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Recruiting Postmenopausal Women into Randomized Controlled Trials: A Patient Perspective

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Abstract

Purpose: To identify barriers to, and motivations for, recruitment and retention in osteoporosis related clinical trials among postmenopausal women.

Methods: We explored the self reported reasons for and against participation in clinical trials among women who expressed an interest in participating in the Nitrates and Bone Turnover (NABT) study: an ongoing randomized controlled trial based at an urban tertiary care centre (Women's College Hospital, University of Toronto). The study was designed to compare the effects of different doses and formulations of nitrates on markers of bone turnover among postmenopausal women not diagnosed and/or receiving treatment for osteoporosis. We administered a standardized interviewer questionnaire to 53 women to determine their reasons for participation in the NABT trial. To determine reasons for non-participation, we administered a questionnaire to 9 women and reviewed data collected at the time of initial assessment in 56 women who were not interested in participating in the trial. We conducted qualitative analyses using thematic coding of these responses.

Results: The most common reasons for participation were: altruism (26.4%) and potential personal benefits (22.6%). The two most common reasons for non-participation included fear associated with taking medication (23.1%) and lack of time (16.9%).

Conclusions: Postmenopausal women participate in clinical trials to help others and potentially themselves. Barriers to participation in trials may include the intervention being evaluated and time required to participate in the trial. Researchers should consider these motivations and barriers when recruiting postmenopausal women for RCTs.

Keywords: Recruitment; Randomized controlled trial; Postmenopausal women; Osteoporosis

Introduction

About one in four postmenopausal women have osteoporosis [1] and fractures from osteoporosis cause significant morbidity and mortality. Ongoing treatment trials among women at risk for osteoporosis are critical to decrease the sickness and death associated with this condition. One factor that has limited progress in the area of osteoporosis clinical research is the difficulty recruiting postmenopausal women for participation in clinical trials. Generally speaking, there are few studies that have investigated reasons for non-participation in Randomized Controlled Trials (RCTs) among patient populations and an even fewer number that have examined barriers to recruitment among women in particular; women may have different attitudes towards participation in RCTs than men [2]. As well, most studies that report on barriers to recruitment are based on the researchers' perspectives rather than the subjects' opinions.

Our study focuses specifically on self-reported barriers to and motivations for participation in an osteoporosis prevention trial (The Nitrates and Bone Turnover Study; NABT) among postmenopausal women, aims to address current knowledge gaps.

Materials and Methods

Study participants

We utilized data obtained from women who contacted our study coordinator to inquire about the NABT trial; an ongoing randomized controlled trial that compares five formulations of nitrates for their effects on bone turnover markers and headache. The NABT trial consists of an 18 day run in phase during which women are assigned to five different nitrate formulations each for two days with a two-day washout between each formulation. Women who are able to tolerate all five formulations and more specifically do not develop severe headaches are entered into a three month treatment phase. Participants are provided a $10.00 reimbursement per study visit to cover transportation costs. Women are eligible to participate in the NABT trial if they are 50 years of age or older, and at least three years postmenopausal. Exclusion criteria include: self reported history of osteoporosis (by Bone Mineral Density (BMD) testing), a history of hip, wrist or vertebral fracture; current use of treatments that may influence bone metabolism; a history of myocardial infarction, angina, valvular or congenital heart disease; migraine headaches; hypersensitivity to nitroglycerin, or allergies to the adhesive used in nitroglycerin patches. All women must give informed consent and be willing to participate in the study.

Recruitment strategies

Recruitment for the NABT study began in July 2011 and is ongoing; we plan to recruit 420 subjects for the run-in phase. Based on prior experience [3] we anticipate that 50% of these women will continue on to the treatment phase. We will continue enrollment until

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we have randomized 210 women, about 35 women per group. As we did for our previous successful trials, we have and will continue to advertise in local newspapers, on local radio and television stations, and place posters in hospitals, doctors' offices, osteoporosis clinics, community centers, fitness centers, coffee shops (areas that are familiar to postmenopausal women) throughout Toronto. We will also mail study information letters to women who have had BMD tests at hospital based osteoporosis clinics. Eligibility is assessed by telephone questionnaire. Subjects who meet eligibility criteria and are interested in participating after the telephone interview will come to the study centre where they will receive written information about the study. We will also capture data on reasons for non-participation and ineligibility.

