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Variations in Unrealistic Optimism Between Acceptors and Decliners of Early Phase Cancer Trials

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Abstract

Purpose—Research has found that patient-subjects in early phase cancer trials exhibit unrealistic optimism regarding the risks and possible benefits of trial participation. Unrealistic optimism is associated with therapeutic misconception and failures to appreciate research-related information. This is the first study to assess whether those who decline to participate in these trials also exhibit unrealistic optimism. It is also the first study to assess whether there are significant differences in appreciation of research related risks/benefits and therapeutic misconception between these two groups.

Methods—We approached 261 patients at two academic medical centers who were offered enrollment in a phase I, II or phase I/II cancer trial (between 2012–2016). Two hundred and thirty-three patients agreed to enroll in an early phase cancer trial, 171 of whom agreed to be interviewed for the study. Twenty-eight patients declined the offer to enroll, 15 of whom agreed to be interviewed for the study. Subjects participated in a structured face-to-face interview with a research associate trained to administer the study questionnaires.

Results—Acceptors demonstrated a significantly higher level of unrealistic optimism than decliners ($p < 0.05$). Decliners had significantly less therapeutic misconception than acceptors [3.37 (SD=0.85) versus 3.79 (SD=0.77), $p = 0.042$]. There was a significant difference on one of the appreciation questions between acceptors and decliners ($p = 0.009$).

Conclusion—Comparative assessment of acceptors and decliners to early phase cancer trials casts light on whether unrealistic optimism is consequential for the decision to participate in these trials. The different levels of unrealistic optimism exhibited by these groups suggests that it may be a factor that affects the decision to participate.

Keywords

Informed Consent; Research Ethics; Risks; Benefits; and Burdens of Research/ Beneficence and Non-Maleficence; unrealistic optimism; Therapeutic-Misconception

Recent research has found that patient-subjects in early phase cancer trials exhibit unrealistic optimism regarding the risks and possible benefits of trial participation (Jansen et al. 2011, 2016a). Unrealistic optimism is a bias that is present when a person believes that he or she is more likely to experience benefits and/or is less likely to experience harms than similar others who are confronting the same event or outcome (Weinstein, 1980). Applied to early phase cancer trials, unrealistic optimism has been positively associated with therapeutic misconception and failures to appreciate research-related information that is disclosed in the informed consent process (Jansen et al. 2016b). (Therapeutic misconception occurs when patient-subjects confuse the context of research with that of therapy; lack of appreciation occurs when patient-subjects inaccurately apply general information to their own situation.) This body of research, however, has focused exclusively on patient-subjects who are enrolled in an early phase cancer trial. To date no research has been done to determine whether those who decline to participate in an early phase cancer trial, preferring instead to pursue the standard of care, alternative treatment or to forgo treatment altogether, also exhibit unrealistic optimism about the risks and benefits of trial participation. Further, no research has been done to determine if decliners exhibit lower levels of unrealistic optimism than acceptors, no unrealistic optimism at all, or unrealistic pessimism about the risks and benefits of trial participation. Knowledge of how acceptors and decliners to these trials respectively assess risks and benefits could shed light on the decision to participate in these trials. If acceptors and decliners manifest different levels of unrealistic optimism, then it may be consequential to the decision to enroll.

This study is a subsidiary part of a larger multi-center program of research on the impact of unrealistic optimism on risk/benefit assessment and informed consent in early phase cancer trials. It compares unrealistic optimism among patient-subjects who accepted an invitation to enroll in an early phase cancer trial (acceptors) and patient-subjects who were offered an invitation to do so and declined (decliners). The results from the acceptors were published previously (Jansen, 2016b). Research on unrealistic optimism in other health-related contexts has found that it is consequential for behavior (Radcliffe, Klein, 2002). Smokers who exhibit unrealistic optimism about the risks of smoking have been found to be less likely to quit smoking than smokers who do not exhibit this optimism, for example (Dillard, McCaul, Klein, 2006). Based on this research, we hypothesized that decliners in our study would exhibit no unrealistic optimism with respect to a range of research-related risks and benefits. We also sought to determine whether acceptors and decliners differ with regard to therapeutic misconception and appreciation of research-related information. Prior research found a positive association between unrealistic optimism and therapeutic misconception and a negative association between unrealistic optimism and appreciation (Jansen et al. 2016a; Weinstein, 1980). Given these findings, we expected that decliners would display greater appreciation and less therapeutic misconception than acceptors.

