Decentralized Clinical Trials

ESSENTIAL TIPS TO AVOID COMMON PITFALLS

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INTRODUCTION

The shift to DCTs has numerous advantages. Remote solutions for maintaining site visits and drug delivery activities in a variety of situations allowed trials to continue during the global COVID-19 crisis. Such solutions also provide participants with more choice regarding how they engage in studies: patients can now potentially choose between going to a study site or speaking to the study doctor via a televisit and can complete their PROs anywhere. This can lead to a significant reduction in the burden associated with clinical trial procedures, by removing need for patient transportation and paper documentation. Study patients can also choose to use their own smartphone or a provisioned device to complete their eDiary. All this gives a tremendous level of flexibility to study patients and mirrors the lifestyle technologies they are now accustomed to using routinely.

Despite these advantages, reducing on-site visit means that data endpoints need to be captured via other means. **Data must not be lost when patients do not come to site for several weeks, data quality must be guaranteed throughout the project, and data must be protected even when patients use their own mobile.**

How can the common pitfalls that come with DCTs be avoided?

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#1

AVOIDING DATA LOSS WHEN PATIENTS VISIT FREQUENCY IS REDUCED

OFFER FLEXIBILITY

The technology used to support DCTs should offer many options to reduce the risk of data loss. With flexibility comes patient choice, which ultimately leads to a higher data collection rate and a better chance of clinical trial success.

- **Large eDiary data collection options:** BYOD or a Provisioned Device offers patients the possibility of completing their eDiary and ePRO endpoints using the comfort of their own smartphone, or using the device that is provisioned for the study should they prefer to keep real life and study life separate.

- **Customizable reminders and alarms** for patients' duties (ePROs, eDiary completion): when study patients can adapt the time or the volume at which reminders will ring, they have more control over their study-related duties and can fit them better around their own way of life. This has the potential to improve the patient's experience and can be even more applicable in long-term studies, which can have a significant burden on daily life.

- **Back-up options in case the primary mode of data entry fails: WebCOA, spare device, interview mode.** Even if these options are all suitable, they might not all be working for every study or every patient. Although a WebCOA solution might be ideal in

many circumstances, an interview can be the best option when the study targets elderly or visually impaired populations, or in pediatric studies where the caregiver/parent may not feel comfortable using the alternative technology proposed. Each situation requires careful consideration of the protocol specifics and the patient population characteristics, together with rigorous planning to allow the most relevant back-up solution to be put in place from the study set-up and avoid the risk of data loss or unforeseen additional costs.

- **eConsent consideration:** the option of remote electronic *vs* on-site paper consent signature needs to be considered. The use of eConsent has so far been very cautious, and sponsors have preferred to pilot it on individual studies rather than incorporate it more widely. It is well recognized, however, that eConsent technology provides a consistent and traceable way of processing informed consent, secures the versioning, and can facilitate monitoring work. As the rate of protocol amendments in clinical trials continues to grow , the extra efforts and associated costs required to track and resolve consent-related protocol deviations are likely to be reduced with eConsent technology. However, in a highly variable regulatory landscape, the use of eConsent should be evaluated cautiously on a country-by-country basis, and it is vital to have a system that allows a hybrid approach of electronic signatures and print-to sign.

- **Telemedicine option:** accelerated by the pandemic, the use of televisits is expanding and it is now expected that this will become a standard approach in many protocols. Although the value of televisits is largely outside data capture (eg, it avoids travel when a given study visit does not require the physical presence of the patient, and it reduces the burden when a disabled patient cannot easily travel to a site), it can help to avoid data loss in DCTs by helping to keep the patients engaged. It creates an additional avenue for contact with site staff, and when fully integrated within a single platform, the televisit feature can bring comfort and confidence to patients, which are a key drivers of patient retention.

THINK SIMPLICITY

If the technical solution proposed for patient data collection is not easy-to-use, and is not patient- or site-oriented, the whole point is lost. Remembering that DCTs are there to help and not to complicate users' life is paramount. **Who never tried a technology or used a website that – although probably very powerful – was not designed with the end-user in mind, meaning that the experience became a nightmare?**

- **Avoid connecting to multiple systems with multiple credentials**

Using a single platform and implementing robust technology integration will not only help to improve patients' experience, it will be the only way to make the clinical trial journey bearable for both patients and sites. If integrating DCT components means accumulating several layers of technology and asking users to connect to different systems using multiple passwords, the complexity generated will have a significant negative impact on users' experience. By opting to work from the bottom up to ensure that the many functions offered to patients and sites interconnect smoothly, the chances of enhancing the user's experience are higher.

"During a clinical trial, patients must complete multiple study procedures, so their participation in should basically be made as easy as possible. With this in mind, offering them a single digital access point for as many study procedures as possible is of course highly attractive"

confirms Trishna Bharadia, a health advocate & patient engagement consultant.

