Published in final edited form as:

Clin Trials. 2010 ; 7(4): 411–417. doi:10.1177/1740774510373491.

Successful subject recruitment for a prostate cancer behavioral intervention trial

Sue P Heiney^a, Swann Arp Adams^b, Bettina F Drake^c, Lisa H Bryant^d, Lynne Bridges^e, and James R Hebert^f

^a College of Nursing, University of South Carolina, Columbia, SC, USA

^b College of Nursing and the Department of Epidemiology and Biostatistics, The Cancer Prevention and Control Program, University of South Carolina, Columbia, SC, USA

^c Department of Surgery, Washington University School of Medicine, St. Louis, MO, USA

^d Neuropsychiatry and Pediatrics, University of South Carolina School of Medicine, Columbia, SC, USA

^e The Caring House, South Carolina Cancer Center, Columbia, SC, USA

^f South Carolina Cancer Prevention and Control Program, Department of Epidemiology and Biostatistics, University of South Carolina, Columbia, SC, USA

Abstract

Background—Inadequate participant recruitment, which may lead to unrepresentative study samples that threaten a study's validity, is often a major challenge in the conduct of research studies.

Purpose—The purpose of this article is to describe the development and implementation of a recruitment plan and evaluate the different recruitment strategies for a prostate cancer behavioral intervention trial.

Methods—Our recruitment plan was based on a framework (The Heiney–Adams Recruitment Model) that we developed, which combines relationship building and social marketing. We evaluated the success of our model using several different recruitment sources including: mailed letters, physician referral, and self-referral.

Results—Recruitment rates ranged from 67% for a support services department mailing to 100% for physician referral. While our original list of contacted patients was comprised of only 13% African American (AA) men, 22% of our recruited participants were AA.

Limitations—One of the strongest barriers to recruitment was strict patient eligibility. Another significant barrier was the lack of electronic records systems to allow for the identification of large numbers of potential participants.

Conclusions—In conclusion, our model incorporating social marketing and relationship building was quite successful in recruiting for a prostate cancer behavioral study, particularly AA participants. In developing strategies, future researchers should attend to issues of staffing, financial resources, physician support, and eligibility criteria in the light of study accrual.

Background

Prostate cancer (PrCa) is the most common cancer diagnosed among men and the second most common cause of cancer death [1]. South Carolina (SC) has high PrCA incidence and the highest mortality rate of the disease in the world [2]. Further, SC has a relatively high prevalence of relapse after treatment in PrCa patients. Given incidence and prevalence data of SC, we expected to have a large pool of eligible patients for a study in which the primary eligibility criterion was a rise in prostate specific antigen (PSA) after definitive treatment. Although our expectations were not realized, our percentage of patients enrolled out of all eligible patients was much higher than other cancer control studies [3,4]. Reported recruitment for national clinical trials is less than 5% [5] and for behavioral/cancer control studies ranges from 14% to 41% [3]. Of the latter group, most reported recruitment rates of 30% or less. We [6] and others have described the difficulties in recruitment and suggested strategies to increase enrollment [7]. Therefore, researchers need a model to be utilized in developing recruitment plans that would provide direction for the most effective strategies.

Purpose

The purpose of this article is twofold: (1) to describe the development of a conceptual framework for recruitment and (2) to evaluate the application of this framework within the context of a cancer behavioral intervention.

Methods

Study background and summary

In a preliminary study, we found that an intensive dietary intervention coupled with mindfulness-based stress reduction was associated with a reduction in the slope of the PSA rise among men who had undergone definitive treatment for PrCa [8]. Given the results from our pilot study, we conducted a randomized trial, A Diet, Physical Activity, and Meditation Intervention in Men with Rising PSA, which was given the acronym EASE (Eating, Activity, and Stress Education) and approved by the Institutional Review Board (IRB) from the Palmetto Health Hospital System, the University of South Carolina, and the Department of Defense. All participants signed a consent form and a privacy authorization, a document that outlines the use and disclosure of personal health information. The EASE Study tested the hypothesis that PSA would be significantly decreased through the use of a vegetable-based diet, physical activity and mindfulness-based stress reduction. Rising PSA levels in a man who has survived PrCa may indicate that the cancer has returned. Including only men who have rising levels will allow us to determine whether the intervention group experiences a decrease in PSA levels compared to the control group. Results from the study currently are being analyzed. The recruitment goal was a total of 66 men with rising PSA levels after achieving a post-treatment nadir. Each man was enrolled along with a partner of his choice. Half of these pairs were randomized to the intervention and half to usual care. The intervention consisted of 2.5 h weekly classes incorporating cooking, meditation, and exercise, which lasted for 3 months. These were followed by 3 monthly booster sessions.

