

Barriers and Motivations for Women to Participate in Cardiovascular Trials

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Abstract

Background: Cardiovascular disease is one of the major causes of mortality in Canadian women. However, the number of women recruited into cardiovascular clinical trials continues to be low relative to the prevalence of cardiovascular disease. To determine why the recruitment of women into cardiovascular trials continues to be problematic, we prospectively examined the barriers and motivations of women contacted for the Raloxifene Use for The Heart (RUTH) study.

Methods: Two hundred seventy postmenopausal women were surveyed. Regardless of study eligibility, women were asked to comment on their reasons for participating or not participating in cardiovascular trials in an open-ended single question format. All answers were recorded and grouped accordingly.

Results: Fifty-four percent of women surveyed indicated they would not participate in clinical research, and 46% indicated that they would. Motivations reported for participating in a cardiovascular clinical trial included personal health benefits (82.2%), interest in research (44.1%), and the possibility of benefiting society (29.1%). Reasons for declining participation included personal illness (24.8%), transportation issues (17.9%), reluctance to increase medication (15.2%), and concern about adverse health effects (13.1%).

Conclusion: As reported by our cohort of postmenopausal women, the major barrier to entering a randomized controlled trial related to cardiovascular disease was the perception that participation would present an increased burden on health and time. Our experience suggests that researchers need to educate women on the importance of clinical trials and that they also need to provide practical solutions to barriers such as transportation.

Key Words: Clinical trials, women, motivation, research subject recruitment

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Résumé

Contexte : Les maladies cardiovasculaires sont l'une des principales causes de mortalité chez les Canadiennes. Cependant, le nombre de femmes recrutées par les essais cliniques portant sur ces maladies est toujours faible, par comparaison avec la prévalence des maladies cardiovasculaires chez celles-ci. Pour déterminer les raisons pour lesquelles le recrutement des femmes par les essais cliniques portant sur ces maladies continue de s'avérer problématique, nous avons examiné (de façon prospective) les obstacles et les motivations des femmes sollicitées dans le cadre de l'étude *Raloxifene Use for The Heart* (RUTH).

Méthodes : Deux cent soixante-dix femmes postménopausées ont été sondées. Peu importe leur statut en matière d'admissibilité à l'étude, nous avons demandé (en ayant recours à une seule question ouverte) à ces femmes de commenter les raisons motivant leur décision de participer ou de ne pas participer aux essais cliniques portant sur les maladies cardiovasculaires. Toutes les réponses ont été consignées et groupées en conséquence.

Résultats : Cinquante quatre pour cent des femmes sondées ont indiqué qu'elles ne participeraient pas à des efforts de recherche clinique, tandis que 46 % ont indiqué qu'elles le feraient. Parmi les raisons signalées de participer à un essai clinique portant sur les maladies cardiovasculaires, on trouvait des avantages personnels en matière de santé (82,2 %), un intérêt envers la recherche (44,1 %) et la possibilité de contribuer au bien-être de la société (29,1 %). Parmi les raisons du refus de participer, on trouvait la maladie personnelle (24,8 %), des préoccupations quant au transport (17,9 %), la réticence à consommer plus de médicaments (15,2 %) et des préoccupations en matière d'effets indésirables pour la santé (13,1 %).

Conclusion : Comme l'a signalé notre cohorte de femmes postménopausées, la perception selon laquelle la participation compromettrait la santé et s'avérerait vorace en temps constituait le principal obstacle se dressant devant la participation à un essai comparatif randomisé portant sur les maladies cardiovasculaires. Notre expérience semble indiquer que les chercheurs se doivent de sensibiliser les femmes à l'importance des essais cliniques et de leur offrir des solutions pratiques aux obstacles tels que ceux qui sont liés au transport.

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INTRODUCTION

Although cardiovascular disease is the most common cause of morbidity and mortality among women in developed countries, women continue to be under-represented in cardiovascular trials.¹⁻⁵ There is a paucity of information about the reasons for this under-representation. However, suggested reasons include the perception that women tend to withdraw from trials prior to their completion, a general unwillingness of women to volunteer for clinical trials, and a generalized safety concern for pregnant women and women of childbearing age.⁵ In non-cardiovascular research, reasons given by women for participating in studies have included altruism,⁶ the desire to foster the progress of research,⁶ the improvement in health of themselves and others,⁷ and monetary compensation.⁸ Whether these factors act to motivate women to participate in cardiovascular research has not been reported.

