

The Rise of Hybrid Trials



Authored by:
Melissa Newara,
eSource Subject Matter Expert

medrio

Inside This Whitepaper

Are your clinical trials equipped for a modern world?	1
What Makes a Trial Hybrid?	2
The Pandemic's Impact on Hybrid Trial Adoption	4
How to Configure Hybrid Models for Any Study	5
The Impact of Hybrid Trial Design	6
The Future of Hybrid Trials.....	7

Q: Are your clinical trials equipped for a modern world?

Prior to 2020, the answer was likely not very much. Although decentralized trials (DCT) existed prior to the pandemic, COVID-19 undoubtedly had a large impact on the rapid adoption of DCT technologies. As many as 76% of clinical trials had to shift some or all of their trial operations to decentralized solutions.¹ As global regulators became more accepting of these novel technologies and patients became accustomed to using them, it begged the question: is decentralization here to stay?

By all accounts, signs point to yes. But, as DCT enters the mainstream lexicon, it's important to distinguish how and where it will benefit clinical research the most. There is a common misconception that decentralized trials will remove the need for sites and replace many traditional clinical trial roles. Although decentralized tools such as remote monitoring, telehealth, and eConsent alleviate many burdens for patients and trial staff, they often still benefit from a tandem in clinic and remote approach.

In fact, despite the advancements in DCT technology, only a small minority of studies can be designed 100% virtual in their protocol. Even by substituting physical visits for virtual ones and collecting direct data capture (DDC), trials may require in-person site visits for confirmation of a diagnosis or dispensing of an IP.

For this reason, hybrid trial models have risen in popularity and offer an optimal solution for agile clinical trial models. In this paper, we'll define what a hybrid trial is, how it utilizes decentralized technologies, and the reason for mainstream adoption of hybrid clinical trials.

Despite the advancements in DCT technology, only a small minority of studies can be designed 100% virtual in their protocol.

What Makes a Trial Hybrid?

Hybrid clinical trial models derive from decentralized clinical trials (DCT), wherein a combination of virtual and in-clinic workflows are implemented to conduct required trial procedures. Nearly all trials operated today are at least partly decentralized trials because they are enabled by technology and virtual workflows.

But a hybrid decentralized trial is distinctively different from a fully virtual decentralized trial. Fully virtual trials are completely technology-based with no traditional site or face-to-face interaction required throughout the duration of the study. Everything from study start-up, patient enrollment, dosing and dispensing, data collection, testing, and final outcomes are managed end-to-end by digital tools and self-administered treatments.

Although virtual models are slowly migrating from smaller early-phase studies, they are gaining momentum in larger, more pivotal trials.⁵ Nonetheless, virtual trials remain limited to specific use cases such as well-characterized drugs with minimal AEs and endpoints suited for remote monitoring.

Hybrid trials leverage decentralized technology—such as remote data collection and eConsent—in tandem with traditional in-clinic workflows to create a seamless study experience. Hybrid trial designs allow technology to alleviate common patient burdens and streamline site operations so sponsors can better address patient needs and achieve more meaningful outcomes. Trials enhanced with virtual elements have been shown to improve efficiency in recruitment, patient monitoring, compliance, retention, and the overall patient experience.⁷

Consider that 70% of potential patients live over two hours from the nearest trial site.² The demands on patients are mounting, which is why fewer than 5% of eligible patients are estimated to participate in clinical research.⁷ Hybrid trials broaden access to a larger, more diverse range of patients while reducing the workload for investigators through remote screening, direct-to-patient IP shipments, and telehealth visits.³

Hybrid trials broaden access to a larger, more diverse range of patients while reducing the workload for investigators through remote screening, direct-to-patient IP shipments, and telehealth visits.

Patient screenings and consent are aided by hybrid models. Where remote patients can benefit from a web-based portal to access intake and eConsent forms, access ePRO, and track IP shipments securely; in-clinic patients are supported by tablet-based forms and site staff available to answer their questions. Based on the complexity of the study protocol, trial operators can leverage a combination of remote and in-clinic eSource to best meet their unique trial needs.

