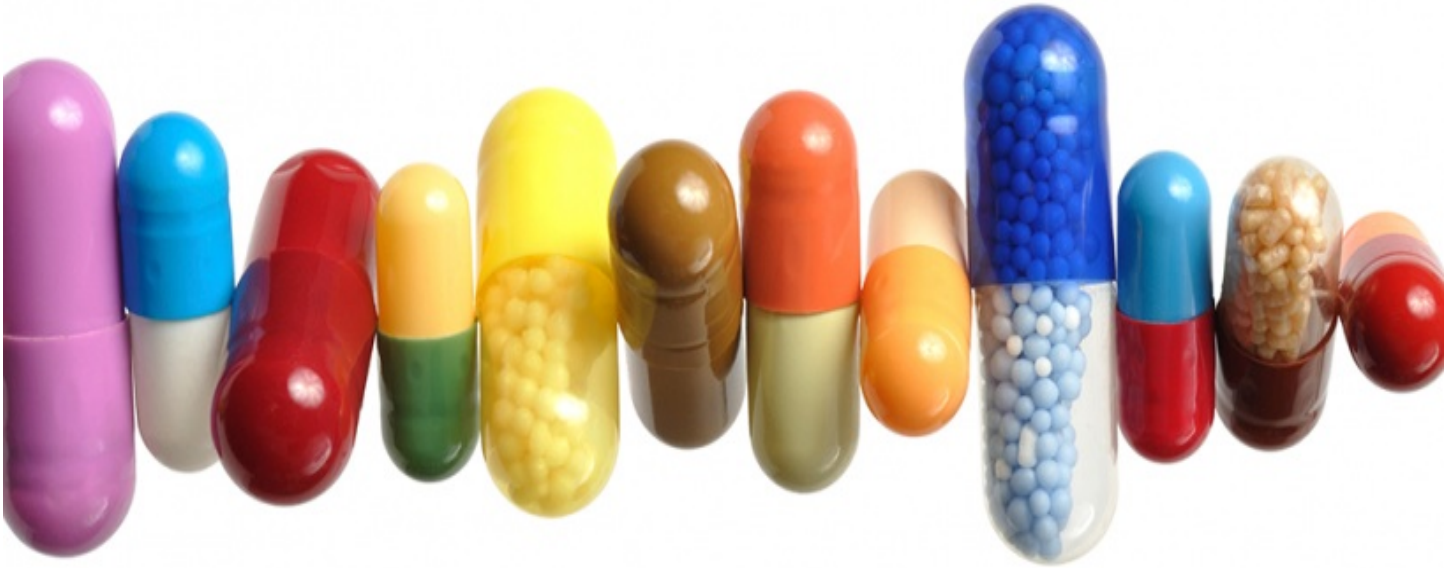

White Paper

Clinical trials: Recruitment strategies

This white paper is dedicated to one of the clinical research communities' hot topics – recruitment. We will discuss different recruitment strategies and their advantages and disadvantages from practical point of view and also we hope to give some new ideas for improving recruitment.

Maybe the most frequently asked question in clinical trials is "How do we improve recruitment?". And this question is coming not just from sponsors but from hospital teams as well. While slow recruitment or lack of recruitment is a serious issue for sponsors who are trying to meet deadlines and collect significant safety information for new products, this is also a major issue for hospitals, which struggle to recruit and waste significant time and resources in attempt to find more participants. Slow recruitment or lack of recruitment does not only increase the financial costs for clinical trials teams in hospitals by increasing the workload and reducing the available resource, but also could damage the team reputation, which will put them in a disadvantage position during future feasibilities. But more importantly this will limit the access of their patients to new therapies.

It is not surprising that in clinical research there is a law - Lasagna's law, which states "*Investigators overestimate, many fold, the pool of available patients who meet the inclusion criteria and would be willing to enrol in a particular trial*". And this is indeed, one of the common issues when setting recruitment targets. The reasons for that overestimation could vary from investigators enthusiasm about the new treatment option, which may not be shared to patients not reviewing properly the eligibility criteria. Whatever the reason is, optimism is in human nature and overestimation is expected result.