Recent recognition of gender differences in cardiovascular risk factors, disease presentation, and treatment outcomes has led to various initiatives aimed at increasing the enrolment of women in cardiovascular trials. Yet significant obstacles to women's participation in these trials still exist. In the HERS (Heart and Estrogen/progestin Replacement Study) trial,⁹ investigators screened 68 561 women by telephone to randomize 2 763. Furthermore, the Women's Health Initiative screened 373 092 postmenopausal women to randomize 16 608 in the estrogen-progestin arm¹⁰ and 10 739 in the estrogen-only arm.¹¹ Identifying factors that encourage or deter women when confronted with the opportunity of participating in cardiovascular research is essential to improving recruitment. In this study, we prospectively surveyed women during the recruitment process for the RUTH (Raloxifene Use for the Heart) trial at one Canadian academic centre to identify self-reported motivations and barriers for participation in cardiovascular clinical trials.

METHODS

The RUTH study was a five- to seven-year international multicentre randomized double-blind placebo-controlled clinical trial investigating whether raloxifene protects against fatal and non-fatal myocardial infarctions in postmenopausal women at risk for coronary events.¹² A total of 10 101 women were randomized worldwide, 56 from our tertiary academic centre. Our recruitment methodology used techniques previously reported as successful, including (1) advertising in local newspapers, magazines, community centres, and hospitals; (2) giving educational rounds in hospitals and the community; (3) approaching potentially eligible women at 10 clinics, nine physicians'

offices, and two catheterization laboratories; and (4) mailing 2181 invitations, signed by both their physicians and the site's principal investigator, to potentially eligible women identified through chart reviews.^{7,13}

During our recruitment period from September 1998 to August 2000, two female nurse study coordinators screened 277 prospective study participants and evaluated eligibility for the RUTH study. Once eligibility was established, oral consent for survey participation was requested. If consent was granted, a 15-minute standardized survey evaluating attitudes towards clinical research participation was conducted. Regardless of study eligibility, women were asked about their reasons for participating or not participating in clinical research, using a single open-ended question: "Can you tell me why you are/are not interested in participation?" All information given about barriers and motivations to cardiovascular research participation was recorded manually and grouped into specific categories of reasons for participation or non-participation in clinical research. Multiple responses were allowed. Responses from both study coordinators were pooled and qualitatively analyzed for similarities and frequency of occurrence. The survey was approved by the University Health Network research ethics board.

RESULTS

We surveyed a total of 270 women with regard to their motivations for or barriers to participating in clinical research. The mean age of the women was 68.6 ± 8.0 years. The percentage of women contacted by each recruitment method is shown in Table 1. The demographics of this convenience sample are outlined in Table 2. This population had a slightly higher level of education than the general Canadian population,¹⁴ and the majority reported English as their primary language. All except two women were post-menopausal.

Of the 270 women surveyed, 125 (46%) indicated that they would be willing to participate in clinical research and 145 (54%) were unwilling to participate (Figure). Of the 125 women who were interested in participating, 56 (21% of all women surveyed) qualified. Of all survey participants, 171 actually met RUTH inclusion criteria and were eligible for study participation. However, 115 (67.3%) eligible women screened for the RUTH study declined participation.

The self-reported reasons for interest or lack thereof in participating in clinical research are listed in Table 3. Motivations offered for participation fell into three major categories: personal health benefits, an interest in participating in medical research, and an interest in benefiting society. A number of barriers to participating in cardiovascular research were also reported, focusing on personal health

Table 1. Percentage of women contacted by each recruitment method

Method of contact	Percent contacted*
Contacted after mailed invitation	40.4
Contacted after chart review	24.4
Responded to mailed invitation	15.2
Response to advertisement	12.0
Referred by physician	8.0
Referred by friend	1.6

*These add up to more than 100%, as more than one method may have been used

Table 2. Characteristics, education levels, and comorbid illnesses of women contacted for the RUTH study through the Toronto centre

Characteristics	Value
Age	68.6 ± 8.0 years
English as a primary language	90.6%
Post-menopausal	99.3%
Current smoker	4.6%
Education	
Less than grade 12	15.4%
Grade 12	47.4%
College/university	37.2%
Comorbid illness	
Hypertensive	59.9%
Previous bypass surgery	52.4%
Hyperlipidemia	43.5%
≥ 1 Myocardial infarction(s)	32.2%
Diabetes	30.8%
Previous coronary angioplasty	27.3%
Angina	28.2%
Lower extremity arterial disease	6.9%

issues such as being too ill to participate, already taking too many pills, and concerns about negative health effects from the study. Other concerns were transportation issues, time constraints, and family pressures. A general apprehension about entering a clinical trial was expressed by 19.3% of women, in that they reported concerns about randomization (2.1%), a fear of experiments, too many visits to the doctor, previous bad experiences with research (4.1%), and a general concern about negative health effects (13.1%). Eighteen percent of women contacted did not provide a reason for non-participation.

