

Successful Patient Recruitment in CT Imaging Clinical Trials:

What Factors Influence Patient Participation?

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Rationale and Objectives: Analyze factors that influence participation in research studies that use coronary computed tomography (CT) imaging.

Materials and Methods: A 12-point survey using a questionnaire was conducted on 80 subjects, of whom 40 agreed to participate in a cardiovascular CT imaging research study (enrolling subjects) and 40 declined participation (non-enrolling subjects). Potential factors that motivated the acceptance or refusal of enrollment were evaluated using a 5-point Likert scale. The following aspects were addressed: (1) additional health information, (2) free imaging, (3) altruistic benefit to society, (4) monetary compensation, (5) radiation exposure, (6) role as an experimental subject, (7) possible loss of confidentiality, (8) contrast or investigational drug use, (9) premedication use, (10) blood draw or intravenous placement, (11) time commitment, and (12) personal medical opinion. Response distributions were obtained for each question and compared between enrolling and non-enrolling groups.

Results: Enrolling subjects gave significantly higher ratings than non-enrolling subjects for the following factors: additional health information ($P < .001$), free imaging ($P < .001$), and the altruistic benefit to society ($P < .001$). For non-enrolling subjects, concern for possible drug use or contrast injection ($P < .001$), concern for possible premedication ($P < .001$), and personal availability or time commitment ($P < .001$) were all given significantly higher ratings. Concern for radiation exposure ($P = .002$) and personal medical opinion ($P < .001$) received significantly high ratings among both groups but did not differ between groups.

Conclusions: Several influential concerns and benefits were identified from potential research subjects. Knowledge of what influences patient participation in studies involving CT imaging may allow researchers to effectively address concerns and highlight the potential benefits related to participation.

Key Words: CT; recruitment; risks; benefits; clinical trial.

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Clinical research is vital for the progress of medicine and clinical practice (1). Because clinical trials depend on patient participation, effective recruitment strategies are imperative for trial success (2). Understanding the factors affecting a patient's willingness to participate in a clinical trial is beneficial for successful patient recruitment (3) because it allows customization of recruitment strategies to address typical concerns and expectations. Inefficiencies in subject recruitment may result in unwanted extensions of study time frames, typically increasing study costs (2) and challenging the completion of expected site deliverables. The investigators' ability to address common concerns puts

research subjects at ease (4), which enables the trial to avoid participant attrition and helps achieve the expected recruitment goals for the study (5).

Several studies have examined factors that affect patients' decisions to participate in different types of clinical trials. The altruistic feeling of helping society has been shown to have a positive influence on participation (6–10). The potential to obtain additional health-related information has been shown to affect participation both positively (3,11,12) and negatively (13). Poor education levels and unfamiliarity with scientific jargon typically have been shown to have a negative impact on study participation (13). Existing studies focus exclusively on the influencing factors on those patients who participate in clinical trials, providing a biased representation of patients' concerns. To our knowledge, no study has yet analyzed the concerns of patients who decline participation.

Unique attributes of computed tomographic (CT) imaging could present additional concerns in these clinical trials involving coronary CT angiography (CCTA). CCTA continues to raise attention because of its radiation levels (12) and potential for harmful effects over time (14). Cost/benefit analyses have shown that the benefits of cardiac CT imaging to detect

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TABLE 1. Patient Distribution

	Accepted Participation	Declined Participation	Total
Patients contacted to participate in CT clinical trial (male, female)	89 (67, 22)	275 (162, 113)	346 (229, 135)
Contacted to participate in questionnaire study (male, female)	55 (37, 13)	79 (36, 43)	134 (78, 56)
Participated in questionnaire study (male, female)	40 (20, 20)	40 (18, 22)	80 (38, 42)

CT, computed tomography.

coronary artery disease (CAD) outweigh the risk of cancer in middle-aged and older patients (15,16). Nevertheless, the levels of anxiety regarding radiation exposure have escalated over the past several years (17). Other unique characteristics involved in clinical trials using CT make recruitment even more challenging, including the use of contrast (18), sublingual nitroglycerine for vasodilation or beta-blockers for heart rate reduction (19). In addition, because radiologists have limited contact with patients, clinical trial enrollment is highly dependent on referring physician support and encouragement (7) and the manner in which patients are educated regarding the risks and benefits of participation (20–22).