New technologies have changed the clinical research environment during the years and have provided new approaches in recruitment, but also placed new challenges. Internet access has allowed potential participants to obtain information about clinical research online and empowered them to be more informed but at the same time has provided ground to scare people interested in research with negative comments and reviews about clinical trials. Another great challenge is lack of access to Internet for many people in developing countries, which prevents them from obtaining information and discovering the opportunities in clinical research. In this review, we will discuss you some recruitment approaches, which our team have observed during the years and also provide some comments, which could be beneficial for hospital teams.

1. Don't shoot yourself in the foot from the beginning

Clinical trials teams should start thinking about recruitment from feasibility stage, before making any commitments to the study. Often sites are eager to take on new studies presuming that the straight forward study title means easy to recruit clinical trial. Hospital teams have to review their records and identify the pool of potential patients before accepting the study. The teams should take into consideration, the fact that they have identified potential participants does not mean they will agree to participate and adjust their recruitment target. It will be very beneficial if the study is discussed during department meeting and all provided feedback is considered. Broad discussion will allow the teams to identify recruitment challenges at early stage and help them make the right decision whether to participate or not.

Accepting a study that the site knows in advance will not be able to recruit for it will be more damaging to the hospital's reputation than declining the study and providing arguments of the decision. Setting up clinical trial requires resources and therefor the teams have to evaluate carefully where to allocate their time and resources.

2. One bird does not make spring

In order to have adequate recruitment you need adequate resources. The fact that you have 2 experienced research nurses does not mean they can handle 50 studies, do data entry and meet all recruitment targets. Recruitment is joint efforts between all members of the clinical trials team. Always be realistic what could be achieved with current resources and have a contingency plan in case of high turn over.

3. Source data review

Source data review is the classical and most used method of identifying potential patients and still widely used in clinical practice today.

There are two approaches in contacting potential participants. The first one is, participants to be reached by phone to confirm their interest in which case the team has to identify team member who has good relationship with the participants or someone who they would trust in their medical decisions and recommendations. The second approach is clinical trials team to send invitation letters to potential participants, which are written on behalf of the treating physician.

3.1 Phone call follow up

Advantages: Source data review is an easy way to identify patients with specific diseases and review if they will meet eligibility requirements. Contacting participants by phone is a quick way to inform them about the study and find out if they are interested.

Disadvantages: Source data review is time-consuming process, requires significant resources to perform regular reviews and does not provide information if potential participant will be interested. Contacting potential participants over the phone could also be quite time-consuming and requires extra soft skills.

3.2 Invitations

This is another smart approach to contact potential participants. Sending written invitation together with informed consent for review to patients who are eligible for the study, gives people more information and time to consider the study.

Advantages: Preparing invitations and their posting could be done by the administrative team, which reduce the workload for the clinical team. This gives opportunity to potential participants to review the information with their family or seek second opinion before making a decision. The invitations could be sent on behalf of their treating consultant.

Disadvantages: Clinical team may still need to follow up if not receiving responses. Lengthy informed consents with numerous adverse events may push away potential participants.

4. Referrals

This is another common approach. Referrals from GPs and community hospitals are often practice and they have a potential to help the recruitment.

Advantages: If the sites have good working relationship with GPs and community hospitals this strategy could be very efficient for them. If the community hospital is included as satellite site this could extend the new treatment options to more patients.

Disadvantages: This approach will not work if you do not have good relationship with the GPs or community hospitals. GPs and community hospitals are short of resources and it could be a challenge for them to get involved. Also they may not necessarily be interested in research. Adding satellite site requires a process for study oversee by Principal Investigator.

5. Using registers

Registers are a new smart way of providing sites with basic information about potential patients who have already expressed interest in research. This could significantly aid clinical trial teams in identifying potential participants.

Advantages: Access to a pool of patients who are interested in research and would like to participate; access to their basic medical history, which could be very helpful to match if anyone fulfills the eligibility criteria.

Disadvantages: Access to registers software or services could be expensive. Maintaining local hospital register could be quite time and resource consuming – someone has to contact patients and maintain the register. People change their minds – the fact that they have agreed at initial stage does not mean they would still be interested later on. Ethical issue – patients who have declined still need to be contacted if there is a new better treatment option for them.

6. Referral networks

These are specially created centres whose main focus is to support clinical research. Such networks may not exist in all countries around the world.

