Patient-Centric Clinical Trials: Turning Opportunities into Standard Procedures

Over the past year, the industry has heard often and at length about patient-focused decentralised trials (DCTs), as vendors and some early adopters report their early experiences in an area that is still evolving. It's important to remember that the industry is still at a very early stage in digital clinical trial development.

Truly patient-focused trials are a goal that we have yet to attain. We still use ePRO and eCOA, as we have for 20 years, only now we talk about these tools as if they are brand new and operate under a decentralised banner. They don't — at least, not yet. We may be using eConsent, but still have patients come to sites to initiate the process. That is not decentralised practice.

At the same time, most trial protocols have not reached a point where patients can participate flexibly based on their own preferences, which change from day to day. If we use multiple technologies to capture data — in essence, the same data from different patients — we must have simple methods to integrate and review that data in one step. That does not happen today. The industry is just beginning to think about common standards for sharing clinical data.

Now that more clinical leaders have experienced, firsthand, the limitations of new tools designed to make trials more patient-centric, many have adjusted their expectations from new technology and are experimenting with different approaches. They've also seen that simply deploying more technology won't make the patient journey any easier if it burdens research sites. In fact, we heard repeatedly at the recent DIA meeting (June 2022, Chicago) how technology overload was slowing down sites and their ability to work with patients. Today, some sites are reporting capacity as low as 30% of pre-COVID levels.

The Changing Role of Standards

One of the fundamental challenges facing the industry is developing standards for sharing clinical data that will enable digital decentralised trials. In the 30 years that Clinical Data Interchange Standards Consortium (CDISC) standards have been in place, industry thinking has changed considerably. Today, standards are no longer seen as intellectual property to be protected, but approaches that must be open and shared, so that the industry can move to one set of clinical data standards. Results will improve efficiency, not only for trial stakeholders, but for regulators, who will be able to inspect data more quickly.

Standards for data transfer will ensure that data is exchanged in the right format. Work will need to focus on two very different areas, designed for two very different purposes: clinical data (under the CDISC)[1] and healthcare data (under Health Level Seven HL 7).[2] Connecting these different data sources, types, and aggregations will require ongoing effort. At this point, as the industry moves into patient-driven data collection, neither, on its own, is a fit. Patients are going to own more and more of their data, and this will likely afford a whole new category, that will lead to yet more complication if new approaches aren't developed. The opportunity therefore is to find a way to generate, collate, and distribute data between point solutions that results in seamless connections between researchers and patients. Only once those connections exist can the industry apply scientific rigor to clinical data, and only then can AI, ML, and NLP be applied to the data in an efficient and scalable manner.

Modern standards development for clinical trial data sharing will require tremendous effort. Even though this work has only begun, interesting ethical questions are already coming up that the industry must address. For example, some healthcare providers have proposed giving every patient a unique record ID. This tokenisation approach would facilitate faster data exchange but could also lead to concerns about data security and privacy and could potentially be vulnerable to misuse. This idea requires open and frank discussion, but it does highlight the raw need to be able to share data quickly and effectively.

An Explosion of Data from Different Sources

Clearly, clinical trial stakeholders today must deal with far more data, from diverse sources, than they did in the past. Some clinical studies today have 10, 20, or even 30 distinct data sources, and, ideally, data should be ingested from these sources in real time. Currently, it must be aggregated and cleaned separately and then brought into the clinical database, a process that can take weeks. Data workbench platforms will be crucial to aggregating and cleaning that data and connecting it to other data in the CDMS. After all, every data point we collect has the potential to create a pattern of interest with every other data point.

These solutions will also fit in well with other approaches such as time-in-motion analyses[3] and advanced analytics, and we can expect to see more collaboration between vendors that specialise in data management and those that apply analytics to that data. The clinical workbench would ingest and aggregate the data and store it in one place, accessible to CDMS, while separate efforts would, for example, consider the cost vs benefit of running more frequent biomarker analysis, or use artificial intelligence to test the soundness of a trial model or individual process. CluePoints,[4] for example, uses AI algorithms, not only to analyse and challenge trial results, but the approaches being used. Analysing all the trial data, not just the clinical but operational, metadata, and audit trail data, offers a detailed picture of the patient's journey. Over time, it will allow the industry to question why certain processes and jobs are even needed and replace them with better approaches. If we can compartmentalise the work that needs to be done, and work together, clinical trials will be able to advance much faster.

Connecting with Patients

The industry is clearly increasing use of eConsent and eCOA tools in today's hybrid trials, and eCOA is already used in roughly half of today's studies. But the question today is whether it will grow because more people are adopting a digital/decentralised trial strategy or just because they simply want more real time, everyday data. We shouldn't confuse the use of those

technologies with the delivery of a true digital strategy.

I think it is important to remind ourselves that decentralising means we push out more of the daily activities from a centralised clinical site to the patient's home. This is not just about collecting more data; it is about changing the core thinking about data collection.

