Recruitment of Participants to a Clinical Trial of Botanical Therapy for Benign Prostatic Hyperplasia

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Abstract

Objectives: The timely recruitment of study participants is a critical component of successful trials. Benign prostatic hyperplasia (BPH), a common nonmalignant urologic condition among older men, is characterized by lower urinary tract symptoms (LUTS). Successful recruitment methods for a trial of medical therapy for BPH, Medical Therapy of Prostate Symptoms (MTOPS), were mass mailing and advertising. The Complementary and Alternative Medicines Trial for Urological Symptoms (CAMUS) was designed to evaluate a botanical therapy, saw palmetto, for the treatment of BPH. The objective of this study was to evaluate recruitment strategies for CAMUS and to contrast the baseline characteristics of CAMUS participants with those recruited to a similar trial using conventional medical therapy.

Design: CAMUS is a randomized, double-blind, placebo-controlled trial designed to evaluate the effects of saw palmetto given at escalating doses over an 18-month period on relief from LUTS.

Subjects: The target enrollment goal was 350 men with LUTS from 11 clinical centers over a 12-month period. The recruitment techniques used and participants contacted, screened, and randomized through each technique were obtained from the clinical centers. Baseline characteristics of the CAMUS participants were compared with participants in the MTOPS trial who met the CAMUS eligibility criteria for LUTS.

Results: The target enrollment goal was achieved in 11 months. The overall monthly recruitment rate per site was 3.7 and ranged from 2.4 to 8.0. The most successful recruitment methods were mass mailing and advertising, which accounted for 39% and 35% of the study participants, respectively. In comparison to MTOPS participants, CAMUS participants were younger, more highly educated, more diverse, and had less severe urinary symptoms.

Conclusions: Successful recruitment methods for CAMUS were similar to those in MTOPS. The use of botanical therapy attracted a less symptomatic and more educated study population.

Introduction

BENIGN PROSTATIC HYPERPLASIA (BPH), a common non-malignant urologic condition among older men, is characterized by lower urinary tract symptoms (LUTS). Treatment of BPH has undergone a significant change during the past decade from surgery to medical therapy. Complementary and alternative medicines are increasing in popularity in the United States,^{1–3} and are frequently used by patients with BP.^{2,4} Since recent reports demonstrated that saw palmetto (*Serenoa repens* (W. Bartram) Small) at a daily dose of 320 mg

was not effective in reducing LUTS,^{5,6} the Complementary and Alternative Medicines for Urological Symptoms (CAMUS) trial was initiated by the National Institutes of Health to determine whether higher doses of this agent would be effective.

The only detailed report on BPH clinical trial enrollment was from the Medical Therapy for Prostatic Symptoms (MTOPS) trial,⁷ which evaluated medical therapy.⁸ This article reports recruitment strategies in CAMUS and compares the characteristics of the CAMUS and MTOPS study populations.

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Materials and Methods

Trial design

The design of the CAMUS trial has been previously described.⁹ Eligible participants were male, ≥ 45 years of age, had an American Urological Association Symptom Index (AUA-SI)¹⁰ ≥ 8 and ≤ 24 with a peak urinary flow rate of ≥ 4 mL/sec and a voided volume of ≥ 125 mL.

The primary endpoint was change from baseline to 18 months in the AUA-SI. Study participants were randomized to placebo or escalating doses of saw palmetto at 6-month intervals (320, 640, and 960 mg daily). The overall recruitment goal for the trial was 350 men over a 12-month period at 11 clinical centers with identical recruitment targets.

CAMUS participants were compared to the subset of MTOPS participants who met the CAMUS eligibility criteria for AUA-SI (8–24) with respect to baseline characteristics using Fisher's exact test or Pearson's χ^2 test for categorical variables and the *t* test for independent samples for continuous variables at the two-sided 0.05 significance level.

Recruitment strategies

Eight (8) institutions used mass mailing. Sources of names for mass mailing included former participants in two large cancer prevention clinical trials: the Prostate, Lung, Colorectal and Ovarian (PLCO) trial¹¹ and the Selenium and vitamin E Cancer Prevention Trial (SELECT).¹² Two (2) institutions sent letters to men who met the age criteria and who had received medical services within their health systems. One (1) institution used a commercial direct mail list.

Mass e-mailing was used by four sites. Most of the e-mail mailings were targeted at university employees and physicians. One (1) institution used a database of individuals from the community who had previously expressed an interest in being considered for research studies.

Nine (9) clinics used both paid and free advertising. While all of these sites advertised in print media, primarily newspaper, several used radio and online ads for recruitment. Posters and flyers throughout the community and university were used by five centers. Six (6) centers reported identifying potential study participants through chart review of medical records of patients who had been previously treated at their urology clinics.

