eCOA and the DCT Slope of Enlightenment

Decentralised clinical trials (DCTs) have become widely accepted across the sector in recent years, and the road to their optimisation has resulted in several key learnings for researchers

Bill Byrom, Anthony Everhart, and Dan DeBonis at Signant Health

The Gartner Hype Cycle is a useful instrument to explore and explain new technology adoption. DCTs are no different, although successful DCT implementation goes beyond simply the enabling technology.

Our industry is traditionally measured and risk-averse when it comes to implementing new technologies – Electronic Data Capture (EDC) and Randomisation and Trial Supply Management (RTSM) solutions both took decades to gain widespread adoption, but are now universally implemented in the majority of studies. This conservative approach similarly applies to DCTs – building gradually from certain key steps such as telephone- and video-enabled clinician ratings in trials for certain disease indications to Pfizer's REMOTE trial experiment in 2011 (1).

Over the next decade, technology providers began to extend capabilities to enable fully remote studies, and new remote site service models began to emerge. This enabled cautious piloting and gave birth to the term 'DCT'. However, the adoption trajectory was accelerated beyond the expected course of the typical Gartner Hype Cycle by the COVID-19 pandemic.

The sequence of typical adoption phases, according to Gartner, starts with a technology trigger, then progresses to the 'peak of inflated expectations', drops to the 'trough of disillusionment', and then increases steadily up 'the slope of enlightenment', leading to productive use and increased adoption at scale. Therefore, it's expected that at some point we should arrive at the trough of disillusionment resulting from variable results from the application of developing, but less mature, solutions. Some clinical trial sponsors believe that they have landed in the trough of disillusionment, but others report a more positive experience. Emerging from the trough, the slope of enlightenment builds from collective experiences and learnings. The question that comes to mind from all of this is whether or not we are already well along the DCT adoption curve and we just didn't realise it. That in mind,

is the term 'DCT' simply an updated label fitting of the times – in some ways a repackaging of behaviours that are actually well-entrenched? We would argue that it is.

While there is a dedicated focus on this nouveau concept of DCTs, it's important to unpack the existing fundamental pieces and best practices of decentralising or optimising clinical research studies. In doing so, we can see that the leap of faith is not so great. There are well adopted and time-tested approaches, along with recent refinements, that can pay off the promise of better trials without the perception of risk or early adopter fears. Let's unpack some of these learnings from the slope of enlightenment and from earlier experiences in decentralising and optimising trials.

Learning 1: Many DCT Methodologies Are Not New

The idea of migrating measures from site to home settings is not new. In addition to patient-reported outcomes, industry researchers have been conducting complex clinician ratings in diseases like depression and anxiety via telephone assessment since the early 2000s, and via video conference before dedicated telemedicine platforms were available (2). As an industry, we have significant experience in decentralising. We should build on this, not reinvent, when considering DCTs.

Learning 2: Mature Solutions Are Vital

The aspiration of a single technology platform to manage all aspects of a DCT is a fine one. Sponsors have wrestled with this for years before DCT was coined. Is a single platform more important than bringing together integrated best-of-breed components from the same, or different, vendors?

To succeed with a single platform, each component from patient recruitment to eConsent and eCOA, telemedicine, and drug supply, must be sufficient to meet the needs of the study. The complexity of functionality needed by many trials cannot always be supported by currently available, single-platform solutions.

Learning 3: Integration and Convergence Where It Is Needed

Patients require a simple study technology experience. This means a single application experience where patient workflow is not complicated by the use of multiple solutions. We need to examine where in their workflow this is most important. Pre-study, the patient is likely to be engaging with web solutions for recruitment, pre-qualification, and consent. Once in the study, it may be that an app is the primary interface with which they will interact. Does it matter if the patient is accessing their required solution via a different modality after they have consented? In our experience, no. eCOA solutions have evolved to enable wider functionality, and to provide a single app experience for enrolled patients. Patients can be guided through all stages of a study, from accessing their visit schedule and receiving important information about upcoming visits, entering PRO data and operating sensors and wearables, connecting with sites via telemedicine, to interacting with couriers for home delivery of medication or sample pick-up.

Accessing eConsent through one modality, such as web, and other study solutions through an app doesn't disrupt workflow. In fact, accessing eConsent via the web enables use on larger screens which is optimal for consuming large amounts of content, whereas ePRO is likely more convenient and discrete on a smaller device, often through an app. It is important to determine where integration and product convergence is needed, and where it is either unnecessary or overly complicated.

Learning 4: ECOA Is the Cornerstone

In our experience, when most sponsors talk about DCTs, they are referencing eCOA with a number of potential add-on solutions that are considered on a per-study basis – like eConsent, patient engagement, and telemedicine. eCOA is a science and an art. It's more than an app, although the app itself is important.

eCOA is the cornerstone. It represents the patient-facing solution that collects clinical evidence to derive vital study endpoints, so it is of utmost importance to get right if the study is to succeed. Good eCOA needs to be functionally rich enough to meet the needs of each study protocol, without needing to bend the protocol to fit. It needs to be implemented in the optimal way, and following best practices, to ensure highest quality clinical data that can be relied upon by sponsors and meet regulatory scrutiny. It needs comprehensive associated features and services like reporting, compliance monitoring, device procurement and logistics, scale and license management, patient-facing helpdesk, and data change processes and functionality. Robust eCOA needs comprehensive and feature-rich tech, strong science, and excellent services to deliver successfully and reliably.

