



8 Strategic Questions to Help Determine Your Path to Decentralization



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In This eBook

In this eBook, we've compiled eight strategic questions that will help jumpstart your path to decentralized clinical trials (DCTs), explaining what qualifies as a decentralized clinical trial, what decentralizing technology means for study teams, and how decentralization benefits patients, sites, and sponsors. Let's start with the basics.

Introduction

What was once an emergent market trend is now an established market need: decentralized clinical trial technology. Decentralized clinical trials, also known as virtual or hybrid trials, were already increasingly appealing, but as of late there has been a rapid acceleration in decentralized trial technology adoption.

The need for decentralized trial technology will certainly continue to remain necessary. According to a report from GlobalData published June 2020, approximately 35% of clinical health experts currently use virtual trials and 67% plan to use them in the future.¹

1. GlobalData COVID-19 Survey, 2020

01

What are decentralized clinical trials?

Decentralized clinical trials, also known as hybrid trials, virtual trials, remote trials, and direct-to-patient trials, are a method of conducting clinical trials in which parts or all of the trial happens outside of a traditional clinic or trial site. Medidata addresses decentralized clinical trials across the clinical trial lifecycle, with technologies that support both patient-facing activities and sponsor-driven oversight and data quality management.

When decentralizing any aspect of a clinical trial, the site and the patient are directly impacted. Patient-facing solutions are designed to lower the burden placed on trial subjects to learn new technologies, limit the number of devices to carry with multiple logins, and facilitate access to remote data capturing tools. With myMedidata, Medidata's patient portal, patients can access all of their clinical trial needs through one web-based portal, removing the need for provisioned devices. At the sponsor level, solutions such as Medidata Digital Oversight provide site monitors remote access to physical sites so they can continue to monitor source data and documents.



The Impact of Decentralized Clinical Trials

According to CenterWatch, the average dropout rate in traditional clinical trials is 30%.² For sponsors, this has a serious financial impact—the median cost per patient in pivotal clinical trials between 2015 and 2017 was over \$41,000.³

In addition, during the COVID-19 pandemic clinical trial recruitment became harder to orchestrate. In fact, according to a Medidata study, there was an 80% drop in new patient enrollment rates during the early months of the pandemic.⁴

These issues point to the need for wider acceptance of DCT procedures as a way to ensure trial stability. According to McKinsey, in December 2019, only 38% of sponsors and CROs expected virtual trials to be a major component of their portfolios. In December 2020, that number rose to 100%.⁵

Decentralized solutions enable patients to remain engaged for the duration of the trial. With technology like connected sensors and direct data capturing tools, convenience for patients ultimately improves data quality. Researchers increase both the size and diversity of their participant pool by opening up access to participation with decentralizing technology, making it more representative of their targeted population. Additionally, the automatic digital transmission of data eliminates human error.

Decentralized Trials vs. Trial Virtualization

“ Although there is some industry-wide concern about varying names for this technology, whether we call it decentralized, virtual, or remote, what we're focusing on is the opportunity to convert some or all elements of a clinical trial to go remote.

From the patient perspective, that may mean that the patient can fill out an ePRO form at home on a phone that's provisioned for them. That type of decentralization has been going on in our industry for over 15 years, and is very common in all kinds of clinical trials. More point solutions have become available to use concurrently, such as eConsent or video visits to replace some or all traditional site visits. One or more decentralizing solutions can be used in any one study, depending on the protocol.

At Medidata, we talk about this idea as a Trial Dial. There's a continuum of fully site-based trials to fully decentralized trials, and we want to enable you to dial that continuum up any way you need to on any type of study, based on geographies, patient population, and indication. Recently, we have also started to see a lot more decentralization of technology that's not necessarily patient facing. An example is remote monitoring, where CRAs don't have to travel to a site to review source documents. They can work remotely, even completing source document review or full site visits from home using the same types of technology that patients use for virtual video visits. We can extend decentralization capabilities beyond just the patient-centered devices and apps, and into other parts of the clinical operation process. ”



Anthony Costello
CEO, Patient Cloud

2. The Issue of Patient Retention in Clinical Trials, CenterWatch, 2016

3. Variation in the Estimated Costs of Pivotal Clinical Benefit Trials Supporting the US Approval of New Therapeutic Agents, 2015–2017: a Cross-sectional Study, BMJ, 2020

4. COVID-19 and Clinical Trials: The Medidata Perspective (Release 9.0), 2020

5. No Place Like Home? Stepping Up the Decentralization of Clinical Trials, McKinsey, 2021

02

What are some key considerations when deciding if a trial can be decentralized? Can all trials be carried out with a decentralized model?

