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Strategies to exclude subjects who conceal and fabricate information when enrolling in clinical trials

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ABSTRACT

Clinical trials within the US face an increasing challenge with the recruitment of quality candidates. One readily available group of subjects that have high rates of participation in clinical research are subjects who enroll in multiple trials for the purpose of generating income through study payments. Aside from issues of safety and generalizability, evidence suggests that these subjects employ methods of deception to qualify for the strict entrance criteria of some studies, including concealing information and fabricating information. Including these subjects in research poses a significant risk to the integrity of data quality and study designs. Strategies to limit enrollment of subjects whose motivation is generating income have not been systematically addressed in the literature. The present paper is intended to provide investigators with a range of strategies for developing and implementing a study protocol with protections to minimize the enrollment of subjects whose primary motivation for enrolling is to generate income. This multifaceted approach includes recommendations for advertising strategies, payment strategies, telephone screening strategies, and baseline screening strategies. The approach also includes recommendations for attending to inconsistent study data and subject motivation. Implementing these strategies may be more or less important depending upon the vulnerability of the study design to subject deception. Although these strategies may help researchers exclude subjects with a higher rate of deceptive practices, widespread adoption of subject registries would go a long way to decrease the chances of subjects enrolling in multiple studies or more than once in the same study.

1. Introduction

One of the challenges to recruiting in any clinical trial is meeting targeted goals of recruitment while maintaining the quality of candidates. One of the more significant threats to the quality of research is sampling from the population of subjects who enroll in multiple clinical trials with the objective of generating income. These subjects, hereafter referred to as “professional subjects,” present a significant risk to the integrity of study designs by providing false information as a strategy for meeting inclusion and exclusion criteria for study enrollment [1–3] and by providing false information about their disease symptoms or medication compliance [4]. Enrolling subjects who use deception in research can substantially undermine the study design by increasing the sample size needed to detect a treatment effect [5]. The impact of the problem is not widely understood and it is unlikely that investigators make sample size assumptions that account for subjects who use deception to gain entry to a study and provide false information while enrolled in the study.

Although investigators may operate with the assumption that subjects are truthful when providing information to researchers, there is mounting evidence that study participants conceal recreational drug use [6], conceal tobacco use [7], lie when answering screening questions [8], enroll in the same study multiple times [9,10], and enroll in multiple studies simultaneously [1,10]. Professional subjects share strategies for evading the restrictive entry criteria of studies [11], share information about upcoming studies using centralized resources online [12], and even have their own smartphone App (“Study Scavenger recruitment App”) to help locate studies based on location, payment, and study topic [13]. It is clear from the literature that subjects use deception, but most of what we know about this is not revealed unless subjects are caught using deception. The true scope of the problem includes both the

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subjects who have been caught using deceptive practices as well as the subjects who have not been caught.

In an attempt to understand how common deception is used by subjects enrolling in research, Devine et al. [1] surveyed 100 "experienced research subjects" recruited from newsprint and online postings to estimate the proportion of subjects who employ deception in research. In this study, the majority of these "experienced subjects" (75%) reported concealing some information from researchers when screening for a study. A significant proportion of subjects reported high rates of concealing information that might exclude them from participation, including participation in more than one study concurrently (43%), health conditions (32%), use of prescribed medications (28%), recreational drug use (20%) and alcohol use (12%). Devine et al. [1] also reported that 33% of subjects admitted to using some form of fabrication to enroll in previous trials; 25% of subjects sampled admitted to exaggerating health conditions to qualify for a study, 14% pretended to have a health problem in order to qualify for a study, and 12% gave researchers false information about symptoms that were the primary focus of the study. Devine et al. [1] also asked subjects about earnings per year and number of studies per year And found that subjects who admitted to using deception averaged $141 US dollars of reimbursement per study in the past year, and reported an expectation of receiving a minimum of $20 (on average) for participating in a study. Professional subjects are known to be attracted to high-paying inpatient phase I studies [3], but these results suggest that studies with reimbursement as low as $20 are also vulnerable to professional subject enrollment. Not all studies are vulnerable to the risk of professional subject enrollment, but some study characteristics may increase the vulnerability including 1) lack of objective testing for primary inclusion criterion (e.g., depressive disorders, anxiety disorders, bipolar and related disorders, pain disorders, substance use disorders), 2) high rates of subject reimbursement, and 3) dispensing study medication that has an inherent potential for diversion.