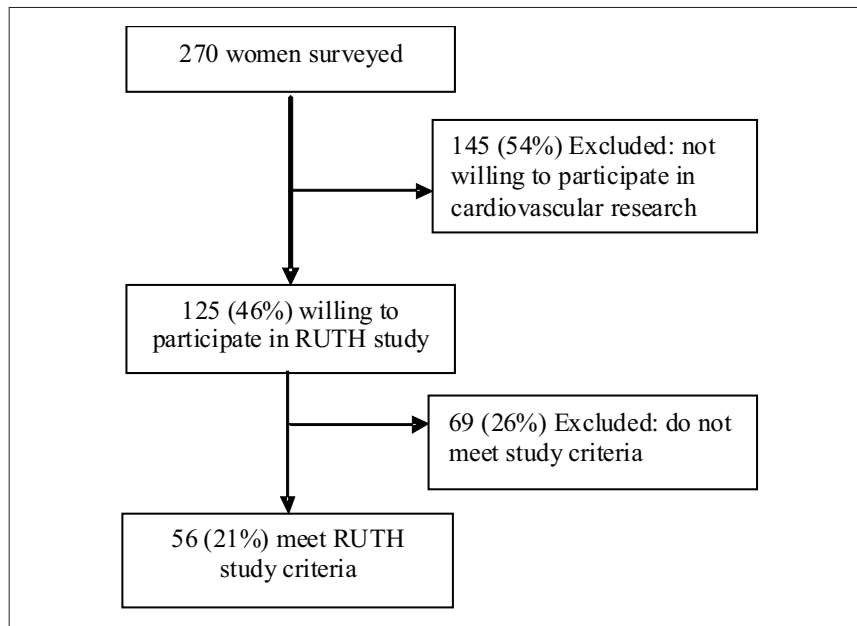
DISCUSSION

A great deal of time and a great many resources are spent on clinical trial recruitment, often with limited success. Gaining an understanding of the reasons why women chose to participate or not in cardiovascular research may lead to improved recruitment strategies. This exploratory study is the first to examine the reasons for interest in participating in postmenopausal cardiovascular research, and the barriers to such participation. The open-ended self-report method used in this study allowed women to express their feelings about medical research participation without prompting or limiting their response, which may have provided a wider scope of information. Of the 270 women interviewed, less than half (125, 46%) expressed interest in participating in clinical research. We found that personal health benefits, the advancement of scientific knowledge, and the benefit to others were the most commonly reported motivators for participating in cardiovascular research. This is consistent with motivations reported by women in other types of clinical research,^{6,7} as well as in studies that did not group responses by gender.¹⁵⁻¹⁸

We also found that, in this group of potential study participants, more than one half of the women surveyed (145, 54%) were not interested in participating in clinical trials. The most commonly reported barrier to participating in cardiovascular research expressed by this sample was the feeling that participation would increase the burden on health, a finding that has been reported in multiple studies in both men and women.^{16,19,20}

Transportation was another significant issue, raised by almost 18% of women surveyed in this study as a deterrent for entering a study. This has been reported previously by clinical trial recruiters who enlist women for research,²¹ as well as by female study participants themselves.^{8,22} However, this appears to be a general obstacle to all participation in clinical trials and is not specific to women. Elderly participants in a diabetes trial reported transportation as a major barrier to participation in clinical studies.¹⁹ Transportation

Flow diagram showing willingness to participate and eligibility of women who were interviewed for potential participation in the RUTH trial



was also noted as a key issue in a retrospective study of the Systolic Hypertension in the Elderly Program (SHEP)¹⁷ and in a study of behavioural therapy for chronic heart failure.¹⁶ Incorporating funding for transportation, parking, or even taxi service to and from the study location into research budgets may alleviate much of the pressure that potential participants experience and may lead to increased enrolment. This, of course, depends on funding institutions considering recruitment and retention items as real costs involved in clinical research. Alternatively, having study coordinators who are willing to travel to the homes of participants for some study visits may be an alternative. Telephone check-ins would also be a low-cost alternative to travelling to a research centre. With the development of web-based forms, instant messaging, and telemedicine, the Internet as a tool for communication between research staff and participants may also be an option in the future.

