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MAXIMIZING CLINICAL RESEARCH PARTICIPATION IN VULNERABLE OLDER PERSONS:

IDENTIFICATION OF BARRIERS AND MOTIVATORS

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Abstract

Objectives—To identify barriers and motivators to participation in long-term clinical research by high-risk elders and to develop procedures to maximize recruitment and retention.

Design—Quantitative and qualitative survey

Setting—Academic primary care medicine and pre-anesthesia testing clinics

Participants—Fifty patients aged 70 or older, including 25 medical patients at high risk of hospitalization, and 25 patients with planned major surgery

Measurements—15-20 minute interviews involved open and close-ended questions guided by an in-depth script. Two planned study protocols were presented to each participant. Both involved serial neuropsychological assessments, blood testing, and magnetic resonance brain imaging (MRI); one added lumbar puncture (LP). Participants were asked whether they would be willing to participate in these protocols, rated barriers and incentives to participation, and were probed with open-ended questions.

Results—Of 50 participants (average age 78 years, 44% male, 40% non-white), 32 (64%) expressed willingness to participate in the LP-containing protocol with LP cited as the strongest disincentive. Thirty-eight (76%) expressed willingness to participate in the protocol without LP, with phlebotomy and long interviews cited as the strongest disincentives. Altruism was a strong motivator for participation, while transportation was a major barrier. Study visits at home, flexible appointment times, assessments shorter than 75 minutes, and providing transportation and free parking were strategies developed to maximize study participation.

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Conclusion—Vulnerable elders expressed a high rate of willingness to participate in an 18-month prospective study. Participants identified incentives and barriers that enabled investigators to develop procedures to maximize recruitment and retention.

Keywords

Clinical trials; Clinical research; Elders; Recruitment; Retention

INTRODUCTION

The older population is the most rapidly growing segment of the American population. In 2000, nearly one in eight Americans was aged 65 or older, and by 2030 this is expected to increase to one in five (1). Moreover, seniors account for >33% of all ambulatory medical visits, and >50% of all hospital days (1). Therefore, research to address issues pertinent to aging is assuming increasing importance.

Several studies have documented that elderly patients are systematically under-represented in clinical research (2-5). Given the high prevalence of elders, this represents a serious problem for translating research findings into clinical practice (6). In some cases, researchers may intentionally limit participation of older adults. They may have concerns about the safety of study procedures, capacity of older adults to consent, or the confounding effects of comorbidity on the interpretation of results. In other cases, unintentional exclusions may result from lack of attention to the practical barriers formed by study activities (7-13).

High recruitment and retention of older adults are critical to ensure adequate statistical power, to minimize bias, and to ensure that research findings can inform clinical practice. Low participation rates lead not only to potential sampling bias and threats to internal validity of the study, but also delays in study completion and increased costs. The available senior population is large, and evidence shows that when approached, older adults are often willing to participate in clinical research. While barriers preventing older adults from participating must be addressed, relatively few research studies have focused on identifying these barriers or developing strategies to overcome them (7-13).

The present study focused on identifying barriers and motivators for participation in a planned clinical research study involving repeated interviews, neuropsychological testing, phlebotomy, neuroimaging, and possibly cerebrospinal fluid assay via lumbar puncture—on 4 occasions over an 18 month period. Specific objectives of the present study were to: 1) identify barriers and motivators to participation in a long-term clinical research study by a vulnerable older population; 2) estimate the importance of incentives to participation; and 3) create optimized study procedures to maximize recruitment and retention. While this study was conducted to address barriers and incentives relevant to a particular study, we believe the results provide practical recommendations to enhance participation and retention of older persons into clinical research more generally.

METHODS

Study design and sample selection

This mixed methods study includes both qualitative and quantitative components. The study involved interviews with a consecutive sample of eligible patients conducted at a primary care medicine clinic and the pre-anesthesia clinic at the Beth Israel Deaconess Medical Center (BIDMC) between March 1, 2007 and June 30, 2007. The BIDMC is a 585-bed acute-care hospital affiliated with Harvard Medical School with over 40,000 admissions and 750,000 outpatient visits each year, serving a large community and referral population. We wanted to

identify barriers and motivators for vulnerable older patients to participate in a planned study to evaluate long-term outcomes of delirium. The study would involve interviews, neuropsychological testing, phlebotomy for laboratory tests, brain magnetic resonance imaging (without intravenous contrast), and might involve lumbar puncture. Patients would be enrolled at baseline, then undergo 3 additional assessments every 6 months over an 18-month period. Given the procedures, multiple reassessments, and long-term follow-up, the future study was rated to have a medium degree of intrusiveness (8).

