# Putting the Patient First: Decentralized Trial Design Increases Enrollment and Representation

Traditionally, clinical trials follow a standardized format, whereby the participant in the trial must attend the clinical site or sites for the purposes of screening, enrollment, treatment administration and data collection. However, the rigid structure of a conventional clinical trial, has limitations for the patient, clinician and the research infrastructure, which were brought into sharp focus by the onset of the COVID-19 pandemic in early 2020.

The pandemic caused huge disruption across industries, including clinical research. Many clinical trials had to be paused or stopped altogether due to the risk to often vulnerable patients of attending clinical sites. In the U.S., an estimated 80% of non-COVID-19-related trials were stopped or interrupted due to the pandemic,[1] and many new trials simply weren't started. The number of trials initiated in the U.S. from February to May 2020 was just 57% of what would have been expected under normal conditions.[2]

However, the pandemic also forced changes in the way clinical trials are designed and conducted. By bringing the trial to the patient, many clinical trials were able to restart and continue throughout the pandemic. Introducing elements of decentralized design shifted the focus of the clinical trial from the site to the patient, which has benefits for the patient and the research establishment. Many are hopeful these changes are here to stay.

Here, we will outline the key components of a decentralized clinical trial (DCT) and its advantages for the patient, clinician and pharmaceutical industry, with a focus on oncology.

---

## The limitations of traditional clinical trial design

There are numerous barriers to access to traditionally conducted clinical trials. This is a particular concern in oncology, where patients may be especially vulnerable or immunocompromised, an issue which came to the forefront during the pandemic. In the United Kingdom, it has been estimated that 14% of cancer patients participate in clinical trials,[3] while in the United States rates of participation may be as low as 8%.[4]

One of the key barriers encountered by patients is the inflexible modes of participation offered by a conventional clinical trial. Traditionally, participants must travel to the clinical site for initial screening, to provide consent, for laboratory tests, imaging, treatment administration and to participate in pharmacokinetic and dynamic studies.[5]

The burden on patients of participating in a clinical trial may have, inadvertently, been exacerbated by efforts to make trials more efficient. Attempts to gather as much information as possible from each study participant, and therefore reduce the overall number of patients needed in a clinical trial, has increased the burden on individual participants.[5] The significant administrative and logistical challenges of participation in a clinical trial often contribute to a poor patient experience, leading to an unwillingness to participate among some patients and even for some to drop out.[6]

As well as logistical factors and inflexible protocols, socioeconomic factors also represent a key barrier and limit the diversity of representations within clinical trial populations. People in remote areas or with complex health needs, for example, may be unable to travel to attend the clinical site.

Lower income patients are also less likely to participate in clinical trials in oncology.[7] The reasons for this are complex and may include the costs associated with participating in a clinical trial (such as the cost of travel to the clinical site), insurance status, and the likelihood of the treating hospital offering clinical trial participation.

### COVID-19 and clinical trials

- In the spring of 2020, clinical trials halted due to the COVID-19 pandemic, forcing perhaps the biggest change in clinical trial conduct since the start of modern oncology.
- Trials subsequently resumed with adapted procedures that allowed patients to continue to access experimental treatments and attend clinical trial sites to collect the data necessary for their study.
- COVID-19 has thus provided an opportunity to reevaluate and adapt clinical trial procedures to put the patient at the center of the trial.[5]

## Patient-centric trial designs can overcome barriers to participation

Decentralized or patient-centric clinical trials can help to overcome some of these barriers, by offering greater flexibility for the patient and using technology to reduce the number of clinic visits. Examples of this include electronic consent forms, telemedicine consultations and self-reported patient outcomes.[8]

An increasing amount of data can be self-reported by patients, also known as electric patient-reported outcomes (ePROs). This has been driven by advances in wearable technologies, such as smart watches, which can be used for the real-time collection of a range of health measures. However, it is important that any device used for data collection in a clinical trial is validated to ensure the data is reliable and comparable across participants.[8, 10]

Research suggests that patients themselves would prefer to enroll in clinical trials that use mobile technology. A survey of patient perceptions of and willingness to participate in mobile versus traditional clinical trials revealed a preference for trials that used mobile technologies. Patients also reported advantages of mobile clinical trials including greater convenience (including fewer in-person clinic visits) and more accurate data collection.[11] Overall, DCTs can reduce the burden on the patient of participating in a clinical trial and improve their safety, comfort and quality of life.[8]

### What are the key components of a decentralized clinical trial (DCT)?

A decentralized clinical trial (DCT), also known as site-less, direct-to-patient, hybrid, remote or virtual clinical trial, offers a patient-centric approach, in contrast to the conventional site-centric model.

