations of optimism are the same, and different types of optimism likely have different consequences for informed consent in early-phase oncology research. *Cancer* 2016;000:000-000. © 2016 American Cancer Society.

**KEYWORDS:** cancer research, dispositional optimism, informed consent, therapeutic misconception, therapeutic optimism.

## INTRODUCTION

Patient-subjects in early-phase oncology trials often report high expectations for personal therapeutic benefit. Although it is true that some participants may benefit, these trials are not designed to provide participants with therapeutic benefit.<sup>1</sup> Therefore, the ethical significance of this optimism has been an ongoing concern among researchers and ethicists.<sup>1-7</sup> Although some have claimed that expressions of optimism alone are never problematic in clinical research,<sup>3</sup> prior studies have documented the potential for optimism to impair informed consent.<sup>5,6</sup> This apparent contradiction may be explained by the fact that optimism is not a unitary psychological construct.<sup>8</sup> Failure to distinguish the different types of optimism can lead researchers and ethicists to disagree when debating its ethical significance for informed consent.

One type of optimism, unrealistic optimism, is an event-specific bias that has been associated with distortions in risk/benefit assessment in a range of health-related contexts, including early-phase oncology trials.<sup>5,9-11</sup> Individuals possessing this bias tend to engage in defensive processing of information, overestimating their prospects for benefit and/or underestimating their susceptibility to the risks associated with the event in question. However, a different type of optimism is an enduring personality characteristic referred to as dispositional optimism. Those high in dispositional optimism tend to expect positive future outcomes in the aggregate. Dispositional optimism has not been associated with defensive

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processing of information, and instead has been found to be positively related to how individuals attend to and process risk/benefit information, as well as effective coping and well-being.<sup>11-14</sup> To the best of our knowledge, no research to date has attempted to determine the extent to which expectations for personal therapeutic benefit reported by patient-subjects in early-phase oncology trials are associated with the generally adaptive dispositional optimism rather than the problematic unrealistic optimism. It is also not known how dispositional optimism relates to other factors commonly associated with these high expectations, such as the therapeutic misconception (TM) (ie, the failure to grasp the differences between clinical research and beneficent medical care).<sup>15</sup>

We conducted a multicenter study to examine these issues. We investigated the relationship between dispositional optimism and expectations of personal therapeutic benefit reported by patient-subjects enrolled in early-phase oncology trials. Given the prevalence of dispositional optimism in the general population, we predicted that it would be present among the participants in the current study. We hypothesized that dispositional optimism would predict high expectations for personal therapeutic benefit expressed by patient-subjects enrolled in early-phase oncology trials, but that it would not be positively correlated with either TM or unrealistic optimism. Past research has found that dispositional optimists “are more flexible and adaptive in their consideration of information about potential problems and stressors.”<sup>13</sup> Therefore, we conjectured that improved information processing could make dispositionally optimistic patient-subjects less susceptible to TM. Furthermore, past research has found that dispositional optimism is not generally correlated with unrealistic optimism, although it may have independent (and possibly interactive) effects with it.<sup>10,16</sup>

## MATERIALS AND METHODS

### **Participants**

Participants were patient-subjects enrolled in early-phase oncology trials (phase 1, 1/2, or 2) at 2 major cancer centers in the United States. They were aged  $\geq 18$  years and were able to speak and read English. The Institutional Review Boards at both sites approved the study.

### **Definitions, Procedures, and Measures**

Participants provided written informed consent and participated in a structured face-to-face interview with a research associate who had been trained to administer the questionnaires.