Although some researchers have offered valuable guidance for reducing the impact of deception in clinical research including using centralized subject registries [14,15], verifying identification through photo ID [16], and using more rigorous assessment [17], there is little published guidance that addresses this problem on an individual site level that may inform recruitment and screening practices. Although the best protection against professional subject enrollment may be widespread adoption of centralized subject registries, single-site investigator-initiated studies that have not enrolled in one of the commercial registries would benefit from building protections into the study protocol. The present paper is intended to provide investigators with a range of practical strategies and suggestions for developing and implementing a study protocol with protections to minimize the enrollment of professional subjects. Given the risk to study integrity that results from subjects concealing and fabricating information in order to qualify for study enrollment, it is important for researchers to have a diverse set of strategies for minimizing the chance of sampling this professional subject population.

2. Strategies

There is no single screening test or method that will likely eliminate the possibility of professional subjects concealing information and fabricating information in order to qualify for a study. A multifaceted approach may provide the best protection against deception in the absence of methods to objectively measure each entrance criterion. The approach described below includes recommendations to minimize deception in research using advertising strategies, payment strategies, telephone screening strategies, and baseline screening strategies. The approach also includes recommendations for attending to subjects' motivation and being alert to inconsistent study data (see Table 1).

2.1. Advertising strategies

At the very outset of conducting a clinical trial, the strategy used for recruitment can have an impact on the rate of professional subject enrollment. Professional subjects are an organized group who search out studies to take part in and share information about trials with high rates of payment [3]. Advertisements, flyers, or other media that includes detailed information about study payments may be a draw for this group of subjects. In studies with a potential for direct benefit, a media campaign that does not mention payments may attract a population that has a more genuine interest in the benefits of research participation than those subjects whose intent is to generate income.

Although it is not intended as a method of advertising, compliance with section 801 of the FDA Amendments Act [18] requires that clinical trials completed in the United States be registered on clinicaltrials.gov. Investigators often include specific information about the inclusion and exclusion criteria for study entrance in the registry, and there is some evidence that professional subjects study this registry and answer screening questions to be consistent with study criteria [1]. Although compliance with section 801 of the FDA is required for many researchers in the US, it is not necessary to provide all of the exclusion criteria within this registry. Limiting the detail of information may increase the rate of screen failure as potential subjects are not aware of the exclusions, but this will also provide some protection against subjects who wish to deceive researchers by eliminating the "study guide" they use before screening.

2.2. Payment strategies

Minimizing subject payments is one strategy to reduce the likelihood of recruiting professional subjects. Models for determining appropriate subject payments have been discussed extensively [19]. However, there is some evidence that increasing payments are related to increasing willingness of subjects to conceal information that would exclude them from enrolling in a study [20]. Although limiting payments could have a negative impact on the rate of subject recruitment, the benefit of limiting the enrollment of subjects who are motivated solely by payments may be a reasonable tradeoff in studies with a high vulnerability to enrolling professional subjects (e.g., clinical trial of narcotic pain medication).

High payments for initial screening visits may make a study vulnerable to professional subjects who are looking for a one-time study payment. Some subjects know that they will not qualify but begin screening with the objective of making money for one visit before being excluded. These subjects may not be a threat to the validity of study data as they will be excluded, but there is a significant cost in staff time to screen them and they occupy screening slots that could be filled with better quality candidates. Over the course of a study, one-session screen failures can undermine the study objectives if they occupy a large proportion of the new subject screening visits to the point that resources are depleted before the recruitment goal can be met. At a minimum, screening these subjects slows recruitment and makes the recruitment phase more costly. Setting a low payment amount for the initial screening visit may deter some of these subjects.

As a further protection against professional subjects who enroll for a one-time payment, one strategy is to withhold any payment for screening if the subject reports a behavior or health condition