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Recruitment and retention of women for clinical leiomyoma trials

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ABSTRACT

Background: Subject recruitment and retention in clinical leiomyoma trials is challenging. We evaluated strategies to increase patient enrollment and completion in leiomyoma trials.
Materials and methods: Randomized trials for treatment of symptomatic leiomyoma published from 2000 through 2008 were evaluated and thirteen trials were selected. Subject enrollment and completion rates, recruitment methods and reasons for patient drop-out were assessed.
Results: Recruitment by study personnel or clinic staff during evaluation for symptomatic leiomyoma was the most common strategy for enrollment. Additional methods included local media, internet postings and physician referrals. Seven to 85% of patients enrolled after screening, with a median enrollment of 70%. Sixty-five to 100% of patients completed the study after enrollment with a median completion rate of 89%. Reasons for drop-out at the screening stage included failure to meet inclusion criteria, patient refusal and patient preference for specific treatment. Commonly reported reasons for drop-out after enrollment were refusal of treatment following randomization, adverse reaction to study intervention and non-compliance with study protocol or follow-up visits.
Conclusion: Women with symptomatic uterine leiomyomas may be attracted to participate in leiomyoma trials, however desire for specific treatment and persistent symptoms following intervention may hinder their participation. Randomization to placebo treatment and stringent inclusion criteria appear to adversely impact accrual. A wide range of recruiting tactics is needed and media sources or direct mailings may prove particularly effective to improve subject recruitment and retention in clinical leiomyoma trials.

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1. Introduction

In the United States, uterine leiomyomas are the most common gynecologic tumor in reproductive-aged women affecting as many as 70% of women by age 50 [1]. Black women are disproportionately affected by uterine leiomyomas compared to other ethnic and racial groups [2–4]. Up to 50% of women with leiomyomata have symptoms of pelvic pain, menstrual irregularities and/or infertility that prompt intervention [1,5]. The treatment for leiomyomas is usually surgical removal of the entire uterus (hysterectomy) or removal of the leiomyomas only (myomectomy). Non-surgical options include medical therapy with hormone-suppressing agents and radiologic procedures to occlude uterine blood supply (uterine artery embolization: UAE) or reduce leiomyomas with targeted ultrasound treatment. Though hysterectomy is curative, leiomyomas and their associated symptoms often recur after other treatments.

Total direct cost to the U.S. health care system for the management of uterine leiomyomas is estimated at $2.1 billion per year [6]. Because the clinical and financial burdens of this disease are large, new treatment strategies would be welcome. Several clinical trials have evaluated the effectiveness of various

Abbreviations: UAE, uterine artery embolization.

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surgical and non-surgical treatments. However, subject enrollment and continuance are challenging, and completion rates are often low.

Many barriers to recruitment and retention in clinical trials exist and it is important to understand how these barriers impact patient participation and the generalizability of reported results. The literature from oncology trials identifies various patient factors such as lack of awareness of ongoing trials, fear or distrust of the medical establishment and concerns over loss of insurance benefits due to participation in "experimental" therapy as causes for low participation [7–9]. This may be particularly important within black communities, where a lower level of trust has been reported as a significant barrier to participation [10,11]. At the healthcare provider level, lack of awareness of ongoing trials, belief that standard therapy is best and concern over loss of control of the patient's care may also lead to lower participation rates [9]. Though these barriers are cited in the context of cancer research clinical trials, they are applicable to other areas of investigation as well. To address low patient participation in clinical trials, more clinical investigators are devising strategies to overcome these obstacles in order to reach recruitment goals.

Though enrollment and completion rates for cancer trials have been evaluated, no reports have examined these measures in leiomyoma clinical trials. Identification of the obstacles to study enrollment and completion may allow us to tailor future recruitment strategies to our target population of women, especially black women, who are disproportionately affected by this condition and who have had low participation rates. To identify such obstacles, we examined enrollment and retention rates and recruitment strategies in published randomized leiomyoma treatment trials.

2. Methods

Clinical leiomyoma studies published from 2000 through 2008 were identified using the PubMed, Scopus and EMBASE search engines and the key words leiomyoma, fibroid and clinical trial. Only randomized controlled trials were selected, as many of these investigations were reported according to CONSORT guidelines and therefore included more complete information on patient flow through the study [12]. Information on the number of patients screened, enrolled and completing each trial was collected. We also collected data on recruitment methods and reasons for patient withdrawal from the studies. Investigators were contacted regarding unpublished data, and additional information they provided was included. We evaluated the reporting of patient demographics, specifically ethnicity, among studies selected. All information was obtained from the published manuscripts or through correspondence with the original authors.

3. Results

The initial search identified 269 abstracts of original articles related to leiomyoma clinical trials and 13 studies met inclusion criteria [13–25]. The studies' duration ranged from three to twenty-four months. The ethnicity of study participants was reported in eleven of the thirteen studies. Black women comprised over 50% of the study population in one-third of the studies identified. The percentage of black participants ranged from <1–72% in these studies.

Four of the thirteen trials provided no information on recruitment strategies. Among the studies providing this information, recruitment by study personnel or clinic staff was employed. Nurses or physicians involved with the study informed patients about the trial during a scheduled visit for evaluation of symptomatic leiomyoma or upon referral from an outside physician. Interested patients were then screened to assess their eligibility for study enrollment.

Three studies reported other recruitment methods in addition to study personnel, with variable overall enrollment rates (7–51%). Additional methods included recruitment through local media, referrals from community physicians, and internet postings (Table 2). In one study, the most successful recruitment methods were television and radio advertisements, word of mouth, and internet sites that described the study. Television public service announcements (PSA) accounted for 25.5% of the referrals while radio, word of mouth and the internet accounted for 18.6%, 17% and 16% respectively. Physician referrals, community outreach through health fairs and collaboration with local churches, recruitment by non-physician providers and newspaper advertisements were individually responsible for less than 10% of the referrals ([15], unpublished data). Although the recruitment strategies of television and radio advertisements were the most successful, they were also the most expensive. Due to reporting of additional recruitment strategies in only a few studies and wide variation in enrollment rates, it is difficult to make comparisons regarding the effectiveness of various methods.

Most patient drop-out occurred at the screening stage. Information on the number of women screened was available for 9 of the 13 studies; a total of 2180 patients were initially screened and 971 (45%) enrolled. The range of patients enrolled after screening was broad (7–85%) with a median enrollment of 70. Three trials reported enrollment >80%; two of these trials included surgical intervention. In the four remaining studies, 361 patients enrolled.

The most frequently cited causes of drop-out during screening were patient refusal to participate after learning about the study, failure to meet inclusion criteria and patient desire for specific treatment.

Though recruitment costs can influence strategies for enrollment and retention, this information was only available for one of the identified trials ([15], unpublished data). Additionally, the clinical investigation by Levens et al. was the only one to report monetary remuneration of study participants (unpublished data).

All thirteen trials provided information regarding follow-up and reasons for withdrawal once patients were enrolled. The median completion rate for enrolled subjects was 89% with a range of 65–100%. Three trials reported <10% of completers per patient screened and two of these trials included a placebo arm (Table 1). Common causes for patient withdrawal once the study was underway were adverse effects from the study intervention, participant non-compliance, withdrawal of consent and failure to follow-up (Table 2). Information on retention strategies was not published.