### **Dispositional optimism**

Dispositional optimism refers to “the generalized positive expectancy that one will experience good outcomes.”<sup>11</sup> Individuals who score high in dispositional optimism generally tend to accentuate the positive and downplay the negative. Consistent with established practice, we used the revised Life Orientation Test (LOT-R) to measure dispositional optimism. The LOT-R was developed by Carver and Scheier and has demonstrated discriminant validity and reliability in numerous studies.<sup>17</sup> This instrument consists of 10 self-report items, 4 of which are filler items. The self-report items ask patient-subjects to respond to statements such as “In uncertain times, I usually expect the best” and “Overall, I expect more good things to happen to me than bad.” Each item is rated on a 5-point scale ranging from 0 (strongly disagree) to 4 (strongly agree). We analyzed the 6 dispositional optimism questions individually, as well as the mean score on all items combined. To calculate LOT-R scores, we dropped the 4 filler questions and reverse-coded the negatively worded questions (eg, “I hardly ever expect things to go my way”) and added them to the positively worded questions (eg, “I am always optimistic about my future”). The total LOT-R score was used as a measure of dispositional optimism (dispositional optimism score). In addition, the optimism and pessimism subscales (obtained from the 3 items each with positive and negative wording, respectively) were analyzed separately.

### **Expectations for personal therapeutic benefit**

Expectations for personal therapeutic benefit refer to patient-subjects’ noncomparative expressions of hope/concern regarding their own participation in the trial in which they are enrolled. Unlike dispositional optimism, expectations for personal therapeutic benefit are event-specific. We used a personal therapeutic benefit questionnaire to measure these expressions of hope/concern. Patient-subjects rated their expectations of experiencing 7 research-related benefits and their personal concern about experiencing 2 research-related risks (the ratings of the latter questions were reversed). Sample questions included “indicate your own personal hope about having your cancer controlled by the drugs you get in the trial” and “indicate your own personal concern about experiencing a health problem caused by the drugs you get in the trial.” Responses were given on a 4-point Likert scale ranging from “I don’t feel at all optimistic/concerned about this happening to me” (1) to “I feel quite optimistic/concerned about this happening to me” (4). A personal therapeutic benefit score was determined by calculating the

mean score of the 9 questions. The personal therapeutic benefit questionnaire was developed by this research team and pilot tested among patients with cancer, and demonstrated ample face validity. The Cronbach coefficient  $\alpha$  was .86, which is considered a good internal consistency.

### Therapeutic misconception

TM occurs when patient-subjects conflate the contexts of research and therapy, thereby inaccurately attributing therapeutic intent to research procedures.<sup>2</sup> The TM scale was used to determine the presence and magnitude of TM. The scale asks patient-subjects to rate their level of agreement with respect to 10 research-related statements.<sup>18,19</sup> A sample statement is “a researcher’s most important task is to make sure that the research will help the people who participate.” Each item was rated on a 5-point scale ranging from 1 (agree) to 5 (disagree). The ratings were reversed to ease interpretation of the results. The scale includes 3 dimensions associated with TM: perceptions of the degree of individualization of the intervention, benefit from participation, and the purpose of the trial. The TM scale was developed by Appelbaum and Lidz and has demonstrated reliability in several previous studies.<sup>18,19</sup> A total TM score as well as a total score per dimension were determined by calculating the mean score of the 10 questions and the mean score of each dimension, respectively.

### Unrealistic optimism

Unrealistic optimism is a bias in which an individual mistakenly believes that he or she is more likely to experience positive outcomes with respect to a specific event compared with other similar individuals facing the same event. Unlike dispositional optimism, unrealistic optimism is event-specific; unlike expectations for personal therapeutic benefit, it is comparative. We used the comparative risk/benefit assessment questionnaire modeled after an instrument developed by Weinstein to measure unrealistic optimism.<sup>5,20</sup> (The comparative risk/benefit assessment questionnaire is the standard method for measuring perceived comparative risk.<sup>9-11</sup>) This questionnaire asks respondents to compare their chances of experiencing 9 research-related events with the chances of other similar individuals experiencing these same events. A sample question is “Compared with other patients invited to participate in the same cancer research trial you are invited to participate in, what are the chances that your life expectancy will be increased by the drugs you get in the trial?” Respondents then answer the question by choosing 1 response on a 7-point interval scale, with values ranging

from -3 (much below average) to +3 (much above average). Comparative risk/benefit judgments are considered unbiased when the mean judgment of the group is zero. Each item score, as well as the mean score of all the items, was used in the statistical analyses.

