Chapter 17
Recruitment and Enrolment

17.1 Introduction

Achieving clinical trial research participant enrolment is clearly essential to conducting a successful trial. Adequate enrolment provides a basis for projected participant retention, resulting in evaluative patient data. Without sufficient patient retention from the time of study initiation to closeout, the number of remaining participants may prove to be too small a pool from which to derive conclusive proof or disproof of the goal of the clinical trial sponsor. Obtaining final evaluative data is dependent on successful patient retention. Patients cannot be retained without an initial pool of enrolled volunteers. This initial pool of screened, then enrolled, participants depends on designing a successful patient recruitment strategy. 'A major focus in all clinical trials is on the recruitment of subjects. Where and how to do this depends on the demographics of the target population and the condition under investigation'. [1, 2].

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17.2 Patient Recruitment

The goal of patient recruitment is to raise awareness of clinical trial opportunities and to encourage enrolment. Services are contracted by pharmaceutical companies, biotechnology companies, medical device companies, CROs or a medical research site. Services include [3]:

Study feasibility: Evaluating whether the study may be performed in a given country and how effective it will be in enrolling patients [3].

Population research: Discovering the motivational drivers of target patient populations is commonly gathered through focus groups and may involve caregivers and physicians [3].

Site selection: Choosing the optimal recruiting sites for study participation may play a role in the type of patients recruited. For example, in breast cancer survivors, evidence indicates that recruiting via letters or at the oncologist's office results in the recruitment of similar patients [4].

Site assessment: Investigating the operational, management, technical and clinical experience capabilities of participating sites helps in deciding what support they will need to successfully recruit patients for the study, improving forecasting and return on investment [3].

Recruitment materials: Patient-directed communications designed to attract study referrals and raise enrolment, which may include brochures, posters, letters and flyers [3].

Media support: Whether directed to patients and/or caregivers, advertising can raise study awareness and drive patient referral volume. Some patient recruitment providers possess in-house capabilities for developing, producing and editing all content, while others rely on

third-party vendors. Some popular media for patient recruitment advertising are television, radio, newspaper, the Web (e.g. banner ads and word links), outdoor notices (e.g. bus stops) and social media [5, 6] (e.g. Twitter messages and YouTube videos) [3].

Media management: To exact the greatest value from media advertising, media buying services ensure placement in patient-rich geographic areas along with current market buying discounts and opportunities [3].

Site training materials: Specially designed instructional tools that assist site staff in introducing the study to patients, explaining study procedures to patients and performing informed consent procedures with patients [3].

Study website: Serving as an online hub for study information and sometimes prescreening, the study website usually describes the study, provides disease-related resources and allows patients to indicate their interest in study participation [3].

Patient referral follow-up: When a site may be short of staff or overwhelmed by a spike in patient referrals, a PRO (define acronym or, better, replace with full term as this acronym does not appear again) may offer administrative support by scheduling site appointments and following up with patients who may present enrolment challenges (e.g. a patient who has recently moved and needs a closer site location) [3].

Translations: Providing cultural and regulatory-compliant translation of recruitment materials into various languages in accordance with country-specific requirements [3].

Community outreach: To expand study awareness, outreach efforts may include participation at local health fairs or networking among community service groups, patient support groups and other neighbourhood

organisations and institutions (e.g. churches and barbershops).

Physician outreach: When study recruitment depends in large part on physician referrals, outreach measures can include forums where doctors, specialists and healthcare providers gather to view a presentation on the study and how their patient pool may be eligible for participation. It may also include direct mail programmes where collateral is sent to physicians with the aim of increasing referral volume [3].

Site support: From resolving pre-trial operational issues to tailored support (e.g. referral processing, subject status updates and protocol clarifications), site support ensures study challenges are immediately addressed [3].

Monitoring and reporting: To assess the effects of patient recruitment activities on enrolment, ongoing monitoring is performed. Assessing study metrics allows the sponsor to adjust recruitment efforts as needed to ensure maximum return on investment [3].

17.3 Patient Enrolment

'Risk' is one of the most important words in the clinical research lexicon. Patient risk is carefully managed and monitored by IRBs and the FDA. But what about risks to clinical trial viability?

Patient enrolment is one of the biggest stumbling blocks in the path of a clinical trial. According to the statistics, most trials do stumble; 80 % are delayed by at least 1 month due to enrolment, and 72 % of trials are delayed by more than 1 month [1]. These delays can filter through the entire drug development pipeline, causing a cascade of missed deadlines.

