Decentralized clinical trials: Meeting patients where they're at

Innovations removing barriers to participation in medical research

Move over, COVID. Decentralized clinical trials (DCTs) is now the hot topic in the pharmaceutical industry. In fact, it was the COVID-19 pandemic that pushed DCTs to the forefront, out of sheer necessity. However, DCTs were around for nearly a decade prior to the pandemic. In 2011, Pfizer completed its first decentralized clinical trial. An article in *Frontiers in Public Health* reports that the earliest studies on the feasibility of "internet trials" date back to 2003 and the first "Trial over the Internet" was patented in the US in 2007.

"The pandemic didn't catalyze innovation. These tools existed," says Craig Lipset, co-chair of the Decentralized Trials & Research Alliance (DTRA) and founder of Clinical Innovation Partners, a consulting agency which provides growth advisory services to organizations developing and implementing innovative approaches for clinical research and medicine development.

Craig Lipset

Let's start with a definition of DCTs. The Food and Drug Administration (FDA) defines decentralized clinical trials as "those executed through telemedicine and mobile/local healthcare providers, using processes and technologies that differ from the traditional clinical trial model." DCTs should not be confused with virtual clinical trials, prompted by the pandemic, which have no face-to-face interactions. DCTs permit physical contact with the patient. Hybrid trials represent a middle ground, in what some consider the best of both worlds: a mix of in-person and virtual/remote elements.

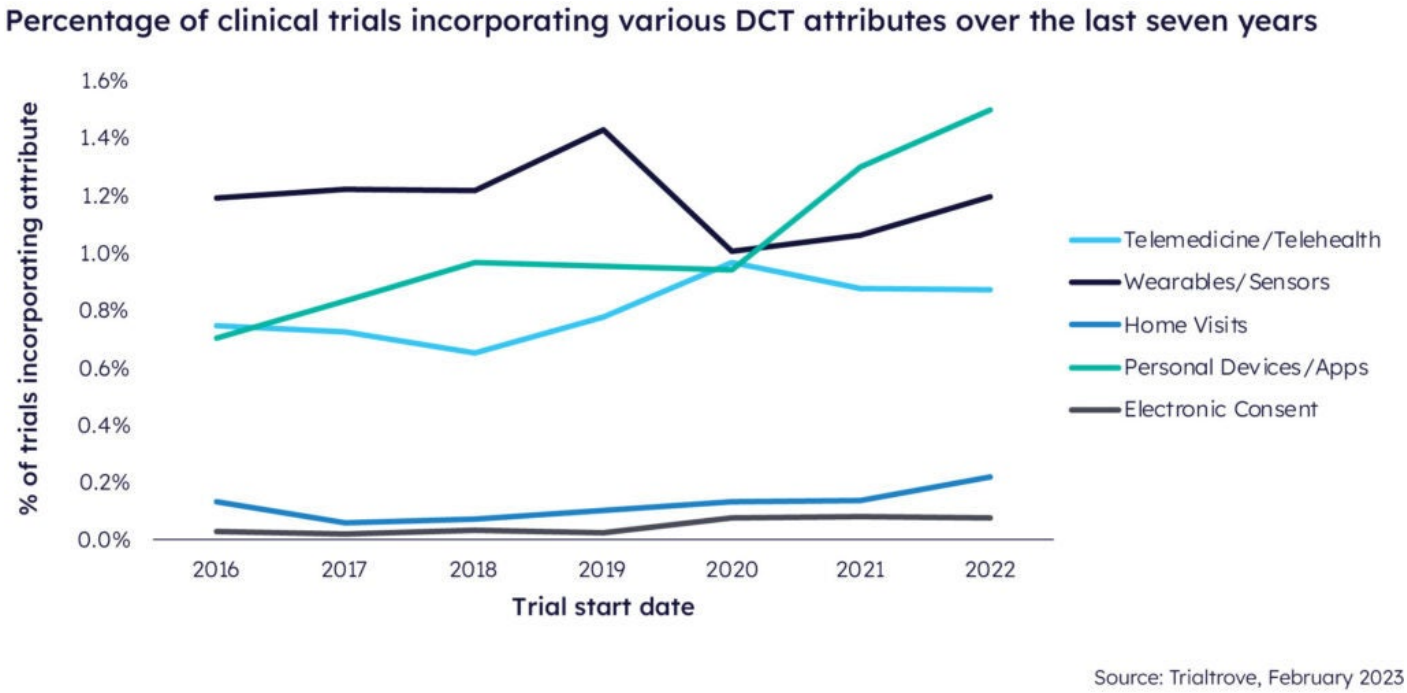
In fact, a recent study conducted on behalf of the Trials@Home consortium, part of Europe's public-private Innovative Medicines Initiative (IMI), calls for standardized terminology around DCTs. The study says DCTs should not be referred to as remote or virtual clinical trials.