### Statistical Analysis

Data were entered into a Research Electronic Data Capture (REDCap) database (project-redcap.org/) using a double-entry procedure. Discrepancies in data entry were identified and corrected by a third operator. Descriptive statistics (eg, percentage for categorical variables, and mean and standard deviation for continuous variables) were used to summarize demographic and clinical characteristics. The Spearman correlation coefficient ( $r$ ) was used to assess the association between dispositional optimism and its 2 subscales with the other measures and the association between TM with unrealistic optimism and expectations of personal therapeutic benefit. The Kruskal-Wallis test or Wilcoxon rank sum test were used to assess the association between the dispositional optimism score and demographic characteristics.

Univariate and multivariate linear regression analyses were performed to further evaluate factors that were independently associated with expectations of personal therapeutic benefit and TM (dependent variables). Factors tested (independent variables) included total unrealistic optimism score; dispositional optimism score; age; sex; study site; ethnicity; education; religion; cancer type; participation in previous research; domestic status; marital status; and, interchangeably, TM and expectations for personal therapeutic benefit. A stepwise procedure was performed for variable selection. Standard model diagnostics were performed, testing first for nonlinearity of independent variables versus dependent variables. In addition, we studied outliers and influential points by examining Studentized residuals, Cook distance, and difference in fit (DFITTS). We then tested for normality of residuals using a kernel density plot, quantile-quantile plot, and the Shapiro-Wilk test. Multicollinearity was inspected using the variance inflation factor. The model diagnostics did not demonstrate any significant deviations from the model assumptions. The scatter plots of response and factor variables demonstrated linearity, and there were no detectable influential points or outliers. The residuals were approximately normal, and there was no indication of significant multicollinearity.

A  $P < .05$  was considered to be statistically significant. Data management and analysis were conducted

**TABLE 1.** Demographic Characteristics

Characteristics		No. of Patients (N = 171)	%	Mean	Minimum	Maximum	SD
Age, y				58.64	18	85	12.78
Age group, y	18–49	31	18.13				
	50–64	73	42.69				
	65–74	57	33.33				
	≥75	10	5.85				
Study site	Site 1	85	49.71				
	Site 2	86	50.29				
Sex	Men	84	49.12				
	Women	87	50.88				
Race	White (non-Hispanic)	146	85.38				
	African American/black of US origin	17	9.94				
	Other	8	4.68				
Education	Grade school/high school	54	31.58				
	College	81	47.37				
	Graduate/professional school	36	21.05				
Religion	Protestant	65	38.01				
	Catholic	26	15.2				
	Agnostic	12	7.02				
	Other <sup>a</sup>	68	39.77				
Cancer type	Blood cancer	54	31.58				
	Lung cancer	26	15.2				
	Breast cancer	23	13.45				
	Other	68	39.77				
Domestic status (do you live alone)	Yes	31	18.13				
	No	140	81.87				
Marital status	Single	28	16.47				
	Married	115	67.25				
	Divorced	17	10				
	Widowed	10	5.85				
Participation in previous research	Yes	53	30.99				
	No	118	69.01				
Phase of clinical trial	1	89	52.05				
	2	63	36.84				
	1/2	19	11.11				

Abbreviation: SD, standard deviation.

<sup>a</sup>Includes Baptist, Christian, Methodist, Buddhist, Spiritual, none, no response, etc.

using SAS statistical software (version 9.4; SAS Institute Inc, Cary, NC).<sup>21</sup>

## RESULTS

### **Patient Characteristics**

We approached 233 patient-subjects who were enrolled in early-phase oncology trials. Of these individuals, 171 (73%) agreed to be interviewed for the current study. Demographic and clinical characteristics of the participants are presented in Table 1. The average age was 59 years. We interviewed slightly more women than men (51% vs 49%). The largest racial/ethnic group was white (non-Hispanic) (85%). A substantial majority of the participants had completed college (68%), were married (67%), and had not participated in a prior clinical research study (69%).