Framework

Our recruitment plan was based on a framework that we developed, which combines relationship building [9,10] and social marketing [11] (Figure 1). For clarity, we have separated these two approaches. However, overlap in recruitment activities occurs, as these are not sequential, especially as the project progresses over time. Relationship building and social marketing have reciprocal influences. Relationship building makes social marketing messages

more credible and the reverse is also true. Thus, both are needed to fully promote an awareness of the study.

Relationship building, based on person centered counseling theory, is the creation of a trusting bond between the research staff and the patient/family [9,10,12]. The relationship is similar to but *not* a therapeutic relationship. The patient and staff connect and develop rapport so that the patient has a sense of affiliation with the research project. The main premises of the relationship building approach are as follows: (1) the patient and staff are equals; (2) staff are empathetic to the patient's situation; (3) staff are appreciative of the patient's thoughts and feelings; and (4) staff are genuine and sincere in interactions. The goal is to create a safe and tolerant discussion in which the patient feels free to ask questions, request more information and decline or accept study enrollment [10]. Relationship building, especially in the African American (AA) population increases trust, identifies benefits, and creates a partnership between the patient and study staff [13].

Social marketing in research is the use of traditional marketing strategies to improve health [14] or recruitment for research studies [15]. For example, social marketing has been used to deliver messages about tobacco use and cancer, problems from drinking and driving and safe sex practices. A social marketing program consists of strategy development and implementation. These activities include identification of target groups and market segments, assessment of media availability and production of materials [11]. Feedback from the community and attention to cultural issues are essential in designing social marketing strategies.

Based on a previous work on recruitment obstacles and our limited resources [6], we planned to use primarily relationship building recruitment strategies to reach eligible patients. We expected that the majority of participants for this study would be drawn from our hospital system's PrCa patient conference. We planned that urologists participating in tumor board meetings would refer patients directly to the study or respect a waiver from the local IRB, which allowed direct release of names of eligible patients.

We developed recruitment materials to fit this relationship building strategy. These included an introductory letter to the potential participant from the study investigator, a cover letter from the patient's physician endorsing the project and a brochure written in lay language using colors that were expected to appeal to men. Colors were chosen by our art director, who used knowledge from marketing research as well as many years of experience. This brochure was intended to be given directly to patients. We emphasized the personal availability of the study staff members using a special e-mail address (EASE@...) and a study voice mail via a dedicated cell phone.

Each potential participant (either self-identified or referred) was contacted by mail using a personalized letter and brochure. The decision to contact patients initially by mail rather than in-person or by phone was based on our experience in which cold calls (i.e., without any information sent previously) are unproductive and do not support relationship building. After the patient had time to review the materials, the recruiter called the patient to assess interest. The script for this and all subsequent calls emphasized focusing on the patient and building rapport. Whenever the patient agreed to enroll in the study, the recruiter sent the patient a thank you note to promote retention.

Social marketing strategy development and implementation

As part of our social marketing strategy, we produced a poster for placement in physician offices, treatment facilities, and other appropriate settings. The poster included a postage paid, self-addressed response card. We created a web site for patients. We used hospital publications

that were available to circulate information. We worked with multiple cancer agencies and grassroots organizations to disseminate information about the study including our hospital's community cancer initiative, the South Carolina Cancer Alliance, and various cancer educational programs. One of the authors (JRH) made presentations to both PrCa support groups in the community. Both the university and hospital sent out public service announcements. The study was featured in several news articles. A researcher colleague mailed information about the study to her participants in a hereditary cancer study. We mailed a letter along with our patient brochure to all urologists and family practice physicians throughout the state informing them of the study and encouraging referral of patients to the study.