Results

Recruitment began in June 2008 and ended in April 2009, ahead of schedule. The overall monthly recruitment rate was

3.7 per site and ranged from 2.4 to 8.0. The overall response rate to the initial mailing was 3.2% (Table 1). University of Colorado enrolled 83% of their participants from direct mailing, which targeted PLCO and SELECT participants. Kaiser and Yale recruited 100% and 93% of their study participants, respectively, through mailings to age-eligible male users of their health systems. University of Texas–Southwestern recruited 45% of their enrollees through mailings using a commercial list. Overall, 39% of the study participants were informed about the study through mass mailing (Table 1).

Electronic mass mailings were done primarily at four sites: University of Colorado, University of Iowa, University of Texas–Southwestern, and Washington University with response rates of 0.4%, 0.3%, 17%, and 10%, respectively. The proportions of participants recruited through e-mail were 17%, 30%, 15%, and 19% for these institutions, respectively. Studywide, 8% of participants learned about the study through e-mail (Table 1).

Advertising through print or radio media attracted 35% of the study participants (Table 1). Cornell, Northwestern, New York University, Queens University, and University of Maryland recruited over half of their study participants through advertisements.

The CAMUS and MTOPS studies differed in entry criteria. MTOPS included men ≥ 50 years of age. CAMUS expanded the age criteria to include those ≥ 45 years of age. In comparison to MTOPS participants, CAMUS participants were younger, more highly educated, and more diverse (Table 2). About 13% of the CAMUS participants were African-American, which reflects the proportion of African-Americans in the U.S. population.¹³ The proportion of participants with a 4-year college degree or technical degree or postcollege education was 66% in CAMUS and 51% in MTOPS. The difference in educational level between the two studies occurred primarily in the non-Hispanic white participants. For most uroflow measurements and the AUA-SI, CAMUS participants had less severe urinary symptoms than MTOPS participants (Table 2).

Discussion

Recruitment strategies that were effective in the MTOPS study,⁷ advertising and mass mailing, were equally effective in the CAMUS study. Some of these similarities may be attributed to the fact that most (eight) of the CAMUS sites also participated in MTOPS. There are, however, differences in the study populations with respect to educational level, diversity, and severity of urinary symptoms. Educational

TABLE 1. YIELD FROM EACH RECRUITMENT METHOD

Method	Number of recipients	Number of contacted participants	Number of screened participants (% contacted)	Number of enrolled participants (% screened)
Mass mailing	34,064	1161	608 (52)	143 (24)
E-mailing	35,000	186	87 (47)	31 (36)
Advertising	—	851	273 (32)	129 (47)
Posters/flyers	—	102	12 (12)	8 (67)
Chart review	—	63	52 (83)	30 (58)
Other	—	—	—	28
Total	69,064	2363	1032 (44)	369 (36)

TABLE 2. COMPARISON OF CAMUS AND MTOPS PARTICIPANTS WITH BASELINE AUA-SI ≤ 24 : DEMOGRAPHIC CHARACTERISTICS

	CAMUS	MTOPS
Race*		
Non-Hispanic white	292 (84%)	2221 (83%)
Non-Hispanic black	44 (13%)	236 (9%)
Hispanic	17 (5%)	177 (7%)
Other	16 (4%)	37 (1%)
College or technical school graduate or postcollege education*	245 (66%)	1354 (51%)
Married	279 (76%)	2060 (77%)
Age (years),* mean (SD)	61.0 (8.3)	62.8 (7.4)
AUA-SI,* mean (SD)	14.6 (4.6)	15.5 (4.7)
Voiding time (sec),* mean (SD)	41.1 (21.3)	51.3 (28.0)
Flow time (sec),* mean (SD)	38.2 (19.1)	46.4 (22.7)
Time to maximum flow (sec),* mean (SD)	9.6 (6.9)	12.6 (12.5)
Maximum flow rate (mL/sec),* mean (SD)	14.9 (6.9)	10.6 (2.6)
Mean flow rate (mL/sec),* mean (SD)	8.0 (1.7)	5.5 (1.7)
Voided volume (mL),* mean (SD)	277.1 (122.7)	240.6 (102.6)
Postvoid residual (mL), mean (SD)	60.0 (70.0)	66.4 (80.9)
Prostate-specific antigen (ng/mL),* mean (SD)	2.1 (1.8)	2.4 (2.1)

* $p < 0.05$.

CAMUS, Complementary and Alternative Medicines Trial for Urological Symptoms; MTOPS, Medical Therapy of Prostate Symptoms; AUA-SI, American Urological Association Symptom Index; SD, standard deviation.

levels are positively correlated with use of complementary and alternative medicine.^{1,3,14-17} There may be a greater interest in botanical therapy among those with minimal symptoms.

Conclusions

It is estimated that approximately 15 million men in the United States had LUTS in 2000, a figure that is expected to increase by 43.6% by 2025¹⁸ with the aging of the population. It is likely that this population will be the target of future clinical trials.

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