Subjects

Over a four-year period, we approached 261 patients at two academic medical centers who had been offered enrollment in a phase I, II or phase I/II cancer trial. Of these, 233 had accepted the offer to enroll, 171 of whom agreed to be interviewed for the present study. Twenty-eight patients declined the offer to enroll, 15 of whom agreed to be interviewed for

the present study. The Institutional Review Boards at both academic medical centers approved the study.

The study planned to enroll 180 patient-subjects, 120 subjects who consent to enroll in an early phase oncology trial and 60 subjects who decline ('decliners'). We were able to identify and approach 28 decliners, 15 of whom agreed to be interviewed. The original sample size provided 89% power to detect a mean difference equivalent to 0.50 standard deviation between two groups with 5% significance level. Even with a smaller sample size of decliners, differences between the two groups enabled us to conduct an informative analysis of the data.

Procedures and Instruments

Subjects were approached after they had made a decision to accept or decline participation in an early phase oncology trial. After providing written informed consent to participate in the study, each subject engaged in a structured face-to-face interview with a research associate who had been trained to administer the study questionnaires: a demographics questionnaire, the Comparative Risk/Benefit Questionnaire, the MacArthur Competence Assessment Tool for Clinical Research and the Therapeutic Misconception Scale.

Unrealistic Optimism

A standard method to measure unrealistic optimism is to ask respondents to rate their personal susceptibility to a prospective benefit or risk from an event to that of similar others who are experiencing the same event. Relying on this method, Weinstein developed the Comparative Risk/Benefit Assessment Questionnaire (CRBA) that has been used to assess unrealistic optimism in a wide range of contexts (Weinstein, 1982; Dillard, Midboe, Klein, 2009). We modified the CRBA questionnaire to the context of clinical research, asking respondents to compare their own chances of experiencing 9 research-related outcomes with the chances of similar others (Jansen et al. 2011). Wording of the questions was slightly modified to reflect differences in subject participation status. Examples of such questions are, (For acceptors) "Compared to others participating in the same research trial that you are participating in, what are the chances that your cancer will be controlled by the drugs taken in the trial?" (For decliners) "Compared to other patients invited to participate in the same cancer research trial you were invited to participate in, what are the chances that your cancer would have been controlled by the drugs you would have received in the trial." Subjects then answer the question by choosing one response on a seven-point 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. Thus, at a group level, we interpreted any optimistic or pessimistic judgment of comparative risk/benefit as being unrealistic. Each item score, as well as the mean score of all items (overall mean UO score), was used in the statistical analyses. The CRBA has ample face validity in the field of social psychology and has been adapted successfully to health psychology, particularly in the field of preventive medicine (Dillard, Midboe Klein, 2009; Prentice, Gold, Carpenter, 2005).

Appreciation

To measure appreciation, we used two questions from the MacArthur Competence Assessment Tool – Clinical Research (MacCAT-CR) developed by Appelbaum and Grisso (Appelbaum, Grisso, Hill-Fotouchi, 1997): (1) “Do you believe that you have been asked to be in this study primarily for your personal benefit?” and (2) “Is it possible that you might get a treatment in this study that is less good than the standard treatment?” We asked respondents to explain their responses to each question and then coded the responses according to the standard scale provided by the MacCAT-CR. With respect to the first question, we classified respondents as either having appreciation, if they answered no, or lacking appreciation, if they answered yes. With respect to the second question, we classified respondents as either having appreciation, if they answered yes, or lacking appreciation, if they answered no.

Therapeutic Misconception

To assess therapeutic misconception, we used the TM Scale, which was developed by Appelbaum and Lidz and has demonstrated validity in several previous studies (Dunn, Palmer, Keehan, Jeste, Appelbaum, 2006). This scale asks respondents to rate their level of agreement as it applies to ten research-related statements. A sample statement is “Being in a research study almost always provides the best possible treatment for a sick person.” (For the decliner group question 8, “The treatment I am getting in this study is definitely the best treatment for me” was rephrased as the conditional statement “The treatment I would have received in this study would have been the best treatment for me.”) Each item was then rated on a 5-point scale ranging from 1 (agree) to 5 (disagree). The ratings were reversed to facilitate interpretation of results. The TM scale includes three subscales: perceptions of the degree of individualization of the intervention, perceptions of benefit from participation, and perceptions of the purpose of the trial. A total TM score, and a total score for each of the subscales, were determined respectively by calculating the mean score of the ten questions and the mean score of each subscale.

