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The effectiveness of small group community-based information sessions on clinical trial recruitment for secondary prevention of Alzheimer's disease

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Abstract

Effective and practical recruitment strategies are needed to ensure successful recruitment into Alzheimer's disease (AD) clinical trials. To facilitate successful recruitment for the NIH-sponsored A4 (Anti-Amyloid treatment in Asymptomatic Alzheimer's disease; NCT02008357) trial for the secondary prevention of AD, we developed a small-group community information session to attract and recruit potential research participants. After a successful media campaign, 213 participants were screened by telephone for eligibility, identifying 127 potential participants. Participants were given the option of a traditional one-on-one recruitment session, or a small-group session. One-on-one recruitment was performed for 15 participants requesting this procedure, and yielded an overall recruitment rate of 67% (n=10). Substantially more individuals (n=112; 88%) requested small-group sessions to learn about the study. After attending the small-group informational sessions, 98% of potential participants self-reported a greater understanding

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of the study, and the recruitment rate from these sessions was 90%. Small-group sessions not only improved recruitment success rates, but also contributed to significantly shorter median time for consent processes (20 vs. 60 minutes) and reduced staff time spent on persons not recruited. Small-group education programs are an effective strategy for enhancing recruitment success and facilitating practical recruitment into clinical trials with high recruitment demands.

Keywords

Alzheimer disease; clinical trial; recruitment; prevention

Introduction

Successful recruitment is considered by most clinical researchers and research organizations to be a major “bottleneck” in the therapeutic pipeline, responsible for a significant delay in bringing promising agents to market¹⁻⁹. As such, effective and practical recruitment strategies are needed to facilitate this process^{10, 11}. This is especially true in the area of clinical research for prevention of Alzheimer's disease (AD), in which thousands of potential participants may be needed to fulfill clinical trial needs^{1, 2, 12}. The Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) trial for the secondary prevention of AD (NCT02008357) is one such study that represents a major effort by the NIH to combat this devastating disease¹³. The A4 Study represents a new paradigm in AD trials, seeking to enroll clinically normal older individuals at high risk for developing AD dementia. To meet trial requirements for enrollment, it is estimated that over 10,000 elderly individuals will need to be screened by 60 centers, with limited site reimbursement for screening procedures. As clinical interventional research in the area of AD prevention moves to the forefront of our efforts, increasing demands for efficient recruitment strategies are expected and desperately needed¹.

Previous scientific research in the area of clinical trial recruitment is limited. Several studies have published on desired trial attributes that might facilitate recruitment¹¹, but few have focused on the scientific study of strategies that might improve recruitment success prospectively¹⁰. Low risk, high potential benefit, easy access, and ease of engagement are the central themes identified in retrospective studies that may enhance research participation¹¹. One study prospectively examined recruitment through outreach to health care providers (continuing education program) vs. community engagement (interactive health fair for community members) and demonstrated that a community-based approach was superior to approaches that target health care providers¹⁰. With limited scientific study in this area, the field has much to explore in order to meet the current and future demands for the research participants needed to move drug discovery programs forward.

In order to address the recruitment needs of the A4 study¹³, we designed a small-group, community-based, education program to recruit potential participants with a high likelihood of engagement. The program was evaluated in regards to recruitment success and practical improvements in recruitment processes in a prospective study.

Methods

Media outreach

The University of Kentucky Public Relations (UKPR) and Marketing Departments were connected with the investigator at the local site and the Alzheimer's Disease Cooperative Study recruitment specialists. Following a national media release, UKPR arranged free, public service, and informational TV, radio, and newspaper press releases across the local region. Data presented below represent the comprehensive impact of this outreach activity but do not include data on specific media outreach activities in relation to potential participant contacts with site.

Participants

Only persons who self-identified to the site after exposure to the local press releases are included in this analysis. Interested participants (n=213) contacted the local investigational site by telephone only. Alternative contact methods including conventional mail and social media were not options provided in the media outreach for interested participants, nor were subjects engaged in this manner included in the present analysis as there were only two over the study period. The potential participants underwent a telephone screen addressing relevant health history, current medical diagnoses including the existence of a diagnosed memory problem, exclusionary conditions and medications, and reaffirmed interest in research participation. All potential participants who completed the telephone screen were naïve to research activities at the investigational site and were offered the opportunity to participate in one-on-one engagement or to attend small-group community sessions (n=127), while many contacts (n=86; 40.4%) were prescreened as ineligible for study participation based on inclusion/exclusion criteria.

Recruitment methods

Based on the expert opinions of study doctors, social workers, and site personnel, a practical engagement capacity of 12 participants per small-group session was selected to promote optimal interaction between study staff and participants.

