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Site selection a continuing conundrum

Finding alternatives to older methods proves challenging

By Marilyn Fenichel

For many companies, searching for clinical trial sites begins with a look at paper-based and spreadsheet tools that document where they had held earlier trials. Returning to familiar sites allows clinical trial teams to work with principal investigators with whom they have built relationships over time.

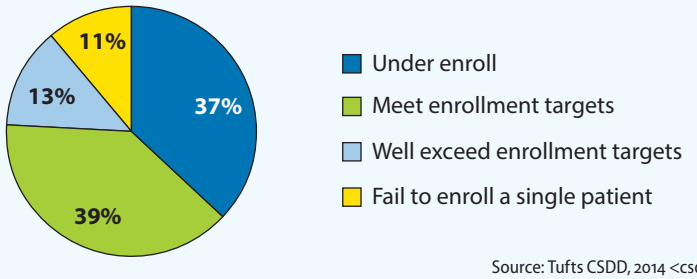
On the surface, this approach makes sense. But in reality, it is time-consuming, inefficient and may not result in the best sites for a given study.

"We have data showing that sponsors work at familiar sites with investigators they know about 65% of the time," said Ken Getz, M.B.A., director of sponsored Research Programs and research associate professor at the Tufts Center for the Study of Drug Development. "As a result, companies are competing for the same investigators, and if they are not available, each company has to start from scratch. The system is fragmented and unsophisticated."

Jae Chung, founder and president of goBalto, a company specializing in study startup software for the life sciences industry, concurred, adding that "these methods lack verification and are slow, taking 3.2 months, on average, to go through the site section process. 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."

Patient enrollment achievement rates

Typical multicenter clinical trial



Source: Tufts CSDD, 2014 <csdd.tufts.edu>

Although the industry is in agreement about what the problems are, finding a solution has proven to be much more difficult. Many alternatives are in the marketplace, and others are in the pilot development phase. It remains to be seen whether any will turn out to be the magic bullet.

Building integrated platforms

One approach that has gained some traction in the marketplace is the use of online databases designed to match investigators to pharmaceutical companies. DrugDev, a technology company with offices in Philadelphia, London, Boston and Washington, D.C., was founded in 2009 specifically for this purpose. The company has since expanded its online network to include 80,000 investigators in 115 countries.

But over the years, it has become increasingly clear that a database alone isn't enough to improve site selection processes. The industry needed a more holistic solution. Several companies have developed online platforms that are a "one stop shop" for clinical trials, providing tools for site feasibility, selection and activation. Each platform is unique and brings together data in different ways.

DrugDev is a case in point. It rolled out its latest concept, called DrugDev Spark, a unified clinical operations solution suite, in the beginning of 2017. The idea is for clients to go through the whole clinical trials process from one interconnected clinical operations platform. Through the site selection and planning module, they learn about investigators and sites from a number of sources, including DrugDev's investigator and site online profiles. These

profiles highlight previous clinical trials experience and other relevant information. The profiles data are then made available to all member companies on the platform.

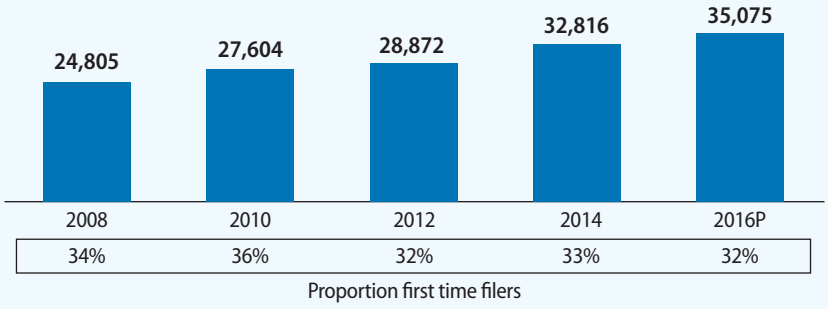
"The profile-sharing component saves time because the investigators only have to answer questions about their capabilities once. Appropriate consents and permissions are in place as well," explained Claire Sears, data solutions communications director at DrugDev.

DrugDev Spark also set out to tackle another problem facing the industry: multiple listings under different names for the same person or institution. For example, an investigator named John Smith may be listed as J. Smith in one database and Jon Smith in another. Using proprietary algorithms, the system can identify and match the records of the same person and then assign that person a number the company calls the "DrugDev Golden Number."