Statistical Considerations—Data were entered into the REDCap (<http://project-redcap.org/>) database using a double data-entry procedure with discrepancies resolved by a third reviewer. The following scores were calculated for each instrument: (1) a question-specific mean score was derived by calculating the mean score of a specific question on the instrument among all patient-subjects by group (acceptor vs decliner); (2) an overall mean score was derived by first calculating the mean overall score for each patient-subject (the mean of all questions on the instrument) and then calculating the mean of the overall score among all patient subjects by group. Additional calculation for the TM subscales included (1) mean individualization score, derived by calculating the mean score of questions 1, 2 and 3; (2) mean purpose score, derived by calculating the mean score of questions 4, 5 and 6; and (3) mean benefit score, derived by calculating the mean score of questions 7, 8, 9 and 10. Mean scores were calculated among all patient-subjects by group (acceptor vs decliner).

Descriptive statistics were used to summarize demographic and clinical characteristics. Cronbach’s alpha was used to evaluate the internal consistency and reliability of the modified CRBA instrument for unrealistic optimism. Wilcoxon signed-rank test was used to

assess the difference in unrealistic optimism and therapeutic misconception between subjects who agreed to participate in trials compared to those who declined. Chi-square tests or Fisher's exact tests were applied to gauge the association between groups of subjects (acceptors versus decliners) and demographic characteristics and MacCAT- CR questions. A p-value of .05 was considered statistically significant. Data management and analysis were conducted using Statistical Analysis System (SAS) version 9.4.

RESULTS

Patient Characteristics

Demographic and clinical characteristics are presented in Table 1. These characteristics for the acceptor group were previously described (Jansen, 2016b). Except for the type of cancer, there were no significant differences between acceptors and decliners with regard to demographic or clinical characteristics.

Difference in Unrealistic Optimism between Decliners and Acceptors

Mean unrealistic optimism scores varied significantly between acceptors and decliners with acceptors expressing significantly higher levels of unrealistic optimism than decliners with respect to 8 of the 9 outcomes (Figure 1). The overall mean unrealistic optimism score for acceptors was 1.00 (SD=0.97) compared to -0.56 (SD=0.95) for decliners, $p<0.0001$). See Table 2. Cronbach's alpha confirmed that the modified scale has an acceptable internal consistency and reliability (Cronbach's alpha of 0.85 for acceptors and 0.88 for decliners). No demographic characteristics were associated with unrealistic optimism.

Difference in Therapeutic Misconception between Decliners and Acceptors

Patients in both the acceptor and decliner groups manifested substantial levels of therapeutic misconception. However, decliners had significantly less therapeutic misconception than acceptors [3.37 (SD=0.85) versus 3.79 (SD=0.77), $p=0.042$]. The difference in therapeutic misconception scores between the two groups was most pronounced with respect to the expectations of benefit subscale (3.82 vs. 3.07) ($p=0.012$). See Table 3. Gender and education were significantly associated with therapeutic misconception scores. Given that there was no significant difference between acceptors and decliners for these demographic factors, it is unlikely that the difference in therapeutic misconception between acceptors and decliners is explained by difference in gender and education between the two groups.

Difference in Appreciation between Decliners and Acceptors

There was a significant difference on one of the appreciation questions between acceptors and decliners (whether they could receive a treatment in the study that was less beneficial than standard treatment) ($p=0.009$). Fifty-three percent of decliners, compared with 21% of acceptors, appreciated that they could get a treatment in the trial that was less beneficial. We found no significant difference between acceptors and decliners concerning their appreciation of their role in the study ($p=0.398$) See Table 4.

Discussion

Although most cancer patients do not participate in cancer trials, most of those who are approached to do so, do not decline to participate (Van Der Biessen, 2013; Catt, Langridge, Fallowfield, Talbot, Jenkins, 2011; Moorcraft, Marriott, Peckett, et al., 2016). For this reason, it has proven difficult for researchers to study decliners. Little is known about how decliners think about the risks and benefits of trial participation. Our study looks at social psychological mechanisms, such as unrealistic optimism, that may distinguish decliners from those who agree to participate in early phase cancer trials. We also investigated whether factors widely considered to be relevant to informed consent, such as therapeutic misconception and appreciation of research-related information, help to discriminate between these two groups of patients.

