**RDP CLINICAL OUTSOURCING**

# Considerations For Improving Patient Recruitment Into Clinical Trials

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Imagine yourself to be a Fund Manager or Angel Investor considering an investment into the pharma or biotech industry and you become aware of the following statistics about recruitment of patients into clinical trials[1]:

- Nearly 80% of all clinical studies fail to finish on time, and 20% of those are delayed for six months or more
- 85% of clinical trials fail to retain enough patients
- The average dropout rate across all clinical trials is around 30%
- Over two-thirds of sites fail to meet original patient enrollment for a given trial
- Up to 50% of sites enroll one or no patients in their studies

Clinical trials account for nearly 40% of the US pharma research budget and total around $7 billion per year and the estimated cost of patient recruitment is 40% of the total budget, or $1.89 billion. Thus, patient recruitment is the very weak link in the development pipeline and one that an experienced investor would want to know what steps are being taken to address the issue and thus accelerate the time to market and thus profitability.

Patient recruitment is now evolving from what has been a relatively staid process into something much more sophisticated and strategic. This is certainly going to be needed as the competition for sites, investigators and patients is increasing and is fuelled by the rising demands of regulatory agencies for more clinical data.

As part of the evolving strategy, it becomes important here to take a step back and perhaps consider clinical trials from the patient's perspective and to investigate the reasons why an individual may or may not participate in a clinical trial. For example, among people who suffer from a chronic illness, only 6% will ever participate in a clinical trial. Furthermore, a survey in May 2008[1] indicates that 94% of Americans have never been informed by their doctors of medical research studies in which they might be suitable as potential subjects. Even more fundamentally, in order to improve the recruitment rate it is necessary to understand that the reasons a potential patient chooses to enter a trial are not necessarily in direct contrast to why patients choose not to enroll. Llewellyn-Thomas et al[2]., reported that patients who agree and those who refuse clinical trial participation may differ in attitudes towards decision control and the perceived benefits, or otherwise, associated with the trial. For example, patients who said they would refuse to enter a particular clinical trial demanded more participation in decision making and a greater increment in treatment benefit. Over 60% of those refusing to enroll in the study reported an aversion to randomization as their primary reason for their decision. If these differences do in fact exist in the overall population then they have implications for the process of obtaining informed consent and for the generalization of results from a clinical trial.

Data from an ECRI Evidence Report[3] which reviewed 11 studies investigating the reasons for participating and not participating in clinical trials revealed there to be no consistent findings. However, by using random-effects calculations to combine results from all the studies, the authors were able to estimate the typical percentages of patients who cited reasons for participation in three general categories: potential health benefits (45%), physician influence (27%) and potential benefit to others

(18%). Four of the eleven studies asked patients why they had decided against participation in clinical trials. Random-effects calculations yielded estimated percentages of 25% for inconvenience, 20% for concern over experimentation, 19% for lack of potential health benefit and 14% for physician influence. In a study of oncology patients, Meropol et al[4]., found that a fear of side-effects was the greatest barrier to obtaining patients' agreement to participate in a clinical trial. The authors of this study found that important discrepancies existed between the perceptions of the oncologist and those of the patient regarding what are the psychosocial barriers to participation in clinical trials. A review of participation in clinical trials by patients with cystic fibrosis[5] revealed that reasons for non-participation could be considered as either social constraints or health constraints. In examining the reasons for participation and non-participation of patients in a review of 26 clinical trials, Verheggen et al[6]., found that the patients make their decision based on a personal balance account. This comprises the physical and emotional added values patients hope to gain from the trial treatment compared to the non-trial treatment, minus the risks they expect in the trial and minus the extra time they expect the trial will take. Relatively long-term patients show a slightly different motivation to participate in a clinical trial than short-term patients. Spaar and colleagues[7] took an alternative approach and investigated the barriers to recruitment from the investigator's perspective by conducting a survey among recruiting physicians of a multi-center trial. The results from their survey suggested that time constraints and problems of enrolling eligible patients were the greatest barriers to recruitment from the physician's perspective.

The vast majority of studies reporting data on reasons for enrollment and non-enrollment have come from oncology studies and it is estimated that less than 2% of patients choose to enroll in clinical trials for cancer therapies in the United States. A modest increase of two to three percentage points would make a major impact and dramatically reduce the time in the recruitment phase of a clinical trial[8]. With what now seems to be an achievable target, studies have sought to identify and overcome barriers to enrollment. An ongoing study called IMPACT (Improving Methods for Patient Accrual to Clinical Trials) is a project to assess the problem of recruitment from a socio-psychological perspective using the specialized methods of risk communication. This will allow the researchers to examine specific factors about how patients inform themselves about a clinical trial and how they decide whether to participate. Such considerations by the patient might include whether they are embarrassed by their medical condition or perhaps whether a daily office visit might be too painful a reminder they are living with a disease. As has been mentioned previously, patients who agree and those who refuse clinical trial entry may differ in attitude towards decision control and the benefits associated with the trial arms. Having established some of the reasons why patients choose not to enroll, strategies can be developed to overcome or reduce these barriers.