While most clinical trials may not be suitable to be fully virtual, they can leverage decentralized elements based on their unique endpoints, patient populations, and treatments. This allows clinical trial operators to unlock the benefits of virtual trials while balancing the need for in-clinic procedures.

What Makes a Trial Hybrid?

CLINICAL TRIAL DESIGNS

FULLY DECENTRALIZED



Every trial procedure is conducted virtually and enabled by digital technologies + direct-to-patient trial supply

HYBRID



Majority of trial is supported by digital technologies + remote workflows with in-clinic reserved for complex trial procedures



Mix of in-clinic and remote telehealth, consent, data collection, and trial supply

FULLY CENTRALIZED



Every trial procedure is conducted in-clinic



Majority of trial is complex and requires in-clinic workflows supported marginally by digital technologies

Image Source

The Pandemic's Impact on Hybrid Trial Adoption

Although hybrid decentralized trials are not new, there was a significant shift in adoption due to the pandemic. A December 2019 study found that 38% of pharma and CROs expected virtual trials to be a major priority moving forward and 48% expected to run a mostly decentralized clinical trial.² When the same question was posed by McKinsey in 2020, the responses changed to 100% and 89%, respectively.²

Clinical trial investigators believe this adoption is attributed to three major shifts:

- **Rising Comfort with Technology:** Consumers are using digital health technology such as wearables and telehealth in more areas of their daily lives. This daily comfort paired with increased use of remote health technologies during the pandemic resulted in a threefold increase in comfort with remote patient interactions.²
- **Focus on the Patient Experience:** Struggles with patient recruitment and retention were amplified during the pandemic, forcing trial operators to rethink the burden placed on patients. DCT allows for patient-centric trial features such as remote monitoring, direct-to-patient trial supply, and telehealth that alleviate common burdens while strengthening recruitment and retention efforts.
- **Maturation of Tools:** DCT technologies have been around long before the pandemic, but are being increasingly validated and given guidance by governing bodies.⁶ As digital endpoints become the primary endpoint, regulatory frameworks and maturing tools are helping trial operators feel more confident digitizing and decentralizing their studies.²