Our sample selection process identified a group of patients who would meet eligibility criteria for the planned study, specifically, being at high-risk for hospitalization during the subsequent year, but who were able to participate in interviews and likely to survive until study completion. Thus, selection criteria for all patients included: age ≥ 70 years, no dementia or active delirium, life expectancy > 6 months, English-speaking, and residing within 30 miles of BIDMC. For medical patients, additional selection criteria to identify a high-risk group for hospitalization included meeting 3 of the following 5 criteria: age ≥ 85 years, Deyo-Charlson comorbidity score ≥ 2 (14,15), any hospitalization in the previous year, ≥ 6 primary care visits in the previous year, and either a low hematocrit ($<30\%$) or albumin (<3.0 mg/dL) or high creatinine (>1.5 mg/dL) level during the previous year (16). For surgical patients, additional selection criteria were: scheduled for elective vascular, gastrointestinal, orthopedic, or non-cardiac thoracic surgery, planned to receive general anesthesia, and to be admitted to the hospital at least overnight (17). Thus, the eligible sample has a substantial degree of vulnerability and illness burden, and thus, might pose a challenge for study enrollment. For this feasibility study, we chose to enroll a total of 50 patients (25 medical and 25 surgical), based on previous similar studies.

Study procedures

The 15-20 minute interviews involved close-ended and open-ended questions guided by an in-depth interview script. All recruitment and interview procedures were conducted by one trained clinician-interviewer. Consecutive patients were screened for eligibility through the online medical record in advance of scheduled appointments. Physician approval (via email, telephone, or direct contact) was obtained to approach the patients. The patients were then approached at the time of their scheduled visit. Written informed consent for participation was obtained from the patient using procedures approved by the BIDMC institutional review board

The interview began with an explanation about the future planned study and its procedures. Lumbar puncture (LP) was being considered for inclusion in the planned study, and was regarded as the most intrusive aspect; therefore, subjects were presented two separate study scenarios: one including LPs and the other not including LPs. To assess the influence of the LP, all of the interview questions were asked in sequence first about the LP study, and then repeated for the non-LP study. For each scenario, patients were asked to rate a list of barriers and incentives to participation on a 3-level ordinal scale in terms of intrusiveness or importance. They were further probed with open-ended questions to provide other barriers and incentives not listed by the interviewer. They were encouraged to give examples and vignettes to illustrate their remarks. The interviewer recorded all open-ended comments verbatim.

Analysis

For each study protocol, descriptive statistics were calculated for overall stated participation rates, strongest disincentives, reasons for refusal, barriers, and motivators. Comparisons of participation rates between protocols and among subgroups were performed with chi-square tests. The qualitative analysis used an adaptation of the Framework Approach to categorize data and identify themes (18). Two individuals (JA, SKI) coded the themes. Verbatim

quotations were provided to highlight important themes. All statistical analyses were conducted using SAS Version 9.1 (SAS Institute, Cary, NC).

RESULTS

Of 58 elders approached, 50 (86%) agreed to be interviewed for this study. In general, this was an older population, with a mean age of 78.4 ± 5.7 years, with 50% from the primary care medicine clinic and 50% from the pre-anesthesia clinic. Of the 50 participants, 28 (56%) were female, 22 (44%) were married, and 40% were nonwhite, including 19 (38%) African-American and 1 (2%) Hispanic. When the 50 participants were asked about their willingness to participate in the hypothetical study (See Methods), 38/50 (76%) stated that they would be willing to participate in the protocol without LP, while 32/50 (64%) stated they would be willing to participate if the LP was included.

We then examined correlates of willingness to participate in the proposed research. Single elderly subjects were significantly more likely to state willingness to participate than married subjects (non-LP protocol: 22/28 single vs. 10/22 married, $p=0.02$). Interviewed seniors stressed that recruitment efforts were more likely to be successful if spouses and family members were involved. One participant noted,

“I have been married 52 years and my wife is my biggest support, I can’t involve myself in anything no matter how strongly I feel about it unless she approves, I think it is best that her and my children be present when I am being asked about such things. After all they will be as involved in the research as I since they will have to bring me here.”

When asked about preference for location of study participation, the vast majority of participants (49/50, 98%) preferred to be studied in their own homes, rather than traveling to a study site. In fact, 14 (28%) reported that they would not participate in the study if they had to travel to the hospital. One participant stated,

“It takes me 20 minutes to go to the bathroom by myself. My kids took my car keys away 2 years ago and I am dependent on someone else for all my daily needs. It is unreasonable to expect me to come to the hospital again and again for research.”

