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Understanding why older people participate in clinical trials: the experience of the Scottish PROSPER participants

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Abstract

Background: over the next 20 years it is anticipated that there will be a significant increase in those aged 75 and over, and a consequent increase in cardiovascular disease, cancer and chronic illness. As this shift takes effect, there will be an increased need for treatment strategies that are of known benefit to this age group and a consequent rise in demand for clinical trials that are conducted specifically with the older population. Because factors that motivate older individuals to participate in clinical trials may differ from those that influence younger adults, it is important to evaluate the strategies used to encourage recruitment and retention and to determine how appropriate these are.
Aim: evaluation of the reasons why subjects agree to participate in a controlled clinical trial of vascular disease prevention and the strategies used to improve compliance and protocol adherence.
Setting: Scotland.
Subjects: 2,520 Prospective Study of Pravastatin in the Elderly at Risk participants, aged 70–82 with either pre-existing vascular disease or at least one major vascular risk factor (hypertension, cigarette smoking, or diabetes mellitus).
Design of study: two-stage iterative survey. Stage I was exploratory.
Results: curiosity, or an interest in finding out more about the study, 'a desire to support research', and anticipated personal benefits, such as health screening, were the most important motivators for generating initial interest in the trial. Ongoing health monitoring was the most important recruitment and retention motivator ($P = 0.001$).
Conclusions: curiosity, self interest and altruism may act as motivators at different points in the study time-line. However, fostering positive relationships between staff and recruits, and keeping recruits informed about the progress of the study are likely to maximise the retention of older subjects to long-term trials.

Keywords: *PROSPER, ageing, randomised controlled clinical trial, recruitment, retention*

Introduction

Projected estimates of demographic changes anticipate that in the period 1996–2020, the global population of older people will have risen at twice the rate of the total population. An even greater increase is expected in those aged over 75 years with a subsequent rise in cardiovascular disease, cancer and chronic illness [1]. These changes are likely to result in a greater demand for health strategies that are of known benefit for the prevention and treatment of disease in older individuals. However, identifying these will be particularly problematic in an older population [defined by the United States Food and Drug Administration (U.S. FDA) as ≥65 years] [2] because of the higher incidence of co-existing disease, multiple drug dosing and altered drug metabolism [3–5]. In clinical trials, such problems make it difficult to evaluate the effects of new treatments and may explain why, traditionally, older individuals have been excluded from clinical trial participation on the basis of advanced age [6].

The FDA has expressed concern about the lack of information regarding variation in drug response across different age and ethnic groups [2]. These concerns may influence

trial sponsors and investigators to ensure that older people and ethnic minorities are proportionately represented in future. However, subject recruitment into trials and patient retention within them are, in general, problematic [7], particularly in pharmacotherapeutic trials that have a placebo arm [8]. Although it is not clear whether age influences recruitment and retention [9], factors that motivate younger adults to participate may differ from those that influence older individuals. Therefore, strategies may be required that are specifically tailored to the needs, concerns and motivations of the older adult.

Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) was a randomised, double-blind, placebo controlled multi-centre trial conducted over a 5-year period between 1997 and 2002. Its aim was to determine whether using pravastatin to lower cholesterol reduced the risk of major vascular events in an older population. The study recruited 5,804 patients based in three centres (Cork, Glasgow and Leiden) who were aged 70–82 years of age and had either pre-existing vascular disease or at least one major vascular risk factor (hypertension, cigarette smoking, or diabetes mellitus) [10].

Recruitment was initiated by inviting patients ≥70 years of age to attend their GP surgery for a health check and initial screening visit. Eligible patients were randomised to receive either active treatment (pravastatin 40 mg) or placebo. Eligibility criteria [10] and primary results [11] are published elsewhere. Study follow-up consisted of a 3 monthly health check for a minimum of 3 years. In recognition of their contribution to the trial, and to maintain communication, recruits received an annual newsletter, an invitation to a lunchtime meeting and, a variety of 'token' gifts.

The purposes of this study were threefold: (i) to identify why PROSPER subjects choose to participate in the study; (ii) to examine factors that supported continuation in the study; and (iii) to evaluate the strategies developed by the Scottish arm of the PROSPER team to enhance compliance and protocol adherence.

Methods

A two-stage retrospective survey of 2,520 men and women aged 70–82 years who participated in the Scottish arm of PROSPER. The three study time-points identified for investigation were: initial invitation; enrolment; and study persistence.

Stage I

A semi-structured questionnaire was mailed to 2,472 Scottish participants following their enrolment to the study. The purpose of Stage I was: to explore why recruits responded to the initial PROSPER invitation letter, and subsequently enrol in the study; to identify recruits' perceptions of the study.

Stage II

We contacted 2,228 PROSPER recruits directly or indirectly about Stage II of this study (292 died before their final study visit). This involved the use of a structured close-out questionnaire developed from the results of the exploratory questionnaire, relevant recruitment and retention literature, and data held at the Scottish Clinical Trials Unit. Ranked response questions were used to (i) identify which factors most influenced Scottish recruits' decisions to enrol in PROSPER, (ii) continue until study close-out and (iii) to evaluate the strategies used by the PROSPER team to support continued participation.