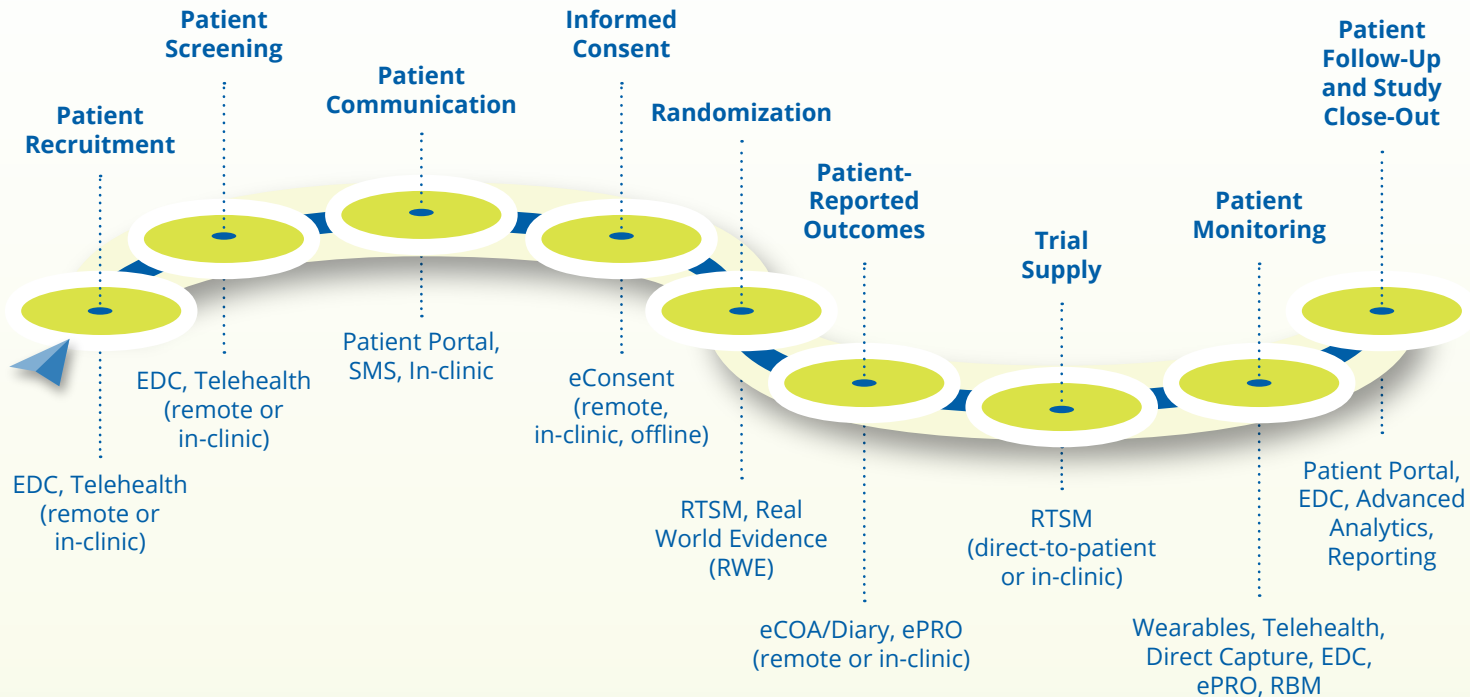
How to Configure Hybrid Models for Any Study

Clinical trial sponsors and CROs that are creating hybrid protocols have a host of decentralized technologies to choose from. They need to identify where traditional site visits are still needed for complex procedures or specialized assessments and where patients would benefit from virtual workflows. Smart, agile hybrid design is necessary.

In order to find a strategic balance between virtual and traditional workflows, try answering these questions:

- ⦿ Where will decentralization add the most value to your trial design and which technologies are necessary to capture it?
- ⦿ What capabilities are needed and who must be trained on these new technologies?
- ⦿ What capabilities would strengthen internal support of a shift toward decentralization?

The Patient Journey in Hybrid Decentralized Trials



The Impact of Hybrid Trial Design

There is a common misconception that decentralized trials will remove the need for sites and replace many clinical trial roles. In reality, the emergence of hybrid trial technology is bringing greater ROI to sponsors, simplifying complex trial management for CROs, empowering site staff, and enabling a more diverse and informed patient population.³

When Linear Clinical Research aimed to digitize their paper processes with Electronic Data Capture (EDC) and direct data capture (DDC), they were mindful of how it would impact their site staff.

“We wanted to gain efficiency in the back end, dealing with what we call ‘administration paper,’” said an Enterprise Data Architect at Linear Clinical Research.⁴ “We wanted to focus on our [site] staff’s strengths, which are taking care of patients and facilitating a clinical trial, and not on copying forms and managing paper.”

Not only was Linear able to enhance site operations through a hybrid approach, they reduced their paper usage by 95%.⁴ In addition, the sponsor-contracted CRA was able to reduce clinic visits by 50% by remotely logging in to review forms and data, allowing the trial to stay on time and on budget.

“Eliminating those on-site visits increases efficiency, reduces delays, and accelerates the overall progress of the trial. The clinic team loved using the tablets for mobile data capture during that first study,” says the Enterprise Architect.

Swing Therapeutics had similar hesitations when kicking off their first decentralized hybrid study using Electronic Patient-Reported Outcomes (ePRO), but their fears were quickly mitigated.

“There were a lot of moving parts in this study. On a site level, they were responsible for the in-person visits, telehealth calls, and compliance follow-up,” said Nicolette Vega, Clinical Project Manager at Swing Therapeutics. “At the participant level, they had to complete sessions in their digital therapy application daily and complete ePRO questionnaires weekly via the patient portal. It was important that the study staff understood the difference between the two systems and who to contact for quick issue resolution.”