To assess the impact of lumbar punctures on participation, the interview questions were repeated with and without LPs. Table 1 indicates the strongest disincentives to study participation under the two study scenarios. For the protocol including LP, the LP was the strongest disincentive, cited by over half of participants; no other disincentive was cited as strongest by more than 12%. Importantly, many participants stated that a strong disincentive would not necessarily result in refusal to participate in the study. Among the 18 patients who stated they would refuse participation, Table 1 indicates the leading causes for refusal; again, only lumbar puncture was cited by more than half (61%). However, of the 11 participants who initially stated they would refuse the study due to the lumbar puncture, three later said they would be willing to participate in the study if their own physician encouraged them to participate. One participant stated,

“I don’t like the idea of a spinal tap (lumbar puncture) and have heard bad things about it, but I trust my doctor and if he tells me there is no risk I will participate”.

Without LP, the 3 most frequently cited disincentives were phlebotomy in 36%, an interview of ≥ 90 minutes in 24%, and MRI brain scan in 12% (Table 1). Among the 12 patients who stated they would refuse participation in the non-LP study, the leading causes were phlebotomy, MRI brain scan, and spouse refusal (Table 1). Notably, the refusal rate was not significantly higher in the LP protocol compared with the non-LP protocol (18/50 vs. 12/50, $P=0.19$). However, the primary reasons for refusal were qualitatively different. Repeated phlebotomy

was only third most important reason for refusal in the LP study (after LP and MRI); it became the most common reason for refusal in the study without LP.

“It hurts to get blood taken out. I don’t like that every time I have to come and get it done, but I can’t help it if the doctor needs it. I will not do it for a research study”.

Long study duration was an important barrier in 10%, as exemplified by one patient,

“The only problem I see if you want me to be a part of this is that I might not be around for the wrap-up and I want to be there when the results come in, so maybe if it was something shorter say one year or so, I would say yes.”

Other barriers included patients’ views that they were too sick to participate in 10 (20%), that the research was a “waste of time” in 5 (10%), and that older persons should not be bothered in 2 (4%). Importantly, 20 (40%) patients did not believe in the importance of clinical research or distrusted researchers, as exemplified below,

“I have seen that research is mostly an attempt by these big hospitals and companies to prove they are do-gooders. I have no faith in them. They are here just to make money.”

Leading motivators for study participation for those who would agree to enroll are indicated in Table 2. The 4 leading motivators were similar between the study with and without LP and included the opportunity to benefit mankind, ability to learn more about the disease under study, personal benefit, and having something to do. Most patients rated free meals as unimportant, and monetary stipends were rated as the leading motivator by only one participant. As an example of personal benefit, one participant stated:

“I am a very sick man, I spend most of my free time either taking medication or visiting doctors and nurses. If participating in a study can ensure that I will be treated well and with respect, I would do it without thinking.”

Leading incentives for participation included: provision of transportation (if required) and free parking (90%); flexible appointment times that did not interfere with their schedules (76%); provision of written results (62%); monetary stipend (50%); and provision of educational materials or newsletter (46%). In terms of educational incentives, one participant stated,

“I would like to know what results you get, I like to keep myself aware of new discoveries. If there is a free newsletter I’d like to receive it.”

Other incentives cited by some respondents included free or early diagnosis of problems (40%); providing assistance with medical treatment or access to healthcare (36%); providing education about their health condition (36%); and bringing older people together with similar problems and providing socialization (10%). One participant stated:

“My mother was never the same after her surgery, I would love to be a part of research that helps figure out what happened to her”.

The results regarding monetary stipends were mixed. While monetary stipends were considered important by 25 (50%), another 10 (20%) stated that they believed that the study was a “noble cause to benefit mankind” and that it was unethical for participants to expect a monetary benefit. One participant stated,

“If I participate in this research and help you guys find out more about Alzheimer’s Disease or delirium, it will be the most important thing I ever did in my life. I think it is immoral to translate such a noble cause into money.”

Another participant stated,

“Maybe some people will do this for money. I will do it because it is God’s work and money should not be a part of this.”

Based on our study results, we have identified several study solutions to address identified barriers or incentives (Table 3). Patients will be interviewed in their homes whenever requested, and intrusive procedures will be minimized (i.e., phlebotomy will be minimized by adding tests to clinical blood draws whenever possible; the duration of the interviews will be minimized to less than 75 minutes). Education and counseling about the study procedures will be provided for spouses and family members to encourage participation. In addition, identified incentives will be provided throughout the study, including transportation, free parking, flexible appointments, written results, monetary stipends, and educational materials/newsletter. These solutions will be put into place for the proposed study to maximize participation and retention.

