The Subject of Recruitment and Retention

Patient-oriented (clinical) research is the link between drug discovery and useful therapeutics, and the cornerstone of any clinical study is the involvement of study subjects. However, it has been estimated that 80% of all clinical trials fail to meet subject recruitment goals, and dropout rates of 15% to 40% are common. Thus, you, as the principal investigator (PI), will be investing significant time and effort in recruiting and retaining participants. This chapter discusses many of the aspects of recruitment and retention, including strategies that foster recruitment and retention success.

Recruitment

Assessing Your Site

Before agreeing to participate in a clinical trial, it is important to evaluate the ability of your practice to recruit patients. You should compare the inclusion/exclusion criteria of the particular protocol to your general patient population and the community at large. For example, a protocol that requires healthy females between the ages of 18 and 35 years would be problematic if your practice comprises mainly older patients. Restrictive inclusion/exclusion criteria may pose a challenge for recruitment. For example, it may be difficult to recruit for a study that seeks elderly persons with osteoporosis but no concomitant conditions, such as hypertension, hyperlipidemia, or diabetes.

You should also review the study protocol to assess the balance between the benefit to the patient versus the risk and inconvenience. It may be prudent to decline a protocol that provides little benefit or is too burdensome.

You may wish to contact several practices that are engaging in similar research to determine information such as enrollment numbers and length of accrual. You should also be aware of recruitment methods used by other research centers in your area by checking local media outlets (newspapers, Internet sites, radio/television spots). Reviewing active clinical trials in your clinic and surrounding communities will help ensure that your study will not compete for subjects. You may want to delay the start of a study if other ongoing trials involve a similar patient type. However, potentially competing studies may be complementary, with subjects failing screening for one satisfying the criteria for another. An example might be a psoriasis trial of a systemic medication requiring 10% body surface area (BSA) and one that involves a topical medication in patients with less surface involved. As some communities experience seasonal population fluctuations, time of year may influence recruitment. Furthermore, the disease or condition under study may be seasonally influenced, such as worsening atopic dermatitis and psoriasis during the winter and worsening superficial fungal infections during the summer.

Recruitment Methods

Any successful recruitment plan has two key steps: 1) raise awareness about the trial among potential subjects; and 2) once a potential subject has contacted you, provide the appropriate information so an informed decision can be made regarding participation.

The first population to approach is your practice. Patients in your care may be more willing to participate based on your recommendation because your opinion is one they trust. Many office practice software is capable of generating a list of patients with a specific diagnosis.
In our experience, telephoning patients you have identified to inform them of the trial is more effective than sending a mailing if the number of patients is manageable. The Study Coordinator should clearly state that he or she is calling on your behalf regarding the study, and a script should be prepared so that all important information is conveyed. Mailings should contain the purpose of the study, as well as the participant parameters, information about the disease state, how long and involved their study responsibilities will be, and a balanced description of the benefits and risks of the study, plus contact information. Because you will need to provide a thorough description of the study when you obtain informed consent (more on that below), this letter can be brief (see example 1). Another method of informing your patients about the trial is to prepare a fact sheet, which provides details regarding a particular trial, and display it in your waiting room (see example 2). It is important to note that any material involved with the recruitment process, including the fact sheet, letter, and the script, must be approved by your site’s Institutional Review Board (IRB). In most cases the sponsor is also interested in reviewing the materials to ensure accuracy.

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Oregon Dermatology Research Center

July 14, 2007

Fellow Members of the Oregon Dermatology Society:

Oregon Dermatology Research Center is currently enrolling pediatric patients aged 4-17 years with moderate to severe psoriasis.

This study is being sponsored by Vitality Pharmaceuticals and involves treating this age group with an experimental topical agent. So far the response to the drug has mirrored that of the adult population.

Patients will be paid for their time and travel and will receive the drug free of charge.

This study presents an opportunity for deserving patients who otherwise might not have access to this treatment.

We would appreciate any referrals that you might have in this age group. If you have any questions about the study, please do not hesitate to contact us at XXX-XXX-XXXX.

Respectfully Yours,

John Smith, MD
Jane Jones, MD

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Example 1. Letter to local physicians for referrals to the clinical trial.
DO YOU HAVE TOENAIL FUNGUS?

Males and females, aged 16-75 years, are needed to participate in the research study of an investigational drug for **FUNGUS OF THE TOENAILS**. There is no charge for study visits or study procedures. Requires 8 visits over a 52-week period. Qualified subjects will be compensated for their time and travel.