The most expansive social marketing strategy (in terms of individuals contacted) was to send direct mail letters to PrCa patients identified from multiple sources, including a hospital psychosocial oncology database, a local oncology practice, and two urology practices.

The second largest strategy to reach individuals occurred as a piggyback to The Prostate Cancer Follow-Back Study (PCFBS), a cross-sectional assessment designed to assess treatment decisions regarding PrCa and factors that may influence those decisions through a short mail questionnaire. This strategy was possible through protocols outlined by the Cancer Control Advisory Committee, South Carolina Department of Health and Environmental Control. For the PCFBS, PrCa cases in an eight county region of South Carolina were identified through the SC Central Cancer Registry for the PCFBS. All these 1866 PrCa cases were sent the PCFBS survey, which included a single question about willingness to be contacted for participation in future research studies. The PCFBS received responses from 465 of these cases (response rate = $465/1866 = 25\%$), indicating permission for future contact.

Statistical methods/evaluation of recruitment strategies

Evaluation includes measuring the success of strategies and describing the population. Privacy policies prevented us from obtaining information such as social security number or birth date of patients on mailing lists. Therefore, we were unable to eliminate overlap in our appeals to patients. Enrollment into the EASE study occurred over a 2-year period. Descriptive statistics were calculated on enrolled, eligible, ineligible, and declining patients. We calculated recruitment rates by dividing the total number of recruited participants for each source by the pool of patients from that source.

Results

Profile of patients referred

Any patient who was referred to the study or referred himself was entered into a database for tracking recruitment. Where possible we gathered demographic data on patients entered into the tracking database. Of those patients ($n = 440$), 354 (80%) were white; 56 (13%) were AA, 2 (< 1%) were Hispanic, 1 (< 1%) was Native American, and in the case of 27 people (6%), the race was not known.

Not eligible—Of the 440 patients, 262 (59%) were not eligible. Numbers and reasons for ineligibility were as follows: 4 (2%) current or past malignancy; 46 (18%) were on hormone therapy; 189 (73%) had no PSA rise; 5 (2%) had treatment that excluded them from the study; 9 (3%) had another major comorbidity; 1 (<1%) had weight loss greater than 5 pounds; 1 (<1%) had cognitive impairment; 1 (<1%) was taking thyroid, steroids, antibiotics, or diuretics, 4 (1%) miscellaneous, and 1 (<1%) had post-traumatic stress disorder. Of the ineligible patients ($n = 262$), 219 (84%) were white; 23 (9%) were AA, 1 (< 1%) was Hispanic, and in the case of 19 people (7%), the race was not known. Of the original pool of contacts, the ineligibility rate was higher in white patients ($219/354 = 62\%$) than in AA ($23/56 = 41\%$). For AA patients,

the major cause of ineligibility was no PSA rise (87%). In comparison, only 71% of ineligible white men had no PSA rise.

Decliners—Of the 440 patients in the pool, 71 (16%) patients were unwilling to participate in the study. Reasons given were as follows: 13 (18%) too far to travel, 5 (9%) too ill, 14 (20%) diet too strict, 21 (28%) were not interested after hearing the study requirements; 5 (7%) had time conflicts, 2 (3%) had personal reasons, and 11 (15%) did not provide a reason for not participating. The race of the patients declining to participate was 64 (85%) white, 8 (11%) AA, and 3 (4%) race was not known. Rates of declining were 18% for white patients and 14% for AA.

Profile of patients enrolled

The demographic characteristics of the study population ($n = 59$) can be found in Table 1. Nearly a quarter of participants (22%) were AA. The majority of the patients had some college or completed college, were married or living with a partner, were current or former smokers, and were retired or unemployed.