"The DrugDev Golden Number ensures that the client is looking at the same investigator whose experience may span many years at many different institutions," explained Sears. "It also means that we can integrate information about that investigator from a variety of data sources. With a richer view of investigators' experience, clients can spend their time matching the right investigators with the right trials. This process facilitates data-sharing across companies and with other partners, reducing investigator burden and allowing us to provide additional services, such as financial/aggregate spend data."

To date, more than one-third of global interventional industry clinical trials are now indexed to the DrugDev Golden Number, and this proportion is growing as new companies onboard the system.

A fragmented global community of FDA-regulated investigators



Source: Tufts CSDD; <csdd.tufts.edu>

"We're seeing a shift in the companies' mindset," noted Sears. "They are embracing the benefits of data-sharing through collaborative projects, such as the TransCelerate Investigator Registry and the Investigator Databank."

Although still too early to have hard data, anecdotal evidence suggests that the platform is saving clients time and effort. Factors that are having a positive effect on a customer's return-on-investment (ROI) include reducing the time spent on selecting and prioritizing sites, decreasing the number of rescue sites needed and increasing investigator engagement.

"We invite the highest-performing sites for each indication to join the catalyst network, which also includes representatives from institutional review boards (IRBs), technology partners and laboratories, to build a unified team that works together to implement each trial. By inviting everyone to work together from the get-go, the process is much more targeted and efficient."

—Clare Grace, Ph.D., vice president of Site and Patient Access, INC Research/InVentiv Health

A rating system for sites

Like DrugDev, goBalto, a San Francisco company, also has an integrated platform for clinical trials that carries clients from site identification to activation, incorporating innovations designed to save time and money.

The first is the use of a cloud-based system to house the platform. According to Chung, this approach frees up resources so that businesses can focus their time and energy on the pursuit of innovation and growth. This occurs largely because the cloud system is easier to use, has greater flexibility, is less expensive and affords more ways to scale up and ensure availability and optimal performance.

Equally important is the ability of clients to send out targeted queries to the platform, which includes a composite of data from internal sources, such as goBalto's performance metrics, and external sources, including Citeline, PubMed and ClinicalTrials.gov. Using all this data, the system assesses the query, automatically composed by the system from the study protocol, and comes back with a list of possible sites rated on a scale of one to 100. The client can then hone in on the top sites with the highest scores.

"Think of our approach as the Yelp of the industry," explained Chung. "The system will tailor its results to the specific requirements spelled out in the query. We're not creating a database. The value proposition we bring to the table is merging data from other databases and providing a user-friendly way for clients to search and find the best sites for their study."

This product has been on the market for about a year and half. The company has data showing the system's capacity to uncover sites. "We have evidence of increased efficiency, cost savings and productivity gains," said Chung. "Using de-identified patient data associated with target sites should increase the likelihood of those selected sites meeting their patient recruitment goals on-time and on-budget."

Similarly, Medidata Solutions, in New York, has a cloud-based platform called the Medidata Clinical Cloud, which allows clients to conduct all of their clinical trial business from one portal. Data from multiple sources are curated, enabling clients to get a quick snapshot of what sites are available. The system can also use this information to predict how many patients can be enrolled at each site. Based on the data, clients can submit very specific queries to find the right site.

"If a company is starting a phase I trial, it may be less concerned about high enrollment numbers and more concerned about cost," explained Andrew Cassel, managing director of Data and Data Analytics at Medidata Solutions. "The platform can find appropriate sites for that trials. It can also accommodate a phase III trial that has a big budget and is looking for sites with historically high enrollment numbers and good data quality."

Recognizing the problem of multiple listings for the same investigator or institution, Medidata, like DrugDev, has developed a solution. In addition to having an algorithm cross-referencing the listings, the company has hired staff to check the data. "We have a team of 30 people who spend all day, every day, curating our data asset," explained Cassel. "We have invested more than 100 years in the curation and quality assurance of our data."

Superimposed onto the Medidata Clinical Cloud is another feature, still in the pilot phase. This feature, called operational performance analytics (OPAL), is scheduled to be released in the fourth quarter of 2017. The advantage of OPAL is that it enables clients to look at their historical performance data compared to their peers in the industry.

