

Keeping your finger on the pulse

Of the thousands of clinical trials that are conducted globally each year, around 80% will fall short of their recruitment targets. It is further estimated that 75% of these studies will fail to meet enrolment deadlines. A CenterWatch Europe survey revealed that patient recruitment and retention were the most frequently cited causes of delays in 40% of studies. Each day of delay is estimated to cost pharma companies US\$600,000–1.2 million in lost revenues.

Historically, many study managers have chosen instead to work with investigator sites to exhaust existing databases and patient lists. Although this can be an effective route, the success of a study that relies on this as the sole means of recruitment largely depends on the therapeutic indication.

Numerous factors may affect success rates at the investigator sites including the prevalence of the condition, among others. It is easy to underestimate recruitment costs and this may lead to 'budget creep' or over spending of the budget allotment later when patients drop out and additional enrolment is needed.

A key element in the success of clinical trials is the ability to set transparent budgets, which realistically reflect recruitment and enrolment costs. Once a budget has been set, it is crucial to monitor expenditure closely. Richard Anderson and Liz Moench suggest three ways of keeping the budget on track, including using real-time performance metrics

Active clinical trial marketing to accelerate recruitment is the only option in many cases but creating a realistic study budget can be difficult; get it wrong and the study will be set up to fail when it comes to recruiting patients. Even if you do it right, it may look as though you're overestimating costs, because on the surface, it can appear that you are accounting for more patients than the study needs.

Steps to success

There are three keys to developing and keeping the study within budget parameters. The first two, which need to occur up front, are detailed recruitment forecasting and accurate estimation of patient recruitment

requirements. The third, occurring during implementation, is real-time performance metrics, which allow ties with non-performing sites to be cut quickly, enabling investment in only those sites that are recruiting and screening patients. Using all three keys permits fiscal risk to be managed effectively.

Employing accurate data during the budgeting process to determine what is spent and where, helps build more accurate, transparent budgets. Budget creep occurs in situations where recruitment vendors are pressured by study managers to bid on price. If vendors deliver a price that is going to be competitive, the price will often increase after

How site performance can affect costs					
Market	Total media cost to date	Total referrals	Cost per referral	Total enrolled	Cost per enrolled
Excellent performers					
Charleston, SC	\$2,920	113	\$26	9	\$324
Iowa City, IA	\$13,683	85	\$161	16	\$885
Average costs: Excellent performers	£16,603	198	\$83,85	25	664
Average performers					
Springfield, IL	\$11,452	55	\$208	2	\$5,726
Pittsburgh, PA	\$22,568	113	\$200	4	\$5,642
Topeka, KS	\$11,354	49	\$232	5	\$2,271
New Orleans, LA	\$11,214	52	\$216	3	\$3,738
Average costs: Average performers	\$56,588	269	\$210	15	\$3,772
Poor performers					
Sacramento, CA	\$17,464	68	\$257	1	\$17,464
New York, NY	\$32,842	35	\$938	1	\$32,842
New York, NY	\$32,842	39	\$842	0	\$32,842
Average costs: Poor performers	\$50,306	142	\$2,037	2	\$25,153

5.6x higher

6.6x higher

Common mistakes:

- Fear of not supporting all sites
- Long decision-making process

Risks:

- Wasted investment
- Budget spread too thin – eventual budget creep
- Recruitment delays

Source: Defacto Communications

Figure 1: Only two-thirds of sites perform; one-third is poor. Site performance can undermine the cost-benefits of good advertising and other media deals.

the project is awarded because a study fails to deliver the required number of patients. This scenario occurs all too often and is frustrating for clinical teams, who wonder why the vendor they selected failed to deliver, and also for vendors who planned correctly, but whose proposal was overlooked.

Companies that focus only on price often do not realise that they are getting what they pay for – budgets based on the delivery of fewer patients and/or budgets that fail to be tied to any projection forecasts. Cost differences may be justified by specifically projecting the number of subjects to be delivered and by committing to the prevention of budget creep later in the study.

Forecasting. Patient forecasting is essential to accurate budgeting. The Leaky Pipe model considers the patient flow through the study and is the foundation of the budgeting process. If recruitment companies and clinical teams do not know how many patients will flow through the study, given its particular protocol specifications, then an accurate plan and budget cannot be developed. The Leaky Pipe model accounts for the loss of subjects for a variety of reasons ranging from health problems through to not granting informed consent, to the patient simply moving away from the research site.

If a study needs 150 patients to produce sufficient results, clinical operations and project managers could need to screen 1,500 patients. This 10:1 ratio may seem high, but it can be affected by many factors, some of which include the prevalence of the condition, the risk involved in participating in the study, and the competition for the type of patients in the study. If clinical teams only budget for 150 recruited patients, the study will invariably run into problems, miss its timeline, expend its budget and come to a standstill.