DISCUSSION

We identified barriers and motivators for research participation among a group of community dwelling elders who are at high risk of hospitalization or scheduled for major surgery. While the majority of this vulnerable older population expressed a willingness to participate in the study (64% in the protocol with LP and 76% in the protocol without LP), the decision to participate appeared to be influenced heavily by the perceived intrusiveness of the study weighed against the perceived benefits of participation (8). The strongest contributors to perceived intrusiveness included LP, repeated phlebotomy, MRI brain scans, and long duration of interviews with neuropsychological testing. Notably, altruistic motivation (i.e., the opportunity to benefit mankind) was a strong motivator for the majority of subjects, and in fact, many viewed study participation as their chance to leave a lasting legacy or as the “most important thing they would ever do in their lives”, particularly as they perceive themselves drawing near the end of life. This has been documented in previous studies (19). Other motivations included educational or other personal benefits, and the chance to socialize with study staff and participants. Interestingly, a monetary stipend was not considered important by the majority of participants, and in fact, was felt not to be indicated by many. Thus, perceptions on the importance of monetary stipends may differ between study investigators and participants.

The strengths of this study include the detailed interviews on a representative cross-section of patients who would be eligible for the actual study. In addition, the study included representation of diverse patients from both medical and surgical clinics. Finally, the questions were asked in a general way, and provided open-ended responses that would extrapolate broadly to other types of studies.

Several important caveats deserve comment. First, this study is based on self-report information, and patients may not actually do what they say. Thus, the enrollment rates in the actual study may not reflect the stated participation rates. To account for larger potential refusal rates, the screen to enroll ratio for the future study will be inflated beyond that required by the current data. In addition, for this study, the patients were selected based on a high risk for hospitalization and were interviewed about a specific future planned project; thus, the results might not extrapolate to all study populations or study types. Future work will be required to extrapolate the results to less vulnerable populations, and to compare medical and surgical populations, which was beyond the scope of our present study. However, the findings carry face validity, correlate well with findings from previous studies (7-13). We therefore believe the results have broader applicability and relevance to other clinical research. Finally, the sample size was relatively small and representation of Hispanic and Asian minority populations was low, due to language barriers. These factors may limit the generalizability of our findings.

From this study, specific strategies to directly enhance participation in the planned study have been developed and refined. These strategies may have broad applicability to clinical research studies in the older population. Importantly, this study may also serve as an example of a useful preliminary study during the planning stages for large clinical research studies. Given the challenges of assuring adequate recruitment, studies of this type may be essential to develop optimized recruitment and retention procedures customized to the target population and the specific study procedures prior to initiating any research study.

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TABLE 1

BARRIERS TO STUDY PARTICIPATION*

Leading barrier identified	Study with lumbar punctures		Study without lumbar punctures	
	Strongest disincentive	Primary cause for refusal	Strongest disincentive	Primary cause for refusal
	(N=50)	(N=18)	(N=50)	(N=12)
	n (%)			
Lumbar puncture	27 (54)	11 (61)	--	--
[†] MRI brain scan	6 (12)	4 (22)	6 (12)	3 (25)
Long interview/neuropsychological testing [‡]	5 (10)		12 (24)	
Enrollment during illness	5 (10)		7 (14)	
Long study duration	3 (6)		5 (10)	
Repeated phlebotomy	2 (4)	1 (6)	18 (36)	7 (58)
Spouse refusal	2 (4)	2 (11)	2 (4)	2 (17)

* Both studies include interviews, neuropsychological testing, MRI brain scans, and phlebotomy

[†] MRI= magnetic resonance imaging without intravenous contrast

[‡] Defined as 90 minutes or longer

TABLE 2
MOTIVATORS FOR STUDY PARTICIPATION*

Leading motivator identified	Study with lumbar punctures	Study without lumbar punctures
	(N=32)	(N=38)
	n (%)	
Benefit mankind	18 (56)	18 (47)
Learn about disease(s) under study	5 (16)	5 (13)
Personal benefit	4 (13)	7 (18)
Something to do	3 (9)	6 (16)
Benefit study physician(s) or hospital	1 (3)	1 (3)
Incentives/stipend	1 (3)	1 (3)

* Both studies include interviews, neuropsychological testing, MRI brain scans, and phlebotomy. Includes all participants who did not refuse study participation

TABLE 3

SOLUTIONS TO MAXIMIZE STUDY PARTICIPATION (N=50)

Barrier identified (n)	Study solution
Traveling to study site (49)	Interview in patient's home whenever requested
Repeated phlebotomy (18)	Minimize blood draws by adding on study tests to planned draw in clinic
Duration of interviews > 90 minutes (12)	Minimize duration of assessments (75 minutes maximum)
Spouse refusal (2)	Education and counseling for spouse and family members (including educational materials, available staff)
Incentive identified (n)	Study solution
Provide transportation if needed (45)	Study will provide transportation whenever needed for interviews
Provide free parking (45)	Study will provide parking vouchers for all interviews
Provide flexible appointments (38)	Interviews will be scheduled at the participant's convenience
Provide written results (31)	Study will make available results of neuropsychological testing as requested
Provide stipend and other incentives (25)	Study will provide stipend and other incentives for all participants
Provide educational materials (23)	Study will publish a quarterly newsletter with educational materials and study updates