Advantages: Referral centres could do pre-screening activities and take some of the workload from the sites. They could be very successful if the target patient population is local to the referral centre and the site.

Disadvantages: There are high costs of getting referral centres involved, which would usually be covered from the sites budget. They would create additional work for Principal Investigators who have to oversee their processes too because they will be considered as satellite site.

7. Patient organisations and charities

Patient organisations have access to potential clinical trials participants and lately more often these organisations are approached for support.

Advantages: Patient organisations could help spread the word for new clinical trials and influence people's decision to participate. They could be very helpful in promoting clinical research in rare diseases. University research groups could build good relationship with patient organisations and this could help their recruitment.

Disadvantages: Patient organisations may not be willing to be involved in endorsing a study if they think the reason behind the clinical trial is to promote particular drug. Generally they prefer not to be involved with specific pharmaceutical company to avoid conflict of interests but this may vary between different organisations.

8. Recruiting web sites

There are some companies that offer services to pharmaceutical companies to help them boost recruitment. These web sites are specific for each clinical trial and provide the main information about the study. They also allow potential participants to register and send their contacts directly to the site which is recruiting for the study.

Advantages: Such campaigns combined with advertising have the potential to reach many participants. This approach will be very good for phase 1 studies where the targets are volunteers in general population.

Disadvantages: The cost per referral is relatively high. People change their minds and the fact that they have registered does not mean they will participate – this could significantly increase the workload for sites, which will spend extra time in attempt to reach such potential participants. There is a risk that people who may not be eligible have registered in the web sites, which could increase the screen failure rate.

9. Advertising

Advertising is another common method in phase 1 studies but it is not limited in this stage alone. It includes newspapers, build boards, social media, etc. Always check your local regulations before considering advertising as it may not be acceptable in some countries.

Advantages: This could be an efficient method to bring awareness of the clinical trial to general public and recruit volunteers. Generally, quality campaigns have good response. This could be effective tool in phase 1 and epidemiology studies.

Disadvantages: It is difficult to target specific patient population. It is difficult to provide details and people who are not eligible may be contacting the site, which could increase the teams' workload.

10. Educational programmes at community centres, university campuses, radio stations, TV programmes

This approach is still not particularly popular due to limited resources and time; however the future of clinical research depends on informing people about the benefits of participating in research. USA statistics in oncology studies show that approximately 5% of the oncology patients participate in clinical trials, which means that many patients miss the opportunity to access new therapies.

Advantages: Majority of the general public is not aware of the benefits of clinical research and still consider participation in clinical trials as being a "guinea pig". Proper educational programmes could significantly benefit clinical research and boost interest in clinical trials. Such programmes could help fight stigma associates with specific diseases like HIV.

Disadvantages: Organising educational programmes requires resources, time and commitment.

11. Patients engagement and advocacy

Patient engagement is becoming a hot topic in the new connected Internet era.

Advantages: Positive experience from clinical research could affect patients' participation in clinical trials. This is particularly applicable for patients with chronic diseases who attend clinic regularly and tend to know other patients with the same condition. They could be valuable advocates in promoting research.

Disadvantages: This may not be applicable for all disease areas. Negative experience of one patient may have negative impact on other patients' willingness to participate.

12. Recruitment of minority populations

It is a regulatory requirement that minorities are represented in clinical research and in the last years this led to examination of new approaches to attract minority populations to clinical trials. The ethical consideration behind this requirement is that minorities should be given equal access to new therapies. However, reaching out minority populations is still a challenge due to variety of reasons. But while there are no clear guidelines how to approach minority groups there are some strategies that are worth considering:

- Language barrier –Using translator or native speaker to help explain the study to participants could be very beneficial. Providing patients with translated flyers and brochures could also have positive impact on helping them make a decision.
- Community centres – It is worth exploring the option to get involved the community centres in educational programmes.
- Provide relevant information – for example, disease prevalence in the minority group.
- Clinical trials awareness days for patients attending clinic.
- Reduce technical and jargon language to minimum to make discussions about clinical research easier for patients to understand.

When we talk about recruitment there is no "one size fits all" strategy. Recruitment strategy could be combination of different approaches and it should consider the specific trial, patient population, budget and resources.