Recruitment vendors and clinical teams alike need to plan for attrition under all circumstances. However, the process of recruiting patients can be even more difficult when the study protocol demands low-prevalence subjects, such as people with migraine headaches who are on certain kinds of pain relievers, or advanced Alzheimer's patients who are treatment naive. For example, if the study calls for drug-naive, advanced Alzheimer's patients, about 75% of callers will be screened out.

Every single study requires its own Leaky Pipe model that drives the budget. Without having that picture up front and agreed to by the clinical team, the budget is meaningless.



The 'leaky pipe' model accounts for the loss of subjects for a variety of reasons ranging from health problems through to not granting informed consent, to the patient simply moving away from the research site

Without accurate planning, significant budget creep is inevitable.

Market-by-market budgeting. A major patient recruitment expense is advertising in local newspapers, radio and other media. Clinical teams must also take into account the cost of buying advertising in different markets. A one-size fits all budget is not appropriate across all sites. The classic mistake companies make is to allot a fixed amount for each site, such as €2,000 (US\$2,407) or, usually, the 'magic' €5,000. This is a major error. What advertising buys for €5,000 in Riga, Latvia, is quite different from what it buys in London or Munich.

Instead of making an average-based estimate of advertising costs, a recruitment budget must determine how many patients each market is projected to deliver, and then estimate how much advertising will be required to reach this number of patients. This must be done on a market-by-market basis, until the big picture equals the number of patients needed – Leaky Pipe and all.

Another error is to let the study sites decide how and where the media budget should be spent. Study coordinators are not marketing experts. When sponsors provide recruitment budget directly to sites, the responsibility shifts to study coordinators to do the research on local media outlets, negotiate media buying costs and process payment. While some study

coordinators may choose to rely on what they believe to be tried and trusted media, the target population of one study may be quite different from another and this can result in failure to promote the study properly and to recruit effectively.

Many coordinators make media decisions based on their own behaviour or beliefs and not on the specific patient population demographics. With a background in nursing or clinical research, study coordinators rarely have the expertise to plan and execute the media campaign or to negotiate added-value advertising, such as bonus airings or sponsorship mentions at no additional cost. This entails identifying the target audience, determining the media reach needed to generate patient response and evaluating the relative benefits and costs of each media method. Lacking this expertise will result in wasting money on ineffective advertising.

Account for non-performance. Across all studies and therapeutic areas De Facto and the MediciGroup have well documented evidence that only two-thirds of sites actively enrol patients. For example, in a study with 30 sites, 20 will be performing sites and 10 will be non-performers. This fact must be accounted for in recruitment budgets and plans. Another third will overachieve, turning in more results and recruiting more patients

than projected, possibly ahead of schedule. And finally, a third of the study sites will perform as expected.

Realistic budgets should be created by assuming that support will be given to 100% of the study sites selected. Within two or three weeks, however, real-time performance metrics will guide continued recruitment investment decisions to two-thirds of the sites, those that are meeting or exceeding projected results. Severing ties with the non-performing sites before additional recruitment investment occurs preserves the budget and eliminates wasted spending.

Fiscal risk management for recruitment requires clinical teams to not grant a site all, or part, of its advertising budget until staff at that site have at least done some groundwork on their own by recruiting from the site's patient database, even if this has involved screening without a patient yet being enrolled. This effort demonstrates study commitment, a characteristic that is likely to continue over the course of the study.

Furthermore, if a study is set up for 'competitive enrolment,' it only makes sense

to have 'competitive recruitment resources.' With only a limited recruitment budget, clinical teams cannot afford to invest in non-performers who deliver zero or limited returns. Those who enrol are rewarded with additional support to help them get to the finish line faster. It means targeting the recruitment budget for the greatest return on investment.

Understanding the big picture

Using the Leaky Pipe model to more accurately estimate patient recruitment needs will probably inflate part of the recruitment budget. However, with real-time metrics, the budget is often decreased by weeding out non-performers early – which requires the daily monitoring of study sites. Clinical procurement teams need to understand the big picture when considering recruitment budget proposals and the differences between them.

For example, budgets that require comprehensive planning and forecasting and budgets based on these models are more likely to complete recruitment on time. As a result, these sites are much less likely to incur

unbudgeted costs for extra time and monitoring as they compensate for patients who drop out.

Smaller companies appear to be more understanding of the zero-based budget approach. They understand the budget's composition, and clearly understand how financial consequences for ill-planned studies can affect their ability to stay in business. They understand that time is money – often venture capital – and they cannot afford to exceed their projected burn rate.

The cost of a comprehensive recruitment plan and budget focused on completing the study on time is considerably less than the cost of maintaining a delayed study with ongoing CRO costs for monitoring. Recruitment budgets must be carefully assessed.

You get what you pay for.





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