



Removing the Blinders in Site Selection

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Investigative sites are the heart and soul of the life sciences sector as they perform the all-important clinical trials. This is a massive undertaking, as clinical trials are a complex, multi-step process starting with first-in-human studies, moving through to pivotal trials for regulatory submission, and ending with post-marketing initiatives. One of the most difficult aspects is the selection of the right sites by sponsors and contract research organizations (CROs), who 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. Using this approach, site selection, a critical step in study startup (SSU), has long been an intense challenge with limited success. More recently, however, purpose-built technologies have emerged to address this problem, using data from multiple sources and algorithms to direct sponsors and CROs to the right sites, increasing their chances for better study execution.

The numbers tell a sobering tale. According to research from the Tufts Center for the Study of Drug Development (CSDD), 37% of sites selected for clinical trial studies under-enroll, and 11% fail to enroll a single subject. Eventually, 89% of studies meet enrollment goals, but often at the expense of sponsors faced with doubling the original timeline due to poor enrollment.¹ Other research cites slow patient enrollment as the top reason clinical trials are behind schedule.² Overall, poor site selection, the inability of sites to predict the rate of enrollment,³ and the subsequent need for study rescue may increase cost of trials by 20% or more.⁴ And perhaps most disturbing is the fact that cycle time has not changed in more than two decades.⁵

This article describes why site selection remains highly inefficient and problematic, and how purpose-built technologies are starting to reverse that trend. New technologies offer intelligent site selection, which is a data-driven approach to creating a target site profile. Specifically, data on site performance and site characteristics are gathered from various sources, and using a scoring algorithm, a complete target site profile emerges, along with a list of sites that conform to the profile. This disruptive strategy lifts the “blinders” from sponsors and CROs who have used less systematic methods over the years and replaces them with a transparent and collaborative process for selecting optimal sites.

Why Such Inefficiency in Site Selection?

This 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 select sites as they house a degree of institutional knowledge about specific sites based on previous studies. Teams have also relied on relationships with principal

investigators built over time. And while these methods seem logical, they lack verification and are slow, taking 3.2 months, on average, to go through the site selection process.⁶ Unfortunately, the institutional knowledge is frequently dated 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 suggests that for a typical multi-center study, 30% of sites selected are new,⁷ meaning they would not appear in existing spreadsheets, thereby undermining the value of the older approach and possibly placing a study at risk.

With the increasing globalization of clinical trials and more complicated protocols, continued reliance on older methods has resulted in various industry initiatives designed to fuel widespread adoption of technology meant to improve clinical trial operations (Chart 1). One example is the call to action by Kramer and Schulman on the need to transform how clinical research is conducted.⁸ They suggest that a multi-stakeholder initiative is needed to encourage adoption of technology in tandem with new business models. They point out that the economic opportunities enabled by technology have been stalled by legacy costs and processes shaped by previous generations of processes. The older methods bear tremendous labor costs, including those linked to patient recruitment efforts. A report by the Institute of Medicine (IOM) makes a similar claim, noting that as long as stakeholders cling to older business practices, they will not benefit from the power of new technology. Under those conditions, clinical trial execution, including functions such as patient recruitment and enrollment, are destined to remain inefficient.⁹ These observations are critical, as new technologies and business processes designed to jumpstart site activation drive better patient recruitment and enrollment. Specifically, site activation accounts for nearly 70% of patient enrollment cycle time.¹⁰

Industry Initiatives to Improve Clinical Trial Operations

- Alliance for Clinical Research Excellence & Safety (ACRES)
- The Clinical Data Interchange Standards Consortium (CDISC)
- Critical Path Institute (C-Path)
- Clinical Trials Transformation Initiative (CTTI)
- HealthCarePoint
- Metrics Champion Consortium
- TransCelerate BioPharma

Chart 1

Given this background, it is time to remove the blinders in site selection and move forward with technology based on study fit, site performance, and site experience. This effort aligns with growing regulatory interest in more efficient SSU activities. Recently, The Wall Street Journal reported on a joint initiative launched by the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) to ease the barriers to patient recruitment and enrollment.¹¹ Specifically, they released a proposed new format for researchers to use when preparing study protocols, which includes clearly stating their purpose, the risks and benefits, recruitment and retention strategies, and simpler informed consent documents.