### **Magnitude of Dispositional Optimism, TM, Expectations for Personal Therapeutic Benefit, and Unrealistic Optimism**

Descriptive statistics on the LOT-R questionnaire (dispositional optimism), the TM scale, the personal therapeutic benefit questionnaire, and the comparative risk/benefit assessment questionnaire are reported in Table 2. Neither dispositional optimism nor unrealistic optimism was found to be significantly associated with study site, age, sex, race/ethnicity, education, religion, or type of cancer ( $P > .05$ ) (Table 3).

### **Association Between Dispositional Optimism and Expectations for Personal Therapeutic Benefit**

Consistent with our hypotheses, dispositional optimism was found to be significantly associated with higher expectations for personal therapeutic benefit (Spearman  $r$ ,

**TABLE 2.** Dispositional Optimism, Therapeutic Misconception, Expected Therapeutic Benefit, and Unrealistic Optimism Descriptive Statistics

Variables	Theoretical Range	Mean Scores	SD	25th Percentile	75th Percentile
Dispositional optimism	1.67 to 5	4.07	0.24	3.67	4.67
Therapeutic misconception	1.30 to 5	3.79	0.77	3.4	4.4
Expected therapeutic benefit	1.66 to 4	3.16	0.59	2.67	3.67
Unrealistic optimism	-1.77 to 3	1	0.97	0.33	1.67

Abbreviation: SD, standard deviation.

**TABLE 3.** Association Between Demographic Characteristics and Types of Optimism

Demographic Characteristics	Level	No.	Dispositional Optimism			Unrealistic Optimism		
			Mean	SD	P	Mean	SD	P
Study site	Site 1	85	3.959	0.711	.054	0.928	0.779	.195
	Site 2	86	4.184	0.573		1.074	1.127	
Age group, y	18-49	31	3.919	0.722	.344	0.853	0.878	.288
	50-64	73	4.071	0.670		1.026	0.967	
	65-74	57	4.114	0.611		0.981	1.057	
	≥75	10	4.317	0.506		1.400	0.713	
Sex	Men	84	4.030	0.678	.499	1.089	0.882	.236
	Women	87	4.113	0.630		0.917	1.046	
Race	White (non-Hispanic)	146	4.078	0.653	.821	0.994	0.912	.684
	African American/black of US origin	17	4.088	0.693		0.974	1.387	
	Other	8	3.938	0.642		1.194	1.082	
Education	Grade school/high school	54	3.935	0.626	.130	0.940	1.072	.795
	College	81	4.111	0.694		1.058	0.917	
	Graduate/professional school	36	4.190	0.578		0.966	0.945	
Religion	Agnostic	12	4.111	0.613	.847	0.630	0.518	.179
	Protestant	65	4.097	0.639		0.906	0.981	
	Catholic	26	4.109	0.757		1.192	0.882	
	Other <sup>a</sup>	68	4.027	0.643		1.085	1.038	
Cancer type	Blood cancer	54	4.065	0.607	.342	0.961	0.880	.636
	Breast cancer	23	4.196	0.670		1.184	1.161	
	Lung cancer	26	4.205	0.675		1.158	0.987	
	Other	68	3.985	0.674		0.912	0.968	

Abbreviation: SD, standard deviation.

<sup>a</sup>Includes Baptist, Christian, Methodist, Buddhist, Spiritual, none, no response, etc.

0.333;  $P < .0001$ ). With regard to the subscales of the LOT-R, expectations for personal therapeutic benefit were strongly positively associated with the optimism subscale (Spearman  $r$ , 0.404;  $P < .0001$ ) and weakly negatively associated with the pessimism subscale (Spearman  $r$ , -.192;  $P = .012$ ).

**Association Between Dispositional Optimism and TM**

Consistent with our hypotheses, dispositional optimism was not found to be associated with TM (Spearman  $r$ , -0.075;  $P = .329$ ). The optimism and pessimism subscales also were not found to be associated with the total TM score (Spearman  $r$ , 0.085 [ $P = .267$ ] and Spearman  $r$ , 0.136 [ $P = .077$ ], respectively), although the optimism subscale was correlated with perceptions of likelihood of benefit (Spearman  $r$ , 0.156;  $P = .041$ ).