So how should the enrolment risk be managed? In the clinic, powerful decision-making tools such as the risk-benefit ratio,

treatment benchmarks and monitoring procedures are used to guide patient care. The same approaches can be adapted to prevent and mitigate clinical trial enrolment problems [5].

17.3.1 The Patient Population

The broad boundaries of every patient population are set by the ethical guidelines laid out in the Declaration of Helsinki. The patient population is further restricted by enrolment criteria in a clinical trial protocol. Every inclusion and exclusion criterion affects enrolment; that may sound obvious. But how much does a certain inclusion and exclusion requirement affect enrolment? The answer to that question is far from obvious [5].

17.3.2 Enrolment Planning

Enrolment planning is a necessity for every study, every time. Organisers should consider the following [6]:

Determine your site's feasibility: Should you even take this study? Every protocol has its challenges, but some are more difficult than others. If your first instinct is one of doubt, then it may be best to pass on the opportunity entirely. Overestimating your site's capabilities and not being able to deliver on it are likely to hurt you more in the end.

It's not always about advertising: Many sites turn to advertising first, without mapping out a plan. Keep in mind that advertising is only one tactic that can be employed when trying to reach your enrolment goals.

Pick the 'lowest-hanging fruit': Reach out to the best qualified and easiest-to-contact potential participants first. You may find great success here, thus minimising your need to do anything else.

Exhaust low-cost options first: Community outreach, networking and physician referrals are a few examples of low- or

no-cost recruitment options, which your site should first explore.

Work 'inside out': Simply put, work your database! Phone calls, e-mails, postcards, Facebook posts and Twitter tweets should all be parts of your plan of attack for helping to fill your study [6].

17.3.3 Take the Time to Research and Understand the Potential Participant

Who is the ideal participant? It is best to narrow this down from the inclusion criteria on the protocol. Find out where the peak prevalence/incidence rates are, and let that help guide your decisions [6].

What is going to motivate the patient to participate? There has to be a motivational factor driving someone to consider participation. Is it because they are seeking new treatment? Or perhaps they do not have health insurance and the medical exams provided at no cost are a benefit for the subject.

Who is the ideal target? While most times this is the potential subject himself/herself, there are many studies that require the attendance of a caregiver or family member; an example would be a moderate-to-severe Alzheimer's study. For studies like this, it is important to keep both audiences in mind as you develop your plan and any messaging [6].

17.3.4 Engage with Sponsors

What do sponsors and CROs want to see with respect to enrolment planning?

A written plan, specific to your site: Just the act of putting an actual plan on paper will go a long way in the eyes of a sponsor or CRO. This demonstrates accountability and a willingness to succeed.

'Smart' planning: As mentioned previously, exhausting low- or no-cost options, in addition to working 'inside out', will be viewed positively. Planning right from the start, even at feasibility, is your best approach.

Allocation of budget for each tactic: Site recruitment budgets are often incredibly lean. Sponsors and CROs will appreciate you assigning estimated costs to each recruitment tactic.

Justification for recommendations and costs: Along with costs for each endeavour, it will help to explain why you are making your recommendations. Perhaps you are recommending television; your position will be supported if you mention that television is the most widely used media vehicle in your market in relation to your target audience.

Metrics, funnel or yield: In the simplest terms, 'What will this deliver?' Constructing a funnel with an estimated return on a sponsor's or CRO's investment will demonstrate stewardship over the budget they have provided to you [6].

References

1. Frank G. Current challenges in clinical trial patient recruitment and enrollment. SoCRA Source. 2004;2(February):30–8.
2. De Looze F. Clinical trials in general practice: recruitment models. Presented at the international clinical trials symposium. 1999.
3. Patient recruitment. Wikipedia. https://en.wikipedia.org/wiki/Patient_recruitment. Accessed online at 19 Oct 2015.
4. Zhou ES, Dunsiger SI, Pinto BM. Proactive versus reactive recruitment to a physical activity intervention for breast cancer survivors: does it matter? Clin Trials. 2013;10(4):587–92.
5. Abelson MB, Welch D, McLaughlin J. Patient enrollment: risks to clinical trial viability. http://www.retinalphysician.com/articleviewer.aspx?articleID=100315. Accessed online at 19 Oct 2015.
6. Patient Recruitment and Retention in Clinical Trials. 10 strategies for success. Forte Research Systems, Inc. Madison, 2013. www.forteresearch.com. Accessed online at 19 Oct 2015.