- **Allow access to DCT components in one click**

Making the features seamless is key: after having connected to the solution, it is necessary that users are able to find the different features very easily and can activate them in a single click.

When a televisit is planned in a study protocol, for instance, accessing the feature that is embedded in the App and available on the same device helps to improve the user's experience and so supports patient retention and promotes complete data capture.

When a patient needs to refer to study information or solution training material , again, accessing this material in a single click on the same device will ease their experience and contribute to the success of the study.

#2

TACKLING TECHNOLOGY ADOPTION RISKS

Even though technology has invaded our lives, further accelerated by the COVID-19 pandemic, some aspects can impair DCT adoption. It is often said that some specific populations, such as elderly patients, view technology as a barrier to running a DCT but in our opinion it is often the technology itself that creates its own adoption challenge. When poorly thought out and designed, a system will not be easily accepted. As clinical trials stakeholders, we must adopt a 'User-oriented' approach.

UNDERSTAND THAT NEEDS OF THE TECHNOLOGY USERS DEPEND ON WIDE RANGE OF CRITERIA

Technology users' needs differ according to the study target patient population, cultural diversity, and the patients' individual appetite to using digital solutions. These needs also vary depending on whether or not patients have prior experience with clinical trials. And not only do these needs differ across individual patients, but they also evolve with time. Who would have thought that 2 years ago, almost 90 % of patients would have chosen a hybrid or fully DCT clinical study , should they have a say in the next trial in which they would participate.

The whole clinical trials industry must take these needs into account, acknowledge their variability, and monitor them. This can only happen by working directly with study patients and sites.

WORK WITH PATIENTS TO ADJUST TO THEIR NEEDS

Working with patient experts, associations, and/or advocates, will allow these needs to be accurately characterized, and allow solutions and technologies to be adjusted accordingly. Thinking with a fresh pair of eyes is not easy and using patient input will help to make the right adjustments, ensuring that the numerous patient types are taken into account as well as the cultural differences that influence patients' habits and requirements.

The FDA strongly supports the involvement of the patient's voice in clinical research and has released a program of guidance to help structure such collaborations, 3 out of 4 guidances have now been released under the FDA Patient Focus Drug Development (PFDD) program.

DEVELOP LONG-TERM RELATIONSHIPS

When involving patients and potentially experienced site representatives in the research or the development of a new feature that will support DCT, the capability to develop long term relationships and trust will be important. When a solution is designed for patients, it should be designed in collaboration with patients (and potentially sites), which often requires time. Establishing trust-based relationships with users will not only help to make the right decisions and to develop appropriate tools or technical solutions, but it will also contribute to changing peoples' perception of clinical trials, which has been described as an additional barrier for patients consenting to clinical research.

By partnering with patients, the chances of tackling the right technology hurdles are increased, which will also help to reduce the frustration that goes with issues not being properly managed. As such, patients are more likely to remain compliant and interested in the research, and longer term they might even spread the word of their positive clinical trial experience which is exactly what the clinical trials industry wants to see spread across patient communities!

HELP STUDY PATIENTS UNDERSTAND THE STUDY FLOW

One reason for losing patients' attention during a study and for them pushing back on their duties and on the use of the technology is a lack of understanding of the overall study objective and the value of the data they provide. One way to address this issue is to help patients perceive the clinical trial as a single stream, rather than a series of disjointed activities. This means that clinical site staff need to take the time to explain the study at the time of patient consent, irrespective of the solution that is used for consenting. We need to help patients understand the flow of the study, through appropriate training material and educational information. We all have a role to play in supporting patients understand why they need to be compliant with study procedures and how they can be.

Patient engagement, therefore, is supported by showing that the different steps and duties in a clinical trial are connected and lead towards answering a protocol question.

TRAIN, TRAIN, AND TRAIN!

Another key element is ensuring that users are well informed of the clinical trial requirements. They need to understand the goal of the research and the importance of the data they provide, as well as must be familiar with the solutions they will use during the study.

- **Prepare appropriate material for both patients and sites:** keeping the end-users in mind, solution providers must create simple and accessible training material. User guides and training material will be much more helpful, for example, if we reduce the amount of documentation and focus on the essentials, and if we limit the amount of text by adding illustrations and using simple language.

- **Multiply training opportunities**:
  - **Limiting site staff training to the Investigators meeting (IM) is a mistake**, as the participants in the IM may not include all of those who will be hands-on, using the solutions during the study. And even when those trained during the IM use the digital systems themselves, *"The positive effect of training does not last"* according to the Head of PRO Strategy from a large pharma company a few years ago. Therefore, multiplying the opportunities to share information is a golden rule: webcasts of IMs, additional webcast training,

short videos or recordings organized in a way that they bring focus on specific aspects of the eCOA set-up process could all be helpful site-centric solutions. Offering refresher sessions, recordings of complete training sessions, or short, focused, and easily accessible material can allow specific questions to be asked, which can be very helpful in some circumstances.