A brief presentation was developed that highlighted: (1) the scientific rationale for the study, (2) inclusion and exclusion criteria, (3) overview of human subjects protections in research, (4) details of study participation, (4) potential risks and benefits from published studies on the investigational agent, and (5) education on study procedures such as required amyloid-PET imaging, disclosure of amyloid status, MRI scans, and optional donation of cerebrospinal fluid. The structure of the program was vetted by the aforementioned expert panel and assembled into a 50 minute presentation with an additional 10-15 minutes allotted for group discussion.

Outcome measures

Outcome measures included the actual number of participants recruited, time to complete the consent processes (estimated in 20 minute intervals for consent procedures only, not including time for informal or formal informational exchange), subjective evaluations of the small-group, community-based presentation, and overall recruitment success by group. The

subjective evaluation was completed by small-group attendees and included four questions that evaluated participant reports of: 1) Understanding of the A4 study, 2) Understanding of the importance of research participation, 3) Readiness to participate in the A4 study, and 4) Likelihood of participating in the A4 study that were graded on a Likert scale including terms for strongly agree, agree, neutral, disagree, and strongly disagree. The subjective evaluation was only collected after the small-group sessions, precluding pre-/post-assessment and between group comparisons.

Statistical analysis

Standard comparative statistics including Student's t, Fisher-exact, and Mann-Whitney u tests were used to compare groups between one-to-one and small-group sessions on recruitment rate, consent time, and availability of medical records.

Human subjects protections

The A4 research protocol and the recruitment procedures were approved by the University of Kentucky Institutional Research Board.

Results

Recruitment activities for 213 participants were analyzed. A flow chart of study recruitment is provided in Figure 1. Telephone screen identified 127 of 213 (60%) subjects eligible for the protocol, and 86 subjects ineligible due to inclusion/exclusion criteria. The reasons for telephone screen ineligibility were varied (See Figure 2), but most often involved contacts made by family members on behalf of potential participants rather than by the potential participants themselves (26%) or contact made for potential participants that already had been diagnosed with mild cognitive impairment or dementia (29%). Basic demographics including age, gender, education, and minority status did not differ between subjects participating in small group informational sessions and those requesting traditional one-on-one informational and consent procedures (Table 1). Most of the eligible participants opted to attend a small group information session (n=112, 88%) rather than come in for a one-on-one enrollment session (n=15, 12%). Participants who attended small group sessions were more likely to enroll in research than those who engaged in one-on-one enrollment (90% vs. 67% respectively, $p<0.05$; Fisher Exact test).

Post-program evaluations for the small-group, community sessions showed that the majority of attendees self-reported improved understanding of the A4 study, improved understanding of the importance of research participation, increased readiness to participate in the A4 study, and increased likeliness to engage in the A4 study than prior to the educational session (Figure 3). Objective measurement of understanding the study was not performed, and the data reported is restricted to perception of understanding only. This should be noted as a limitation of the current study.

Consent process time was reduced from a median of 60 minutes to 20 minutes for attendees of the small group sessions ($p<0.05$; Mann-Whitney u-test). An increased availability of medical records for review to determine eligibility in the study was seen in the small-group attendees compared to one-on-one enrollees (100% vs 60%, $p<0.05$; Fisher exact test).

Discussion

The data presented demonstrate that small-group community informational sessions are an effective strategy that can facilitate recruitment and reduce one-on-one consent time, lessening burden on study staff. The development and empirical testing of strategies to enhance and streamline recruitment processes are important in helping to overcome this critical bottleneck in clinical research engagement, yet few studies exist in the literature to provide guidance in this regard^{1, 10}. While it was expected that small-group community sessions would lessen one-on-one consent time, the increased recruitment success using this protocol was not anticipated. Increased recruitment rates for those engaged in small-group sessions cannot be explained on the basis of study understanding as full discussion of the consent form and research processes was identical between those requesting one-on-one informational sessions and those attending the small-group sessions.

It is possible that the social engagement in the small-group sessions created a group dynamic that encouraged research participation. Group dynamic theory was developed and popularized in the mid-20th century as a method for creating social change¹⁴. The theory rests on eight key principles that encompass aspects of group composition, purpose, perceptions and individual influences on group behavior (Table 2). The small-group community sessions implemented as part of our efforts to facilitate recruitment into the A4 study included several favorable aspects of group dynamic theory that potentially contributed positively to the enhanced recruitment success seen with this methodology. For example, group composition included individuals that were from the same community, all recognized as normal in cognition, and all with strong desire to learn more about the study. This homogeneity in group composition and purpose potentially contributed to a strong sense of belonging and purpose in the group that facilitated group dynamics. The information presented to the group was directly related to the purpose of the group, further facilitating group dynamics. Time for social interaction, discourse, and a shared question and answer session may have influenced individual resistance to deviate from the main group purpose of engagement in the clinical trial activities. Irrespective of whether group dynamic theory can explain the increased engagement of those attending the small-group community sessions over one-on-one individual informational sessions, it is clear that the group session format represents an effective method of enhancing research participation.