The emergence of hybrid trial technology is bringing greater ROI to sponsors, simplifying complex trial management for CROs, empowering site staff, and enabling a more diverse and informed patient population.

Due to ePRO’s ease of use, SMS notifications for patient reminders, and a bring-your-own-device (BYOD) model, the study saw high patient engagement and achieved 97% patient compliance.

In both of these examples, hybrid trials relied on an orchestrated effort between patients, providers, and sites to create a seamless study experience. By automating manual processes where possible, clinical teams can reprioritize their efforts to more pressing matters like the patient experience.

The Future of Hybrid Trials

The pandemic highlighted the importance of decentralization and emphasized the need for clinical trials to adopt more agile, virtual approaches. Hybrid trials are creating a new patient- and site-centric paradigm shift by making clinical research more accessible, convenient, and configurable. As the industry moves towards mass digitization, hybrid studies are anticipated to lead the way.

But as hybrid and virtual studies grow in popularity, they will inevitably generate challenges with managing and storing data. Sponsors and CROs should look to partner with vendors that preserve data quality and prioritize data security. Operating all apps, ePRO tools, and wearable devices on validated, trusted technology is necessary to ensuring trusted outcomes.

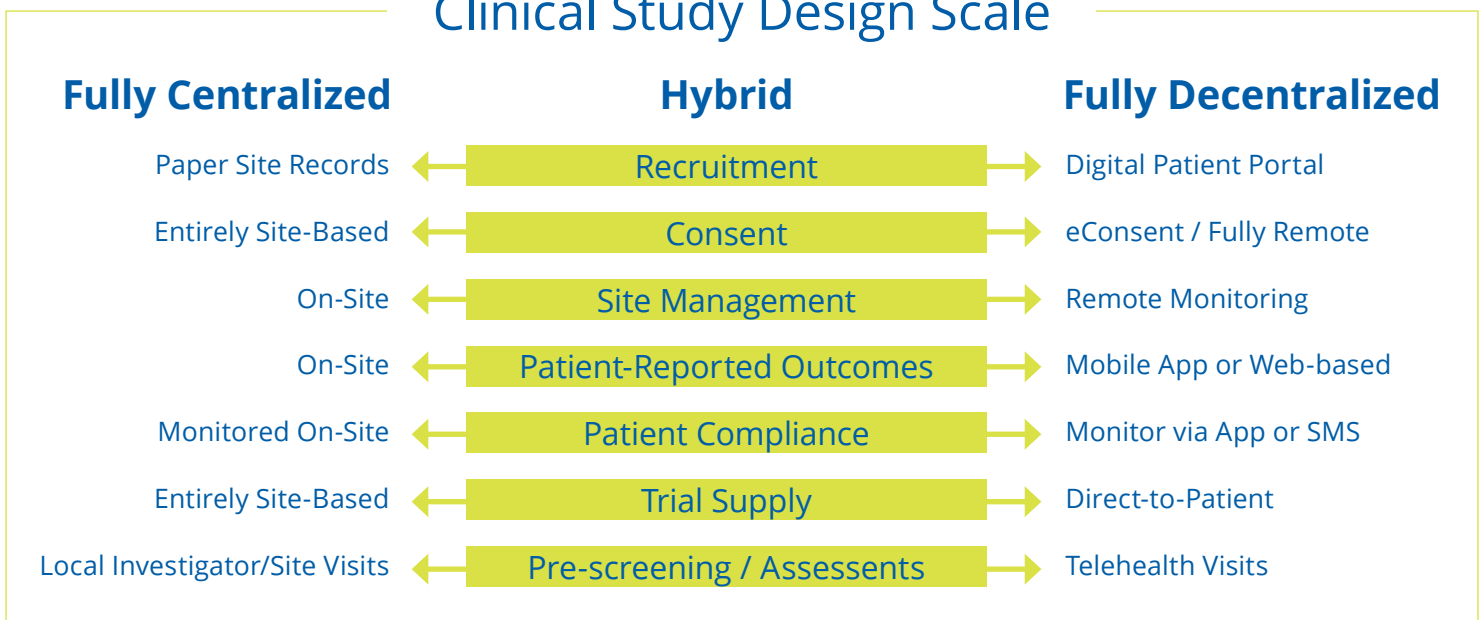
Time should also be taken to introduce new decentralized technologies and procedures to all trial operators and patients. Patients have varying degrees of comfort with clinical research and access