Recruitment evaluation

An examination of our tracking database revealed that patients originated from four sources: PCFBS, direct mailings (urology clinic, oncology clinic, and support services), physician referral, and self-referral. Tables 2 and 3 summarize the results of the recruitment model which incorporates social marketing with relationship building. Recruitment proportions were calculated for each source from the total number we attempted to contact or sent a letter; the total number responding to our solicitation (either letter or phone); and the total number of eligible individuals.

Prostate cancer follow-back study—Of the 465 patients from the PCFBS who indicated they could be contacted for other cancer studies, a subset ($n = 206$) were contacted about their interest and eligibility in the EASE study. We recruited 84.6% (11/13) of the eligible patients (Table 2).

Physician referral—Through professional networking, we encouraged physicians to refer patients directly to the study. Referrals originated from urologists and from oncologists. We received 24 referrals from physicians. Our recruitment rate was 100% of eligible patients ($n=13$), which was expected, given the inherent endorsement by the physician (Table 2).

Direct mail—Of the 2500 patients from our direct mail pool (two urology clinics, oncology clinics, and support services department), 170 called or e-mailed to express interest in the study. We recruited between 67% (2/3 for support services department) and 79% (15/19 for oncology clinics) of those eligible (Table 3).

Self-referral—We had no way of measuring the total number of individuals exposed to our social marketing strategies such as posters and newspaper articles. However, we assume that the sum total of our social marketing strategies resulted in 40 self-referrals, from which we recruited 10 patients (recruitment rate = $10/12 = 83.3\%$) (Table 3).

Using these four approaches within the context of our conceptual framework, our goal was to recruit 66 patients. Consequently, we were able to recruit a total of 59, yielding an overall recruitment rate of 83% of eligible individuals.

Limitations

It should be noted that our framework and evaluation were applied to a behavioral intervention trial, which was quite different from typical private industry-sponsored clinical trials or cooperative agreement treatment trials. The principal investigator was not a physician with a large pool of patients from which we could recruit. Hence, all participants were derived from 'indirect' sources. Nevertheless, there are applications of our framework in the more traditional clinical trial environment. In this setting, the relationship building component of the framework would be particularly important to ensure high enrollment and retention.

Conclusions

Our model, which combines social marketing and relationship building, was successfully applied to recruit PrCa patients to a behavioral intervention trial. Successful accrual ranged from 67% to 100% of eligible patients, depending upon the source from which identified. We believe that inability to reach our recruitment goal was not due to our recruitment plan. Factors that inhibited recruitment included restrictive inclusion and exclusion criteria (e.g., 59% of patients contacted were not eligible to participate), our inability to contact target populations directly due to Health Insurance Portability and Accountability Act (HIPAA) regulations, competing industry-sponsored trials, and high mortality from both co-morbid conditions in the target population and PrCa.

Our results demonstrate that while the time and resources of direct mailing are minimal, recruitment rates, which we defined as the ratio of number recruited to the total pool *contacted* ranged from 7% to 15%. In comparison, physician and self-referral required greater staff and financial resources, yet yielded higher recruitment rates (24% to 54% of the *contacted* pool). Additional financial resources would have helped to expand our social marketing campaign (more brochures, mailings, multimedia ads, and public figure endorsement), which would have enhanced our recruitment plan. Based upon our experiences, we estimate that a comprehensive social marketing campaign for recruitment would cost between \$12,000 and \$20,000, depending on the scope of the proposed work. For this particular study, we only had approximately \$6000 available for our campaign.

The number of AA patients we were able to recruit (22% of all enrollees) was very good when comparing the population of our catchment area, which is 30% AA [16], with that in other studies [17]. Anecdotal feedback from our recruiter indicated that AA men and partners responded well to the relationship building strategies that we used.

Recruitment obstacles

It is critical to have the physician's support in behavioral intervention in studies, because physicians have such a great influence over patient decisions. The majority of physician referrals were from oncologists. Physicians were not comfortable with our identification of their patients through alternative sources such as the local tumor registry system.