The purpose of this study was to analyze factors that influence patient participation in research studies that use coronary CT imaging. Patients who expressed interest in participating in CCTA imaging trials were surveyed to determine the factors that influenced their decisions. Standard factors in clinical trial participation were analyzed as were those unique to CT imaging. Results were compared based on whether the subjects ultimately decided to participate so that their opinions were included to provide a more complete representation of patients' concerns.

MATERIALS AND METHODS

Over a 9-month period, research personnel contacted potential research subjects to participate in clinical trials involving CCTA. Subjects were recruited from the main medical center and one satellite cardiology clinic. All subjects were pre-screened by research personnel to assure qualification for one of the trials. Within 1 week of receiving a referral to undergo a cardiac stress imaging exam, qualifying patients were sent informational material through standard mail that explained the trial they would qualify for, including the different steps and processes involved as part of the research examination. Interested patients were provided additional information regarding participation over the phone, after which they made the decision whether to participate. A list of the patients who expressed interest over the phone was maintained for the purpose of this study. Later, patients were randomly selected from this group and asked to complete a questionnaire ranking various factors that affected their decision to accept or decline participation.

This study focused on patients recruited for three institutional review board–approved, Health Insurance Portability and Accountability Act–compliant clinical trials: PROspective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) (23), Randomized Evaluation of Patients

with Stable Angina Comparing Diagnostic Examinations (RESCUE) (24), and an investigator-initiated, single-center, industry-sponsored trial funded by Siemens. The aim of the PROMISE trial was to recruit patients who experienced new or worsening chest pain that was suspicious for clinically significant CAD but excluded those with known CAD. In the trial, patients were randomized to either the “functional test arm” involving one of three standard of care imaging methods (echocardiography, electrocardiogram exercise stress test, or nuclear medicine imaging) or to the “anatomical test arm” involving a CCTA. The aim of the RESCUE trial was to recruit patients with symptoms of stable angina or angina equivalent and without prior revascularization. Patients were randomized to either the functional test arm involving standard of care nuclear medicine imaging or to the anatomical test arm involving a CCTA. In the industry trial, potential subjects who underwent stress nuclear myocardial perfusion imaging within the previous 3 months were offered participation involving a CCTA with stress nuclear myocardial perfusion imaging.

In total, 346 patients were contacted to participate in one of the three clinical trials, 89 of whom ultimately participated. Of the initial 346 patients, 134 were randomly selected and asked to participate in this survey, 80 of whom agreed to participate in the questionnaire (Table 1). Confirmation was obtained from each subject who participated in the survey that he or she indeed received the informational material regarding one of the three clinical trials, read through the material, and that he or she made a conscious decision to accept or decline participation. No subjects surveyed participated in more than one clinical trial. Because of the difficulty of enrollment into this study, a cutoff of 40 patients was set for both groups of patients, enrolling (PROMISE: 17; RESCUE: 12; and industry trial: 11) and declining (PROMISE: 19; RESCUE: 9; and industry trial: 12).

A structured phone interview was conducted with each patient and the answers were immediately documented during the conversation. The survey consisted of 12 questions that evaluated the importance of various factors in each patient's enrollment decision. The survey was structured into four main categories: benefits (both personal and societal), risks and discomforts (such as radiation exposure, the “guinea pig syndrome” (25), and possible loss of confidentiality), possible side effects (from contrast, investigational drug use, premedication, and intravenous placement or blood draw), and personal influence (such as time commitment and individual medical opinion) (Table 2). The survey was administered to each patient by the same interviewer to ensure

TABLE 2. Categories and Questions from Questionnaire

Benefits	Risks/Discomforts	Possible Side Effects	Personal Influence
The chance to obtain additional health information	Concern regarding possible radiation exposure	Concern for possible contrast or investigational drug use	Personal availability and/or time commitment
The opportunity to obtain free imaging	Role as an experimental subject ("guinea pig")	Concern for possible premedication use	Personal medical opinion regarding your own health
Altruistic benefit to society	Concern for possible loss of confidentiality	Concern for possible blood draw/intravenous placement	
Monetary compensation			

consistency in the delivery of each question and the way each was explained. For example, altruism was defined for subjects as a selfless benefit to society, and individual medical opinion was explained as the influence of patients' own opinion regarding their health on their decision to participate.

