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Patient Perception, Preferences and Participation

Factors associated with participation in a prevention trial aimed at reducing biomarkers of breast cancer risk

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ABSTRACT

Objectives: Poor enrollment into prevention trials is a major obstacle to the conduct of clinical investigations. This study focuses on cognitive and affective influences on the decision to participate in a clinical trial aimed at reducing biomarkers of breast cancer risk.
Methods: Following a decision to participate or not in a clinical trial focused on reduction of breast cancer risk, women were recruited into the present study. Data were gathered via telephone survey.
Results: One hundred healthy women took part in the current study, 72 of whom had participated in the clinical trial, and 28 of whom had declined participation. Women who decided to enroll perceived more benefits and fewer costs, and they experienced more positive emotions and fewer negative emotions. They also made the decision more quickly, more easily, were more satisfied with it, and had fewer regrets than women who declined participation in the clinical trial.
Conclusions: Participants to this clinical trial differed from nonparticipants in terms of antecedents, process, and outcomes of the decision to enroll.
Practice implications: Although obstacles exist, accrual might be improved by greater emphasis on the practical and psychosocial benefits to participants.

1. Introduction

Clinical trials are the gold standard for evaluating options for treatment and/or prevention of cancer. While there are many challenges to conducting a valid clinical trial, perhaps the single biggest obstacle is recruitment of participants. Although as many as 20% of patients are eligible to participate in clinical research, only 2–7% actually choose to do so [1,2]. Recruitment is particularly problematic in prevention trials which include healthy subjects who fear toxicity from the intervention more than they appreciate the reduction in cancer risk [3]. Low rates of participation create serious problems for health care delivery. Under-enrolled trials take longer than they otherwise would, which delays the introduction of new regimens and postpones rejection of ineffectual alternatives. Poor accrual to trials also endangers medical science at a fundamental level. Low enrollment may produce non-representative samples, thereby constraining the generalizability of the findings and threatening the validity of the trial's conclusions.

Improved understanding of how individuals decide to enter a trial could lead to strategies for increasing enrollment [4]. In this project, we sought to deepen our understanding of the participation decisions along several lines. First, rational models of decision making emphasize the costs and benefits associated with different options. In a study of enrollment into breast cancer treatment trials, Avis, Smith, Link, Hortobagyi, and Rivera [5] asked participants and nonparticipants to evaluate seven perceived benefits and 15 perceived drawbacks of joining a trial. We sought to test the utility of the same set of predictors in a breast cancer prevention trial.

One limitation to rational models of decision making is that they do not readily accommodate non-rational influences on decision making, such as emotion. Given research showing that emotions can have important effects on decision making, [6–8] we included measures of both positive and negative emotions associated with the enrollment decision. Evidence of the unique effects of discrete emotions on judgment led us to maintain the measures as separate indices, rather than collapse them into the broader categories of positive and negative [9].

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Enrollment decisions are binary: participate or not. However, other features of the decision can be examined in more nuanced ways [10]. For example, analysis of the speed and difficulty of the decision may yield insight into processes that undergird enrollment [11]. Post-decision phenomena, such as satisfaction and regret [12,13] index psychologically important outcomes [14] that could influence subsequent decisions [15].

We expected that studying the decision process broadly might contribute to a fuller understanding of the problem of accrual. Hence, we examined antecedents of the decision, aspects of the process itself, and outcomes of the choice to enroll vs. not to enroll.

2. Methods

2.1. Sample

A clinical trial is conducted at Hershey Medical Center under the direction of one of us (AM) to assess the efficacy of combining Raloxifene with Lovaza (the FDA approved formulation of the omega-3 fatty acids docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) as a means of reducing breast density, a biomarker of breast cancer risk [16]. The details of the clinical trial (NCT00723398) have been recently published by us [17]. Briefly, the trial targeted healthy, postmenopausal women deemed to be at high risk of breast cancer based on breast density in excess of 25% at their yearly routine screening mammogram. Additional inclusion/exclusion criteria are detailed in our report [17]. Consistent with the demographics of the catchment area, 98% of the sample was white and 2% were of African descent.