Study design

The primary purpose of our current study was to determine barriers to and motivation for participation in the NABT trial. Barriers and motivations to participation were identified through review of data collected as part of the initial telephone questionnaire or, if reasons for participation or non-participation were not captured during the initial questionnaire, by administering standardized questionnaires (Appendix 1 and Appendix 2; discussed below). We also evaluated our recruitment strategies by collecting information about how women heard about the trial. At the time of the current publication 260 women had contacted the study coordinator to find out more about the NABT trial. We classified subjects based on their interest for and against participation (Figure 1): 82 women gave consent to proceed with the screening questionnaire, were eligible for study entry and gave consent to enter the study (Group 1), 27 women gave consent to proceed with the screening questionnaire, were eligible for study entry, and decided against study participation (Group 2), 57 women declined the eligibility screening questionnaire (Group 3), and 94 women were ineligible (Group 4).

We utilized two standardized interviewer questionnaires in our study. The questionnaires were developed after an extensive literature review with a focus on previously published literature that reported on the use and development of interviewer administered questionnaires as a means to understanding reasons for participation or non-participation in clinical trials. One trial, the *Trial of Management of Borderline and Other Low-grade Abnormal smears (TOMBOLA),* used questionnaires to explore reasons for participation and non-participation [2]. We used similar questions, modifying the wording and components that were unique to either the TOMBOLA or the NABT trials. We also replaced the structured response options that TOMBOLA created for each of the questions to open-ended questions with the aim of allowing the women to truly express their perspective by emphasizing the points that they felt most strongly about. The questionnaire was pilot tested in five women to assess: clarity of questions and to ensure that we were capturing appropriate responses. Questionnaires were reviewed for missing data, poor completion and responses to open-ended questions. The Nitrates and Bone Turnover (NABT) trial as well as the content and administration of the questionnaires were approved by the Women's College Hospital Research Ethics Board.

We utilized Questionnaire 1 (Appendix 1) for women who had agreed to participate in the NABT trial, including those who were currently participating women who had entered the study but decided to drop out at the run-in or randomization phase, and women who had completed the trial. We administered Questionnaire 1 to 53 of the 82 women in Group 1 and were unable to contact the remaining 29 women. Questionnaire 2 (Appendix 2) was administered to women who declined participation in the NABT trial. Of the 27 women in Group 2, we administered the questionnaire to 4 women, 14 provided a reason at the time of declining to participate and we were unable to contact 9 women. Of the 57 women in Group 3, we administered Questionnaire 2 to 5 women, we obtained data on reasons for non-