The study is conducted by:

**Dr. John Smith and Dr. Jane Jones**
_of ABC MEDICAL RESEARCH CENTER, P.C._
100 ABC Street
Adjacent to Hampton Square

Call: **XXX-XXX-XXXX** and ask for **Toni** for more information

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*Example 2. Trial fact sheet or print advertisement.*

The introduction of the Health Insurance Portability and Accountability Act (HIPAA) has changed study recruitment in the United States. Contacting your own patients about a clinical trial is allowed, but you must use caution if you want to contact patients under the care of another physician, unless that physician’s practice is covered by the same HIPAA consent. Sending letters requesting referrals from local physicians may be effective, and would be appropriate under HIPAA guidelines because the other physician would be the initial contact for the patient. Also, health maintenance organizations and other third-party payers, as well as large medical centers, often have extensive databases of patients, but may require a substantial fee. Because HIPAA prevents you from contracting these patients directly, it may be beneficial to partner with these organizations, who would then contact their patients on your behalf. A fee for the organization’s time would most likely be involved, but it may be worth considering if other avenues of recruitment prove unsuccessful. Posters about the trial displayed in community clinics and hospitals may also be successful and avoids HIPAA restrictions because the patients would be contacting you.

You may also identify potential participants through conducting a mass mailing. A list of potential subjects may be attainable from a national patient-oriented organization (eg, the American Diabetes Association, National Multiple Sclerosis Society) or a local chapter (eg, the New Jersey chapter of the American Heart Association). Again, due to HIPAA, the organization would have to distribute the mailing on your behalf.

Media campaigns are a common method of informing the greater community about your trial, and may include print, radio, and/or television. The choice of which media outlet is determined by the success of past recruitment attempts, the receptiveness of the local population to the various media channels, and the advertising budget for the particular trial.

*Newspaper Advertising*

Deciding on the newspaper in which to advertise your research study should be based on the population that you want to reach. If you need a specific ethnic, gender, or age group you may want to investigate specialty publications, but the daily newspaper may be the best choice if a broad population is desired. To determine if you should advertise during the week or on the weekend, you can acquire circulation numbers from the newspaper’s marketing department who should also know the
demographics of their readership. For example, an advertisement in the Entertainment section may reach a younger audience than an advertisement in the World News section. The size of the advertisement and the frequency of publication will most likely be dictated by your budget; however, the key elements should include the demographics of the target population, the purpose of the study, and contact information. If you practice out of a large clinic or hospital, your facility may have restrictions governing the use of their logo. Example 2 represents a short print advertisement. As mentioned previously, your IRB will need to review and approve the advertisement before you can submit it for print.

Radio Advertising

Radio may be more expensive than newspaper advertisement, but may be a more targeted approach to reaching the desired population. Radio stations exist for a variety of music preferences, which often translate into different ethnic, cultural, gender, and aged listeners. For example, radio stations that play top 40 hits may appeal to younger individuals, and Spanish-speaking stations may be a good way to recruit a Hispanic population—just make sure that the advertisement is in Spanish. When deciding to place a radio advertisement, you should consider many of the same factors as for newspaper advertisements: day of the week, time of day, and frequency. Radio stations know their demographics and can assist you in finding the best avenue for reaching your target population. In many cases, a single company will own several radio stations, each with different audience demographics. In some cases, radio ads might be run on several stations at different times. Costs could be prohibitive depending on the market. For example, a single ad placed on a popular New York City FM station might exceed the cost of placing the same ad in a smaller market for two consecutive weeks.

Television Advertising

Television may be the most expensive medium, but it may also be the most effective. Television advertising possesses many of the same characteristics as radio and involves the same decision-making process. The benefits of television over radio include an even more targeted approach (a multitude of cable channels exist), and the person who hears your message is usually in an environment conducive to writing down the relevant information, unlike radio, which is frequently listened to while driving, necessitating the listener to remember the information for the duration of the trip. Scripts used for radio or television advertisements will need to be approved by your IRB.

Internet Advertising

With the Internet, several other avenues exist for promoting your clinical trial. Web sites, like CenterWatch Clinical Trials Listing Service™, maintain a database of clinical trials that patients can search. While there is a fee to the clinical trial organizer for this service, the sponsors of the study may post the trial on their own patient-oriented Web site for no charge. Other Web sites may also facilitate recruitment, such as those supported by national disease organizations (eg, American Cancer Society) or patient support groups (eg, Colon Cancer Alliance). In addition, e-mail can facilitate mass mailings, but the same HIPAA concerns that apply to postal mail also relate to e-mail.

