Making Site Selection Precise And Accurate

25**MAY**2016
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Underperforming investigative sites have long been a puzzling issue for clinical trial stakeholders. There are lots of reasons for sub-optimal performance, ranging from inadequate processes for study execution to overly complex protocols. Current thinking suggests that at least some of the problem stems from continued reliance by many sites on paper-based or simple spreadsheet methods for numerous aspects of study conduct. The problem is compounded by sponsors and contract research organizations (CROs) who operate in a similar manner—using older methods to track site performance, resulting in a lack of transparency as to what is happening in real-time and an inability to mitigate risk that could stall clinical trial conduct.[1] This scenario is played out as clinical trials unfold, with the notoriously slow study startup (SSU) phase particularly hard hit. Sites are selected during SSU, a task that is best performed when sponsors or CROs use a data-driven approach to create a target site profile based on an algorithm that uses a weighted average of feasibility, SSU metrics, and site experience. Fortunately, this approach is now possible with the recent launch of purpose-built technologies designed to consolidate data from multiple sources that point sponsors and CROs toward the right sites, increasing the chances for better study execution.

This article presents statistics that document the urgent need to improve site selection, and ultimately, SSU activation and performance. Key to that effort is new technology that embraces big data as a source of algorithms for intelligent site selection. The result is a transparent, risk-based process that optimizes selection of the right sites at the right time, and reduces the number of under-performers.

Data Tell the Story

As clinical trials become increasingly global, it is taking a lengthy 3.2 months, on average, to complete the site identification process for Phase II and Phase III studies.[2] Often, that process has inconsistencies in the practices sponsors and CROs implement, which has a direct bearing on cycle time. Most commonly, it reflects the use of ingrained methods that contain a degree of institutional knowledge about specific sites based on previous studies. This includes an understandable reliance on relationships with principal investigators nurtured over time, but these methods lack verification and reliable metrics, and do not include any new sites, which, for a typical multi-center study, can represent 30% of sites selected.[3] These new sites would not be found in existing spreadsheets, raising concern about the value of this older approach.

As evidence, statistics on study performance are discouraging. Despite enormous attention paid to the subjects of clinical trial inefficiency and the need for transformation,[4] clinical trial cycle time has remained unchanged for two decades, stagnating at nearly seven years.[5] For the site selection process in particular, slow cycle time reflects too many sites under-enrolling or failing to enroll. Research suggests that 37% of sites chosen for clinical trial studies under-enroll, and 11% never enroll a single subject. Most studies, 89%, do eventually meet enrollment targets, but only when timelines are essentially doubled.[6]

The costs associated with this scenario are steep. Poor site selection, the inability of sites to predict the rate of enrollment,[7] and the ensuing need for study rescue can boost clinical trial costs by 20% or more.[8]

Qualitative interviews with stakeholders conducted recently by the Tufts Center for the Study of Drug Development (CSDD) gathered information about why site selection practices remain so inefficient and ineffective2. Core themes fell into three categories, following the clinical trial timeline:
- Planning and site identification phase
- SSU and site initiation phase
- Ongoing execution and completion phase

For the planning and site identification phase, research found that most organizations perform very limited upfront planning. Many companies reported collecting incomplete selection criteria, and of those collected, many of the criteria used to identify and select sites were not directly associated with site performance. In addition, the interviews documented a number of rather unsophisticated approaches to site identification, such as word of mouth, literature searches, internet searches, chart review, and conferences. On a positive note, use of internal and commercial databases do reflect a growing interest in a more data-driven approach.

Interviews about the SSU and initiation phase revealed that too often, sponsors and CROs re-invent the wheel every time they recruit sites, using and re-using selection criteria when they already have sufficient knowledge about how specific sites perform. And as for study execution and completion, the research showed little or no transparency of information or real-time ability to offer remediation and risk mitigation to help sites succeed. Rather, sponsors or CROs continue to measure site performance at various time points that do not give the sites enough time to adjust mid-stream.

These findings indicate that sponsors and CROs would benefit from adopting internal practices that support more sustainable site performance. For site selection, this means disrupting the heavy reliance on legacy methods. While these are valuable resources, they need to be complemented, or in some instances, replaced with technology that allows stakeholders to embrace intelligent site profiling, made possible with purpose-built technology that uses data-driven algorithms.

Big Data Key to Choosing the Right Sites

Site selection is complex and multi-factorial, especially as clinical trials become more global. The therapeutic area, eligibility criteria, treatment requirements, site infrastructure, and staff capabilities are among the basic characteristics that sponsors and CRO must consider when evaluating sites. Technology has become standard practice in the form of electronic data capture (EDC), the clinical trial management system (CTMS), the interactive web response system (IWRS) and more, but these systems do not focus on SSU tasks, such as site selection. What they do offer, however, are rich datasets from past performance, but these disparate datasets are not useful until they are consolidated for the purpose of fine tuning site selection.