DCTs can be defined as “those executed through telemedicine and mobile/local healthcare providers, using procedures that vary from the traditional clinical trial model” and might involve:

- **Recruitment** by web-based methods, such as social media and telemedicine.
- **Informed consent** by remote electronic document access.
- **Trial activities** completed remotely, such as through video conferencing.
- **Physical examination** by in-home nurse visits.
- **Laboratory specimen collection** at a local site or an in-home phlebotomist visit.
- **Data collection** through digital health devices, such as smart watches and other validated wearable technology.[8, 9]

## Change is backed by regulators

DCTs are backed by regulators, who have advocated for their use to mitigate the impact of the COVID-19 public health emergency. The U.S. Food and Drug Administration (FDA) and the National Cancer Institute (NCI) first issued guidance on the conduct of clinical trials during the pandemic in March 2020.[12] The guidance recommended drastic changes in clinical trial conduct including implementing procedures for obtaining informed consent remotely, remote (virtual or phone-based) safety and clinical outcome assessments, and delivering therapeutics to patients’ homes or allowing at-home infusions for intravenous therapeutics.[5, 12]

The European Medicines Agency (EMA) issued similar guidance on the management of clinical trials during the pandemic,[13] including changes to informed consent, distribution of treatments, and patient monitoring procedures. The EMA recommended converting physical visits to phone or video where possible and performing laboratory, imaging and other tests at clinical sites closer to participants' homes.

As we transition out of the pandemic, there is an argument that elements of a decentralized design should be retained. Indeed, a recent white paper from the NCI's Clinical Trials and Translational Research Working Group recommends that changes to clinical trials initiated by COVID-19 become permanent.[14]

## New trial technology could accelerate drug development timelines

The pandemic has highlighted the feasibility of using telemedicine technology in clinical trials. Doing so can increase patient recruitment, reduce cost, save time and—crucially during the pandemic—reduce the risk of infection.[8] A decentralized design may also reduce inequality by removing barriers to access, such as geographic, transport, financial or health-related limitations.[5,8]

As well as providing important benefits for patients, there are also significant advantages for those involved in designing and conducting clinical trials in introducing decentralized elements.

Making a trial easier to access and take part in increases patient enrollment and could reduce the number of protocol deviations and the rate of patient dropout in a trial. Furthermore, collecting data directly from patients themselves, from wearable devices for example, could provide unprecedented longitudinal data for clinical trials and collected in a real-world context. Increasing the use of patient-reported outcomes also reduces the need for manual data collection and entry, saving time and labor.[8]

This highlights one of the most important potential benefits of DCTs—making the drug development process more efficient. The average cost associated with bringing a new drug to market has been estimated at $1.3 billion,[15] with an average of 12.5 years between discovery to licensing and approval.[16] Incorporating virtual and decentralized elements into clinical trials, such as electronic consent forms, telemedicine consultations and self-reported outcomes, could change this.[5, 8]

The pandemic has demonstrated that streamlining clinical trial processes is very much possible, and as a result many are starting to take the prospect of decentralization more seriously. For example, the Oncology Center of Excellence (OCE), has begun to advance the science of ePROS, digital health technologies, real-world evidence and health equity in oncology drug development.[5]

Although a fully decentralized process is unlikely to be possible for most oncology clinical trials, given the need for delicate discussions, intravenous drug administrations and medical imaging, decentralizing some components of the clinical trial process can have significant benefits for patients, oncologists and the research establishment.

### What are the benefits of introducing decentralized elements to a clinical trial?

- Patient convenience.
- Improved patient quality of life.
- Increased recruitment and retention.
- Enhanced cost, time and resource efficiency.
- Shorter trial timelines.
- Real-world, longitudinal data.
- Increased diversity in clinical trial populations.
- More meaningful results for unmet medical needs and patient populations.