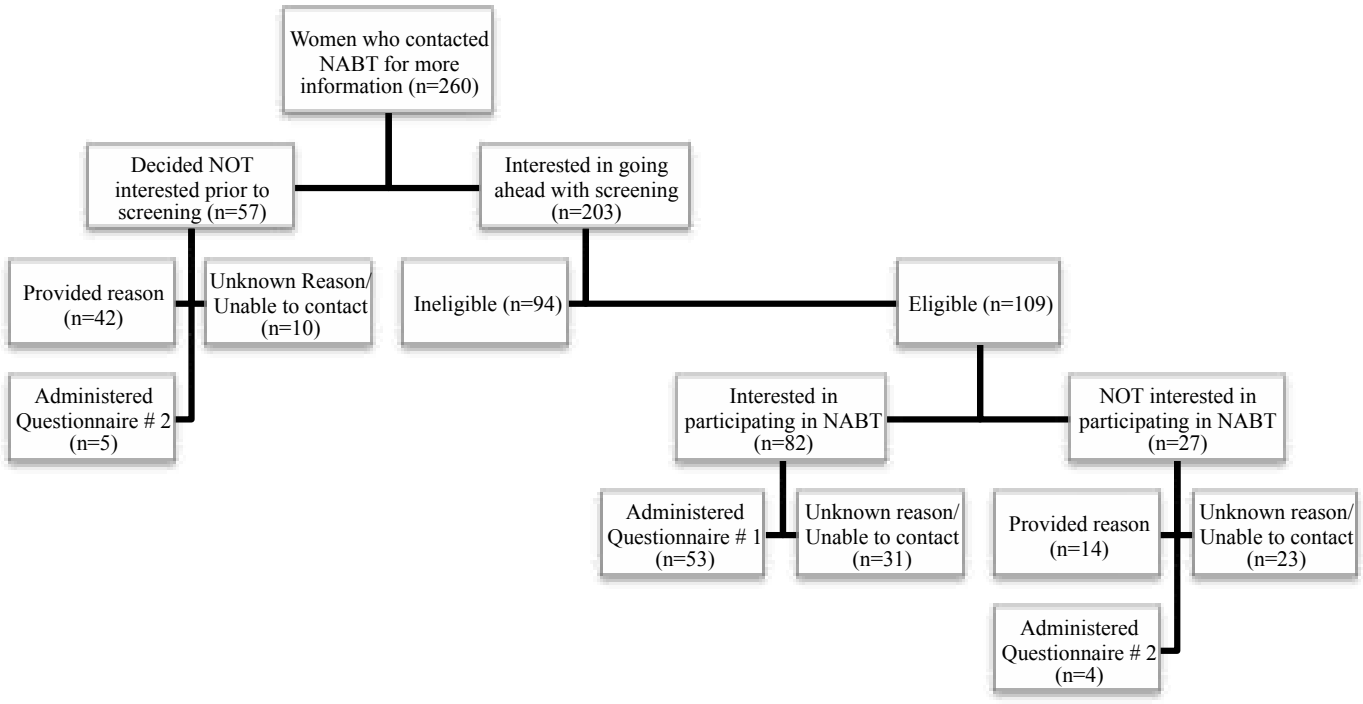

Figure 1:

participation for 42 of the women at the time that they decided not to participate, and were unable to contact the remaining 10 women. Questionnaires were administered by telephone from May to August 2012.

We transformed the qualitative data from the questionnaires into categories for statistical analyses. We first identified common themes that arose from the open-ended questions. For Questionnaire 1, responses to reasons for interest in participation could be grouped into the following themes: altruism, potential personal benefits, noticing a poster or direct contact by Women's College Hospital, curiosity to learn, participation in previous trial, physician's recommendation and interest in research. Any response that did not fit with these themes was categorized as "other". For Questionnaire 2 reasons for disinterest in participation were grouped into: fear and concern associated with taking medication, lack of time, wanting greater monetary compensation, travel/commute constraints, personal health issues, concern about headache side-effect, moving out of the country, and physician recommending non-participation. Reasons not captured in these groupings were categorized as "other". Multiple responses were welcomed, however, only the top reason was used for categorizing the results. In the case of close-ended questions (those that had either yes or no responses) we counted the number of yes and no answers. We also recorded their individual reasoning, or the 'why', behind their response. Questionnaire responses were organized within Excel workbooks using thematic coding based on frequencies of themes conveyed in interviews. For example, a response such as "I wanted to give back and help out" was given a code of "1" to symbolize altruism. We analyzed the data by counting the number of responses for each theme and calculating percentages relative to the total number of respondents across categories.

In addition to determining the barriers to and motivations for participation in the NABT trial, we also evaluated our recruitment strategies. Specifically, we asked all women who contacted the study centre how they had found out about our study. Responses were categorized as: posters in the community, posters in a hospital, participation in previous trial, direct mailing, and contacting research institute on own initiative due to personal interest in osteoporosis, a friend's recommendation, or other. We then calculated the frequency for each response.

Results

The mean age of participants in this study was 65.2 ± 11.8 years. About 25% of the women reported that the number one reason for participating in a trial was altruism and an additional one-fourth cited personal gain as a reason. Another 15% of the women stated that their reason for participation was because they were persuaded by effective recruitment methods (they noticed a poster, received direct mailing, etc.). The top motivations for participation are listed in Table 1.

We found that 100% (n=53) of the postmenopausal women who were participants would encourage others to participate in similar research studies, the top reason participants believe other women do not participate in research studies is because they simply may not know of the opportunity (n=17 of 53, 32.1%), and while 30% of women (n=16) believe that they face specific barriers as women, in being able to participate in research studies.

Among non-participants, approximately 25% of the women said the number one reason for not participating in the trial was fear and concern associated with taking medication. Another 20% said that they could not participate due to a lack of time. Of note, about 12% of women did not participate due to inadequate monetary compensations. Self-reported reasons for lack of interest in participation are reported in Table 2. With regards to recruitment strategies, 147 (56.0%) of the 260 women who contacted the study centre provided information about how and where they heard about the study. About one third of the women (n=45 or 30.6%) saw a poster in the community (coffee shops, clothing stores, fitness clubs and community centers) while ¼ of the 260 women contacted us because they had participated in our previous trial. These women contacted us in response to a mailing or phone call inviting them to participate in the new trial. Twenty-seven (18.4%) women saw the poster at a hospital and another 27 (18.4%) had received an invitation to participate in the mail. Seven women (4.8%) took the initiative to contact the research institute themselves because of a personal interest in osteoporosis. Two (1.4%) women said a friend who participated in the study recommended it, and 5 (3.4%) of the women had other reasons.

