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Start-up Costs Can Be an Uphill Slog in Need of Change

By John W Mitchell

Frustration about clinical trial start-up costs is not unlike Sisyphus' dilemma. A host of long-standing expense and inefficiency realities continues to create such uphill headwinds for the clinical trial sector. According to some sources, such problems even threaten the viability of the sector. Sites complain they incur more overhead costs driven by regulatory documentation, antiquated data collection and the demands of precision medicine to name a few — all without increased compensation from sponsors and CROs. A recent study supports this concern. Researchers at the Tufts Center for the Study of Drug Development found that the study start-up phase of five to six months for clinical trials has remained unchanged for the past decade. The study also concluded that CROs making investments in technology are getting trials done faster. None of this bodes well for smaller, independent players.

"Sites are doing more work for [fewer] patients. We used to enroll about eight patients per study 10 years ago, and today the number is less than three," says Jeff Kingsley, CEO at IACT Health. His company operates 13 locations in Georgia and a few outside the state in a network of about 100 clinical specialists. "The protocols are longer, and there are more procedures per patient per day. So, you're doing loads more work, but you're only paid when you put patients in trials. The averages speak for themselves — you put fewer patients in trials today."

According to Kingsley, the only way to continue this financial model is to participate in three times as many concurrent trials. However, he says it's far more efficient from an overhead standpoint to have one trial that places eight patients, rather than three trials that place eight patients.

Also, at a time when technology is conquering inefficiencies in other industries, technology is compounding problems in the clinical trial sector. In each of the three studies he cites above, it's likely that three different electronic health records, tablets and wearables are used by the different sponsors. When each sponsor uses their own networks and devices for patient-reported outcomes, it adds to site workload and time.

"We have no ability to standardize technology," Kingsley says "We have to do so many trials with so many sponsors, and they have their own decision-making… Our industry suffers from adoptive phobia (standardization between sponsors and sites)."

As an example, he cites the advantages of sites adopting electronic platforms such as eSource. Using such a platform could save billions compared to the aggregate cost of monitors flying to sites to review source documents. Clinically, an electronic platform also prevents errors such as entering a blood pressure incorrectly or performing a patient procedure out of order from the test protocol.

"We're trying to convince the industry it's a huge benefit, but the sites can't afford to pay for all this software," Kingsley says. "These costs should be borne by the sponsors, but they're not — they're balking."

Tufts researchers analyzed nearly 10,000 protocols from 178 global pharmaceutical and biotechnology companies based on Medidata PICA standards. They compared data from 2001 to 2005 and 2011 to 2015 — and found that both trial complexity and costs are on the rise. Lead study author Mary Jo Lamberti attributes this to several factors, including site identification, site selection, the submission of regulatory documents, and contract and budget execution. The more exacting needs of precision medicine also play a role, she adds.

Further, the study concluded that while Phase I and Phase II clinical trials are the most complex based on distinct and total procedures, Phase III trials have seen the biggest increase in complexity over the past 10 years. The total number of endpoints rose 86 percent. In response, drugmakers have doubled the number of countries and increased investigative sites by 63 percent in support of Phase III protocols. Yet the mean number of patients has declined 18 percent.

Some new technologies are being utilized, but there's still not meaningful data or system standardization, Lamberi says. And even when sponsor technologies are available, there often isn't any tech support available when clinical coordinators and patients encounter difficulties, Kingley stresses.

"The burgeoning amount of technology is daunting," he says. "Our coordinators went into research to be in front of patients. They are spending an inordinate amount of time with tech support and with patients on unscheduled visits because their

tablet (from various sponsors) isn't syncing or transmitting. These costs should not be borne by sites...but we're doing it for free."

Mark Lacy, Benchmark Research's CEO, reports that just attempting to get selected as a trial sites takes more effort now.

"We are asked to provide more and more information to help the CRO win a bid from a sponsor. This equates to 10 to 15 hours a week completing the same questionnaire from multiple CROs for the same study," he says. "We don't get paid for the work if the CRO doesn't win the bid."

But he notes that if they don't do this prep work, his company risks not landing the study if the CRO wins the bid.

Jill Johnston, President of WCG Clinical support and management, notes that effort, time, technology and pass-through costs have all increased for sites.

"Costs are always a problem," she says. "Technology use in the space is still in its infancy, we are not yet seeing the returns, but we are seeing the increased cost of the technology being added to the process."

Despite these challenges, she says better outcomes are possible with a keen commitment to change such as, for example, adopting new operation approaches in the early stages, rather than tinkering in Phase III of a trial.

"Pass-throughs, like IRB costs and startup fees for sites, have increased with business-savvy site organizations ensuring they are getting paid for their efforts, as well as inflation increases for some of the other pass-throughs," Johnston says.

Of course, the very tenuous nature of clinical trials is always close in the background. Su Linna, managing director at BDO Industry Specialty Services and Life Sciences Practices, says companies can easily spend millions on a product that will never come to market given that only one in 13 products survive Phase I trials. She cited Tufts findings that it takes nearly eight months from identifying a site to initiating studies — and that most sites under-enroll patients.

She also cited data from the clinical trial software company Medrio showing that the average cost per patient enrolled in clinical trials climbed 157 percent between 2008 to 2013. These costs typically account for up to 20 percent of the total tab.

But she says, "New technologies and approaches are promising to create efficiencies...We're seeing larger, more collaborate studies emerge." Plus, federal, state and grant funding options "can help companies defray costs."

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She cited wearable technology as an example of emerging technology, but conceded that upfront investments could be cost-prohibitive for smaller companies.

"The biggest costs are the labor that comes with starting up a trial," says Vivienne van de Walle, medical and managing director/owner of PT&R in the Netherlands..."When I try to get this built into a contract to get reimbursed, I often get a response: 'But this is part of doing the business.' My, by now, infamous response is: 'This is part of doing the business with you.'"

It takes at least three to four patients to begin to break even in the typical clinical trial, according to Walle. She also notes that there are now many portals in the clinical trial world, which is fragmented and time-consuming.

"Training can be protocol specific or generic. Generic trainings from various sponsors on IRT/EDC/eTools is often not acknowledged by other parties," Walle says. "Hence, we are doing the same training over and over again. [It's a] total waste of time that we are not spending with our patients (and in) recruitment."

She also notes that her company often has to invest its own resources in the pre-contract stage; this can be a precarious process. Sometimes, even after being selected as a site, there can be up to a two-year delay to eventually be canceled because the start-up process, including contracting, was never completed. This results in zero compensation for start-up expense.

Such troubles beg the question: why does any capable scientist/manager stay in the clinical trial sector?

"I'm in love with the trial business. I view it as broken," Kingsley says. "The healthcare industry trials the rest of the world in general with new innovation — such as big data, analytics, AI. Research is even worse in general than healthcare. We as a company are adopting eSource and eRegs and AI. I want to help fix it — I want to force change."

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