Decentralised Clinical Trials: How to Overcome the Main Challenges

Despite their definite advantages, decentralised trials have yet to find a firm foothold in the clinical trial paradigm. On the surface, it seems strange that such a positive upgrade to standard models has yet to see widespread clinical uptake: for much of what virtual trials require, technologies and algorithms exist which can suffice. Automation of form-filling and menial tasks is present in many other areas of pharmaceuticals; wearable monitoring technologies and standardised-format messaging systems, such as WhatsApp, are ubiquitous.

Lack of Data Integration

The move to more internet-enabled clinical trials has meant that physicians have access to more data than ever before. While this does provide significant benefits for both clinical study and for the patients, who can now view this information to better understand their progress in the trial and their own development and treatment, problems remain.

The numerous sources of data used in clinical trials (from wearables, instant messaging platforms and e-forms) are yet to be easily integrated into a single, usable source. This disallows effective analysis, meaning that it is that much harder for trials to pass regulatory review.

According to a Tufts University impact report published last year, the amount of data from clinical trials is growing steadily through greater study scope and complexity. As this has happened, 77% of sponsors and CROs have reported difficulty loading the new data into their EDC systems for a number of reasons, in particular compatibility and integration issues and technical problems. To combat this, on average six different applications are used to contain this data.

This difficulty has a knock-on effect for trial time, with the time from "last patient, last visit" to database lock increasing from an average of 33.4 days in 2007 to 36.1 days on average in 2017.

In Oracle's 2019 survey, participants claimed that they felt like technology providers were overly focused on adding more and more functions to products, without considering whether they are interoperable with others.

Participants in the survey also suggested that having numerous technologies in a trial would slow down processes through several separate portals or log-in details. Due to the need to train staff in each technology, there is also a potentially large burden for patients averse to or inexperienced with technology.

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WHAT CAN BE DONE?

Tools that integrate multiple sources of data do exist, and are already being slowly introduced into decentralised trials. This technology allows sponsors to both aggregate and integrate data to improve efficiency. Standardising data across multiple sources also allows for much quicker analysis, a reduction on manual standardisation burden, and increased trial oversight and understanding.

While the right data integration software will vary based on company needs and circumstances, there are a number of guides already online that can narrow down the options available and make a decision considerably easier:

- The Buyers' Guide to Data Integration Software
- Bio-ITWorld's Managing and Integrating Clinical Trial Data report
- A guide to the best clinical trial management software for 2020

Patient Incentivisation

Patient engagement is one of the major troubles facing clinical trials today. As has already been noted above, a significant percentage of patients will drop out of a clinical trial before or during phase 3. There are dozens of reasons for this: patients can feel isolated or unheard during the treatment; they can see limited feedback on their progress during the trial, or lack an understanding of what their place is in the trial; they can be put off by difficulties in any part of the process, from the burden of wearable technology to a lack of compensatory incentivisation offered.

Gareth Powell noted a central reason why clinical trials find patient engagement so difficult: "It comes down to accessibility. Clinical trials can be a burden for both patients and clinicians, with long hours and continuous visits a difficulty. Normal life gets in the way."

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WHAT CAN BE DONE?

Powell suggested that as decentralised trials become more well-known and commonplace, incentivisation will occur naturally. He said that with the increase in electronic patient-reported outcomes (ePROs) capturing both healthcare and lifestyle information, such as social time, the impact of an illness on work etc, the patient is increasingly able to view their own data.

This means that they can better engage with the trial and their healthcare progress, either by seeing improvements as they occur or seeing how the data is operated. This alone gives something back to the patient and makes continuing the trial more appealing.

While steps have always been made to disseminate information with the patient at the end of the trial, doing so during the process is much more engaging. For example, he pointed to LEO pharma's Imagine app. This shows snapshots across the timeline of skin condition treatment, so patients can understand the impact the medicine has had on them.

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Maria Palombini noted that a number of pilot projects are currently active and onboarding patients. A majority of these projects have been focused on patients with rare diseases, as they're often highly incentivised either by potential access to a last-resort trial or to receive better therapy for quality of life.

She said that full virtualisation of trials was a fundamentally exclusionary concept. Patients who are already disillusioned with the process are unlikely to sign up to a trial which lacks human contact or inclusion. Hybridised trials, however, still have that human connection alongside the added bonus of automation and digital technologies, blockchain for data management, and increased diversity due to greater population inclusion.