Discussion

About 1/4 of women who participated in our study did so for altruistic reasons. Our finding is consistent with previous studies and emphasizes the importance of highlighting the societal and greater good of research as a strategy to enhance recruitment [4,5]. About 1/5 of women who participated in our clinical trial did so for the potential personal health benefits: specifically, women enrolled in our study with the hope that participation would improve their bone health. This is not surprising- previous work has demonstrated that a postmenopausal women's perceived risk for developing the disease being studied is the most important factor in their decision to participate in research [6].

About 1/3 of women we questioned noted that women had specific barriers to recruitment into clinical trials compared with men; namely balancing work and family commitments. Of note, in our study some participants commented that the barrier of work family balance lessened after retirement. For example, one woman stated, "younger women may have commitments such as child care, but not at my age". Similarly, another woman explained, "now that I am retired I can

Reason for interest	Number (%)
Altruism	14 (26.4)
Potential personal benefits	12 (22.6)
Noticed poster or was contacted by Women's College Hospital	8 (15.1)
Curiosity to learn	6 (11.3)
Participation in previous trial	6 (11.3)
Physician's recommendation	3 (5.7)
Interest in research	2 (3.8)
Other	2 (3.8)
TOTAL	53 (100)

Table 1: Reasons for interest in participation.

Reason for disinterest	Number (%)
Fear and concern associated with taking medication	15 (23.1)
Lack of time	11 (16.9)
Want greater monetary compensation	8 (12.3)
Travel/commute	7 (10.8)
Personal health issues	6 (9.2)
Concern about headache side-effect	4 (6.2)
Moving out of country	4 (6.2)
Physician suggested against participation	3 (4.6)
Other	7 (10.8)
TOTAL	65 (100)

Table 2: Reasons for disinterest in participation.

get downtown (to the Woman's College Hospital Research Institute) easily, with lots of time".

It is important to note that almost half of the women screened for NABT (47.1%) did not satisfy the eligibility criteria. Failure to recruit subjects is one of the main reasons for not completing trials and strict eligibility criteria, while increasing internal validity, may play a role in recruitment failures [7-9]. Of women who were eligible and did not participate in our study the number one reason given was due to fear and concern associated with taking medication. While some women may have been uncomfortable taking any medication, another common issue that limits recruitment into clinical trials with a medical intervention is the concept by potential subjects that they are already taking too many medications and/or are too ill to participate in a trial [5]. As co-morbidity increases with age this barrier to recruitment may become more prevalent among elderly men and women [10]. Lack of time was a significant issue that was raised by 17.0% of the women who declined participation in NABT. Methods to overcome this barrier might include monetary compensation for time, electronic assessments (using home computers), and mail out kits for sample collection. Only a small number of women (4.6%) declined or agreed (5.7%) to participate in our trial based on the recommendation from their family physician. Our finding is different from what has been previously reported but the previous study utilized theoretical scenarios, which may elicit different responses [6]. In contrast to previous studies, [5,7] we did not find transportation was a major barrier to recruitment perhaps because we provided modest compensations (10 dollars per visit) for transportation (parking or public transit). With regards to recruitment we found that the most effective method of advertising the study was to poster in the community. Of the women who contacted us, 30.6% obtained our information through an advertisement at a fitness club, community center, coffee shop or another similar location throughout the city. Our finding differs from previous data that has reported that the best recruitment strategy is personalized mailings inviting participation [5].

Our study had some limitations. We were unable to collect detailed data on non participants and thus could not examine factors (such as age) that might influence the willingness to participate in a clinical trial. We were unable to contact all of the potential participants and it is possible that those we could not contact had different reasons for not participating. In some cases there was a long lag time between subjects agreeing to participate in the NABT and administration of our questionnaire, which may have resulted in recall bias concerning details of rationale for participation and non-participation. Indeed, some study subjects we contacted did express difficulty in remembering details regarding recruitment.

In conclusion, we have found that strategies to enhance recruitment of postmenopausal women into clinical trials include promoting altruism and the potential personal benefits. Barriers to recruitment include fear and concern associated with taking medication and lack of time, both of which may be perpetuated by age and gender. Recruitment strategies that emphasis these benefits and clearly address these particular barriers may be more successful in achieving stronger participation of postmenopausal women in future clinical trails.

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