DRUG DISCOVERY & DEVELOPMENT

Are Clinical Research Sites a Dying Paradigm?

24**AUG**2017
By Craig Morgan

A recent analysis by the Manhattan Institute determined that Phase III clinical trials account for 90% or more of the cost of developing an approved drug from laboratory to pharmacy. Given that reliable estimates put the cost of developing, and gaining marketing approval for a new drug, at well over a billion dollars, it's clear that human trials are pivotal to the pharmaceutical industry scrambling to find ways to reduce costs and speed timelines, while maintaining the quality and efficacy of the research.

Investigative sites have come under scrutiny in this pursuit, as the site selection and activation process is a perpetual bottleneck in starting studies. According to research conducted by the Tufts Center for the Study of Drug Development (Tufts CSDD), it takes on average 17 months to get from protocol approval to 100% approved sites initiated for a study, with costs ranging into the millions of dollars.

Patient recruitment and retention are additional challenges for investigative sites that drive up overall costs. Some estimates have indicated that patient recruitment is responsible for 30 percent of the time it takes to conduct a clinical trial, and sadly, a significant number of sites never enroll a single patient. Additionally, according to Forte Research, the average patient dropout rate across all clinical trials is 30 percent, with 85 percent of all clinical trials failing to retain enough subjects to successfully complete a study. These avoidable delays drive up overall study costs and negatively impact timelines.

mHealth Technologies and the Site-less Clinical Trial Model

The emergence of disruptive mobile health (mHealth) technologies is fueling an industry push towards a more patient-centered approach (also known as site-less trials, remote trials and virtual trials.) Instead of requiring study volunteers to visit an investigative site multiple times over the course of the study, this approach utilizes various mHealth and telehealth technologies to allow patients to accomplish study visits from the comfort of their own homes. Study volunteers communicate with study personnel remotely via

technology and receive their medications in the mail, while health data is transmitted over the web via mHealth technologies. This effectively eliminates the need for site selection and activation activities on multiple sites, thereby saving study sponsors significant amounts of time and money, while reducing trial participation burden on patients.

In addition to mHealth and telehealth technologies, site-less clinical trials may also rely on home visits to patients by skilled nursing resources. This eliminates the burden of a site visit and may improve overall patient retention. There is significant precedent for home visits in clinical trials, particularly for rare diseases or other serious indications which leave the patients home-bound. Home visits have been leveraged successfully over the last few years to avoid low recruitment or high drop-out rates. A recent study on rare disease patients published in Neurology reported that over half (54%) indicated that home-based research visits would increase the likelihood of clinical trial participation.

With the rise of siteless trials and the confluence of factors contributing to high costs and slow timelines - Are clinical research sites a dying paradigm?

Technologies that Support the Siteless Clinical Trial Model

The siteless clinical trial model leverages the power of the internet as a communication tool. Various connected mHealth devices like Fitbit, Apple Watch, Telcare and Scanadu allow subjects involved in clinical trials to transmit remote, real-time patient data (e.g., sleep duration and quality, blood pressure, blood sugar, activity levels, heart rate, etc.) directly to the central study site, eliminating the need for a site visit by patients.

Other technologies are utilized to provide a communication channel between patients and those who administer and conduct the study protocol from a centralized location. A technology firm known as Exco InTouch, for example, specializes in supporting patient-centric trials with digital solutions for patient engagement and data capture that help patients integrate clinical studies into everyday life. The Exco InTouch Gather platform connects patients with study personnel in ways that facilitate more effective data gathering and patient convenience.

eClinicalHealth has developed a patient-centric, cloud-enabled platform called Clinpal that improves patient engagement and data acquisition through every step ofthe clinical trial journey. This platform was utilized recently in a 100 percent remote diabetes study conducted in partnership with Sanofi where all patients were recruited via Facebook. This study also utilized an electronic informed consent form that patients were able to receive and sign remotely.

Other technologies supporting the site-less clinical trial model include an iPad app from a firm called Mytrus that is used to distribute clinical trial consent forms. Additionally, Radio Frequency Identification (RFID) chip technology is being utilized to allow study personnel to monitor at home dispensing to determine whether the patient has received the correct medication and is taking the correct dose.

