Life Science Leader

Alternative Fact: Site Identification Is Not Critical To Clinical Trial Efficiency

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On the surface this may seem to have some validity, as sponsors and CROs often lack a transparent, evidence-based strategy for this task. Instead, they frequently rely on archaic paper-based or spreadsheet methods to identify sites across the globe with a reasonable chance of enrolling the contracted number of patients on schedule, and the ability to generate quality data. Moreover, the practice of adding more sites per study than necessary and requiring each site to recruit fewer subjects per site is a standard, although questionable, risk mitigation practice. So how important can site identification be to the efficiency of clinical trials?

Reality paints a starkly different image. Clinical trials that get off to a good start are more likely to be successful trials. According to research from Tufts Center for the Study of Drug Development (CSDD), 37 percent of sites selected for clinical trial studies under-enroll, and 11 percent fail to enroll a single subject. Eventually, 89 percent of studies meet enrollment goals, but often at the expense of sponsors faced with doubling the original timeline due to poor enrollment. Other research cites slow patient enrollment as the top reason clinical trials are behind schedule. Overall, poor site selection, the inability of sites to predict the rate of enrollment, and the subsequent need for study rescue may increase cost of trials by 20 percent or more, according to research by Citeline.

And it all starts with site identification, the first step in the process toward activating sites to enroll their first trial subject, known as First Patient In (FPI). Ideally, the protocol for a clinical trial is complete before site identification begins and study startup (the collection of activities associated with site identification, site feasibility assessment, site selection and site activation, through to conduct) gets underway. The reality is that oftentimes the protocol is still being finalized as study startup kicks off.

Identifying high-performing investigative sites is one of the most critical decisions made by a sponsor or CRO, it is a key driver in ensuring recruitment is completed on time and that the data is delivered in a timely manner with excellent quality. The process can be cumbersome and time-consuming, as it requires evaluation of current data on performance and patient accessibility, as well as, the future potential of sites to execute the study. Recruiting quality investigators and investigative sites directly correlates to quick subject enrollment, subject retention and quality data for any clinical study. When done well, investigators provide better results not only for the study but also for the patients themselves who seek out and participate in the study. But this is typically easier said than done.

Competition for trial sites, investigators and patients continues to rise. The changing landscape of clinical trial site selection and patient recruitment is attributed to increasing complexity of trial protocols, competition for patients in certain therapeutic areas, as well as, the changing regulatory requirements, culminating in 80 percent of trials failing to meet enrollment timelines.

Why is there such inefficiency in site selection? What data sources are used to identify potential investigative sites? And what are the common pitfalls in current approaches to site identification?

Finding and Evaluating Potential Sites

There are four common methods used to identify investigative sites. Often a combination of these methods is used to quickly find the right sites for clinical studies. Each has varying degrees of effectiveness and drawbacks.

Internal databases

The source of inefficiencies is a question often asked about an industry deeply rooted in paper-based and spreadsheet tools for clinical trial conduct. Study teams have continued to use these older tools to identify and ultimately select sites as they house a degree of institutional knowledge about specific sites based on previous studies.

Sponsors and CROs don’t need to reinvent the wheel for every new clinical study. They already have internal databases readily accessible and pre-populated with sites that they’ve worked with in the past. Maintaining an internal database helps them cultivate long-term relationships with sites that have performed well historically and that they would like to use for future studies.

One drawback is that internal databases need to be actively maintained. Manually entering new data and tracking changes to the database becomes increasingly labor intensive, and prone to errors, as the database grows.

While an internal database provides a great starting point for established sponsors and CROs, the data is limited and often needs to be expanded upon to include new investigative sites. Many investigators do not return to conduct another clinical trial with investigator turnover rates reaching 35 percent in the United States and 55 percent in Europe. This makes it difficult to gain transparency with regards to who will perform well in your study.

Unfortunately, institutional knowledge is frequently dated (shouldn't sites be evaluated base on recent performance?) and siloed within departments, and may not be relevant to the therapeutic area under investigation. Moreover, study teams are blinded to problems inherent with this approach—namely, it limits opportunities to engage with new sites that could be more effective than those familiar to the study team. Research from Tufts CSDD suggests that for a typical multi-center study, 30 percent of sites selected are new, meaning they would not appear in existing spreadsheets, thereby undermining the value of this approach and possibly placing a study at risk.

Contact a CRO

Engaging a CRO as a development partner is a common industry practice for sponsors when starting up clinical studies (outsourcing of trials is estimated by Research and Markets to exceed 70 percent by 2020.) CROs can provide a wide range of services to sponsors including site identification. CROs that provide site selection services also provide their own list of investigative sites. While several CROs help identify sites, there are important distinctions to consider.

Larger CROs generally have a wide-breadth of expertise and capabilities to handle multiple indications and service the sponsor. However, their list of sites may be out of date because they are spread across multiple indications.

Smaller, niche CROs typically have a more focused and up-to-date list. However, because smaller CROs are niche providers, many of their sites may already be dedicated to other competing studies.

Peer Referrals and KOLs

Key Opinion Leaders (KOLs) are professionals with firsthand knowledge and experience working in a particular indication and will be sought out by their peers for advice and clinical care directions for their own patients. Due to their significant interaction with their peers, KOLs can provide referrals of investigators who have patient populations and skills to execute the study. In addition, the selection of a well-known KOL will help to provide incentive for other sites to join the study based on the sponsor or CRO finding a KOL by scouring scientific publications, conference agendas and professional blogs.

While having a KOL on your study is a good thing it should be taken into consideration that KOLs tend to have large practices and will be highly sought after, which may leave them with a challenge to enroll patients and collect data in a timely manner for your study. You must determine if the benefit of the KOLs influence is greater than the need for patient enrollment at their individual site for your study.

Current sites may also be a good source to tap when trying to identify new sites. Most sites will refer other sites to a sponsor or CRO that can accommodate a clinical study.

Physician Directories/Registries

Sponsors and CROs utilize both online and offline directories to identify sites and cast a wide net for site nominations and selection. Some online directories allow them to search for sites free of charge, while others require a fee. Directories can be large and help exposure to sites that they were not aware of previously; however, ability to judge the quality of the sites remains a challenge. They will need to spend more time researching the quality of each new site – a labor intensive and time consuming process. Since many directories are static and not regularly maintained they may be receiving data, which is not relevant at the time when a decision on site selection needs to be made.

No matter the list or database used, it is critical to know how often the content is updated. Principal investigators and sites change, and their areas of research expertise and site capabilities can also fluctuate. The utilization of the information from registries/directories is a starting point in the selection process and is enhanced when combined with internal and external information about site performance and patient populations, yielding the best results.

Reinventing Site Identification

Sponsors/CROs are finished finding and initiating sites when they enroll an adequate number of subjects in an acceptable amount of time. Precise and accurate site identification is too complex, too manual, and too inefficient. With more than 80 percent of all clinical trials running overtime and over budget there is intense pressure to speed clinical trials and restrain costs. Sponsors and CROs need ways to automate and reduce the time it takes to get investigative sites up and running.

Better managing clinical study startup, starting with optimizing site identification, represents a substantial opportunity to reduce clinical study timelines, and costs, enabling therapies to get to those in need faster.

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