Both questionnaires were piloted before their use in the main study. The close-out pilot population ($n = 50$) was not included in the main study.

Statistical methods and analysis

Data were analysed using SPSS™ Version 9.

In Stage I, all closed response questions were analysed using frequency counts. A consecutive sub-sample ($n = 470$) of open question responses were analysed using a content analysis procedure. For the sub-sample, sample size was determined at the point of data saturation [12].

In Stage II, ranked data were analysed using Friedman's test for multinomial variables and Wilcoxon signed rank for paired data. Unpaired data were analysed using a Kruskal–Wallis test. Where categories were combined and data were treated as nominal, a chi-squared goodness of fit test was used. As in Stage I a content analysis procedure was used to analyse open responses [12].

Results

Stage I

In Stage I, an overall response rate of 58% ($n = 1,439$) was achieved. Please see Appendices 1, 2 and 3 (available as supplementary data at http://www.ageing.oupjournals.org).

Motivators for positive response to initial invitation and enrolment

Seven main categories were identified as motivators resulting in a positive response to the initial invitation letter and subsequent study enrolment (Table 1). Overall, 'personal benefit' and a desire to support research were the most frequently cited enrolment motivators. However, in the pre-screening phase, 'curiosity' prompted most positive responses ($n = 86$).

Once enrolled, personal benefit, in particular the health checks received, and altruistic motivators such as 'supporting research' or 'helping others', were perceived to be the most positive aspects of participation.

Stage II

Of the 2,178 Scottish PROSPER recruits contacted about Stage II of the study 1,417 responded. Therefore an overall response rate of 65% ($n = 1417$) was obtained. Of these respondents, 61.9% ($n = 878$) also commented openly on their general perception of PROSPER and the recruitment experience.

Motivators for continued participation

The close-out results confirmed those of the exploratory questionnaire that most recruits enrolled in the study because of self interest ($n = 607$; 52.9%) (defined in this study by factors such as 'health checks' or 'peace of mind') or altruism ($n = 455$; 39.6%) (defined by factors such as 'help research' or 'help others'). However, ranked response

Table 1. Factors motivating PROSPER recruits ($n = 470$) to respond positively to the initial invitation letter and subsequently enrol in the study as reported by recruits following study enrolment

	Initial response*		Enrolment**	
Motivators	*n*	(%)	*n*	(%)
Curiosity/interest	86	(19.6)	11	(2.4)
Support research	78	(17.8)	102	(22.8)
Personal benefit	70	(15.9)	111	(24.8)
Input of health care professionals	52	(11.9)	29	(6.5)
Impact of vascular disease on self/others	47	(10.7)	73	(16.3)
Help others	46	(10.5)	61	(13.6)
Self-interest and to help others	22	(5.0)	39	(8.7)
Other reasons	37	(8.4)	22	(4.9)
Total	438	(100)	448	(100)

Missing data = *32, **22.

questions indicated that the number in the former group was significantly higher ($P = 0.001$) (Chi squared). Self interest was also the most significant incentive for continued participation ($P = 0.001$) (Chi squared).

Respondents motivated to continue in the study for reasons other than self interest did so mainly to find out the outcome of the study ($n = 216$) or because of interactions between themselves and the study team ($n = 180$).

Acceptability of study incentives

Respondents' rankings of the study incentives (1, least preferred; 9, most preferred) indicated that three were favoured over the others (Table 2). A millennium calendar with prints of local (Scottish) landmarks was ranked first choice with the lunch-time meeting and annual newsletter ranked second and third choice, respectively ($P = 0.001$) (Friedman; Wilcoxon signed rank).

Lunch-time meeting

Regardless of gender, the social aspect of the lunch invitation was significantly ($P = 0.001$) more important to attendees than the lunch itself. Most recruits attended in order to meet the medical staff involved ($n = 239$), meet other recruits ($n = 196$), or obtain information about the progress of the study ($n = 149$). Of those who did not attend lunch, and indicated why ($n = 484$), lack of time ($n = 250$), mostly due to having another appointment, was significantly more likely to account for non-attendance than venue ($n = 95$), disinterest ($n = 83$) or illness ($P = 0.001$).

Annual newsletter

Newsletters were read by most respondents ($n = 1302$). However, the most favoured topics were those that provided information about the set-up and progress of the study (Table 3) (Friedman; Wilcoxon signed rank). Although men were more likely to rank the newsletter higher than were the women ($P = 0.001$) (Kruskal–Wallis), there was no significant difference in their ranking of preferred topic.

Perceptions of PROSPER and the recruitment experience

Four main categories ('Trial Staff', 'Perceived Benefits', 'Self Esteem' and 'Personal Sentiments') were identified from recruits' comments about the recruitment experience.