Within a year of being offered the opportunity to enroll in the clinical trial, 305 women were contacted by mail and invited to participate in the current study about their decision regarding enrollment in the clinical trial. This included 100% of the trial nonparticipants. Ultimately, 72 trial participants and 28 nonparticipants agreed to provide data about their enrollment decision. Rate of accrual to the clinical trial itself may have been depressed by the risk of venous thromboembolism associated with the use of raloxifene. The response rate was 54% for trial participants and 16% for nonparticipants, which gave an overall response rate of 32% for the current study. Data were collected via telephone interview. Because inclusion/exclusion criteria combined with the catchment area produced a homogeneous sample, no additional demographic data were collected for the decision study.

2.2. Measures

The primary variable of interest was measured with a single item *What decision did you make concerning the preventive breast cancer trial (Yes, to participate vs. No, not to participate)?* Other outcome measures included speed and difficulty of decision making, satisfaction with the decision, and regrets following the decision. The exact wording of these and all other measures appears in the text and tables of the Results section. Single items designed to measure a variety perceived costs and benefits were taken directly from Avis et al. [4] although some items were excluded because they were not relevant to this preventive trial (e.g., "too much blood drawn"). The emotion measures were single items whose validity was established in previous studies [18].

2.3. Statistical analyses

Multiple imputation was used to estimate the 0.8% of the data that were missing.

Bivariate analyses utilized t or χ^2 statistics as appropriate to ordinal or categorical data. Given the difference in group sizes (72 vs. 28), equality of variances was not assumed when estimating t values. A forward step logistic regression model was used to estimate the multivariate associations with enrollment decision.

3. Results

3.1. Perceived costs of participation

Respondents made judgments of the importance of 13 possible costs to participation in the clinical trial using a three-point response scale: (1) = Not at all important, (2) = Somewhat important, and (3) = Very important. Table 1 summarizes mean responses broken by participants and nonparticipants. The means are ordered from highest to lowest in the participant group; standard deviations appear in parentheses. Significant differences at $p < .05$ were observed on three of the thirteen items: Nonparticipants reported higher perceived costs regarding (a) the possibility of side effects, (b) riskiness of the trial, and (c) the amount of time required by the trial.

3.2. Perceived benefits of participation

The importance of seven possible benefits to participation was assessed on a three-point response scale: (1) = Not at all important, (2) = Somewhat important, and (3) = Very important. Table 2 summarizes mean responses broken down by participants and nonparticipants. Three of the eight items showed significant differences at $p < .05$. Participants saw more benefit in trial enrollment as: (a) a way of helping others, (b) a way of doing something positive, and (c) a way of being involved in new treatments.

Table 1
Perceived costs of the decision to enroll.

	Participants	Non participants	t	p
	Mean (SD)	Mean (SD)		
The possibility of side effects	1.99 (0.70)	2.57 (0.57)	4.29	.0001
Didn't know what to expect	1.54 (0.60)	1.86 (0.84)	1.83	.07
Might get less effective treatment	1.42 (0.66)	1.44 (0.82)	0.34	.73
It was too risky	1.31 (0.57)	2.00 (0.90)	3.78	.001
Might not get the best treatment	1.18 (0.48)	1.40 (0.80)	1.20	.23
It disrupted your daily routine	1.14 (0.38)	1.38 (0.62)	1.78	.083
It took too much time	1.14 (0.38)	1.45 (0.70)	2.21	.030
Medical research can't be trusted	1.12 (0.44)	1.08 (0.38)	0.57	.56
You would have felt like a guinea pig	1.11 (0.39)	1.14 (0.35)	0.38	.70
Researchers care more about research than people	1.10 (0.38)	1.07 (0.26)	0.35	.72
Transportation was a problem	1.08 (0.32)	1.19 (0.55)	0.89	.37
Might have changed your relationship with a health care provider	1.08 (0.27)	1.13 (0.32)	0.44	.65
Lack of privacy	1.04 (0.26)	1.20 (0.40)	1.77	.08