**Association Between Dispositional Optimism and Unrealistic Optimism**

Dispositional optimism was found to be weakly associated with unrealistic optimism (Spearman  $r$ , 0.215;  $P = .005$ ). The optimism subscale of the LOT-R held a stronger association with unrealistic optimism (Spearman  $r$ , 0.279;  $P = .0002$ ); the pessimism subscale was not found to be associated with unrealistic optimism (Spearman  $r$ , -0.127;  $P = .097$ ).

**Factors Associated With TM**

On univariate regression analyses, 5 factors were found to be significantly associated with TM: male sex ( $P = .004$ ), an educational level of ≤high school ( $P < .0001$ ), participation in previous research ( $P = .007$ ), total unrealistic optimism score ( $P = .0003$ ), and expectation for personal therapeutic benefit ( $P = .007$ ) (Table 4). However, on

**TABLE 4.** Univariate Linear Regression Analysis to Evaluate the Association With Expectations for Personal Therapeutic Benefit and Therapeutic Misconception<sup>a</sup>

Variable	Comparison	Expectations for Personal Therapeutic Benefit			Therapeutic Misconception		
		Estimate	SE	Overall <i>P</i>	Estimate	SE	Overall <i>P</i>
Age		-0.002	0.004	.639	0.006	0.005	.222
Study site	Site 1 vs site 2	-0.081	0.091	.376	-0.170	0.117	.149
Sex	Man vs woman	0.013	0.091	.889	<b>0.338</b>	<b>0.115</b>	<b>.004</b>
Ethnic group	White vs other	-0.057	0.217	.852	-0.538	0.276	.073
	African American/black of US origin vs other	-0.131	0.256		0.326	0.326	
Education	Grade school/high school vs graduate/professional school	0.053	0.128	.655	<b>0.572</b>	<b>0.157</b>	<b>&lt;.0001</b>
	College vs graduate/professional school	0.107	0.119		0.029	0.146	
Religion <sup>b</sup>	Agnostic vs other	-0.135	0.187	.887	-0.448	0.237	.062
	Protestant vs other	-0.050	0.104		-0.317	0.132	
	Catholic vs other	-0.011	0.138		-0.157	0.175	
Cancer type	Blood cancer vs other	-0.004	0.108	.373	-0.070	0.140	.273
	Breast cancer vs other	0.213	0.143		0.067	0.185	
	Lung cancer vs other	0.131	0.137		0.283	0.177	
Participation in previous research	Yes vs no	-0.027	0.098	.784	<b>-0.342</b>	<b>0.125</b>	<b>.007</b>
Domestic status (do you live alone)	Yes vs no	-0.117	0.118	.323	-0.077	0.153	.615
Marital status	Single vs widowed	0.115	0.219	.243	-0.035	0.285	.816
	Married vs widowed	0.227	0.196		0.110	0.255	
	Divorced vs widowed	0.422	0.236		0.119	0.309	
Total dispositional optimism		<b>0.274</b>	<b>0.067</b>	<b>&lt;.0001</b>	-0.054	0.090	.548
Total unrealistic optimism		<b>0.453</b>	<b>0.032</b>	<b>&lt;.0001</b>	<b>0.217</b>	<b>0.059</b>	<b>.0003</b>
Total therapeutic misconception/ total expected therapeutic benefit		<b>0.158</b>	<b>0.058</b>	<b>.007</b>	<b>0.264</b>	<b>0.097</b>	<b>.007</b>

Abbreviation: SE, standard error.

<sup>a</sup> Bold type indicates statistically significant association.<sup>b</sup> "Other" includes Baptist, Christian, Methodist, Buddhist, Spiritual, none, no response, etc.

multivariate regression analysis, expectation for personal therapeutic benefit and participation in previous research dropped out of the model and the factors that were found to be independently associated with TM were male sex ( $P = .004$ ), lower educational level ( $P < .0001$ ), and unrealistic optimism ( $P = .0001$ ) (Table 5). Thus, whereas dispositional optimism was not found to be independently associated with TM, unrealistic optimism was.

