Decentralized Clinical Trials: Driving Economic Value In Clinical Development

The advantages of decentralized clinical trials (DCTs) are well recognized. COVID-19 showed that the DCT model was not only viable but practicable as a means of overcoming physical constraints on patient access to trial sites. Additional benefits are increasingly in evidence, such as speed, efficiency, patient convenience and diversity, improved recruitment/retention or data enrichment.

Nonetheless, clinical trials are expensive, and the attrition rate can be brutal. Trial sponsors want to know that, if they take DCTs on board, their bottom line is going to benefit too. Making a case for the economic merits of DCTs, though, can be challenging. The baseline costs of DCTs may not ultimately look that different from those of a conventional trial.

A better argument can be made for outcomes, but those may be hard to pin down, especially at the stage of deciding how a clinical trial is going to roll out. The inherent complexity of clinical trials also complicates generalized claims of economic value. No two studies are quite alike, given variables such as study design, duration, therapy area, patient population or disease prevalence.

A recent analysis by the US-based Tufts Center for the Study of Drug Development, quantifying the financial value of DCTs, provides an opportunity to open up the discussion. The Tufts report found evidence of substantial value in DCT strategies, as measured by changes in expected net present value (eNPV).

The Tufts study looked at three measurable factors with a known impact on the financial value of drug development: clinical-phase cycle times; screen failure rates; and the number of substantial protocol amendments. All of these KPIs improved in the DCT setting. In Phase II, for example, substantial protocol amendments fell from an average 3.3 (non-DCT) to 2.4, screen-failure rates from 31.5% to 24.1%, and Phase duration from 30 to 27 months.

In both Phase II and Phase III, the Tufts analysis calculated that, on this parameter, the increase in sponsor eNPV from DCTs in Phase II was $8.8m per investigational drug. That amounted to base-case RoI of x 4.62. On the same parameter, base-case eNPV inn Phase III rose by $41.2m to deliver RoI of x 13.2.

The Impact Of Time On Cost

Not all of these components had equivalent value in relation to costs, though. In some instances (e.g. Phase II protocol amendments and screen failures), investment in DCT methodologies did end up diluting RoI for those particular

elements. Nonetheless, points out Harpreet Gill, vice president, decentralized clinical trials at ICON, factors such as protocol amendments, “aren’t necessarily baked into the initial trial budget and the impact is difficult to predict at the outset”.

However, reductions of 27% in substantial protocol amendments at Phase II, and of 6% at Phase III, are “going to affect the long-term lifecycle of the overall drug-development programme”, Gill comments. “Logically, that will improve the return on your investment and reduce the overall cost of drug development.”

As the Tufts study underlined, duration is a key driver of cost inflation in clinical trials. This can be mitigated in DCTs through faster patient recruitment and site start-up, that are typically inflationary components.

Decentralization increases the speed of patient recruitment and reduces costs through digital and community outreach campaigns. This increased direct to patient outreach will often decrease the number of sites needed to recruit the same number of patients and associated site initiation costs including, Institutional Review Board (IRB) approval.

Driving Value With Patient Diversity and Retention

DCTs also deliver economic value by addressing patient diversity and retention.

Direct and broader digital patient recruitment also expands the diversity of patients with access to trials, an area that is seeing increased interest from regulators. As Gill points out,

regulatory bodies such as the US Food and Drug Administration have been vocal about the importance of diversity in clinical trials. Here, ICON has seen some "quite phenomenal" outcomes, such as 17% diversity in a heart-failure study, higher than would be expected from this type of study. Typically, a clinical trial will involve a very specific patient cohort, then regulators may ask for additional studies to provide evidence from different study populations. Covering a broader patient base from the outset should help reduce this demand and associated costs from follow-up studies.

Once patients are recruited, there is the further challenge of patient retention and compliance: 85% of clinical trials fail to retain enough patients and the average dropout rate is 30%. Here, the decentralized model increases patient centricity and optionality, by offering services such as home health. This reduces the burden on patients and increases retention and compliance. Moving the trial increasingly onto the patient's own turf, lowers the barrier to participation and brings benefits in terms of patient diversity, protocol compliance, engagement and patient retention with patients no longer having the burden of travel to the study site. According to a Baird report on DCTs, with remote visits, 38% fewer patients discontinue early and patient completion rates improve to 89% versus 60% in traditional trials.

One other key challenge and cost driver is delays due to data quality. DCTs alleviate this risk by driving better compliance generating data directly from source leading to higher-quality more reliable data. The Baird analysts found a 33% reduction in data variability for decentralized clinical versus traditional studies.

As Gill explains, DCTs enable the sponsor to be more agile with the collection of data directly from patients in real time. They can take early action to avoid protocol deviations or patient non-compliance, while delivering "cleaner" outcomes and outputs over the longer term.

Where The Value Sits

In making the economic case for DCTs, ICON draws on experience from more than 60 decentralized or hybrid studies conducted over the last few years, as well as over 400 in-home service projects. These have yielded "very clear proof points" of where DCT methodologies generate value, Gill says.

For example, providing focused support to patients throughout the trial, and within the patient's own ecosystem, whether through home-health visits or concierge services, "really does improve patient retention, reduce drop-out rates and keep the patient engaged in the study", Gill notes. In economic terms, this may be less about baseline costs *per se* than how costs shift with the transition to a decentralized model.

For example, the initial impact and investment of setting up home-health or digital health technology may be inflationary. On the other hand, and depending on the needs of the study, there may be compensatory deflationary elements that balance the investment out, such as fewer sites, reduced on-site monitoring, reduced fees for IRB reviews.

Concierge services may be seen as an additional cost to the sponsor upfront however, steering the patient through every step of the clinical-trial journey will ultimately bring real benefits to the study. These services can include everything from timely provision of sensors & wearables, ensuring patients can set up and log on to the technology, training older patients to manage the technology, helping a patient prepare for a pending telehealth visit, to providing ongoing technical support where necessary.

All of this helps to avoid protocol deviations and keep patients' interest levels up – both key components of value in clinical trials. "Every time you recruit a patient, there is cost involved," Gill points out. "If your patients don't drop out and are compliant, that's also going to have an overall effect on the economic outcome and value of the study."

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Driving Metrics That Reflect Economic Value

These are the kinds of metrics ICON is now focusing on, and will continue to measure and quantify throughout its studies, to drive home the message that DCTs really can elevate the bottom line. That means first sitting down with clients, right at the start of the study, taking them through the DCT model, and showing where costs are likely to arise and/or shift.

"Most of the studies are going to be hybrid, so there will be some movement," Gill elaborates. "From there on, though, we want to concentrate very much on the metrics: things like compliance with eCOAs (electronic clinical outcome assessments), recruitment rates, speed of recruitment, patient retention. We can look at all those factors during the study as leading indicators to see how DCT methods influence the study's economic value."

For the moment, publications such as the Tufts study are helping to put these issues into perspective for clients who may wonder where and when the economic benefits from DCTs are really going to emerge. "Some clients have never worked on a heavily decentralized study, and they view these as a risk," Gill acknowledges. "Industry research really does help us to have these discussions and develop the narrative around increased value."