This initiative follows on the heels of earlier guidance documents on risk-based monitoring, which state that plans to reduce risk should begin from the beginning of clinical trials, and that electronic tools facilitate this effort, including identifying rates of enrollment at various sites.^{12,13} A more recent rule, namely the European Union's new Clinical Trials Regulation (CTR) EU No 536/2014, makes mention of clinical trial technology as part of the effort to remove duplication of effort and risk of delays in starting new clinical studies.¹⁴

Optimizing Site Selection

The expansive regulatory push to better execute SSU tasks suggests that it is the responsibility of stakeholders, such as sponsors and CROs, to implement state-of-the-art technologies.¹⁵ For site selection specifically, purpose-built platforms are available to aid in industry-wide efforts to optimize this function by identifying the right ones and reducing the risk of choosing under-enrolling and non-enrolling sites.

To start the process, new solutions offer workflows that advance sites through feasibility and activation within a workspace using a data-driven approach to intelligent site selection. The data come from internal and external sources that can be combined into a single meta-database, allowing the information to be re-used to inform future site selection, building institutional knowledge. The data sources include SSU performance metrics, and information from tools, such as the clinical trial management system and electronic data capture systems to create algorithms that assign weights to the data and build a target site profile. Querying the database using parameters from a specific protocol helps generate a list of sites. Finally, workflows guide the global study team to select the sites from that list, conduct the feasibility screening, and accelerate the sites to activation.

The weighted score is composed of study fit (i.e., feasibility); SSU performance, such as enrollment, patient volume, and cycle time performance; and experience of the site and investigator (Figure 1). With this information, the solution ranks and prioritizes the most suitable sites for a particular protocol, mitigating risk factors for recruitment and retention. In addition, there are built-in reports that provide insight into start-up time, patient retention, and quality at the site and country levels.

Overall, this approach brings an innovative disruption to the manual process of site selection, facilitates real-time collaboration with globally dispersed clinical research teams, and helps remove the blinders in identifying the right sites. The technology has many benefits (Chart 2), and is part of an end-to-end solution that brings workflow-based processes to study teams, helps sponsors and CROs identify bottlenecks, and provides intelligent site profiling for better site selection.

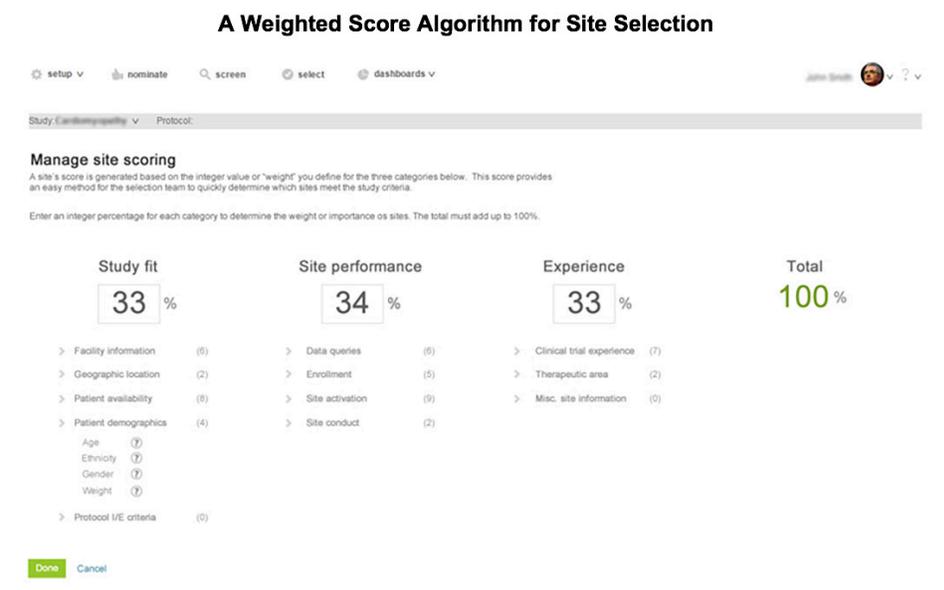


Figure 1

Taking Off the Blinders

Purpose-built technologies rooted in multiple data sources provide sponsors and CROs with a data driven approach to selecting sites most likely to enroll patients on time and on budget. The resulting data are actionable intelligence that allows stakeholders to fulfill their responsibilities for better execution of clinical trials, and mitigating risk. Importantly, to improve site selection, new technologies are allowing stakeholders to take off blinders that have remained due to ongoing reliance on older methods that lack verification and transparency. That older approach is being replaced by **a more thoughtful and analytical method that advances the process starting with feasibility through to site activation.**

Key Benefits of Intelligent Site Selection Technology

- Automates site identification, feasibility and selection processes
- Reduces risk of under-enrolling and non-enrolling sites
- Expedites collaboration with global study teams
- Analyzes patient-to-site proximity
- Provides built-in reports into start-up time, patient retention, and quality
- Drives data-based business decisions
- Assigns permissions to individual team members, such as access to data and ability to perform specific tasks

Chart 2

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