This is where purpose-built study startup (SSU) site selection and feasibility tools can make the biggest impact. They re-define the site selection process by combining internal and external data sources into a single meta-database. This big data approach allows for the creation of algorithms that assign weights to the data based on the protocol, enabling the building of a target site profile that uses study fit, site performance, and experience of the

Site Profile Algorithm Uses Weighted Average

Study Fit (Feasibility)	Site Performance (SSU Metrics)	Site & Investigator Experience
Facility information	Enrollment	Enrollment
Geographic location	Data queries	Data queries
Protocol inclusion/exclusion criteria	Site profiles	
Patient demographics	Site activation	
		Chart 1

site and investigator (Chart 1). A list of sites can then be generated by querying the database using parameters from the protocol and filtering options. Next, workflows built into site selection solutions steer study teams to choose sites from that list, conduct the feasibility screening, and accelerate the sites to activation. This approach mitigates the risk of choosing underperforming sites by finding the optimum alignment of top-performers with substantial patient databases.

The Tufts interviews showed an interest among stakeholders in shifting the landscape to include these sorts of new workflow tools offering real-time visualization and big-data analytics for better site selection, and ultimately, site performance. Other benefits include built-in reports that provide insight into start-up time, patient retention, and quality at the site and country levels. These solutions also include workflow tasks and allow tracking of project status by country and by site in real time. Tasks range from inviting sites to participate, through to choosing potential sites, and ending with approving and making final site selection (Figure 1). Significantly, cycle times that are generated along each step become part of the big datasets that can be re-used in future studies.

Analytics Mitigate Risk

The need for intelligent site selection is a driving force among clinical trial stakeholders anxious to implement new tools for transitioning away from legacy systems. This is made possible by purpose-built technologies that consolidate multiple data sources into a meta-database. As a result, sponsors and CROs can benefit from a data analytics approach to site optimization, whereby the best sites with the right profile for enrolling patients on time and on budget are identified.
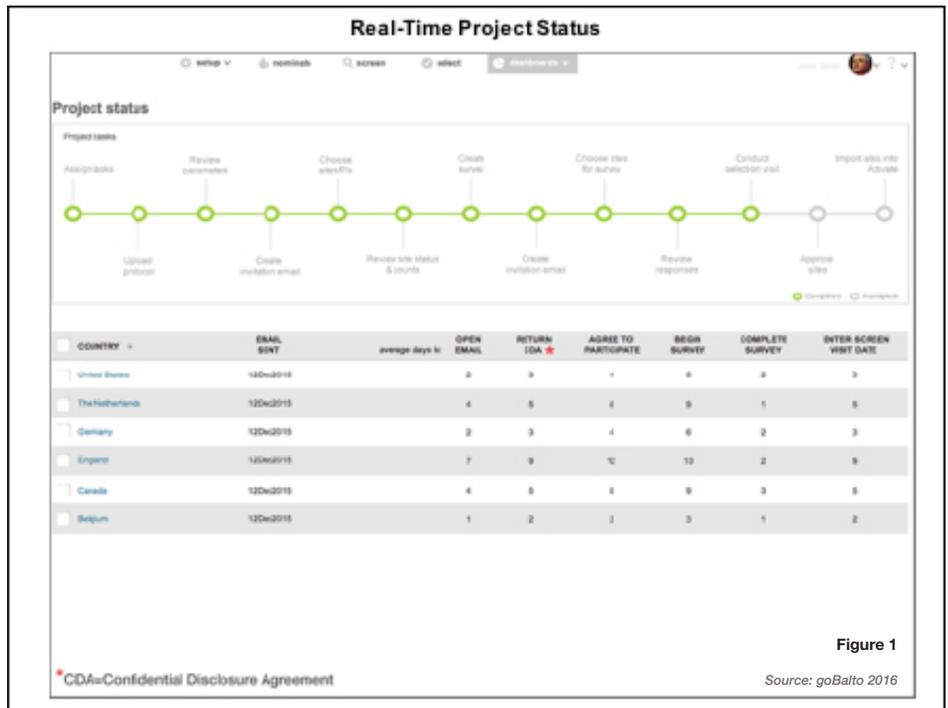

Figure 1

*CDA=Confidential Disclosure Agreement

Source: goBalto 2016

This method mitigates risk by reducing the number of underperforming sites, and offers a process yielding actionable intelligence that is useful in shortening cycle times, a much coveted outcome of the clinical trials industry. With better site selection functionality in place, the technology is ready to move forward by integrating with a site activation tool that can streamline activation and real-time reporting of study progress.

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