Table 2. Study incentives ranked by respondents ($n = 929$) in order of preference

Study incentives	Mean rank (1 least preferred, 9 most preferred)
Millennium calendar	6.46
Lunch invitation	5.93
Newsletters	5.72
Card holder	5.31
Year calendar	5.25
Key ring	4.78
Post-it pad/pen	4.71
Pen emblem	4.40
Competition	2.43

Table 3. Newsletter topics ranked by respondents ($n = 1120$) in order of preference

Newsletter topics	Mean rank (1 least preferred, 9 most preferred)
Study set-up	6.93
Study progress	6.86
Health advice	6.0
ECGs	4.82
Your questions answered	4.69
Nurse's profile	4.63
Data centre	4.12
Study team	4.01
Biochemistry lab	2.95

Trial staff, in particular the research nurses who monitored recruits' progress, were perceived as 'caring', 'friendly', 'competent' and 'efficient'. Many respondents commented that they felt 'looked after', 'safe', or 'special' while taking part in the study and expressed gratitude for the researchers' 'concern for the elderly'.

Discussion

Previous studies have identified many variables that impact on the recruitment and retention of clinical trial subjects. Often, it is not possible to identify whether results are applicable to recruitment in general, or only to a particular

phase of recruitment. Our results show that personal benefit and altruism motivated more individuals at the point of enrolment. However, during the pre-enrolment phase, 'curiosity' prompted more positive responses. Mattson *et al.* [13] also identified 'curiosity' to be an important motivator, although numbers were small in comparison to the other motivators reported. However, Mattson *et al.* were investigating motivators for enrolment [13]; therefore, it could be argued that if 'curiosity' is satisfied during the pre-enrolment stage, other motivators such as personal benefit and altruism [8, 13, 14] will supersede it.

Personal gain and altruism encompass a number of factors and it is not always clear whether one is more influential than the other. However, the respondents in our study stated factors associated with the former significantly more often. Moreover, regardless of primary motivation for joining the study, when given the opportunity to provide a personal view of PROSPER and the recruitment experience, many respondents chose to re-iterate these benefits. Given that study enrolees are thought to be significantly more concerned about their health than non-enrolees [15], and that older individuals worry more about their health than younger adults [16], regular health monitoring may be an appropriate and ethical [17, 18] recompense for older trial recruits.

It is not clear whether the use of incentives in clinical trials influences recruitment and retention rates. Recipients of PROSPER incentives rated 'token' gifts lower than the annual newsletter and lunch meeting. It is worth noting that articles relating to study progress were the most favoured topics in the newsletter while the most appealing aspect of the lunch time meeting was the opportunity to meet the investigators and other recruits, and to find out more about the study. Since older adults, in general, prefer face to face as opposed to written contact [19], it is possible that the newsletter and lunch time meeting provided by PROSPER helped recruits 'put a face' to those involved. Furthermore, respondents clearly indicated that the relationship between themselves and study staff was very positive. Therefore, although continued health monitoring was the most significant factor for persistence in PROSPER, it is likely that in the absence of positive staff–participant relationships it might have been less so.

Limitations of the study

The extent to which the results of this study can be generalised are limited by the response rate achieved and because it was not possible to identify whether the motivations of non-responders differed from those of responders. However, mailed questionnaires often have a response rate <60%, and as individuals, particularly those with cognitive or physical disability, are likely to have more difficulty completing questionnaires than others [12] we believe that the response rate was acceptable. Moreover, as PROSPER participants were recruited from a random sample of elderly people at risk of vascular disease [10], there is no reason to suggest that those who did not respond differed significantly from those who did.

Conclusion

Curiosity is an important pre-enrolment motivator and should therefore be fostered early to optimise study recruitment.

At the point of enrolment, there may be a greater need to emphasise the potential personal benefits for recruits themselves and for future generations. However, feeling involved in, and being kept informed about, the study will help recruits foster a positive attitude toward the study and maintain recruits' interest in it. Such strategies are likely to maximise retention of older subjects to longer term clinical trials and have a greater impact on study persistence than the provision of token gifts.

Recruitment may be enhanced if the motivators identified in this study are adopted for use in future studies. However, it may be beneficial for future researchers to build into the study plan a means of identifying reasons for non-participation.

Key points

- Curiosity is an important pre-enrolment motivator for older adults.
- Perceived personal health benefits and altruism are important enrolment motivators.
- Keeping recruits informed about the progress of the trial helps retain interest and maximise retention.
- Regular health monitoring may be an appropriate and ethical recompense for older recruits.

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Loss of partner and suicide risks among oldest old: a population-based register study

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Abstract

Background: while mortality among the oldest old has improved over recent decades, these improvements are not reflected in the suicide mortality of this age group. We do not know the reasons why the suicide mortality is still very high among the oldest old.
Objective: the aim is to analyse the impact that loss of a partner has on the suicide risks of the oldest old (80+) compared to younger age groups.
Subjects: the entire Danish population aged 50 during 1994–1998 ($n = 1{,}978{,}527$).
Methods: we applied survival analysis to calculate the changes in relative risk of suicide after a loss by using individual-level data.
Results: the majority of older persons who commit suicide are widowed, although only a relatively small proportion of the oldest old who commit suicide have experienced a recent loss of partner (men: 18%, women: 6%). In absolute terms, the oldest old men experience the highest increase in suicide risk immediately after the loss (15-fold; 95% CI 10.2–23.6) compared to middle-aged men who are still married. Oldest old men seem to suffer more from the loss and need longer time to recover than women.