Unlike health promotion or early detection studies, behavioral intervention trials may encounter many obstacles to direct communication with the target population of eligible patients. One such obstacle in our situation was the lack of electronic systems in the physicians' offices that would have allowed identification of eligible patients on a mass scale. For example, while we could obtain a listing from a local oncology office of all patients with an ICD-9 code for PrCa, we had no way of knowing whether these patients were alive or met PSA eligibility requirements. Thus, the letters sent to potential patient participants had to be clear about the eligibility (rising PSA); at the same time we had to reassure the patient that the letter did not mean that his cancer had relapsed or that he had experienced a rise in PSA. Even with our best

efforts, patients were confused by the content of the letter and time was consumed in making telephone calls to reassure patients.

In conclusion, a model and plan for recruitment are essential requirements for the evaluation of strategies. Our model incorporating social marketing and relationship building was quite successful in recruiting participants for a behavioral intervention study for PrCa. Future researchers are advised to take into account issues of staffing to ensure selection of personable recruiters, adequacy of financial resources, elicitation of physician support, and realistic eligibility criteria, when planning study accrual. In our case, we had limited resources and strict eligibility criteria; thus we had to utilize general social marketing strategies and rely heavily upon relationship building between the recruiter and eligible candidates to encourage participation. Application of the principles of relationship building and social marketing ensures not only successful recruitment, but also benefits the study validity by minimizing selection bias due to refusals to participate by eligible patients.

Acknowledgments

The study (PC020466 A Diet, Physical Activity and Meditation Intervention in Men with Rising Prostate-Specific Antigen (PSA) is partially funded by the Department of Defense US Army Medical Research and Materiel Command (USAMRMC) Congressionally Directed Medical Research Programs (CDMRP), and 2002 Prostate Cancer Research Program (PCRP), grant DAMD17-03-1-0139.

References

1. Cancer Facts and Figures. [accessed 1 August 2007]. Available at: www.cancer.org
2. Drake BF, Keane TE, Mosley CM, et al. Prostate cancer disparities in South Carolina: early detection, special programs, and descriptive epidemiology. *J S C Med Assoc* 2006;102:241–49. [PubMed: 17319238]
3. Motzer S, Moseley J, Lewis F. Recruitment and retention of families in clinical trials with longitudinal designs. *West J Nurs Res* 1997;19:314–33. [PubMed: 9170990]
4. Carlson L, Specia M, Patel K, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of Cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. *Psychoneuroendocrinology* 2004;29:448–74. [PubMed: 14749092]
5. Doctors, patients face different barriers to clinical trials. [accessed 18 January 2008]. Available at: <http://www.cancer.gov/clinicaltrials/developments/doctors-barriers0401>
6. Heiney SP, Adams SA, Cunningham JE, et al. Subject recruitment for cancer control studies in an adverse environment. *Cancer Nurs* 2006;29:291–99. [PubMed: 16871096]
7. Berger AM, Neumark DE, Chamberlain J. Enhancing recruitment and retention in randomized clinical trials of cancer symptom management. *Oncol Nurs Forum* 2007;34:E17–E22. [PubMed: 17573292]
8. Saxe GA, Hebert JR, Carmody JF, et al. Can diet in conjunction with stress reduction affect the rate of increase in prostate specific antigen after biochemical recurrence of prostate cancer? *J Urol* 2001;166:2202–07. [PubMed: 11696736]
9. Corey, G. Theory and practice of counseling and psychotherapy. 6. Brooks-Cole/Wadsworth Publishing; Pacific Grove, CA: 2001.
10. Overholser J. The central role of the therapeutic alliance: a simulated interview with Carl Rogers. *J Contemp Psychother* 2007;37:71–8.
11. Manoff, RK. Social Marketing. Praeger Publishers; New York: 1985.
12. Cross, J.; Cross, P. Knowing yourself inside out. Crystal Publications; Berkeley, CA: 1998. p. 1-300.
13. Watkins-Bruner D, Linton S, Konski A, et al. Successful strategies for African American recruitment to prostate cancer research. *Int J Cancer Prev* 2005;1:295–306.
14. Watkins-Bruner D, Konski A, Feigenberg S, et al. Benchmarking African American recruitment to cancer control trials with social marketing and direct response radio. *Oncol Nurs Forum* 2005;32:180.