We found significant differences in unrealistic optimism between acceptors and decliners, thus confirming our primary hypothesis. Acceptors had higher expectations for personal benefit and perceived less risk from trial participation than those who declined to participate. These differences in unrealistic optimism between the two groups, in turn, were found to align with differences in therapeutic misconception and appreciation of research-related information. Although both groups had high therapeutic misconception scores, decliners had a better understanding than acceptors of the nature and purpose of trial participation. They also had a greater appreciation that the drug available in the trial could be less beneficial to them than treatment outside of the trial, including no treatment. It remains unclear what accounts for these differences.

Acceptors and decliners made their decisions after an informed consent discussion with a clinician-investigator. It might be wondered whether variations in how information was presented and explained could account for the differences we observed between the two groups. However, both groups participated in an informed consent process at one of two medical centers; and in previously reported data we found that there was no difference in unrealistic optimism among subjects across the two sites. Nonetheless, we cannot rule out person-to-person variation in disclosure that might have accounted for some part of the effect.

Best Practices

Our data are cross-sectional and causal inferences cannot be drawn directly. Nevertheless, a plausible explanation of our findings is that unrealistic optimism affects the decision to enroll in an early phase cancer trial, i.e., that those who manifest unrealistic optimism are more likely to accept the offer to enroll in a trial than those who manifest no unrealistic optimism or even unrealistic pessimism. Unrealistically optimistic patients, after all, anticipate experiencing greater benefits and less risk from trial participation. This explanation is consistent with research in other health-related contexts that has found that unrealistic optimism is consequential for behavior (Radcliffe, Klein, 2002; Dillard, McCaul, Klein, 2006; Dillard, Midboe, Klein, 2009). If correct, this explanation for our findings would cast doubt on the claim, sometimes advanced by ethicists, that most phase 1 trial participants “would still consent to being in these trials even if they suffered no defects in understanding or appreciation relevant to informed decision-making” (Miller, Joffe, 2013 p.

762). Researchers and ethicists interested in informed consent may need to attend to social psychological mechanisms related to risk/benefit assessment and consider how these mechanisms could bear on the decision to participate in a clinical trial.

Our study has some limitations. Fifteen out of 28 decliners we approached agreed to participate, which is a good response rate. But the sample size for the decliners was small, compared to the sample size of the acceptors. Despite the small sample, our study reveals statistically significant results between acceptors and decliners. A larger sample size of decliners would provide greater understanding of the magnitude of the responses from the members of this group and enable stronger comparative assessments. Although we found no significant variation in unrealistic optimism among acceptors with different cancers, a larger sample of decliners would allow broader sub-analyses by cancer type. Our sample population from both acceptors and decliners also was predominantly White (non-Hispanic), and thus our findings may not generalize to other demographic groups.

Research Agenda

Decliners in our study exhibited modest levels of unrealistic pessimism with respect to some of the outcomes they were asked about. This raises interesting and unstudied questions about what may have given rise to this pessimism and about its significance. It is possible that some of these respondents suffered from depression, which has been associated with unrealistic pessimism in other contexts (Strunk, Lopez, DeRubeis, 2006). It is also possible that some respondents adjusted their expectations for benefits and their concerns about risks after their decision to decline enrollment in a clinical trial (Jansen, 2014). Possibly, when decliners were considering enrollment in the trial, their risk/benefit expectations were more favorable. Another possibility is that decliners exhibit unrealistic optimism about the benefits of treatment options outside the trial, and that this optimism conditioned their assessment of the risks and benefits of trial participation. Further research would be needed to confirm or disconfirm these possibilities.

Whatever best explains the unrealistic pessimism we observed, it appears to be less detrimental to informed consent than unrealistic optimism. Decliners exhibited less deficits in understanding and appreciation of relevant risk/benefit information than acceptors. Although unrealistic pessimism may affect the motivation to participate in a clinical trial, and researchers may wish to investigate this possibility in more detail, it does not appear to impair informed consent.

Educational Implications

Risk/benefit assessment is a key component of informed decision making in clinical research. Past studies have documented a number of barriers to accurate risk/benefit assessment (Horng & Grady, 2003; Pentz, White, Harvey, et al. 2012). Our findings suggest that efforts to improve understanding of these barriers may require researchers to focus on those who decline, as well as accept, enrollment in clinical trials. There appear to be significant differences between these two groups concerning unrealistic optimism, therapeutic misconception, and appreciation of research related information.

