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Recruitment methods in a clinical trial of provoked vulvodynia: predictors of enrollment

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Abstract

Background—Successful recruitment in clinical trials for chronic pain conditions is challenging, especially in women with provoked vulvodynia due to reluctance in discussing pain associated with sexual intercourse. The most successful recruitment methods and the characteristics of women reached with these methods are unknown.

Objective—To compare the effectiveness and efficiency of four recruitment methods and to determine socioeconomic predictors for successful enrollment in a National Institute of Health (NIH)-sponsored multicenter clinical trial evaluating a gabapentin intervention in women with provoked vulvodynia.

Methods—Recruitment methods utilized mass mailing, media, clinician referrals and community outreach. Effectiveness (number of participants enrolled) and efficiency (proportion screened who enrolled) were determined. Socioeconomic variables including race, educational level, annual household income, relationship status, age, menopausal status and employment status also were evaluated regarding which recruitment strategies were best at targeting specific cohorts.

Results—Of 868 potential study participants, 219 were enrolled. The most effective recruitment method in enrolling participants was mass mailing (P<.001). There were no statistically significant differences in efficiency between recruitment methods (P = 0.11). Relative to clinician referral, black women were 13 times as likely to be enrolled through mass mailing (adjusted odds ratio [αOR] 12.5, 95% confidence interval [CI], 3.6 – 43.1) as white women. There were no differences

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in enrollment according to educational level, annual income, relationship status, age, menopausal status, or employment status and recruitment method.

Conclusion—In this clinical trial, mass mailing was the most effective recruitment method. Race of participants enrolled in a provoked vulvodynia trial was related to the recruitment method.

Keywords

Recruitment methods; predictors; provoked vulvodynia

Background

Clinical trials for chronic pain conditions, often do not meet recruitment goals due to many reasons, including reluctance of subjects to enroll in these trials. Limited recruitment strategies can potentially lead to a highly selective enrollment process, especially if there is a placebo arm and potential subjects are reluctant to go off of pain medication.[1] Recruitment of women with provoked vulvodynia is particularly challenging not only due to a placebo arm in most of these studies, but also due to the reluctance in women and clinicians in discussing this condition and the sexual issues, such as dyspareunia, that result.

Successful recruitment methods are often gauged by whether they are effective (meet enrollment goals), efficient (low screened/enrollment ratio), and reach the intended target population. If a recruitment method results in a large pool of candidates, but many are not eligible and enroll, then this approach may not be efficient. Of particular importance in vulvodynia clinical trials is the aim to recruit women with different subtypes, including those from different socioeconomic backgrounds, in order to better characterize the disorder and to determine differences in treatment responsivity.[2] Although these indicators of successful recruitment are instrumental for timely completion of clinical trials, they have not been investigated in vulvodynia.

Many clinical trials in vulvodynia have used clinician referrals as the only recruitment method,[3–10] where potential participants are readily available and may be enrolled within a brief period of time with minimal resource requirements. However, this recruitment method may reach a limited population and be susceptible to selection bias as these participants may have better access to health care due to socioeconomic factors or have more complex or severe conditions.[11]

Studies have shown that clinician-referred participants tend to be white, better educated, more likely to be in a partnered relationship and younger than those in the wider population,[11] and a similar demographic profile has been observed in randomized clinical trials in women with vulvodynia.[3– 10,12–15] Whether these characteristics are related to the recruitment method, or are a true reflection of the patient population deserves study, as epidemiological studies have shown that menopausal women, those of Hispanic descent and those of the black race also report symptoms of vulvodynia.[16–18]

Mass mailing and the media are other common recruitment methods that reach a more representative population and may target groups of interest through use of zip codes and

radio and television stations that reach certain subpopulations. However, use of a “broad net” to enroll potential participants may be less efficient. Community outreach has been shown to be highly effective in recruiting minority participants,[19] but may be limited by time commitment of investigators and staff.

Since no recruitment method satisfies all criteria for global representation of subjects, there is a trend to actively use more than one recruitment method.[12–15,20] However, the success of multiple recruitment strategies in meeting recruitment goals has not been reported. We compared the effectiveness and efficiency of clinician referrals, mass mailing, media and community outreach recruitment methods and determined socioeconomic predictors of enrollment for each of these recruitment methods in a National of Institute (NIH)-sponsored multicenter clinical trial evaluating women with vulvodynia.

Methods

Women were recruited for a multicenter clinical trial studying the therapeutic effect of gabapentin, the results of which will be reported at a later date. Institutional review board approval was obtained from the from the University of Rochester School of Medicine and Dentistry, Rutgers-Robert Wood Johnson Medical School and the University of Tennessee Health Science Center, and all subjects signed an informed consent before participation.