Our results showed that 19.3% of the women surveyed in this study voiced some apprehension about clinical research as one reason for not participating in the RUTH study. Concerns ranged from negative health effects of study medication to fear of experimentation, and previous negative experiences in clinical research. Patient concerns about the clinical research process have been cited as barriers to research participation in a number of previous clinical trials,^{18,22–24} suggesting a level of skepticism about the research process. As medical patients are perceived as a vulnerable group,²⁵ media coverage of the lack of transparency that occasionally occurs in research, coupled with publicized

events such as the Tuskegee Syphilis Experiment,²⁶ may foster these concerns. It has been shown that a relationship of trust between the clinician and participant is crucial to recruitment.^{27,28} Furthermore, lack of knowledge and understanding of the research process was found to be an important barrier to women's participation in clinical cancer research.²² Whether this is true for cardiovascular trials has not been well documented. Conversely, it has been shown that giving potential study participants information about the explicit purpose of clinical studies helps to improve enrolment of women and minorities in HIV research²⁹ and in studies of lung cancer patients.³⁰ Our experience suggests that if women are informed not only about the importance of clinical trials but also about the clinical research process, they may eventually have greater confidence and trust in the clinical research setting and thus enrolment may improve.

There is little available information on the different recruitment rates in men and women, because most studies do not separate recruitment information by gender.^{15,16,19,23,27} However, a number of reports do suggest that women are more difficult to recruit than men. While recruiting elderly study participants for a diabetes clinical trial in 1995, Anderson and colleagues¹⁹ found that women tended to decline study participation more often than men. Recruitment for participants in the New Mexico Elder Health Survey also showed that women were less likely to participate.³¹ Gitanjali et al.³² and Petty et al.¹⁸ also reported that women were less willing to participate in clinical research in Asian and European studies, respectively.

Table 3. Women's reported motivations for and barriers to participation in cardiovascular clinical trials

	(%)*
Interested in clinical trial participation (n = 125)	
Personal health benefits	82.2
Interested in research	44.1
Benefit society	29.1
Not interested in clinical trial participation (n = 145)	
Too many health problems or too ill	24.8
Transportation problems	17.9
Already taking too many medications	15.2
Concerned about negative health effects	13.1
No time (5.5% care-giving, 2.8% social activities, 0.7% other)	9.0
Family not wanting woman to participate	4.1
Only 50% chance of taking the drug	2.1
Other (perceive low risk, don't like /scared of experiment, too overwhelming, too many doctor's visits, previous bad experience with another study)	4.1
No specific reason given	18.6

*These add up to more than 100%, as multiple reasons were accepted.

Gender differences in self-report motivations for and barriers to participation in clinical research are also not well documented. However, Stone et al.²⁴ reported similar barriers to AIDS research participation by both genders, specifically those involving lack of interest and fear of experimentation. Five percent of our surveyed population reported time constraints arising from caregiving as a barrier to participation, and another 4% reported that they felt their family members would not agree with their participating in research. One previous study has reported that women, and not men, tended to report time constraints arising from caregiving as a barrier to participation.²⁰ Determining whether these gender-specific barriers are widespread, and whether providing child or elder care at the study centre would improve enrolment of women in clinical research trials has yet to be studied.

The under-representation of women in clinical research in general¹ and in cardiovascular research specifically²⁻⁵ is well documented. Although efforts towards increasing the number of women and minorities in clinical research have been made, the proportions of these groups enrolled in clinical research are still well below their representation in the overall population of cardiovascular patients, and no sizeable change has been seen over the last two decades. As additional information is gathered on barriers to participation in medical research, we gain a broader perspective on the issues as well as insight into how to solve them.

CONCLUSION

Because of a history of exclusion from clinical trials, women may need reassurance of their value in the clinical research setting. The apprehension of clinical trials shown by our sample of women indicates that as clinical researchers, we still have a long way to go in terms of education and development of trust. We also need to provide practical solutions, such as transportation to study centres or follow-up at local sites in the community, to overcome participation barriers. Otherwise, the high screening-to-randomization ratio will continue to pose a significant obstacle to recruiting adequate numbers of women in clinical trials.

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