One of the first components of any new recruitment strategy must be to increase the size of the patient pool and to consider how to encourage the 94% of patients that do not currently come forward to participate in clinical trials by more effective communication. The communication has to not only encourage patients to come forward by pre-identifying them or by indirect solicitation but it also needs to ensure that patients are sufficiently educated to understand all the facts about enrolling into a study. This will require modifications to the conventional outreach programs as well as the integration of social

media. Furthermore, communication with doctors referring patients into studies will need to be improved as data indicate that fewer than 4% of all US physicians actively participate in conducting clinical trials although 60% of physicians surveyed by CenterWatch in 2006 said they have referred patients to clinical trials[1]. In addition to improved communication with physicians, there also needs to be a change in thinking from the Sponsor's clinical teams. Often, there is a lot of emphasis from the Sponsor asking investigators to believe they have a superior new treatment and thus pushing the investigator to do this study while dropping everything else. It is imperative not only to convince the Investigator of their potential contribution to the study but to maintain that initial enthusiasm throughout the course of the entire trial.

Many companies are now developing alternative strategies to identify potential patients. The previous traditional advertisement and media based recruitment programs can reach a broad array of potential patients but they can be untargeted and costly. Recent literature would suggest that e-recruitment methods are generally considered to be more cost-effective than traditional media tactics for outreach. With this in mind, it is important to understand that in order for patients to be comfortable receiving clinical trials information via social media, the potential gains will have to greatly outweigh the losses. For e-patients, the traditional search and internet browsing remains the status quo of online health information seeking. By and large, social media profiles about clinical trials do not provide anywhere near the value of search engines for consumption of trial information. Sponsors and recruiters are beginning to address the more widespread use of text messaging and smart phone applications. iPhone and iPad applications are growing in number. Even though e-recruitment offers some potential, of itself it is highly unlikely to produce the quantity of patients required to fill the enrollment needs of the large phase 3 studies.

A strategy using several tactics will most likely achieve the best outcome. Using a clinic center enrollment focus will involve the use of existing databases detailing sites with historically good recruitment campaigns combined with patients with specific diseases who have already indicated their willingness to participate in a clinical trial. Moreover, with selective targeting, patients living within a certain distance of the site can be identified, thus removing one potential barrier to participation which is often quoted by patients, that of the requirement to travel to a "distant" hospital. In a report by the consulting firm Cutting Edge Information[9], the second most important motivator for a patient to enroll in a clinical trial was the convenience of the trial site. Where necessary, this can be combined with a patient-centric enrollment focus which might involve the use of social media and conventional media. It is important to realize that site staff and patients need to remain motivated to maintain retention within the study. This can be done by such strategies as appointment reminders or transportation assistance.

Recruitment consultants are now coming more and more to the fore and offer expertise by working with experienced physicians to review demographic factors and historical data before initiating a recruitment program. Their input is to help recruitment messages, either to respective individual patients or to targeted social media websites, be clear and effectively reach the intended population of potential patients. Recruitment specialists will have site assessment tracking tools and hands-on field support to quickly identify and act upon any problems in a pro-active rather than reactive manner. The report mentioned above by Cutting Edge Information also revealed that forming strategic partnerships with -

CROs that have dedicated patient recruitment groups and databases with site-specific demographic information could benefit a drug sponsor's recruitment efforts. Thus, with the delay of completing clinical trials estimated to cost $1million per day in unrealized sales, it might be safely assumed that investors into a company developing a new drug might well question not only the risks of not gaining market approval but also the measures taken to speed the recruitment process during the clinical trial.

REFERENCES


1. http://www.ciscrp.org/professional/facts_pat.html
2. Llewellyn-Thomas HA, McGreal MJ, Thiel EC et al. Patients willingness to enter clinical trials: measuring the association with perceived benefit and preference for decision participation. Soc Sci Med (1991);32:35-42
3. https://www.ecri.org/Documents/Clinical_Trials_Patient_Guide_Evidence_Report.pdf
4. Meropol NJ, Weinfurt KP, Burnett CB et al. Perceptions of patients and physicians regarding phase I cancer clinical trials: implications for physician-patient communication. J Clin Oncol (2003);13:2589-2596
5. http://www.cfww.org/pub/english/cfwnl/10/273/Motivations_in_Clinical_Research_Why_do_people_participate
6. Verheggen FWSM, Nieman F, Jonkers R. Determinants of patient participation in clinical studies requiring informed consent: why patients enter a clinical trial. Patient Education and Counselling (1998);35:111-125
7. Spaar A, Frey M, Turk A et al. Recruitment barriers in a randomized controlled trial from the physician's perspective- a postal survey. BMC Med Res Method (2009);9:14-21
8. http://www.sciencedaily.com/releases/2007/09/070917115305.htm
9. http://www.centerwatch.com/news-online/article/982