Recruitment methods

Recruitment took place from 1 August 2011 through 31 July 2015. Recruitment methods were categorized into 4 main categories according to those used in previous studies: mass mailing, media, clinician referrals and community outreach.[21]

Clinician referral—Each of the investigators recruited potential participants from their practice and through chart review. In addition, letters containing brochures and a 4” × 4” card containing inclusion/exclusion criteria were mailed to obstetrician-gynecologists and family practice physicians in the community.

Mass mailing—A paid advertisement was placed in a monthly utility bill within a 15-mile radius of the research site at the University of Tennessee Health Science Center, and direct mail advertising at the other research sites within the same 15-mile radius. Specific zip codes from a mailing house were selected for target populations according to age, educational status, and annual household income and race at all three study sites.

Media—Media included fliers and printed advertisements, local newspapers and magazines, the National Vulvodynia Association newsletter, 30-minute spots in local radio stations, website advertisements placed on clinicaltrials.gov, craiglist.com, nva.org, Facebook and university home pages, and the development of a website.

Community outreach—Investigators contacted community leaders and organizations and gave presentations at grand rounds, professional meetings and community events. Research staff set up tables and booths at local events and health screenings.

Terminology

Effectiveness was defined as the number of participants who enrolled. Efficiency was defined as the proportion of those screened who enrolled in the study (signed informed consent), or the "recruitment fraction."[1]

Participants

Participants were screened through an online screening questionnaire developed for the research study and through a toll-free telephone number where research staff used the same screening questionnaire to determine eligibility.

Eligible participants were 18 years of age or older and had greater than three continuous months of insertional dyspareunia, pain to touch, or both with tampon insertion (modified `Friedrich's Criteria').[22] They were required to demonstrate moderate to severe tenderness in the vulvar vestibule, which was greater than the score in the outer vulvar area or the score in the vagina on the cotton swab test[23] during the pelvic examination and report an average pain level of 4 or greater (0, no pain to 10 worse pain imaginable) with two tampon insertions during a two-week screening period.[24] They were excluded from study participation if they had other vulvar conditions, including dermatoses, vulvitis, atrophic vaginitis or active vaginal infection, a prior vestibulectomy, were pregnant or at risk for pregnancy without use of a reliable birth control method, had any unstable medical or psychiatric condition, or use of centrally acting antidepressant or anxiolytic medications, with the exception of the long term, stable dose use of selective serotonin reuptake inhibitors.

Participants who were eligible for enrollment completed a 72-item self-report questionnaire.[25] The questionnaire included items assessing the women's demographic characteristics, including race, ethnicity, educational level, annual household income, relationship status, age, menopausal status and employment status.

Data analysis

Data were analyzed used SAS version 9.3 (SAS Institute Inc., Cary, North Carolina). Chi-square tests were used to assess differences between the four recruitment methods in effectiveness and efficiency and to assess differences between each of the recruitment methods and the demographic variables. Multinomial logistic regression was then used to fit the data, using demographic variables to describe the likelihood of those enrolled through different recruitment methods, clinician referral being the reference level.[26] The significance level was set at 0.01 to account for multiple adjustments.

Results

Data from the community outreach recruitment method was excluded from statistical analyses because only one community outreach-derived participant was screened and none enrolled. We were also unable to analyze data by ethnicity based upon self-reported Hispanic ethnicity being limited to three study participants.

Among 868 potential participants screened, 303 were eligible and 219 were enrolled. The average age of enrolled participants was 38.4 ± 12.8 years of age. The majority were black, premenopausal, less than 52 years of age, not employed full time, had less than a college degree, made less than $25,000 per year, and were not in a partnered relationship (Table 1).

Mass mailing was significantly more effective than the media or clinician referrals in the number of women screened (54% vs. 27% vs. 19%), respectively. It was also more effective in the number of subject's enrolled (50% vs 26% vs. 23%), respectively. The proportion of those screened who enrolled (recruitment fraction) was 25%. The recruitment fractions did not differ significantly by recruitment method (mass mailing (23%) vs media (25%) clinician referrals (31%)).

Relative to clinician referral, black women were 13 times as likely to be enrolled through mass mailing as white women (Table 2). There were no statistically significant differences in enrollment of participants according to educational level, annual income, relationship status, age, menopausal status, or employment status and recruitment method.

Discussion

We compared the effectiveness and efficiency of four recruitment methods. We found that mass mailing was most effective in screening and enrolling women compared to clinician referral, media, or community outreach. These findings are consistent with one of the largest clinical trials conducted in women, the Women's Health Initiative, where the most effective recruitment strategy was mass mailing, accounting for 67% of total participants enrolled, followed by 14% from newspapers or magazine advertisements.[27]

Nevertheless, the finding that clinician referral was a less effective recruitment method than mass mailing is somewhat surprising, since this method is commonly used with the assumption that recognition of the study by a patient's clinician would generate a large population of subjects. However, clinicians may be reluctant to refer patients to research studies because it diverts time and resources away from their practice.[28] Our study provided no strong evidence of differences in efficiency of the recruitment methods other than the inferiority of community outreach.