An important but often disregarded component of successful recruitment is having a system to respond promptly and appropriately to any contacts from potential subjects. A dedicated phone line and clinic employee should be designated for recruitment. This person’s responsibilities include maintaining a phone log, ensuring that calls are returned within 24 hours, and reporting the recruiting status of each study on a scheduled basis. A telephone script describing each study should be developed and approved by the investigator and IRB. This script should include a very brief overview of the study
disease and major inclusion/exclusion criteria, study length, number of visits, medication(s) under study, and compensation when appropriate. Care must be taken not to “phone screen,” and not to instruct subjects regarding their disease or care. It is appropriate to describe the study and, if the prospective subject is interested, make an appointment for him/her to visit the clinic for a discussion with the investigator about the protocol and informed consent issues. The recruiting staff should then be able to quickly schedule a clinic visit for any potential subject.

Barriers to Recruitment

The majority of individuals who are eligible for a clinical trial choose not to participate. Reasons for not participating include being unaware, inconvenience, concern over experimentation, potential lack of health benefit, and physician influence. In addition, treatment of conditions that may lead to denial of insurance coverage are strong disincentive to research participation.

Addressing these concerns is an important part of the recruitment process. Obtaining proper informed consent is critical and provides an excellent opportunity to explain all of the risks and advantages of participating in the trial. Potential subjects who are adequately informed are more likely to participate because they can see the benefits to their own health, a top reason individuals agree to participate.

Retention

It does little good to recruit subjects only to have the majority of them discontinue the study. Having a patient-centered approach to the conduct of a clinical trial to retain participation is essential.

As mentioned previously, informed consent is critical to patient recruitment and retention. A chapter has been devoted to informed consent, but a discussion about how it relates to the retention of participants is presented here. The role of the informed consent process is to ensure the balance between the benefits to the subjects versus the risks/inconvenience, and to clearly define subject responsibilities, such as adherence to the assessment schedule and appointment windows, maintenance of diaries and medication logs, and the need for laboratory studies. This will help prevent dropout because the participants will not be surprised by any of the procedures. Adverse events are one of the most common reasons for discontinuation, but if subjects are aware of the extent of the possible side effects, they may be more tolerant of mild or transient uncomfortable events. Also, patients often prematurely discontinue a study because they do not perceive benefit; however, some therapies take time to show activity, and subjects who are aware of this may be more likely to finish the trial even if positive effects are not initially apparent.

The informed consent document must be thoroughly reviewed by the potential participant, but to guarantee that the individual understands the document and the specifics of the trial, you, the principal investigator (PI), should also personally speak to the individual. You should both ask for and answer questions from the individual, so that you can confirm that he or she has a good understanding of all relevant aspects of the study. The decision to participate in the trial should be made jointly between you and the potential subject. How you interact with each person seeking to enter your trial has a significant impact on both the recruitment and retention of this person.

The experience of the potential subjects during the enrollment phase will influence their opinion of the entire process and their decision not only to start the study, but also to continue until its completion. It is important for the PI and the Study Coordinator to establish a personal relationship with the subject at the beginning of the process. This personal rapport should be maintained throughout
the study, and everyone in your practice should treat the subject with courtesy and respect. Because clinical research trials usually involve many office visits, you should ensure that the research subjects are given priority in the schedules, flexibility in the context of the research schedules, and allowed windows for each visit. This is critical. Sometimes extraordinary measures might be required to keep a study subject on schedule. For example arranging for transportation to the visit, having a staff member provide childcare in the office while the patient is at the visit, and even going to a subject’s home for follow-up. Throughout the trial, you should maximize the ease of scheduling appointments by always having someone available while the subject is at the clinic and also to answer the phone if the subject needs to change an appointment. Your physical facility should be a comfortable environment, including the examination rooms and the waiting room, especially if the subject will need to stay at the clinic for any length of time.

You can encourage continued trial participation through active monitoring of the adherence of the patient to the study regimen and assessment visits. Telephone calls the day before the appointment and postcard reminders are an effective means of prompting your subjects to keep their appointments. You should have discussions with those subjects who are not adherent, and if necessary, offer assistance.

Conclusions

From the initiation of recruitment throughout the treatment and assessment phases, your human subjects must always be your first priority. However, recruiting subjects and then retaining them for the duration of the study can be a challenge. Start by analyzing the patient population of your practice and the community to determine if a particular protocol is appropriate for your clinic. Then create an advertising campaign to inform potential participants about your trial. Have a system to accept the influx of inquiries about the trial and a way to begin the initial enrollment process. Discuss the goals, risks, and benefits of the trial, and explain informed consent so that the subject understands the participation parameters. It is your responsibility to provide an environment that is pleasant and a treatment/assessment regimen that is as convenient as possible. All it takes to reach enrollment goals and avoid dropout is a little careful planning.

Resources