Determining if a trial can be conducted using a decentralized model begins with protocol review. Ideally, key stakeholders, such as the company offering decentralizing technologies, will join the sponsor early enough to be involved in protocol development. This ensures that the decentralization methods and potential impacts on sites and patients can be evaluated early on, instead of requiring later protocol amendments. Key considerations when analyzing the protocol are the phase of the trial, disease/condition being researched, the data analysis plan, the patient population, risk profile, method of therapy administration, storage requirements of the treatment/drug, visit schedule, and feasibility of collecting the endpoints.

After reviewing the protocol, the next step is to determine which procedures and oversight activities can be managed outside of the traditional trial setting and which ones can be virtually managed at the patient's home or other non-site location.



SOME KEY CONSIDERATIONS:



Does the protocol require wearable sensors and devices that can be used independently at home or does usage require the assistance of a home health nurse or other healthcare professional?



Will the majority of the study monitoring activities occur off-site?



Can the patient store and administer the treatment on their own or do they require assistance?



How is the patient's perspective being captured in the study? What PROs are included and when?



During this analysis, a key consideration is if telemedicine or live video visits with a healthcare professional or clinical research staff can be used in lieu of clinic visits. Once the varying categories of remote procedures and activities have been identified, you can determine how to operationalize them using one or varying vendors. Patients can learn and consent to their trial using eConsent, while many endpoints can be collected passively through sensors or wearable devices or actively through eCOA/ePRO.