Since both acceptors and decliners had substantial levels of therapeutic misconception, but only acceptors exhibited unrealistic optimism, therapeutic misconception appears to be a factor that explains expectations for therapeutic benefit, even when patient-subjects do not report unrealistically optimistic assessments of their personal likelihood for benefit compared to others in the same trial. If patient-subjects mistakenly think that by participating in a research study people will get the best treatment for their medical problems, then they may overestimate the likelihood that they will benefit from trial participation, even if they are not themselves optimistically biased. Interestingly, however, unrealistic optimism is associated with therapeutic misconception. Consistent with prior research (Jansen, et al. 2011), our findings suggest that patient-subjects with unrealistic optimism tend to think they are special in the sense that they are more likely to benefit from trial participation than others receiving the very same drugs in the trial.

Some writers have suggested that when respondents answer questions from therapeutic misconception questionnaires they may be taking this as an opportunity to express hopeful or positive attitudes (Kim et al., 2013). That decliners in our study exhibited significant levels of therapeutic misconception casts doubt on this suggestion. It is unlikely that patients would express hopeful or positive attitudes about a trial for which they declined to enroll. Hopeful attitudes aside, the crucial issue is whether unrealistic optimism and therapeutic misconception impair the understanding and appreciation of the risks and benefits of trial participation. Our findings suggest they may. They provide clinicians and researchers with a better understanding of unrealistic optimism and its potential relevance for decisions to enroll in early phase cancer trials. Decliners appear to have a better understanding of the nature and purpose of research, and a greater appreciation of their own susceptibility to risks and benefits from trial participation, than do acceptors. More research is needed on larger groups of decliners, but our findings suggest that they differ significantly from acceptors in ways that affect the quality of informed consent.

Conclusion

Studies on early phase cancer trials have focused on whether participants in these trials have given genuine informed consent. Little research has been done on those who decline to participate in these trials and the research that exists has been motivated largely by a desire to identify barriers to recruitment. By studying defects in informed consent among those who decline trial participation, clinicians and researchers can come to a better understanding of the significance of these defects for the decision to enroll in the trials.

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Figure 1. Difference in mean Unrealistic Optimism (UO) between decliners and acceptors
Mean UO score (blue circle) and associated 95% confidence intervals. Green line: acceptors.
Red line: decliners. Small sample size accounts for the wide confidence interval among
decliners.

Table 1

Demographic Characteristics

Patient Demographic Characteristics				Acceptor Group (N=171)				Decliner Group (N=15)				Fisher's Exact P-Value
	Mean	SD	Min	Max	Mean	SD	Min	Max				
Age	58.64	12.78	18	85	62.8	14.83	22	86	0.131			
Age Group	No. of patients		%		No. of patients		%		0.754			
	31		18.13		2		13.33					
	(18–49)											
	73		42.69		5		33.33					
(50–64)	57		33.33		7		46.67					
	(65–74)											
(75 +)	10		5.85		1		6.67					
	(75 +)											
Gender	84		49.12		5		33.33		0.241			
	Male											
Female	87		50.88		10		66.67					
	Female											
Race	146		85.38		12		80.00		0.360			
	White(non-Hispanic)											
	17		9.94		3		20.00					
	African American/or Black of US origin											
Other	8		4.68		.		.					
	Other											
Education	54		31.58		9		60.00		0.083			
	Grade school/High school											
	81		47.37		4		26.67					
	College											
Graduate/Prof. School	36		21.05		2		13.33					
	Graduate/Prof. School											
Religion	101		59.06		2		13.33		0.543			
	Protestant											
	26		15.20		2		13.33					
	Catholic											
Agnostic	12		7.02		1		6.67					
	Agnostic											
Other	32		18.71		10		66.67					
	Other											
Cancer Problem	54		31.58		1		6.67		0.013			
	Blood cancer											
	26		15.20		7		46.67					
	Lung Cancer											
Breast cancer	23		13.45		2		13.33					
	Breast cancer											
Other	68		39.77		5		33.33					
	Other											
Domestic Status (Do you live alone)	31		18.13		1		6.67		0.259			
	Yes											