Subjects were asked to evaluate each factor using a 5-point Likert scale (26) to describe the extent of each factor's influence on their decision to accept or decline participation in the CT clinical trial. Respondents gave responses ranging from 1 (not at all important) to 5 (extremely important). Precise responses and ratings of each factor in the survey were recorded for each subject, respectively.

The data are divided into two categories of responses: those who participated in a clinical trial and those who declined participation. One-sided Wilcoxon rank-sum tests were used to find which questions generally had higher responses than the overall response distribution. Two-sided Wilcoxon rank-sum tests were used to determine significant differences between the two groups. In addition, two-sample Kolmogorov-Smirnov tests were used to determine if response distributions differed based on gender, and analysis of variance was used to determine if average responses differed between subjects of different studies. A significance level of 0.05 with Bonferroni correction for multiple comparisons was used to determine statistical significance and tests were performed using the MATLAB statistical toolbox (version 7.10.0, MathWorks Inc, Natick, MA). This study was approved by the university institutional review board and in compliance with the Health Insurance Portability and Accountability Act guidelines.

RESULTS

Data are reported on the total sample of 40 respondents in each group. The two-sample Kolmogorov-Smirnov test indicated no statistical significance in response distribution between sexes. Subjects from the three studies were not found to have significant differences in mean response either overall ($P = .78$) or in the benefits, risks/discomforts, possible side effects, or personal influence categories ($P = .09$, $P = .90$, $P = .97$, and $P = .41$, respectively).

Five of the 12 factors analyzed in the survey were found to be significantly more important in subjects' participation decisions. Subjects generally gave these factors higher ratings regardless of whether they declined or accepted participation

TABLE 3. Average Response Values for Enrolling and Non-enrolling Subjects

Questions	Enrolling	Non-enrolling
Benefits		
The chance to obtain additional health information	4.5 ± 1.1	2.7 ± 1.7
The opportunity to obtain free imaging	4.1 ± 1.3	2.4 ± 1.7
Altruistic benefit to society	4.5 ± 0.9	2.8 ± 1.5
Monetary compensation	2.1 ± 1.3	1.7 ± 1.4
Risks/discomforts		
Concern regarding possible radiation exposure	2.7 ± 1.5	3.6 ± 1.6
Role as an experimental subject ("guinea pig")	1.7 ± 1.2	2.1 ± 1.3
Concern for possible loss of confidentiality	1.6 ± 1.1	2.1 ± 1.5
Possible side effects		
Concern for possible contrast or investigational drug use	1.8 ± 1.1	3.1 ± 1.7
Concern for possible premedication use	1.6 ± 1.1	2.9 ± 1.6
Concern for possible blood draw/intravenous placement	1.4 ± 0.9	1.4 ± 0.9
Personal influence		
Personal availability and/or time commitment	2.0 ± 1.2	3.7 ± 1.6
Personal medical opinion regarding your own health	3.2 ± 1.3	3.3 ± 1.6

in the study. Three of these factors, additional health information ($P < .001$), free imaging ($P < .001$), and altruistic benefit to society ($P < .001$), were found to be significant overall but were also significantly more influential for enrolling subjects. The remaining two factors, possible radiation exposure ($P = .002$) and personal medical opinion ($P < .001$), were found to be significant overall but responses did not differ significantly between the enrolling and non-enrolling subjects.