#### Factors Associated With Expectations for Personal Therapeutic Benefit

On univariate analyses, high expectations for personal therapeutic benefit were found to be significantly associated with unrealistic optimism ( $P < .0001$ ), total TM score ( $P = .007$ ), and dispositional optimism ( $P < .0001$ ) (Fig. 1). However, on multivariate linear regression analysis, only dispositional optimism ( $P = .02$ ) and unrealistic optimism ( $P < .0001$ ) were found to be independent predictors of high expectations for personal therapeutic benefit (Table 5).

#### DISCUSSION

Discussions of optimism in clinical research elicit mixed opinions. Some contend that optimism among trial participants is never ethically problematic.<sup>3</sup> Others express concern that optimism within this context reveals a failure of informed consent.<sup>5,6</sup> The current study addresses part of this disagreement by exploring 2 distinct phenomena represented by the term "optimism," each of which may have different ethical implications.

We investigated whether dispositional optimism could help to explain, in part, the expectations for personal therapeutic benefit expressed by patient-subjects in early-phase oncology trials, without entailing commonly studied problems in informed consent. We confirmed our expectation that dispositional optimism among the patient-subjects we studied would be associated with high expectations for personal therapeutic benefit. In fact, dispositional optimism predicted high expectations for personal therapeutic benefit independently of other variables. These findings are not unexpected because dispositional optimism is commonly defined in terms of generalized

**TABLE 5.** Multivariate Regression Analysis of Factors Independently Associated With Personal Therapeutic Benefit and Therapeutic Misconception

	Variable	Comparison	Estimate	SE	P
Independent factors of therapeutic misconception	Sex	Man vs woman	0.310	0.105	.004
	Education	Grade school/high school vs graduate/professional school	0.601	0.146	<.0001
		College vs graduate/professional school	0.036	0.136	
Independent factors of expectations for personal therapeutic benefit	Total unrealistic optimism score		0.215	0.054	.0001
	Total dispositional optimism		0.112	0.048	.020
	Total unrealistic optimism		0.434	0.032	<.0001

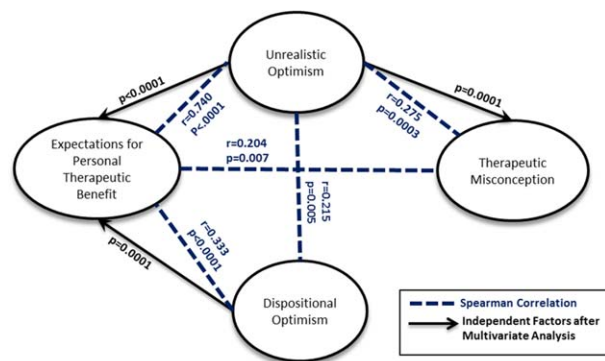
Abbreviation: SE, standard error.

positive outcome expectancies.<sup>22</sup> Given that dispositional optimism is regarded as a trait and not a product of misunderstanding or irrationality, it should not provoke ethical concern among researchers unless it is associated with other factors that have been found to impair informed decision making. Indeed, expectations for therapeutic benefit that result from a dispositionally optimistic orientation and are not associated with either misunderstanding or bias may reflect hopeful feelings rather than any failure to appreciate relevant information.

It is important to note that we found that dispositional optimism was not significantly associated with TM. Although a substantial number of the patient-subjects we interviewed manifested TM, dispositional optimism did not appear to be a factor that accounted for it. Research regarding dispositional optimism within other contexts has found that, when confronted with a stressful life event, dispositionally optimistic individuals are more likely than those not dispositionally optimistic to process and retain the full range of information provided to them, including negative or unwelcome information.<sup>12-14,22</sup> On this basis, we conjectured that dispositional optimism would not be associated with TM. In contrast to some recent suggestions in the literature,<sup>23,24</sup> the fact that the dispositionally optimistic participants in the current study were neither more nor less likely to demonstrate TM suggests that TM does not merely reflect participants' hopeful expressions concerning the results of their participation in a study.