Industry practice will become more interesting, and much closer to the patient-centric ideal, when patients can be given more choice in how they participate in a trial. In one scenario, a patient would provide his or her consent remotely and would download an app to automatically become part of a trial. Day by day, she'd be able to choose whether to use home or remote monitoring or come to the clinic. This may not be possible with MRI or other procedures that require the patient to physically visit a location, but, in most cases, the patient would determine the degree of decentralisation. However, different clinical study teams would have to accept these options in order for this model to be delivered to patients.

At this point, sponsors are actively exploring the use of digital technology in clinical trials, but for each problem any new application solves, it may create several new challenges, especially for research sites, which will see it as a burden if it doesn't offer immediate benefits. In discussions with sponsors and partners, I advise them to consider both patient and site needs when they start writing the protocol; not afterwards. Applying new technology to a final trial design is simply too little too late. It is the same advice I consider for all technology companies - think about the user experiences we are seeking, across multiple different therapeutic needs, before you try to design a new product. Tackling the issues of the day, from concept to conclusion, is paramount and the only way to drive real change.

In the end, patient convenience is key to patient compliance and future trial enrollments. Today, most digital patient-facing technologies require too much work from patients. The following guidelines can help ensure that application development results in a win-win for patients, sites, sponsors and CROs.

- **Consider closely the interests of each stakeholder in the trial.** What are the key needs and interests for each group, and how are you delivering them? Are you currently using technology that solved one problem but created new problems that you couldn't anticipate? The fewer changes to the patient's normal daily activity we introduce, the better.

Success boils down to making the right data available at the right time in a highly consumable way. From a sponsor's perspective, it's about making processes repeatable, attainable, and defendable.

- **Determine the impact that each application will have on each stakeholder in the trial and consider overall cost.** How likely will auditors accept the data, how well will patients respond to the strategy, and how easily will sites be able to execute the approach? On top of that, of course, costs must also be considered. Remember that, if patients like the approach, accept it readily, and comply with requirements, you'll also be able to recruit them more easily in the future.

- **Don't make research sites the help desk for each trial. Ensure strong site-patient engagement and don't burden sites with new technology that does not add value to the work they do.** We're hearing anecdotally that some patient-focused apps are adding to clinical staff workloads and slowing trials down significantly. Before the COVID-19 pandemic, some sponsors say, research sites used to see six to seven patients per day. Now, they are seeing one to two patients a day, as site staff adjust to the need to educate and support patients on the use of new apps. At the earliest planning stages, sponsors must consider the potential burden that any new technology will place on sites and ensure that any tools that they develop will benefit sites and strengthen engagement between sites and patients. Better site-patient engagement needn't result in patients visiting sites more frequently. It means ensuring that the level of contact is right for the patient on that particular day. If a patient is doing well, there's no reason to have him or her come in. But if she isn't, she will need to visit the site at the right time to ensure that the trial is right for her or determine whether changes are needed.

- **Integrate applications into the devices that patients already use in their daily lives, whether phones, smart watches, or Fitbits, and reduce the number of steps required to register and use each tool.**

Be sure that the tools selected for any trial can communicate with each other, to make it easier for clinical site staff to check patient health and treatment records.

Think about how patients behave in the real world. Saddling them with apps on different devices plus an iPad will not be convenient. Integrating apps into tools that patients already use and accept, whether smartphones, smart watches, or Fitbits, will make it easier for them to comply with trial procedures. You may not be able to avoid having patients download an app, but why not give them a QR code to complete registration and other steps for them, carrying over user details and automatically creating data flows? This way, everything is connected in one step, rather than having patients go through a 20-step checklist just to get up and running.

- **Use a holistic healthcare framework for developing trial technology. For example, ensure that trial apps also give patients data that will help them better manage their overall health and interact more effectively with their HCPs.**

A scorecard approach will be extremely helpful for most patients. For example, diabetic patients who are overweight could receive a personalised daily diagnostic message from their physician, as in: "This is the amount of insulin you've taken today, this is your HbA1c result from the lab, and this is your blood glucose level. You're taken 10,000 steps today. Great work. Keep going." Or "I need to see you. You haven't taken any steps today, and your insulin, blood glucose and HbA1c levels are up. We need to talk." This type of approach would motivate patients and make the patient-physician interaction part of the trial, moving trials in the direction of holistic medical care. In the end, that is exactly what digital clinical trial technology should deliver.

Now that the initial buzz over DCTs has begun to fade, the real work is beginning as the industry explores how technology can best be used to bring patient centricity and efficiency to each trial. One test for digital will be adaptive trials, which would change continuously in response to trial results, requiring a central control point and seamless data transfer. At this point, we're a long way from being able to run adaptive trials digitally, just as we can't yet give patients real choice in how they participate in clinical trials every day. The key to advancing clinical trials is realising that digital strategies are in their very formative days. Accepting this fact, instead of acting as if decentralised patient-focused trials had already arrived, will allow us to work together and advance to truly flexible, patient-centered digital trials in the future.

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