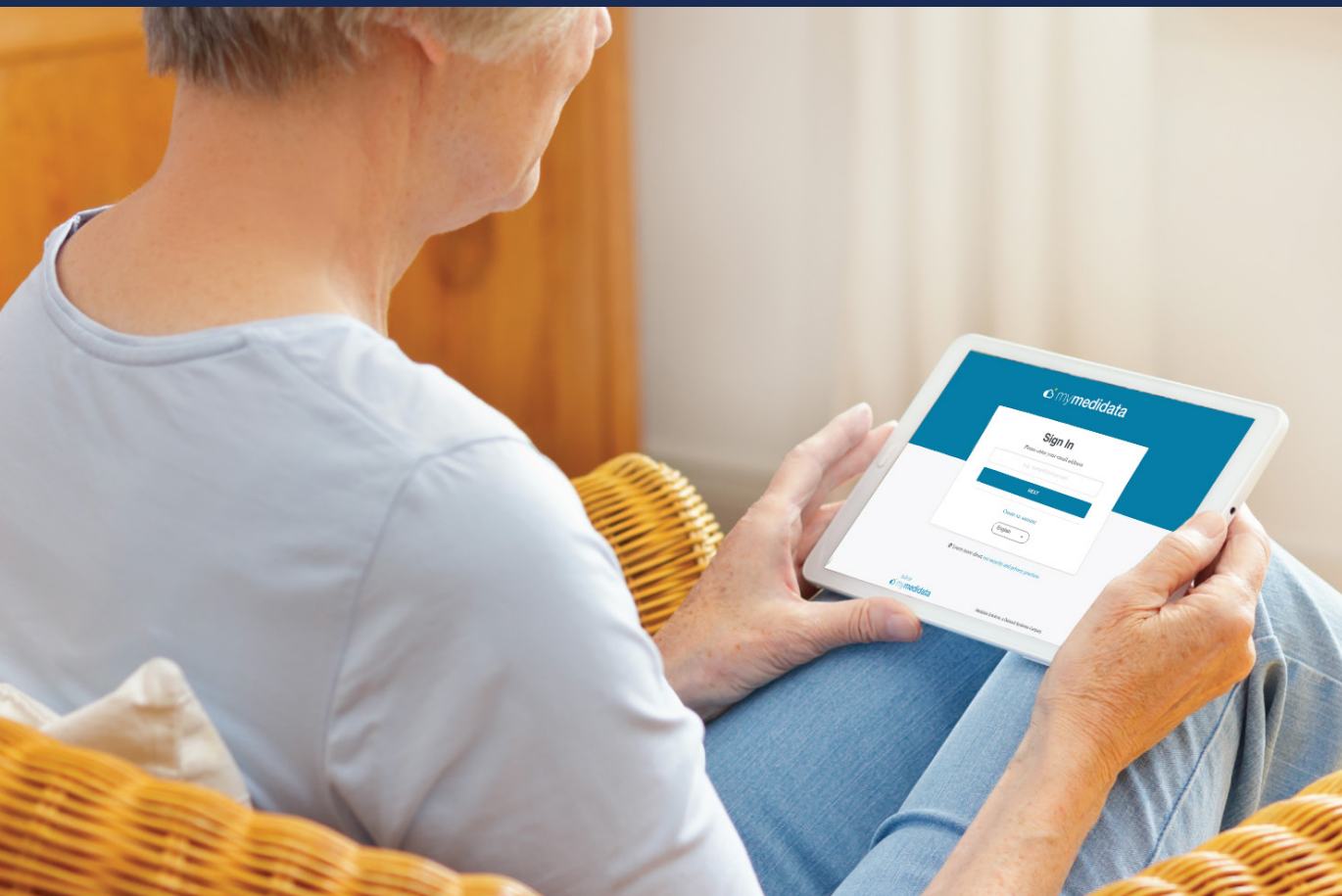
Aside from patient-facing technologies, there are many other tools that can be used by sites, sponsors, and CROs to enable trial decentralization. For example, remote monitoring and source data verification enables remote review of critical data and documents to help keep trials running smoothly by assisting sites and monitors in document acquisition, task workflow automation, and source document review in cases where travel to sites is infeasible or impossible. Using a randomization trial supply management (RTSM) solution with a direct-to-patient capable depot or pharmacy would send the Investigational Medicinal Product (IMP) to the patient's home.

There are also payment considerations when running a decentralized trial. Having a technology that streamlines the collection of data and automates the site payment calculation and invoicing process enables fewer manual touch points. When developing site budgets and clinical trial agreements, it's also important to consider whether traditional payment triggers are appropriate. For example, source data verification (SDV) may not be an appropriate payment trigger when dealing with infrequent monitoring visits.

Finally, when all possibilities for decentralization have been identified, a major consideration is the use of a unified platform to enable these technologies. It's often possible to integrate multiple point solutions through varying vendors. However, a robust platform offering an end-to-end range of technologies not only mitigates risk but also ensures consistent reliable data and a better user experience for patients, sites, and sponsors. myMedidata, built on Rave EDC, enables a suite of decentralizing technologies through one web-based portal for the patient while streamlining data capture directly into Rave EDC.

03

How are patients recruited and enrolled to participate through a decentralized trial model in comparison to traditional methods?



By removing geographic barriers to participation, patients gain access to trials from a broader range of locations. Channels of recruitment include digital advertising, social media, advocacy groups, direct to patient advertising, or patient registries. Opening up access to participation empowers patients to learn and register for research they are interested in.

With myMedidata, Medidata's patient portal, patients have access to one dashboard for life for the duration of all of their studies. myMedidata Registries enables pre- and post-trial engagement, providing participants with continued support and engagement before they join a study and after they finish their clinical trial.

Once a recruitment strategy has been developed and modalities of recruitment established, the patients entering the recruitment funnel must carefully be screened for eligibility. With a traditional approach, patients living close to trial sites and able to commute frequently are typically the participants for the duration of the study. By enabling decentralized enrollment and participation, a larger range of ethnic, racial, and socioeconomic status of patients are given the opportunity to participate.

04

What does the patient journey look like in a decentralized clinical trial?