One expected benefit of the small-group sessions was facilitation of consent processes leading to reduced burden on study staff. This was borne out, with individual median consent time reduced from 60 minutes (for the one on one sessions) to 20 minutes (for individuals who had participated in the group sessions). This represents a substantial improvement in the efficiency of research engagement activities, allowing staff to more fully focus on post-consent engagement and activities.

Several key questions remain unanswered in regards to facilitation of recruitment using small-group community sessions. It is unknown whether the small group community sessions are generalizable as a recruitment approach for trials with the clinical AD population. Additionally, it remains unclear if the approach is practical as a general community outreach effort, or if the facilitation of recruitment was dependent on

homogeneity of attendees and group purpose predicted as influential in outcome success by group dynamic theory¹⁴. The optimal size for group participation should be explored further. While larger sessions would lead to a greater facilitation of the consent process and time saved by study staff, it might sacrifice some of the potential benefits (i.e. recruitment success) that could be attributable to group dynamics. Further studies examining these and other key questions are needed to fully understand important aspects of practical implementation of such unconventional recruitment strategies.

While no statistically significant differences were seen between subjects engaged in traditional one-on-one vs. small-group sessions, the sample size is small, and a potentially important trend towards lower engagement of minority participants in the small-group sessions was seen (4.3 vs. 13.3 % respectively). Re-evaluation of the generalizability of small-group sessions in varied settings with larger sample sizes will be needed to fully evaluate these considerations. Indeed, minority recruitment successes at our center have been largely dependent on more focused outreach engagement than that provided by generalized media press releases¹⁵. Thus, while small-group community sessions may represent an important strategy for outreach, multiple approaches may be needed to ensure successful recruitment for the many dementia prevention trials that are planned and underway currently.

A major limitation of the current study is that recruitment efforts for the A4 study (on which this experiment was designed) are ongoing, and the data collected and presented to date represent only a fraction of that expected to be available at the end of study recruitment. As such, it should be recognized that the data remain quite fluid. Despite this caveat, it is important to share this early data on recruitment success within the field, as A4 recruitment already lags nearly a year behind projections and many other large scale prevention trials using similar populations are planned or in process currently. Such efforts may significantly benefit from adoption of similar recruitment strategies. In addition, our strategy of formalizing scientific exploration of the effectiveness of specific recruitment strategies, examined in a prospective fashion, should serve as a translational model for the rational evaluation of other disparate efforts to enhance recruitment for prevention trials in AD and many other disease states.

Despite limitations in our understanding of how or why the approach of small-group community informational sessions were so successful, it is clear that this strategy led to several positive outcomes including increased recruitment rates and reduced staff time for engagement activities. As recruitment and successful engagement are one of the key barriers to efficient and timely clinical trial completion^{1-4, 7, 8, 10}, the results of this study serve as an important example of how science can be applied to aspects of clinical trials that have not traditionally been examined in an empiric sense¹⁰. Further studies of non-traditional methods for recruitment and engagement in clinical trial activities that can reduce total time to trial completion are needed in order to maximize therapeutic development in our search for new medicines and interventions designed to prevent or treat AD.

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Figure 1. Flow chart of study recruitment

Figure 2. Reasons for telephone prescreen ineligibility for study participation for subjects contacting the site after media outreach activities

Figure 3. Post small-group evaluation participant-reported outcomes

Table 1
Basic demographic information for subjects attending small-group community sessions
vs. traditional one-on-one information and consent sessions

Demographic	Small-group sessions (n=88)	One-on-one sessions (n=15)	p-value
Age in years (mean $\pm$ s.d.)	72.3 $\pm$ 5.5	73.5 $\pm$ 5.9	0.46, Student t-test
Education in years (mean $\pm$ s.d.)	16.7 $\pm$ 2.3	16.8 $\pm$ 2.6	0.89, Student t-test
Gender (% male)	53.3	53.2	1.0, Fisher exact test
Minority status (%)	4.3	13.3	0.24, Fisher exact test

Table 2
Eight key principles of group dynamic theory¹⁴

Principle	Description
1	If the group is to be used effectively as a medium of change, those people who are to be changed and those who are to exert influence for change must have a strong sense of belonging to the same group.
2	The more attractive the group is to members the greater is the influence that the group can exert on its members.
3	In attempts to change attitudes, values, or behavior, the more relevant they are to the basis of attraction to the group, the greater will be the influence that the group can exert upon them.
4	The greater the prestige of a group member in the eyes of other members, the greater the influence they can exert.
5	Efforts to change individuals or subparts of a group which, if successful, would have the result of making them deviate from the norms of the group will encounter strong resistance.
6	Strong pressure for changes in the group can be established by creating a shared perception by members of the need for change, thus making the source of pressure for change lie within the group.
7	Information relating to the need for change, plans for change, and consequences of change must be shared by all relevant people in the group.
8	Changes in one part of a group produce strain in other related parts which can be reduced only by eliminating the change or by bringing about readjustments in the related parts.