15. Keyzer J, Melinkow J, Kuppermann M, et al. Recruitment strategies for minority participation: challenges and cost lessons from the power interview. *Ethn Dis* 2005;15:395–406. [PubMed: 16108298]
16. Heiney SP, Adams SA, Cunningham JE, et al. Subject recruitment for cancer control studies in an adverse environment. *Cancer Nurs* 2006;29:291–99. [PubMed: 16871096]
17. Coward DD. Facilitation of self-transcendence in a breast cancer support group: II. *Oncol Nurs Forum* 2003;30:291–300. [PubMed: 12692663]
18. Gordon R, McDermott L, Stead M, Angus K. The effectiveness of social marketing interventions for health improvement: what's the evidence? *Public Health* 2006;120:1133–39. [PubMed: 17095026]
19. Brown B, Long H, Gould H, et al. A conceptual model for the recruitment of diverse women into research studies. *J Womens Health Gend Based Med* 2000;9:625–32. [PubMed: 10957751]
20. Airhihenbuwa CO, Kumanyika SK, TenHave TR, Morssink CB. Cultural identity and health lifestyles among African Americans: a new direction for health intervention research? *Ethn Dis* 2000;10:148–64. [PubMed: 10892821]
21. Heiney SP, Adams SA, Wells LM, Johnson H. Evaluation of conceptual framework for recruitment of African American patients with breast cancer. *Onc Nurs Forum* 2010;37:E161.

Figure 1.
 Heiney-Adams Recruitment Framework [6,10-12,18-21]. Adapted with permission from Heiney et al. [21]. Copyright 2010 by the Oncology Nursing Society

Table 1

Demographic characteristics of the EASE participants, 2003–2007

Characteristic	Participants
Age mean±SD (range)	70 ±9 (44–85)
	<i>n</i> (%)
Race	
White	45(76)
African American	13(22)
Native American	1(2)
Missing	0
Marital Status	
Married/Living with partner	47(84)
Widowed, divorced, single	9(16)
Missing	3
Education	
High school or less	13(23)
Some college	20(36)
College graduate	23(41)
Missing	3
Employment	
Full-time	12(22)
Part-time	8(14)
Retired/Unemployed	36(64)
Missing	3
Smoking status	
Never	22(41)
Current	5(9)
Former	27(50)
Missing	5
Enrollment source	
PCFBS	11(19)
Direct mail	25(42)
Physician referral	13(22)
Self-referral	10(17)
Total	59

Table 2

Recruitment rates for participants contacted directly for the EASE study, 2003–2007

	PCFBS ^a	Physician referral
Contacted directly	206	24
No answer	45	0
Pool 1 ^b	161	24
Refused pre eligibility	22	2
Pool 2	139	22
Not eligible	123	9
Eligible	13	13
Refused	2	0
Recruited	11	13
Overall recruitment (%) ^c	5.3	54.2
Contact recruitment (%) ^d	6.8	54.2
Eligible recruitment (%) ^e	84.6	100.0

^aThe Prostate Cancer Follow-Back Study.^bPool of respondents who answered our calls.^cRecruited divided by number contacted directly.^dRecruited divided by Pool 1.^eRecruited divided by eligible patients.

Table 3

Recruitment rates via mailings for the EASE study 2003–2007

	Oncology clinic	Urology clinics	Support services department	Self referral ^a
Sent letter	1384	759	350	NA
Responded to letter or contacted our offices	95	60	15	40 ^a
Refused pre eligibility	17	8	3	7
Pool 1 ^b	78	52	12	33
Not eligible	59	41	9	21
Eligible	19	11	3	12
Refused	4	3	1	2
Recruited	15	8	2	10
Overall recruitment (%) ^c	1.1	1.0	0.6	25.0
Contact recruitment (%) ^d	15.8	13.3	13.3	25.0
Eligible recruitment (%) ^e	79.0	72.7	66.7	83.3

^a Self-referrals contacted our offices directly (no letter was sent).^b Pool of respondents able to assess eligibility.^c Recruited divided by number sent letter.^d Recruited divided by Pool 1.^e Recruited divided by eligible patients.