to technology. Some cohort groups have preferences for in-person visits versus others that consider themselves more privy to telehealth. Making time to train and support patients, tailor interfaces to your patient groups, and give patients the options between a decentralized arm and a traditional arm are key to bridging the gap.

Finally, mitigating concerns with your sites is also imperative. Sites worry that maintaining patient engagement virtually could be challenging and others fear drowning in technical issues. Be sure to set aside time for clear, demonstrative logistical and technical support with your sites to ensure the decentralized workflows help, not hinder, the patient-site experience.

Decentralization is not a one-size-fits-all approach. Each study should be carefully weighed to determine which level of virtualization to embrace. But one thing is clear—hybrid trials are a key driver towards the modernization of clinical research and they shows no signs of slowing down.

Clinical Study Design Scale



About the Author

Melissa Newara is an experienced clinical trial technology professional with over 16 years in the clinical research space. Serving as Medrio's eSource Subject Matter Expert, she supports customers in understanding industry trends and regulations and helps to identify ways to optimize data collection by focusing on the patient and site experience.

Melissa's deep-rooted understanding of patient engagement and eSource collection stems from her extensive background working within clinical research in neuro-oncology, multiple sclerosis, behavioral health and gastroenterology. Most recently, she focused her work in eCOA as a clinical solutions specialist and a proposal operations manager. Melissa received her Master's in Psychology from Drexel University in 2007.

References

1. Survey: COVID-19 the Tipping Point for Decentralized Clinical Trials
2. No place like home? Stepping up the decentralization of clinical trials
3. How Decentralized Trials Strengthen Your Participation Pool
4. Linear Clinical Research, a Phase I Site, Goes Electronic with Medrio
5. Otsuka and Click Therapeutics Initiate First-of-its-Kind Fully Remote Clinical Trial Using Digital Therapeutics as Adjunctive Therapy in Adults With Major Depressive Disorder
6. Hesitant to Embrace Decentralized Trials Because of Regulations?
7. Hybrid and Virtual Trials: Understanding the New Clinical Development Paradigm
8. 5 ways to lower clinical trial patient recruitment costs
9. SubjectWell (2020). Survey of Clinical Trial Awareness and Attitudes
10. Improving Health Literacy in Clinical Trials
11. How far Americans live from the closest hospital differs by community type

About Medrio

At Medrio, we believe that clinical trial technology shouldn't be difficult to use. That's why our full-service eClinical Data Management suite helps streamline your research and unify your solutions so you have more time to focus on your patients, rather than multiple vendors. Since 2005, our flexible technology has evolved alongside our customers to include an integrated suite of EDC, DDC, eConsent, RTSM and ePRO/eCOA solutions that support your teams and sites, while reducing patient burden.

Let our solutions put you back in the driver's seat with adaptive technology that easily powers mid-study changes and accelerates your trials, without compromising data quality. Or lean on our global team of experts who are available 24/7 to support you where you need it most. We've worked alongside Sponsors, CROs, and sites—spanning all therapeutic areas and trial phases—to secure over 770 approvals, because we know it takes a village to achieve a healthier world. Discover the Medrio difference today by visiting us at medrio.com.

medrio

345 California St., #325
San Francisco, CA 94104
+1 800.498.6830
info@medrio.com
www.medrio.com