

An Executive Summary

Virtual, Decentralized, Site-less Trials ... What Does it All Mean?



Katherine Vandebelt
Global Head of Clinical Innovation
Oracle Health Sciences



Dr. Vishaal Mehra
CEO & Medical Director
Artemis

Using virtual components in clinical trials provides many new benefits and requires knowledge, willingness to change and collaboration between sites and sponsors.

Overview

This article explores several features of virtual clinical trials, from the definitions of terms to the impact on workflows, based largely on a discussion with leaders in the clinical trial and pharmaceutical industries. This includes key considerations for staff, patients and sites to improve efficiency in clinical trials while maintaining participant safety and enhancing treatment outcomes.

Looking Back

Before exploring decentralized trials, it is important to understand what it means to use virtual approaches and their roles within decentralized trials. A [webinar](#) hosted by *Applied Clinical Trials* and *Pharmaceutical Executive* and sponsored by Oracle Health Sciences titled “Virtual, Decentralized, Site-less Trials... What Does it All Mean?” discussed various definitions available when considering decentralized elements for trials. These definitions include that of a decentralized trial itself, as well as input from the FDA and others on how some of the previously mentioned terms can lead to some confusion within the industry.

This webinar also provided information on patient-facing technologies, such as electronic devices, that can be used to collect more data (see **Figure 1**). These tools can also increase compliance. Additionally, the differences for patients, site staff and

Figure 1: How work is done is differently with patient-facing technologies.

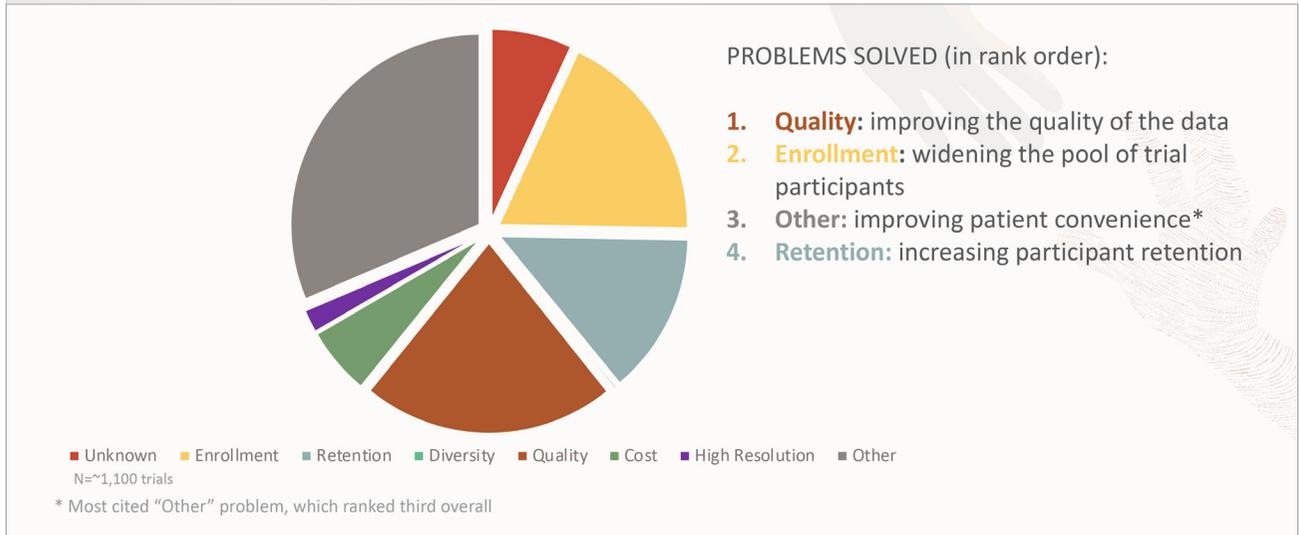


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Figure 2: Results from summit participants on their primary goal for implementing virtual components in trials.

data management when using decentralized approach were explored, as well as regulatory aspects. Once a trial sponsor considers the impacts across all of these factors, the best technologies can then be selected. The decentralized methods are likely to evolve over time as one sponsor adapts to different patient and trial needs.

Asking the Experts

Oracle Health Sciences partnered with the CNS Summit organization for discussions with 28 key industry stakeholders—people from biotechnology companies, clinical research, regulators and so on—with direct experience using patient-facing technology in clinical trials. The participants had 10–40 years of experience across more than 1200 clinical trials that included decentralized components, and they were asked four questions.