Siteless Technology Contract Research Organizations (CROs)

An interesting development in site-less clinical trials is the concept of the site-less technology contract research organization (CRO). Center Point Clinical Services launched the world's first CRO specializing in site-less clinical trials in 2016 "The siteless CRO model enables clinical research to be conducted at an unprecedented scale and scope," said CEO Joe Martinez. "Study sponsors are able to reach and maintain excellent communication with trial participants, wherever they are, as well as secure and retain reliable data that can be instantly accessed and shared. Our model provides an insurance policy to 'de-risk' the clinical trial process and empower study sponsors to successfully manage in the new world of patient-centric and direct-to-patient activity."

While Center Point is currently the only CRO focusing exclusively on siteless clinical trials, there is evidence that other CROs are beginning to move in this direction. Earlier this year, Parexel launched a patient sensor solution that will allow study data collection remotely using wearables and sensors.

Benefits of the Siteless Technology Model

The siteless technology CRO model for clinical trials has a number of benefits including:

Provides a More Diverse and Representative Patient Population. Clinical trial models are currently built around the concept of the geographical investigative site. Unfortunately, this old model eliminates a large number of potential study volunteers who simply do not have convenient access to these sites – elderly patients with mobility issues, patients who live in rural areas, patients who are very sick, etc. The siteless model opens the trial up to a much wider – and therefore potentially more diverse and representative – patient population.

Speeds the Recruiting Process. By significantly increasing the number of potential study volunteers, the site-less model can dramatically speed up the trial recruiting process, and ultimately shorten the duration of the clinical trial itself.

Improves Patient Compliance and Retention. Poor patient medication compliance and retention are a problem for many traditional studies. When study patients are supported by calls from pharmacists on a regular basis to educate and reinforce study protocol, however, patient compliance and retention are

improved significantly. Additionally, patient convenience in the siteless model is a big contributor to patient retention. Data compiled by Center Point shows that studies which they have supported increased patient compliance by 30 percent, and patient retention by 60 percent or more.

More Cost Effective. The lack of multiple brick and mortar study sites, along with improved patient recruitment and retention, saves sponsors significant amounts of money.

Improves Ability to Achieve Regulatory and Commercialization Goals. Use of mHealth technologies with continuous monitoring increases data volume, while improved patient compliance leads to more reliable data. Additionally, the centralization of the study site in site-less trials leads to a reduction in record-keeping inaccuracies and omissions, and adverse events and safety reporting failure. Ultimately, the improvement in data reliability and record-keeping helps sponsors to reduce cost and better achieve regulatory and commercialization goals.[12]

Challenges of the Siteless Technology CRO Model

There are a number of challenges inherent in the site-less CRO model:

May not work for Complex Trials. The siteless model is more difficult to implement for trials that require complex study visit procedures, or those that can only be conducted by expert medical specialists using technical equipment.

Data Security. Given that large volumes of sensitive patient data will be transmitted over the internet, data security is a concern that must be addressed. Patient recruitment and retention can also be affected by data security concerns.

Difficulty Attracting Older Patients. The siteless model is best suited to the millennial generation, who are familiar and comfortable with remote communication and technology. Patients over 60 may be disinclined to participate due to a lack of in-person support in the trial. Additionally, patient recruitment through social media will likely not be very effective for people over 60.

Conclusion

Problems with the traditional multiple study site model include:

- Communication between sites, sponsors, and patients is often not robust and can be a limiting factor in study quality
- Clinical study teams at different sites often work in isolation
- Systems used to support patients and sites are not connected

Siteless clinical trials solve these problems and provide significant benefits for study sponsors and patients alike. Siteless trials will continue to grow in popularity as the industry invests more in patient-centricity.

Hybrid studies, where patients have a choice as to how they interact with study personnel – either attending in-person appointments at a study site or participating remotely using mHealth technologies - will likely become more common.

The ultimate winner in this industry move towards siteless clinical trials may be the patient. As siteless clinical trials drive down costs and speed timelines due to improved patient enrollment and retention, patients will benefit from having faster access to treatments.

Craig Morgan *is a technology and life sciences management professional with more than 15 years experience in the application of informatics and bioinformatics to drug discovery. He currently heads up the marketing and brand development functions at goBalto, working with sponsors, CROs and sites to reduce cycle times and improve collaboration and oversight in clinical trials.*

Craig Morgan
Head of Marketing | goBalto