Specifically for enrolling subjects, the factors that had significantly higher ratings were additional health information ($P < .001$), free imaging ($P < .001$) and the altruistic benefit to society ($P < .001$). Subjects who enrolled in a study gave these factors significantly higher ratings than those who

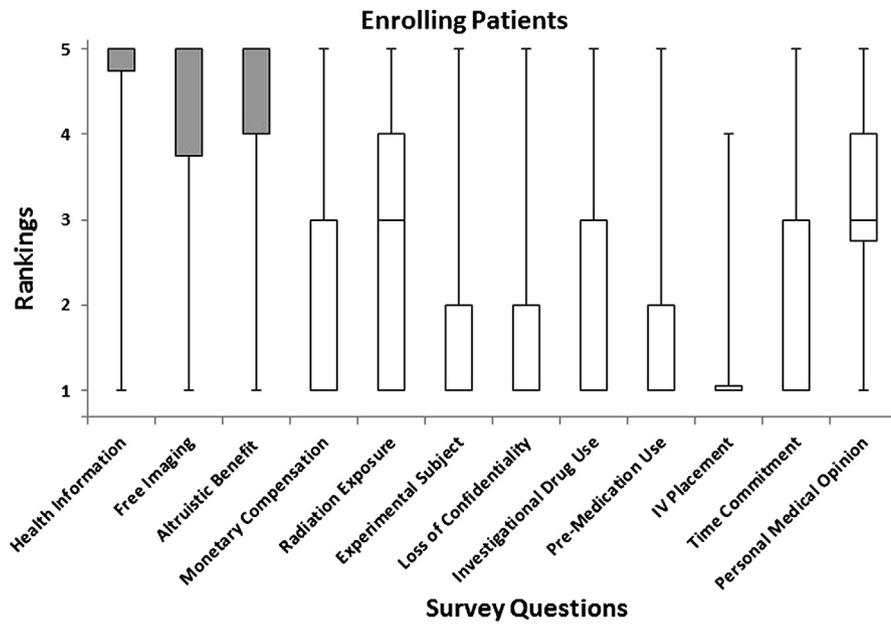


Figure 1. Response distributions for enrolling patients. Box plots show the distributions of questionnaire responses for each question. Response distributions that are significantly higher than non-enrolling patient responses are colored gray. IV, intravenous.

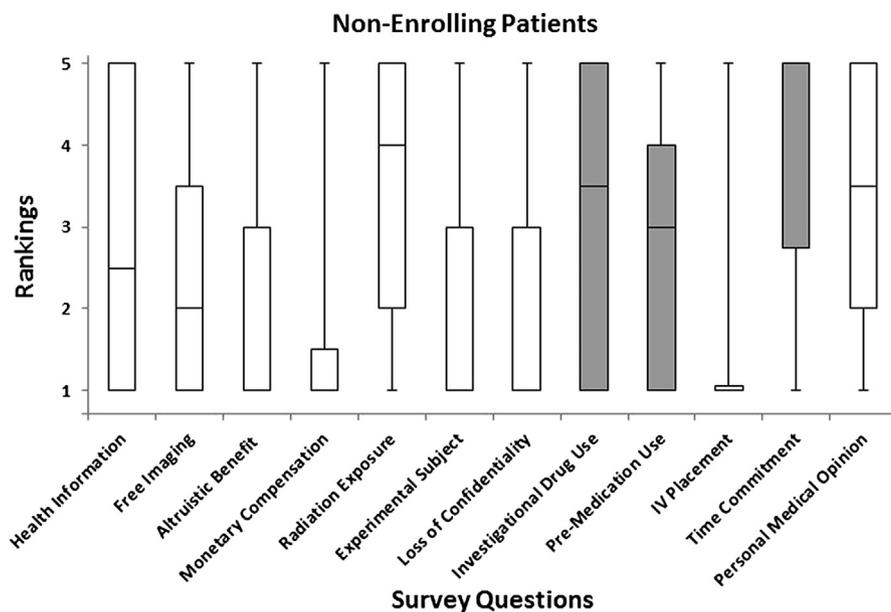


Figure 2. Response distributions for non-enrolling patients. Box plots show the distributions of questionnaire responses for each question. Response distributions that are significantly higher than enrolling patient responses are colored gray. IV, intravenous.

declined enrollment. All three of these influential factors received a rating of 5 (extremely important) from 50% or more of these subjects (Table 3 and Fig 1).