Once a patient has been recruited and screened for eligibility, they are ready to learn study details, requirements, benefits/risks, and ultimately consent for participation. An electronic consent or eConsent is used in lieu of traditional paper and wet signatures gathered at a trial site. The eConsent tool allows patients to learn about their studies through an educational video, followed by written details and guidelines.

With Medidata eConsent, patients first watch a video to better understand the study details. If they have any issues with the consent forms, they can flag areas they don't fully understand to review with a study healthcare professional before consenting.





RTSM USE CASE

In a study where IMP dispensation is weight based, data can be entered by the patient and then used by Rave RTSM to dispense the correct amount of IMP. By allowing the patient to enter their own weight, the burden of travel is removed from the patient. This can result in a significant decrease in dropout rates.

Medidata eConsent also includes a knowledge review to ensure the patient's full understanding of trial specifics before consenting. With myMedidata, the consenting process can also occur virtually from the patient's home. If a patient has a question prior to consenting, they can engage with their study team through a myMedidata LIVE video visit for further clarification on the study requirements. Once patients have enrolled and their information has been entered into Rave EDC, Rave RTSM randomizes and automates trial supply management for these patients. Since RTSM communicates directly within Rave, sites are no longer burdened with separate trial supply management—the randomization takes place and the items to dispense are reported through Rave.

In a decentralized or hybrid model, patients can receive shipments of their IMP directly at home. Many patients require multiple distributions of their trial IMP, creating challenges with continued site visits and supply accountability. By enabling direct to patient shipments of IMP, the site initiates a dispensation of IMP from a depot/pharmacy which is then delivered directly to the patient's home. Patients can use myMedidata to report the receipt of their shipment. This data will be sent to RTSM and visible to the site, allowing the site to take any necessary actions to ensure the patient has the IMP they need.

Patient data capture happens virtually through the wearable devices and biosensors along with data capturing tools such as eCOA and ePRO. Using myMedidata, patients easily log in from their laptop, tablet, or mobile phone to access these tools for at-home data capture. Additionally, data is unified directly into Rave EDC, giving sites access to patient data in near real time. With the use of such digital data capturing tools, studies receive faster and more accurate data with little-to-no transcription errors. Data entered by the patient in eCOA can be passed through Rave EDC, confirmed by the site, and be used by Rave RTSM for dispensation purposes.

With live video visits, patients meet with their study teams and physician investigators virtually. From enrollment to end of study participation, patients can schedule to meet and discuss adverse events with their study teams as needed. During the COVID-19 pandemic, the demand for telehealth services greatly went up, according to site research by SCRS.⁶ With patients' inability to travel to their traditional clinics, investigators and study teams were unable to continue delivering patient care. Through myMedidata LIVE, patients can join live video visits with their physician investigators, enabling both parties to connect as needed and more frequently.

6. SCRS COVID-19 Site Preparedness Survey, 2020

What are some challenges sites have recently faced and how can decentralizing technologies ease some of those burdens?



REGULATORY PERSPECTIVE:

Remote monitoring of source documents was been accepted by some global regulatory authorities (including FDA) in early 2020 as a result of the COVID-19 pandemic.

7. COVID-19 and Clinical Trials: The Medidata Perspective (Release 9.0), 2020

Medidata Detect, a powerful data and risk surveillance tool for centralized monitoring, powers proactive and decentralized data review. Traditionally, sites use paper diaries to collect reported outcomes from the patient then type the data into an EDC. With the use of ePRO, patient data capture happens digitally, rendering transcriptional verification activities by the monitor obsolete. Instead, clinical data from all sources flows directly into Detect, which uses advanced algorithms and machine learning to spot issues in the data. This improves data accuracy and provides actionable insight in near real-time.

Additionally, with Medidata Remote Source Review, monitors can continue monitoring source documents from anywhere. During the global pandemic, CRAs were unable to visit sites to perform critical source document review activities. With the use of Remote Source Review, sites can securely upload documents for CRAs to review without traveling to the site. Centralized monitoring alerts the CRA of a data anomaly, in which case they can virtually access and review the source document.

06

What are the regulatory bodies saying about the adoption of these technologies?