Learning 5: Successful Implementations Need Scale, Service, and Science

Moving from pilot mode to full implementation requires solutions and organisations that operate at scale. Ensuring global reach, operational capacity, architectural scale, and the ability to deal with the complexities of increasingly global studies in terms of logistics and localisation, are all important considerations that enable successful transition from pilot to pivotal trial.

Similarly, service components become increasingly important – for example, ensuring the correct COA versions are implemented and licensed correctly; leveraging relationships and established working practices to work with scale authors and translation vendors efficiently and effectively; providing end-to-end mobile device and wearable device procurement, set-up, and

logistics; and resourcing 24/7 patient support in all languages with a high immediate call resolution rate.

Scientific expertise is also an essential ingredient for successful DCTs, and has been a staple of DCT methods over the years. Clinical and scientific experts provide consulting on study design, helping to develop studies with decentralisation in mind. They ensure that measures migrated to remote assessment are done so in a way that preserves measurement properties while maintaining accuracy and reliability. They can review data throughout the trial for outliers, patterns, and trends, which might require mitigation to ensure ongoing high data quality.

Learning 6: Don't Forget About Drug Supplies

While direct-to-patient medication supply was a key component of Pfizer's REMOTE trial, and is a key component of the current Trials@Home research study, few sponsors and fewer vendors consider direct-to-patient medication supply as a DCT method (1, 3). But, medication dispensing is often a key activity at site visits. If the intention is to eliminate certain on-site activities to reduce the need for clinic attendance, then direct-to-patient medication provision should be an obvious consideration in many cases. Enabling provision of medication to the patient's home requires solutions that simplify the processes while carefully guarding patient privacy and identity, ensuring full oversight of the medication chain of custody, and maintaining investigator dispensing authority. This is an important, yet overlooked, component of DCTs.

Learning 7: Trial Optimisation Is the New DCT

Decentralisation tends to be associated with reducing site visits. A more useful perspective is optimisation – optimising the way clinical trials are run, and how clinical evidence is collected. This needs to be accomplished with speed and accuracy while focusing on ensuring an empathetic patient experience. Decentralising aspects of a clinical trial by reducing the number of on-site visits, through enabling certain procedures and assessments to be conducted away from a site, is one important tactic of trial optimisation. Optimising will focus on collecting the right data at the right time, using the right solutions in the right setting. Thoughtful, optimised study design should consider the number of activities conducted at required site visits, and how the visit experience could be simplified for both patients and sites by migrating certain elements to be conducted away from site. This may not always lead to fewer site visits, but should always lead to a more empathetic experience for the patient.

While some are currently experiencing the trough of DCT disillusionment, we as an industry may well be on our way up the slope of enlightenment without realising it. The focus on single platforms over ensuring that key solution pillars are implemented using best-of-breed components may be one factor driving disillusionment. Another factor may be a focus on decentralising as opposed to optimising study designs and protocol schedules of events. The DCT slope of enlightenment reveals the importance of robust, reliable, and comprehensive eCOA as the critical ingredient of successful DCTs. The addition of newer decentralised methodologies upon the cornerstone of eCOA will lead to greater and more rapid success.

References

1. *Orri M et al, Web-based trial to evaluate the efficacy and safety of tolterodine ER 4 mg in participants with overactive bladder: REMOTE trial, Contemp Clin Trials, 38: pp190-7, 2014*
2. *Kobak KA, A comparison of face-to-face and videoconference administration of the Hamilton Depression Rating Scale, J Telemed Telecare, 10(4): pp231-5, 2004*
3. *Visit: trialsathome.com/*

Bill Byrom, PhD, has worked in the pharmaceutical industry for 30 years. He has authored over 70 publications and two industry textbooks on electronic patient-reported outcomes (ePRO). Currently Principal, eCOA Science at **Signant Health**, his recent scientific work includes the use of wearable technology and bring-your-own-device (BYOD) eCOA in clinical trials.

Dan DeBonis, Principal, Endpoint Solutions at **Signant Health**, is at the forefront of innovation for electronic Clinical Outcome Assessment (eCOA), outcome analytics, and digital technologies. He has authored a patent as well as various publications on clinical research technologies.

Anthony Everhart, MD, Clinical Vice President Internal Medicine is an innovator, educator, and leader in the pharmaceutical and biotechnology industries with over 25 years of experience in the practice of medicine and over 14 years of experience in clinical research. Board-certified in Internal Medicine and a Fellow of the American College of Physicians, he is one of **Signant Health's** experts in decentralised trials, rater training, blinded data analytics, and placebo response mitigation.