- **For study patients, multiplying training options is also necessary.** As well as reviewing study documentation and systems with the relevant study personnel on site, patients have a better chance of staying engaged if they can refer to the material in their own time. Solutions that are easily and quickly accessible and which allow adapted study or solutions information to be conveyed will help. The information provided must be very carefully prepared with the patient in mind, making sure it does not require health literacy knowledge, that it is in the patient's mother language, and using illustrations if helpful.

#3

SECURING DATA QUALITY WHEN COLLECTING DATA FROM MULTIPLE SOURCES

Collecting data from multiple sources and at so many different timepoints requires significant data management and reliable audit trails for guaranteeing data quality. However, digitalizing data collection can bring us beyond where we were with traditional trials in terms of data quality. DCT-associated data management activities can help to reach that level, providing that those activities are well anticipated and implemented.

- **Work with experienced partners**

Not only will experienced data managers (DMs) know how to clean and manage study data, but they will also understand the timeline constraints as well as specific protocol requirements. Furthermore, they will have experience with managing data collected via eCOA questionnaires and will build appropriate edit checks based on the protocol, create all the necessary triggers, and, together with experienced project managers (PMs), will follow the best practices for PRO migration and implementation.

- **Prepare the relevant study documentation**

Using relevant outcomes from the discussions that took place within the study team, experienced PMs and DMs will prepare all the necessary study documentation. The PM will be responsible for the project plan which contains all the operational steps of the study. Regarding data management, the study DM will draft the study specific documentation based on what the team will have discussed, and then create two main documents for data management activities: the Data Management Plan, describing the DM activities, and the Data Cleaning Plan, detailing the data controls.

- **Implement relevant edit checks**

With electronic data capture, limits can be programmed to avoid missing data, prevent the capture of illogical data, and narrow the time window in which certain data should be collected.

- As such, a pop-up message can be implemented when an illogical response is provided, or when the end of the time window for data entry approaches. With the support of experienced teams, any value that triggers a pop-up message will be carefully considered, to ensure it does not bias or discourage participants from reporting accurate but unusual responses whilst still optimizing data capture and preserving data quality.

- These edit checks have to be discussed very early in the set-up process, then programmed, tested and validated before the study goes live.

- User Acceptance Testings (UATs) are also there for sponsor teams to test as many scenarios as possible and test the programmed triggers and edit checks in all relevant situations.

- **Define key study team roles**

Preventing data loss also requires robust tracking of who entered the data. The study team roles should be defined very early in the process, and their associated responsibilities clearly listed. After their creation, the DM will monitor the different study roles and the use of their relevant rights, as well as perform the necessary updates throughout the study. This is a key activity that is necessary to preserve data quality and integrity, and as such safeguard the value of the clinical study data.

#4

ENSURING DATA PROTECTION

With digitizing inevitably comes the question of data privacy, even more important in the healthcare domain where personal data can be very sensitive. Data privacy risks can be a barrier for trial participation in some cases and must be tackled. It is the responsibility of the solution partner to be able to guarantee private data protection, and several actions can be put in place:

- **Make relevant adjustments according to country regulations**

As regulations vary from one country to another about data privacy and technology management, not all countries will be a good fit for implementing digital components in support of DCT. A good example is China, where implementing a BYOD study is impossible. A global trial run in EU, US and Asia required anticipation of the provisioned device solution in China where local rules do not allow for apps to be loaded from the App store/Google store, making the use of the BYOD app impossible. This situation led the team to implement a hybrid study, where Chinese patients (and patients from other countries who did not want/did not have a suitable phone) could use a provisioned device.

- **Make the strategic choices that matter**

The security and privacy of patients' data is essential, but in a BYOD scenario, for instance, clinical study data may coexist with other private data on the same device. Study participants are likely to have sensitive data stored on their device, and some apps installed by the user for

private use have the potential to automatically share data held on or accessed by the device. It is necessary to implement security controls within the solution and opting for a web browser embedded in an App (online solution only) can also be an easy way to prevent a data privacy breach: with an online solution, no clinical data are stored on the patient's device, which significantly reduces the data privacy risk (but requires patients to be online to complete their questionnaires or eDiaries).

CONCLUSION

When transitioning to DCTs, clinical trials stakeholders cannot ignore the associated risks and challenges. These include maintaining compliance and avoiding data loss when patients no longer go to study sites, supporting patients and sites in embracing the necessarily associated technologies, and guaranteeing both data integrity and data protection whilst multiplying the data collection sources and techniques. It is through the alliance of powerful technologies, solid expertise, and strong data management capabilities that DCTs will be run successfully and will bring all their potential to the clinical trials community.

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