

Subject Recruiting: The Missing Links

By Norman M. Goldfarb

Subject recruiting delays 94% of clinical trials¹, so perhaps it is time to consider some new approaches. Four new or uncommon strategies can accelerate subject enrollment.

Investigator Self-selection

Sponsors and CROs are not very good at identifying sites that will meet subject enrollment targets. In fact, about 30% of the sites in a typical study will enroll zero subjects, at an average cost to the sponsor of over \$15,000.² Investigator questionnaires are notoriously ineffective as a tool for identifying investigators that will meet subject enrollment targets. For example, none of the questions used by a large pharmaceutical company in its standard questionnaire reached a 5% predictive ability for subject enrollment.³

Savvy investigators know that sponsors expect them to exaggerate their subject enrollment potential, and will discount whatever numbers they provide. After a site is selected, there is generally no accountability for those numbers. A system based on wink-wink lies and no accountability is unlikely to be accurate.

The problem with the current process for site selection is that we are asking the wrong question:

WRONG QUESTION: "How do we select sites?"

RIGHT QUESTION: "How do we help sites select themselves?"

We can ask the right question by modifying current approaches to feasibility studies. Prior to the site qualification visits, offer sites an optional payment of, say, \$400 to:

- Identify and talk informally to two legitimate study candidates.
- Complete and submit a form for each potential subject with demographics, candidate responses, etc. Subject privacy must obviously be respected.

Ideally, conduct this feasibility study before the protocol is finalized. Give priority to sites that participate. By going through this exercise, sites demonstrate some confidence and interest in the study. They will better understand the recruiting challenge. If either candidate enrolls, the site is already in the top 70% of enrollers. This strategy is best suited for out-patient studies for chronic conditions. It assumes that investigators have an existing population of potential subjects.

Point-of Care Integration

Physician referrals seem like an obvious way to obtain potential subjects for clinical studies, especially for innovative therapies not otherwise available to the general public. Patients are interested: According to a recent Harris Poll, the largest group (51%) of U.S. adults would prefer to learn about clinical trial opportunities from their physicians. The second-largest group (28%) would prefer to learn about them from email notifications of relevant trials. Internet websites came in fifth with 19%.⁴ The reality, however, is that most physicians will look you in the eye and promise referrals, but never deliver. There are three obstacles to physician referrals:

- **Some physicians worry about losing patients to investigators.** Give referrals to get referrals. Clinical research studies can be a rich source of potential referrals to other physicians. Potential subjects who do not qualify for a study are often interested in referrals to new physicians. Physicians understand the quid pro quo of cross-referrals, and there are no legal or regulatory restrictions on the practice. This obstacle disappears when investigators prove in practice that they are not patient thieves.
- **Referral fees are taboo.** Referring patients for a fee is generally considered unethical and is illegal in some states. However, it is perfectly acceptable to compensate physicians for their time in reviewing charts, discussing clinical research with potential subjects, and following subjects during the study. The only limitation is that the payment must not be contingent on the referral. In any case, not paying a physician for a patient that screen-fails is a sure way to eliminate future referrals. Here again, cross-referrals can be useful.
- **Most physicians have very busy schedules, much higher priorities, and limited space in their brains.** The physician's involvement is minimized by moving the primary patient interaction to the intake process. Simply have each patient complete a form stating which areas of research, if any, interest him or her. If the patient is not interested, he or she can check that box instead. The result will be a database of 100% of the physician's patient population. With the proper HIPAA authorization on the form, investigators can contact the patients directly, bypassing the physician bottleneck in many cases. Rather than attempting to access physician patient populations by recruiting them as principal investigators, it would be much more efficient to start them off as "referring investigators."

"The current approach to introducing new investigators to clinical research is akin to drafting baseball players from college and giving them all their own teams to manage."

Community Outreach

Medical science cannot progress without clinical research. Alarmist, one-sided reports in the media discourage public participation in clinical studies. Productive investigative sites often engage in study-specific local community outreach activities, but a more comprehensive, national approach is required to influence public opinion. The Center for Information and Study on Clinical Research Participation (CISCRIP) conducts an active outreach program through the media, but it cannot do the job alone.⁵ We need to create a network of speakers who can address local community groups at schools, churches, health fairs, support group meetings, etc. These speakers can explain clinical research to the public in an objective manner, without taking sides. Our industry has a good story; we just need to tell it. First Clinical Research has therefore launching an industry speakers' bureau. A standard presentation and hand-outs are available on the website.⁶

Metrics and Rapid Response

Few sites track or measure the effectiveness of different subject recruiting approaches such as advertising, chart-reviews, posters, flyers, centralized services, physician referrals, community outreach, etc. Useful metrics include:

- Number of leads
- Number and % of visits
- Number and % of enrollments
- Number and % of evaluable subjects

- Out-of-pocket cost for each of above numbers
- Labor cost for each of above numbers
- Calendar time for each of above numbers

By collecting at least a subset of this data, sites can adjust their recruiting strategies within a study and across studies. Sponsors can also inform sites when certain approaches are working well for a specific study given site characteristics such as community size and demographics.

By collecting data in near-real-time, sites can quickly adapt their recruiting strategies to make effective use of their limited recruiting budgets and not waste time more time than necessary on unreimbursed costs. Sponsors can re-allocate advertising funds, centralized recruiting services, coaching and other resources. They can detect non-and low-performers immediately. They can diagnose problems and undertake remedial action before wasting resources on unmotivated or burned-out sites. If rescue sites are required, action can be taken months earlier than is common today.

These metrics would also be useful in identifying the dozen or more hidden costs associated with subject recruiting, and making them explicit in study budgets.⁷

Summary

The above strategies have the potential to substantially improve subject recruitment productivity. They can help preserve the U.S.'s leadership in clinical research. Clinical research studies are moving out of the United States primarily because U.S. investigators do not enroll adequate numbers of subjects in the required timeframe. Sponsors attempt to address the problem by finding new investigators, most commonly "tourists" without the necessary training to recruit subjects and collect high-quality data. A better approach is to develop preferred-provider relationships with productive sites, and work with them to improve efficiencies and data quality, while reducing costs for both parties.

References:

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