Specifically for the non-enrolling patients, the statistically significant factors for this group were the concern for possible drug use or contrast injection ($P < .001$), concern for possible premedication ($P < .001$), and personal availability or time commitment ($P < .001$). Unlike the subjects who participated in a clinical trial, many of the non-enrolling subjects felt that the chance to obtain additional health information was not at all an important factor in their decision process as 40% provided a rating of 1 (not at all important) (Table 3 and Fig 2).

Factors that were not significant for either group were monetary compensation ($P = .13$), concern regarding being

an experimental subject ($P = .26$), concern for possible loss of confidentiality ($P = .17$), and intravenous placement or blood draw ($P = .76$).

DISCUSSION

This study illustrates the concerns regarding participation in radiological research studies involving cardiovascular CT imaging held by potential research subjects. With any clinical trial, there is an inherent balance between benefits and risks (27). Particularly for a clinical trial involving an imaging method using ionizing radiation, several general and distinct factors need to be considered by potential research subjects.

Subjects in both groups gave significantly higher than average responses to three of four of the questions in the benefits category (additional health information, free imaging, and the altruistic benefit to society). Altruism specifically has been identified previously as a key factor providing an incentive to patients to participate in a variety of clinical trials (3,7,8,12,13) because patients enjoy the feeling of helping society (9,10). These results may have to do with the methods used to administer the survey. It has previously been noted that participants in surveys conducted in a non-self-administered way often tend to give socially desirable responses to survey items (6,10). Furthermore, it is possible that these respondents felt obligated to view clinical trials in a more favorable light because they are treated in an academic medical center (9).

Possible radiation exposure was found to be important in the decision-making process but influence did not differ significantly between the groups. It is possible that this concern comes from a lack of understanding because radiation is a word that often evokes fear and concern, particularly in patients not familiar with the associated medical effects (14). There may be a lack of understanding regarding the risks and benefits of CT imaging (28) or imaging modalities as a whole, leading to the association of potential harm. It is also possible that participating subjects relied on social trust of the institution, assuming that the risks associated with CT imaging are unlikely to affect them individually (29). Assumptions of patient understanding cannot be made (30) and so it is imperative that patients receive sufficient information (21) to make a truly informed decision. Analysis of the effects of providing educational materials on the success of recruitment warrants future investigation.

An unexpected discovery from the results of the survey was that a majority in each group (75% of non-enrolling patients and 55% of enrolling) indicated that monetary compensation had little influence in the decision-making processes. This result seems to contradict the results from a previous study that demonstrated that monetary compensation makes subjects more willing to participate in clinical trials, regardless of the risk (31). The urge to provide socially desirable responses could serve as a potential explanation for these results (6,10). It is also possible that monetary compensation provided in the clinical trials outlined here (\$100) was not enough to be an impacting factor based on the associated costs involved with participating (28). A substantially higher amount may have played a more important role in a potential research subject's decision process. Individual economic status could also play a role in the influence of this factor but it was not recorded in this study.

Reaching patients and receiving responses to the survey was difficult, particularly for patients who did not participate in a clinical trial. As a result, the sample size was relatively small and selection bias may have affected the results. Furthermore, the results presented in this study show correlations and do not necessarily reflect causation. Because the survey was given post facto, it is possible that the enrolling patients' initial concerns about risks were softened by going through the test

without incident. Interviews before enrollment could provide a more accurate account of their concerns. Providing educational material and recording whether a subject's decision changes could also yield a causal relationship between patient understanding and trial participation. Addressing patients' attitudes at the time of making a decision regarding participation via qualitative research methods such as an interview may also provide a more in-depth look into what patients think and feel in the moment.

The findings from this study demonstrate the degree of influence of various factors on the decision to accept or decline participation in a clinical trial involving coronary CT. The outlined findings may allow for ways to more effectively address concerns and highlight the potential benefits related to participation in such trials. This information can be used to develop a more conscientious approach to explain these research studies and lead to the modification of recruitment strategies, consent forms, and clinical procedures to meet the expectations of participants. Furthermore, the results from this study may provide insights into the typical concerns of patients undergoing CT imaging or other imaging procedures that use ionizing radiation in a clinical, non-research based setting.

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