We also determined socioeconomic predictors of enrollment for each of the recruitment methods. We found that white women were significantly more likely to be enrolled through clinician referrals and black women through mass mailing. This demographic profile is consistent with research in previous clinical trials in vulvodynia,[3–10,12–15] and suggests that clinician referral may not reach the broader population of women with this condition, and that recruitment methods should include mass mailing to maximize diversity in the study cohort.

The fact that mass mailing was an effective recruitment method for enrolling black women is a key finding, as enhancing recruitment and participation in clinical trials among underrepresented groups is a national priority. Although the NIH Revitalization Act of 1993 authorized that minorities be appropriately represented in clinical trials, they continue to have lower enrollment rates in health research when compared to nonminority groups.[30]

It is noteworthy that community outreach was not an effective recruitment strategy in recruiting black women, despite the fact that it is commonly used, in part, due to perceived distrust among minority populations of the medical community.[31] Since this method was ineffective, and may be limited by time commitment of investigators and staff, it is not suggested as a primary method of recruitment in vulvodynia trials.

A strength of our study was the large population of black women who enrolled; however, a major limitation was the inability to determine which recruitment method was most successful in enrolling Hispanic women, where vulvodynia is most prevalent.[16–18] Difficulties in reaching these women may have been due to unavailability of Spanish-speaking research staff or the geographic location of the research sites. Larger multicenter trials with available translators are necessary to recruit this subgroup of women.

Methodological issues may have influenced results. We used multiple recruitment methods concurrently, so it is difficult to state whether findings would have been similar if they were run independently. It is also possible that the media may have been a more successful recruitment method if television advertising had been used, but because of costs and budgetary constraints, we limited advertising to newspaper ads, websites and radio.

Future research should explore which recruitment methods are most effective in reaching women of diverse ethnicities and races, age groups, and subtypes of vulvodynia and in women with other medical conditions.

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Table 1

Socioeconomic characteristics of participants.

Demographic characteristics	Percent/mean ± SD[a]
Age (years)[b]	38.4 ± 12.8
Race	
Black	144 (66)
White	75 (34)
Ethnicity	
Hispanic	3 (1)
Non-Hispanic	216 (99)
Education	
Partial high school or less	9 (6)
High school graduate or equivalent (GED)	41 (28)
Partial college/university	38 (26)
College/university graduate	42 (30)
Post-graduate/professional degree	15 (10)
Annual Income (USD)	
< $24,999	66 (45)
$45,000 – 49,999	32 (22)
$50,000 – 99,999	19 (13)
>$100,000	8 (6)
Prefer not to answer	21 (14)
Relationship status	
Single, never married	62 (43)
Divorced/separated/widowed	21 (14)
Married/marriage-like relationship	63 (43)
Age	
< 52 years	178 (81)
≥ 52 years	41 (19)
Menopausal status	
No	116 (81)
Yes	28 (19)
Employment status	
Full time (40 hrs./week)	43 (29)
Part time (17–39 hrs./week)	31 (21)
Occasional (1–16 hrs./week)	4 (3)
Full time homemaker	8 (6)
Student	18 (12)
Retired	7 (5)
Disabled	8 (6)
Unemployed	27 (18)

[a] SD: standard deviation.

[b] Data are n (%) unless otherwise specified.

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Table 2

Multinomial logistic regression for enrollment method.

Variable		Mass Mailing			Media			Clinician Referral[a]
		N	αOR[b] (95% CI)[c]	P	N	αOR (95% CI)	P	N
Race								
	Blacks	93	12.5 (3.6, 43.1)	<0.001	35	3.8 (1.0, 14.9)	0.06	16
	Whites	17			23			35
Educational Level								
	< College Degree	51	3.2 (1.0, 9.9)	0.05	20	1.3 (0.4, 4.7)	0.66	17
	≥ College Degree	16			13			29
Annual Income								
	< $25,000/year	38	1.9 (0.5, 7.4)	0.34	17	3.5 (0.8, 15.3)	0.10	11
	≥ $25,000/year	21			8			30
Relationship Status								
	Non-partnered	43	1.2 (0.4, 3.9)	0.78	23	2.3 (0.6, 8.5)	0.23	17
	Partnered	24			10			29
Age								
	< 52 years	93	1.3 (0.2, 9.3)	0.77	43	0.5 (0.1, 4.0)	0.50	42
	≥ 52 years	17			15			9
Menopausal								
	Yes	11	0.9 (0.2, 4.6)	0.91	5	0.7 (0.1, 4.3)	0.68	12
	No	56			28			32
Employment Status								
	Full-time	21	1.6 (0.4, 6.1)	0.48	8	2.0 (0.5, 8.3)	0.33	14
	Not Full-time	46			25			32

[a] Reference group.

[b] Odds ratios (αOR) were computed through multinomial logistic regression analysis.

[c] CI = confidence interval.