## Conclusion

Clinical trials have followed a prescriptive format for a long time, including elements that have been problematic for the patients participating. The disruptive effect of the COVID-19 pandemic forced changes to this regime and demonstrated that it is possible, and in many ways beneficial, to do things differently. As the world returns to normality, the clinical trial infrastructure has the opportunity to retain elements of these new and more patient-centric trial designs. The benefits of doing so extend from increasing patient participation to increasing efficiency in the process of clinical research.

**Learn more** at oncology.labcorp.com

labcorp | Oncology

**References**


1. Dorn, A. van. COVID-19 and readjusting clinical trials. *The Lancet*, 396(10250), 2020. pp.523–524.
2. Unger, J.M. and Xiao, H. The COVID-19 pandemic and new clinical trial activations. *Trials*, 22(1), 2021.
3. Sinha, G. United Kingdom Becomes the Cancer Clinical Trials Recruitment Capital of the World. *JNCI Journal of the National Cancer Institute*, 99(6), 2007. pp.420–422.
4. Unger, J.M., Vaidya, R., Hershman, D.L., Minasian, L.M. and Fleury, M.E. Systematic Review and Meta-Analysis of the Magnitude of Structural, Clinical, and Physician and Patient Barriers to Cancer Clinical Trial Participation. *JNCI: Journal of the National Cancer Institute*, 111(3), 2019. pp.245–255.
5. Flaherty, K.T., Doroshow, J.H., Galbraith, S., Ribas, A., Kluetz, P.G., Pazdur, R. and Theoret, M.R. Rethinking Cancer Clinical Trial Conduct Induced by COVID-19: An Academic Center, Industry, Government, and Regulatory Agency Perspective. *Cancer Discovery* 2021;11:1–5.
6. Biankin, A.V., Piantadosi, S. and Hollingsworth, S.J. Patient-centric trials for therapeutic development in precision oncology. *Nature*, 526(7573), 2015. pp.361–370.
7. Unger, J.M., Gralow, J.R., Albain, K.S., Ramsey, S.D. and Hershman, D.L. Patient Income Level and Cancer Clinical Trial Participation. *JAMA Oncology*, 2(1), 2016. p.137.
8. Saini, K.S., de las Heras, B., Plummer, R., Moreno, V., Romano, M., de Castro, J., Aftimos, P., Fredriksson, J., Bhattacharyya, G.S., Olivo, M.S., Schiavon, G., Punie, K., Garcia-Foncillas, J., Rogata, E., Pfeiffer, R., Orbegoso, C., Morrison, K., Curigliano, G., Chin, L. and Saini, M.L. Reimagining Global Oncology Clinical Trials for the Postpandemic Era: A Call to Arms. *JCO Global Oncology*, (6), 2020. pp.1357–1362.
9. Clinical Trials Transformation Initiative (2021) *Decentralized Clinical Trials Expert Meeting*. [online] Available at: https://ctti-clinicaltrials.org/decentralized-clinical-trials-expert-meeting/ [Accessed 17 Sep. 2021].
10. Wu, M. and Luo, J. (2019). *Wearable Technology Applications in Healthcare: A Literature Review*. [online] www.himss.org. Available at: https://www.himss.org/resources/wearable-technology-applications-healthcare-literature-review.
11. Perry, B., Geoghegan, C., Lin, L., McGuire, F.H., Nido, V., Grabert, B., Morin, S.L., Hallinan, Z.P. and Corneli, A. Patient preferences for using mobile technologies in clinical trials. *Contemporary Clinical Trials Communications*, 15, 2019. p.100399.
12. US FDA. Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards, 2020.
13. European Medicines Agency. Guidance on the Management of Clinical Trials During the COVID-19 Pandemic. Version 4, 2021.
14. NCI (2020) Clinical Trials and Translational Research Advisory Committee (CTAC) Strategic Planning Working Group. Working Group Report November 4, 2020. Available from: https://deainfo.nci.nih.gov/advisory/ctac/1120/SPWGreport.pdf.
15. Wouters, O.J., McKee, M. and Luyten, J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. JAMA, 323(9), 2014. p.844.
16. Torjesen, I. Drug development: the journey of a medicine from lab to shelf. [online] *The Pharmaceutical Journal*, 2015. Available at: https://pharmaceutical-journal.com/article/feature/drug-development-the-journey-of-a-medicine-from-lab-to-shelf. [Accessed 17 Sep. 2021].


---

**Learn more** at oncology.labcorp.com

labcorp | Oncology