The first question was: How do you define virtual clinical trials that involve a principal investigator (PI)? This question format was used to emphasize that such trials still involve patients and the collection of new data. The key input here was the importance of the PI's role.

In any clinical trial, the PI's role is the same—ensuring the safety of patients and the integrity of the trial data. In the decentralized approach, though, the question becomes: How does a PI accomplish those goals with less physical contact with patients? Plus, a PI could go from 10 patients in a conventional trial to handling 50–100 in a decentralized trial while still needing to maintain the same quality of work.

To get a better sense of audience experience in the previously mentioned webinar, participants were asked: In what therapeutic area did you initially experience a decentralized component in a trial? One of the top replies was dermatology, which is an area undergoing a major

push for decentralized trials. Also, about 15% of the respondents first experienced decentralized components in a clinical trial involving a treatment for psychiatry/neurology. In the webinar, Dr. Mehra also pointed out that patient diaries in decentralized trials can be used for real-time inputs of data.

Problem-solving with Patient-facing Tech

In the summit focus sessions, the second question explored was: When you have employed patient-facing technology in some aspect of a trial, what was the primary problem you sought to solve? The top reply was to increase and improve the quality of the data, as shown in **Figure 2**.

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Collecting patient data in real time can improve the quality of the information. For example, noting a migraine in a patient diary at the time of the indication is better than telling the PI about it a week later. Aside from reducing errors, direct data entry can also give a PI better insight into drug adherence.

The second most common objective among the respondents was to widen the pool of trial participants. The summit respondents also expressed that they want to use virtual trial components to improve patient convenience, which helps patients stay in the trial and meet the expectations of the trial.

The third question dealt with the challenges or obstacles identified in incorporating patient-facing technology into trials. When it comes to addressing these challenges, the best clinical research execution model depends on a protocol's characteristics, which include the following: acute or chronic medical conditions; common or rare conditions; administration that is oral, injection or infusion; and the primary endpoint. Respondents noted that face-to-face interactions will still be required and should be anticipated whether telemedicine is the planned approach or not. For example, a severe adverse event would require a face-to-face interaction.

With new digital endpoints, a trial sponsor should also talk with regulatory authorities, as virtual technologies can produce different kinds of data and increased amounts of it, which require different analytics.

The technology used in a decentralized trial should be considered in a bottom-up approach—meaning from the start. Remote technology can be added incrementally, starting off during pre-study interactions with patients. Additionally, at the site level, technology should be as innovative as possible. Dialog between trial sponsors, PIs, partners and regulators should start early on and continue throughout the trial.

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What it Takes for the Team

When posed the question, “What do you or your team need more of to be more effective and successful with incorporating decentralized components in trials?” webinar participants had the option to select knowledge, skills training, technologies, help/feedback from others or other resources, including finances and staff. The top

answer from the participants was knowledge, which was followed by technologies and resources.

From the site-sponsor level, addressing the need for more knowledge is like starting from scratch. Until the operational level is understood, sponsors will not know what technology, training, resources and so on will be needed. Also, a fully decentralized clinical trial will create different needs than a hybrid, which includes features of centralized (traditional) and decentralized approaches.

Methods for Moving Ahead

The last question addressed at the summit was: What do you believe needs to be done in order to effectively move forward in realizing the potential of patient-facing technology in clinical trials? The answers from the summit participants helped to create a list of suggestions, which include the following:

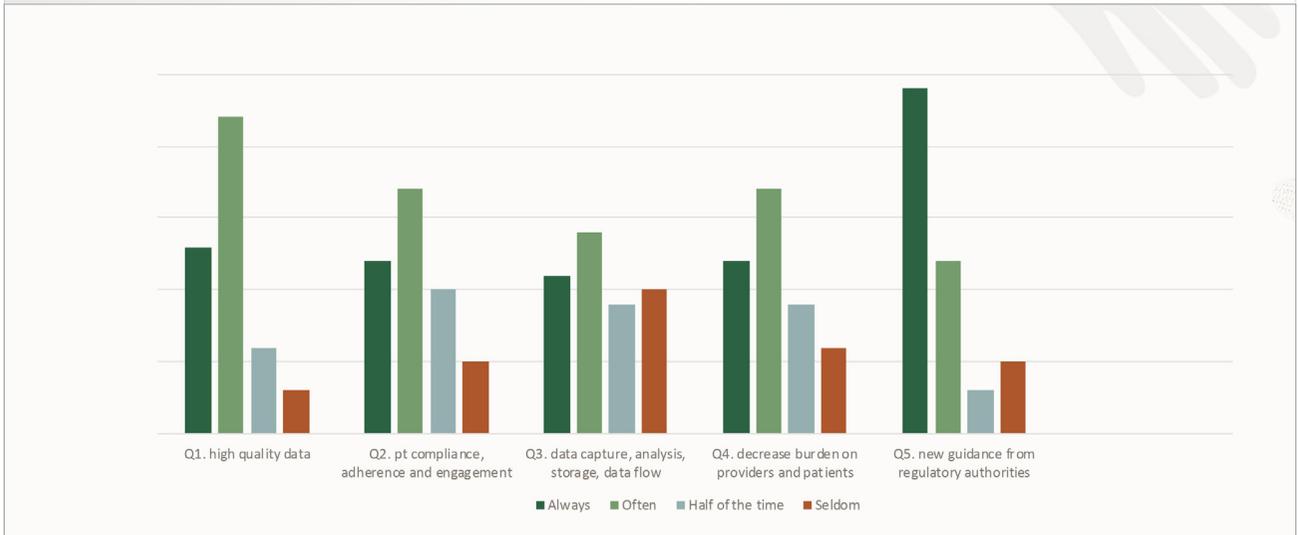
- **DO IT!** Use virtual components in your trials with intention and realize value that has already been proven
- **SIMPLIFY!** Collaborate to address challenges
 - Support new data types, data volumes and data integrations
 - Handle the volume of patient-facing technologies, sign-ons and training burden for patients and site staff
- **BE REAL!** Understand that face-to-face healthcare and professional-to-patient interactions are essential (and not going away!)
- **BE BOLD!** Start early in the compound development (e.g., Phase I-b, Phase II) and evaluate what is the right approach.

To successfully move forward in decentralized trials, sponsors should first involve the site staff in developing solutions. When something does not work, the site staff needs to offer solutions to sponsors that go beyond just sharing the problem. Second, a sponsor should prepare its site staff for the change by having the necessary internal discussions. Third, patient experience—treating them as customers—is the key to success. Thus, patients need to be involved in this process.

Virtual components also dramatically changes the interactions among the trial team and patients. By using the right technology in a decentralized trial, for example, the interactions between site staff and patients can shrink from three hours to 30 minutes.

Going back to the webinar, participants were asked in which trial phase they first worked with decentralized components, with most replying Phase III. It was noted that patient diaries for recording pain are being used moderately in Phase II and III.

Figure 3: Results from a 2020 SCOPE snap poll on ways to reduce the burden on providers and patients.



Polling Protocol Research and More

At the 2020 Summit for Clinical Ops Executives (SCOPE) in Orlando, a snap poll explored the research done in designing a protocol. From 53 people polled, 7% replied that they always do research in designing a protocol, such as reviewing new regulatory guidance from agencies. The people polled also noted doing research on strategies for maximizing patient compliance, adherence and engagement, as well as ways to reduce the burden on providers and patients, as shown in **Figure 3**.

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A snap poll conducted at the Site Solution Summit in October 2019 examined site-staff experience. Of those polled, 38 out of 48 had conducted Phase II or III clinical trials that involved virtual components, such as wearable or mobile technology; web-based diaries and wearable technologies made up the most common virtual components.

With increasing use of this technology, sponsors will want to make it more efficient, but some will hesitate to invest too heavily at this time. As the regulatory and industry expectations become clearer, the investment made in this technology might increase, such as using more expensive and sophisticated systems. In the meantime, it is recommended for sponsors to not get too future-oriented.

However, sponsors can improve tier-1 support. This includes handling patient inquiries, such as questions about the protocol or patient-facing technology. Instead of addressing these inquiries in person, the technology in a decentralized trial should handle this. Therefore, technology should evolve, as needed, to become tier-1 support for the patients in clinical trials.

A poll conducted in the the previously mentioned webinar revealed that participants expect that decentralized trials will be used across the industry at scale in 5–6 years. Dr. Mehra noted, however, that it is likely to happen in the next three years. That is because much of the technology is already here and has been for years. The industry just needs to figure out how to effectively use such technology.

Conclusion

Clinical trial sites need to get involved with sponsors and clinical research organizations, which often requires ongoing dialogue. Additionally, that dialogue must include all staff involved with a trial. All the while, research on protocols, technology and information from other industries will help push ahead decentralized trials. Even if decentralized components are added incrementally, the results will help the industry accelerate and expand drug development.