An association between dispositional optimism and unrealistic optimism was noted, but the association was weak. This finding is consistent with past studies that demonstrated that dispositional optimism and unrealistic optimism are not strongly associated and represent different types of optimism.<sup>11</sup>

Past research has found a link between unrealistic optimism and deficits in informed consent.<sup>5,6</sup> In the cur-



**Figure 1.** Factors associated with expectations for personal therapeutic benefit.

rent study, although dispositional optimism and unrealistic optimism both predicted high expectations for personal therapeutic benefit, only unrealistic optimism was found to predict TM. Thus, dispositional optimism appeared to account for some of the high expectations for personal therapeutic benefit reported by the patient-subjects we studied without being strongly associated with either unrealistic optimism or TM.

The current study provides clinicians and researchers with a more complete and balanced understanding of how optimism relates to the therapeutic expectations of patient-subjects enrolled in early-phase cancer trials and reveals the ethical complexity of optimism for informed consent in these trials. Although one type of optimism can be an ethically benign, and possibly adaptive, dispositional orientation to stressful events, another type of optimism appears to be a bias that has the potential to compromise informed consent. Without carefully distinguishing dispositional optimism from unrealistic optimism, no single conclusion can be drawn regarding the ethical significance of optimistic expectations for personal therapeutic benefit within this context.

The current study was subject to some limitations. First, the sample was predominantly white (non-Hispanic), and it remains unclear whether these findings are generalizable to other demographic groups. The current study included only adult patient-subjects, mostly of middle age, who were enrolled in early-phase oncology trials and therefore we do not know whether our findings are generalizable to other research populations (eg, patient-subjects of other ages, including children and adolescents, or patient-subjects enrolled in later-phase cancer trials or in other clinical research). Second, the current study did not investigate other potentially adaptive consequences of dispositional optimism, such as its association with psychological adjustment or improved coping, or potential negative outcomes. A complete picture of the ethical significance of dispositional optimism for patient-subjects enrolled in early-phase oncology trials would need to take into account these further potential benefits and harms.

### Conclusions

High expectations for personal therapeutic benefit among patient-subjects in early-phase oncology trials should not be assumed to result only from misunderstanding of specific information concerning the trials. Instead, the data from the current study indicate that these expectations may be associated with either a general dispositionally positive outlook on life or biased expectations regarding specific aspects of trial participation.

Although unrealistic optimism may impair informed consent, dispositional optimism likely does not. Because dispositional optimism is a stable personality characteristic, we believe there is little reason to think that it would be dampened by interventions to combat misunderstanding and bias regarding clinical trials. Thus, the findings of the current study suggest that those who have claimed that optimism is not a problem for informed consent in early-phase oncology trials are partly correct and partly incorrect. Investigators need to know that all forms of optimism are not the same, and that different types of optimism likely have different consequences for informed consent.

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### CONFLICT OF INTEREST DISCLOSURES

Daruka Mahadevan has acted as a paid member of the Speakers' Bureau for Alexion and Janssen for work performed outside of the current study.

### AUTHOR CONTRIBUTIONS

**Lynn A. Jansen:** Conceptualization, methodology, investigation, resources, writing—original draft, writing—review and editing, visualization, supervision, project administration, and funding acquisition. **Daruka Mahadevan:** Conceptualization, investigation, writing—original draft, writing—review and editing, supervision, project administration. **Paul S. Appelbaum:** Methodology and writing—review and editing. **William M.P. Klein:** Conceptualization, methodology, writing—original draft, writing—review and editing, and supervision. **Neil D. Weinstein:** Conceptualization, methodology, validation, resources, writing—original draft, and writing—review and editing. **Motomi Mori:** Methodology, formal analysis, writing—review and editing, visualization, and supervision. **Racky Daffé:** Methodology, software, validation, formal analysis, investigation, data curation, writing—original draft, writing—review and editing, and visualization. **Daniel P. Sulmasy:** Conceptualization, methodology, validation, resources, writing—original draft, and writing—review and editing.

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