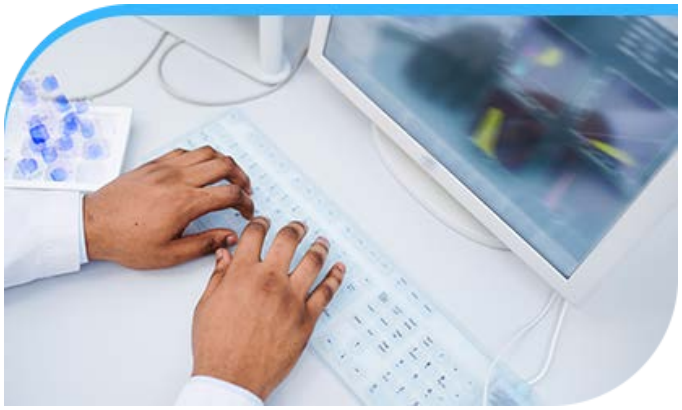
Lack of Patient Safety / Adverse Event Reporting

Concerns have been raised that decentralising trials leads to a fall in patient safety, due primarily to the fact that without direct patient contact, there could be limited recognition of adverse events or dissatisfactory care.

John Reites acknowledged this as a real risk that must be mitigated: "The ability to remotely capture data, capture it more continuously and hold visits outside of the standard trial clinic visit, means that additional processes backed by experience must be setup to support patient safety as the number one focus with clear steps to support AE/SAE reporting."

WHAT CAN BE DONE?

This problem, of course, applies largely to decentralised trials that do not adapt suitably to the change with necessary or advanced technologies. While many doctors have suggested that a lack of face-to-face time with the patient could lead to missed signals, advocates of decentralising trials can point to dozens of technologies that minimise this concern.



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Examples include tracking technologies, like Apple Watches, that can collect and store data, letting clinicians interpret and react to adverse reactions. Many of the more advanced types of wearable or monitoring technology can also automatically detect different forms of adverse event, such as nQ Medical's neuroQWERTY keyboard, which can predict patient disease based on how fast an individual is typing or keypad pressure and was recently awarded Breakthrough Device Designation by the FDA.

Gareth Powell elaborated on this concern: "If someone's having an AER, how can we tell? Well, if we're using Web X calls or video services, the model can work. Remote face-to-face discussions, supported by underlying data like heart rate or blood pressure that can notify of an AER, are seeing greater and greater practice. As the technology improves, we can take more and more measurements and be in a better place to analyse the data."

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Device Selection

A slighter issue with decentralised trials than those referenced above, the selection of tools and devices is also an issue brought up by some clinicians as a problem when moving to more hybrid models of trial.

Issues raised include understanding which devices and models to use, in a field that is only now beginning to develop and be better understood. Reticence to introduce variability into a necessarily structured and highly-ordered process is understandable.

WHAT CAN BE DONE?

Here more than in any other challenge to decentralised clinical trials, the answer lies in knowledge and experience, something which many companies are in short supply of. As the field progresses, physicians and site operators will by default learn more about best practices of the technological aspect, and become more able to discern what will benefit both the patient and the study and what will not.

The answer to this challenge can be difficult for a company to establish on its own. The necessary equipment and processes will of course depend entirely on the trial being run, on patient population size, geographic dispersion, and the level of interaction sites wish to have with their patients.

Without any knowledge whatsoever, a CRO could be the best solution to a company's expertise needs. While some have questioned the necessity of CROs as companies gather more and more technological solutions that easily reduce outsourced work, for newer companies a CRO could be vital.

The CRO landscape now covers almost any task clinical trials need performing, from patient recruitment to working with novel or expensive technology that is more efficiently outsourced than bought and trained around. While CROs require a level of trust, co-operation and short-term expense than is otherwise found simply by internalising procedures and technology, for many companies it is the preferred option when dealing with new processes or technologies that they lack the staff for and experience in.

The use of CROs for technology, data and personnel management allows pharma companies and sites to focus on other tasks, such as developing new frameworks and building new networks with key opinion leaders. The main areas in which CROs can be engaged to perform outsourced work include:

- Medical and scientific, including medical advice, writing medical reports and legal responsibility of trial conduct.
- Statistical, including data entry into databases and statistical analysis of safety data
- Trial management, including investigator selection and recruitment and monitoring the conduct of studies and protocol compliance
- Regulatory, including compilation of technical data for regulatory agreement and interim progress reports to regulators
- Drug safety, including designing safety data collection methods, assessing the study safety profile and assessing serious AEs in a study

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