Patient Demographic Characteristics		Acceptor Group (N=171)				Decliner Group (N=15)				Fisher's Exact P-Value
		Mean	SD	Min	Max	Mean	SD	Min	Max	
No		140	81.87			14	93.33			
Marital Status	Single	28	16.47			2	13.33			0.103
	Married	115	67.65			7	46.67			
	Divorced	17	10.00			3	20.00			
	Widowed	10	5.88			3	20.00			

Table 2

Difference in Mean Unrealistic Optimism between Decliners and Acceptors

Unrealistic Optimism Score Mean (SD) Range (−3, +3)	Acceptors, N=171 mean (SD)	Decliners, N=15 mean (SD)	P-Value *
your cancer will be controlled by the drugs you get in the trial	1.28 (1.31)	−0.60 (1.06)	<0.0001
you will experience a health benefit from participating in the trial	1.40 (1.26)	−0.67 (1.05)	<0.0001
you will experience a health problem from the drugs being tested in the trial	0.56 (1.32)	−0.73 (1.53)	0.001
your cancer will be cured by the drugs you get in the trial	0.12 (1.91)	−0.87 (1.51)	0.054
your life expectancy will be increased by the drugs you get in the trial	1.37 (1.26)	−0.07 (1.22)	0.0001
the growth (or spread) of your cancer will be slowed as a result of the drugs you get in the trial	1.57 (1.21)	0.00 (1.36)	<0.0001
your cancer will be stopped as a result of the drugs you get in the trial	0.94 (1.60)	−0.67 (1.59)	0.001
your cancer pain will be controlled as a result of drugs you get in the trial	0.75 (1.57)	−0.87 (1.30)	0.0002
you will become sicker from the drugs you get in the trial	1.02 (1.47)	−0.53 (1.41)	0.0004
Overall Mean Optimistic Bias Score	1.00 (0.97)	−0.56 (0.97)	<0.0001

* Wilcoxon Two-Sample Test

Table 3

Difference in Mean Therapeutic Misconception between Decliners and Acceptors

Therapeutic Misconception Score Mean (SD) Range (1, 5)	Acceptors, N=171 Mean (SD)	Decliners, N=15 Mean (SD)	P-Value *
This study is designed to give everyone the type of treatment and amount of treatment that best fits with his or her individual needs.	4.04 (1.20)	3.93 (1.16)	0.592
When designing research, researchers must be sure that each person in the study will get the best treatment available for that person's individual needs, just as though they were being treated by their own personal doctor.	4.28 (1.13)	4.07 (1.28)	0.472
Researchers always try to provide each person in a study the treatment that best meets that person's individual needs.	4.04 (1.22)	3.40 (1.18)	0.031
The purpose of the experimental study is to provide the best treatment available for me and others in the study.	4.20 (1.23)	3.93 (1.49)	0.634
Research studies are designed primarily to help those people who participate in them rather than primarily to help future patients with the same disease.	2.47 (1.36)	2.33 (1.45)	0.644
A researcher's most important task is to make sure that the research will help the people who participate.	3.58 (1.41)	3.80 (1.52)	0.450
The reason I was asked to be in this study is that it will provide me with the best available treatment.	4.08 (1.20)	3.20 (1.42)	0.012
The treatment I am getting in this study is definitely the best treatment for me.	4.33 (0.89)	3.13 (1.13)	<.0001
Being in a research study almost always provides the best possible treatment for a sick person.	3.32 (1.20)	3.13 (1.55)	0.755
By participating in a research study, people will get the best treatment for their medical problems.	3.56 (1.14)	2.80 (1.52)	0.049
Mean Individualization Score	4.12 (1.05)	3.80 (1.01)	0.168
Mean Purpose Score	3.42 (0.99)	3.36 (1.01)	0.840
Mean Benefit Score	3.82 (0.86)	3.07 (1.16)	0.012
Overall Mean Therapeutic Misconception Score	3.79 (0.77)	3.37 (0.85)	0.042

* Wilcoxon Two-Sample Test

Note: Higher scores indicate greater TM

Table 4

Difference in MAC-CAT CR between Decliners and Acceptors

MAC-CAT CR		Frequency (Percentage)		P-Value *
		Acceptors (N=171)	Decliners (N=15)	
Role in Study	Appreciation	51 (29.82)	6 (40)	0.398
	Lack of Appreciation	120 (70.18)	9 (60)	
Possibility of Less Beneficial Treatment	Appreciation	36 (21.05)	8 (53.33)	0.009
	Lack of Appreciation	135 (78.95)	7 (46.67)	

* P-Value Fisher's Exact Test