Many of the world's regulatory agencies, including the FDA, the European Medicines Agency (EMA), the UK's Medicines and Healthcare Products Regulatory Agency (MHRA), Singapore's Health Science Authority (HSA), and China's Center for Drug Evaluation (CDE), have issued guidance documents that describe how new processes and methods can be implemented to protect patients and facilitate continued trial execution while maintaining GCP standards (FDA, 2020a; EMA, 2020; MHRA, 2020; HSA, 2020; Taylor, 2020).

While these documents cover many topics, all of them contain components that discuss the use of digital technologies to facilitate trials during the pandemic, such as enabling remote site monitoring, handling informed consent, conducting remote trial visits, and maintaining data integrity and an audit trail. The European Commission has also undertaken various mHealth initiatives, including publishing a legal framework that provides legal guidance on European Union legislation in the field to app developers, medical device manufacturers, and digital distribution platforms.

Finally, many Asian Pacific countries are known to have high adoption rates of mobile technologies and mHealth. A World Health Organization report found that the Eastern Mediterranean Region, Western Pacific Region, and South-East Asia Region had the highest percentage of countries reporting an evaluation of a government-sponsored mHealth program, a critical step to eventually forming a regulation.⁸ A regulatory sandbox initiative launched by Singapore's Ministry of Health in 2018 is intended to bring together the views of HCPs and business so that the ministry can better support innovation. A major topic is telemedicine, which the ministry states "is set to become a key feature of Singapore's healthcare landscape."⁹

8. World Health Organization (WHO), 2016

9. Singapore Ministry of Health (MOH), 2018



There are many new digital health-care-related technologies becoming available through varying vendors. Doesn't the use of many different tools increase patient and site burden with multiple logins and training?

Working with independent point solutions without a unified platform can create significant challenges for sites and sponsors. With multiple logins and the need for device integration, it can become a burden on sites to implement these tools. However, using decentralized technology already built on the EDC being used at the site will mitigate risk and reduce data transcription workload. Medidata's decentralized clinical trial technology is unified directly with Rave EDC, enabling direct eSource data capture to provide more information in real-time, with no opportunity for error. With Medidata Remote Monitoring, there is no need to create a new login. Sites log into Rave EDC and access the data in near-real time for monitoring without the need for data reconciliation.



08

I'm not looking to go fully decentralized on a study. Is this still an option?



Medidata recognizes that trials rarely operate 100% virtually. Our Trial Dial decentralization continuum helps sponsors strike the right balance between site-based and decentralized visits that still delivers a truly patient-centric clinical trial. Ideally, sponsors can customize the design of their trials to reflect the best mix of onsite/virtual touch points for an enhanced experience for the patient. Driven by the increased focus on lowering patient burden associated with trials and minimizing study risk, the industry is interested in turning the Trial Dial to introduce some level of decentralization into more trials.

From a patient perspective, this might include electronic consent from home, followed by a site visit, followed by the remote use of eCOA tools by the patient. Based on data entered in eCOA, direct to patient shipment of IMP can happen, all before the patient returns to the site for lab tests or treatment. From a sponsor or CRO study monitoring perspective, oversight activities begin with on-site study start-up activities, followed by central statistical data monitoring and data review with virtual remote source review, and targeted, risk-based, onsite visits. In some studies, there is a dramatic reduction in site visits with assessments and oversight being provided remotely.

8 STRATEGIC QUESTIONS TO DETERMINE YOUR PATH TO DECENTRALIZATION

About Medidata

Medidata is leading the digital transformation of life sciences, creating hope for millions of patients. Medidata helps generate the evidence and insights to help pharmaceutical, biotech, medical device and diagnostics companies, and academic researchers accelerate value, minimize risk, and optimize outcomes. More than one million registered users across 1,600+ customers and partners access the world's most-used platform for clinical development, commercial, and real-world data. Medidata, a Dassault Systèmes company (Euronext Paris: #13065, DSY.PA), is headquartered in New York City and has offices around the world to meet the needs of its customers. Discover more at www.medidata.com and follow us [@medidata](https://twitter.com/medidata), The Operating System for Life Sciences™.

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