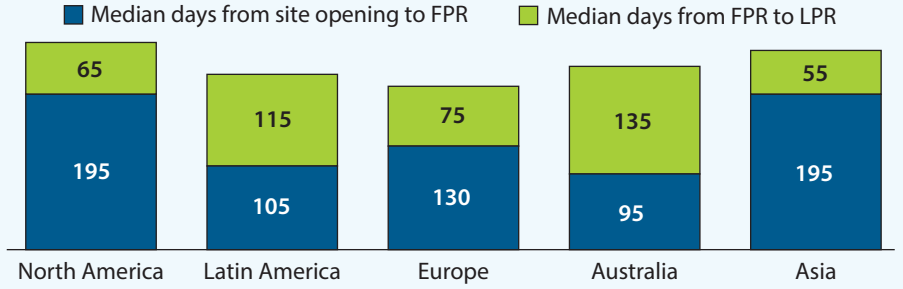
"Clients benefit from the system because they can drill down to each therapeutic area, study and site to analyze reasons for sub-par performance," said Cassel. "By tracking their metrics over time, clients can learn from their prior successes and failures, figure out how to improve and even make corrections in real time."

Selection of current site selection database offerings

Company	Type of service	Unique features
DrugDev	Unified clinical operations suite of solutions providing one-stop services for clinical trials	Member-based; emphasizes sharing and integration of information from multiple data sources.
goBalto	Cloud-based system	Aggregates data from multiple sources and ranks sites.
Medidata Solutions	Cloud-based system	Aggregates data from multiple sources and allows clients to see progress over time, benchmark against their peers, and make corrections.
INC Research/ inVentiv Health	Invitation-only network multiple partners	Organized by therapeutic area and includes only top sites. Brings in external partners for quick startup.

Source: CenterWatch, 2017

Site performance by global region



Recruitment metrics- time from site opening to First Participant Randomization (FPR) and Last Participant Randomization (LPR)

Source: Berthon-Jones Courtney-Vega, et. al. 2015

A team approach

For INC Research/InVentiv Health, a CRO based in Raleigh, North Carolina, improving efficiencies for clinical trials involved more than collecting and aggregating data. Instead, this CRO looked to high-performing sites in specific therapeutic areas to build unique networks that also included key external partners. Called the Catalyst Site Network, the program now encompasses networks in four therapeutic areas: oncology, vaccines, early-phase

research and psychiatric disorders, which just launched in June 2017.

"We invite the highest-performing sites for each indication to join the catalyst network, which also includes representatives from institutional review boards (IRBs), technology partners and laboratories, to build a unified team that works together to implement each trial," explained Clare Grace, Ph.D., vice president of Site and Patient Access at INC Research/InVentiv Health. "By inviting everyone to work together from the get-go, the process is much more targeted and efficient."

The company also has a larger Catalyst Community, which is open to all sites. The purpose of this community is to promote dialogue and to share knowledge about new technologies and best practices. "By sharing information, we raise the game across the industry," noted Grace.

When working with clients, the process begins with a seven to 10 day intensive discussion about how many sites are needed, types of sites and site mix. Once the study begins, this process is normally extended over four to six weeks, when decisions about sites, locations, patients and resources are made. "With the Catalyst Program, the timeframe for startup is significantly reduced," said Grace.

Grace and her team are hoping to have a large set of metrics available by the end of the year. "We understand that each therapeutic area is different," added Grace. "We're trying to build a different, more therapeutically minded mechanism to conduct clinical trials in the most efficient way possible."

Investigative site activity: 2015

	All values are medians
Total number of request for proposals (RFPs)	21
Total number of contracts negotiated	12
Total number of contracts awarded	10
Total number of clinical trials initiated (e.g., protocol approved by IRB and site ready begin screening patients)	12
Total number of clinical trials for which your site was actively recruiting and retaining study volunteers	17
Total number of initiated clinical trials that were canceled	2

Source: CenterWatch, 2015; n=252 investigative sites

Looking to the future

Time will tell whether these new products will make a difference in how sites are selected and clinical trials conducted. Even though many innovations have been made, the industry is aware of new issues that still need to be addressed.

"For some of the newer therapies, such as checkpoint inhibitors being tested in oncology, the issue isn't finding sites, it's finding patients," explained Cassel. "In this space, the competition for patients is fierce. For these trials, we need to figure out a way to target the patient population and then figure out how to set up a trial where the patients are located. We're still working on that."

Another issue that may require some attention down the road is whether investigators will have any recourse if they get a low score. "Investigators should have an opportunity to challenge a low score," observed Getz. "Their feedback could help further improve the quality of sites and keep everyone competitive for future trials."

Getz also wonders whether any of these new products will have widespread adoption. "Over the past three decades, I've seen many ideas come and go," he said. "But none have yet taken hold. We will have to see if any of the new generation of products are able to transform the industry."

Marilyn Fenichel is a freelance science writer based in the Washington, DC, area. She has been working with CenterWatch for about a year. She writes frequently about cancer, healthcare policy and other topics related to health and medicine for numerous magazines and nonprofit organizations. Email mfenichel@rcn.com.