Lipset recognizes that the industry is full of jargon, and emphasizes that the public should know the research community is working to make trials as accessible as possible, to give patients the opportunity to participate from anywhere.

Participation in a traditional clinical trial, in person at a clinical trial site, can be burdensome. This requires travel, may require time away from work plus additional expenses such as childcare. These and other negative impacts could deter potential participants from joining a research study.

Lipset says innovation such as DCTs must come with guardrails. Study sponsors must ensure participants are safe and protected, while maintaining data integrity. This includes using consistent forms of measurement, for both traditional trials and DCTs.

Despite these caveats, according to a recent Citeline white paper, "Unlocking the Potential of Decentralized Clinical Trials," the number of trials with decentralized attributes has gradually increased over time.



As the table above indicates, various tools and techniques are incorporated into DCTs. The FDA uses an umbrella term, digital health technologies, to refer to many of the tools used and has issued guidance on remote data acquisition. In January, the FDA's Center for Drug Evaluation and Research (CDER) also published its guidance agenda for 2023, with plans to issue guidelines on DCTs before year's end.

Likewise, the European Commission (EC), the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) have published recommendations regarding DCTs. The paper acknowledges that clinical trials have already adopted many decentralized elements such as electronic calendars, wearables, phone calls, and online appointments. How the elements are used depends on several factors, including the type of study, the trial population, the disease being treated, the condition of the trial participant, the type of medicinal product, its characteristics, and development stage.

The paper advises that these elements "should be considered individually and in combination."

The Clinical Trials Transformation Initiative (CTTI), another public-private partnership designed to improve the quality and efficiency of clinical trials, has issued recommendations to guide sponsors in conducting DCTs.

The Study Sponsor's Perspective

In addition to being more patient-centric than traditional studies, DCTs have the potential to positively impact a sponsor's bottom line. According to an impact report from the Boston area's Tufts Center for the Study of Drug Development, DCT methods increase value by $20 million per drug, if applied in both Phase II and III trials. In another study, 75 percent of companies that completed remote and decentralized trials reported both financial and time savings, and 50 percent reported streamlined patient recruitment.

Top 10 sponsors, by number of studies, for all ongoing and planned trials

Ranking	Trials with DCT attributes	All trials
1	Pfizer	AstraZeneca
2	Novartis	Merck & Co
3	Takeda	Bristol Myers Squibb
4	AstraZeneca	Roche
5	Roche	Pfizer
6	Eli Lilly	Novartis
7	Sanofi	Jiangsu Hengrui Pharmaceuticals
8	Johnson & Johnson	Johnson & Johnson
9	AbbVie	Sanofi
10	GSK	AbbVie

Source: Trialtrove, February 2023

The Citeline white paper lists the top 10 study sponsors conducting trials with DCT attributes. Pfizer, which took an early lead as noted above, is in the number one spot. Joining Pfizer among the top 10 is Sanofi, at number seven.

Kim Hawkins, Global Head of Clinical Project Operations & Dossier Delivery at Sanofi, shares how her organization has made DCTs a priority since 2015, when it co-developed the VERKKO trial (in collaboration with Langland and Mendor), Europe's first fully remote clinical trial, evaluating a patient-centric online clinical trial platform integrated with a 3G-enabled wireless blood glucose meter. Hawkins says the trial, which was widely recognized in the industry as one of the first fully remote clinical trials, marked Sanofi's desire to study this different model of running clinical trials.

Kim Hawkins

While Sanofi did not have a drug or a device under investigation, it supported the study because it was interested in evaluating remote trial participation and monitoring. The study also evaluated the feasibility and efficacy of patient engagement and patient-investigator interaction through the web-based platform. The VERKKO trial showed that patient compliance improved 18 percent, the study site spent 66 percent less time engaged in study coordination activities, and the online recruitment was completed 56 percent faster compared to the traditionally conducted "sister protocol" second trial.

In 2017, Sanofi partnered with Science 37 in an effort to use its technical and mobile capabilities for DCTs. Because Sanofi started building those capabilities into its portfolio, Hawkins says that, when the coronavirus pandemic hit, "We felt like we were in a good place to continue to support our trials and our participating patients."

She says that, post-pandemic, “We have very strong commitment from our senior management” for DCTs. Sanofi has launched a major initiative, Act for Patients, incorporating digital technology such as DCTs, artificial intelligence (AI), and an integrated patient platform to modernize clinical trials. Hawkins says this is “an integrated solution that our patients can use, our sites can use, and our partners can use — all in one platform.”

Sanofi and the University Medical Center Utrecht are leading the IMI €40 million research project, Trials@Home, to study DCTs, with Hawkins as project co-lead. The five-year project has workstreams to focus on different areas, including best practices, regulatory, data privacy, and stakeholder communication. The consortium will conduct a pilot study comparing three different study arms: traditional, hybrid, and DCT, to compare the pros and cons of each approach (RADIAL study).

The Patient’s Perspective

Ronnie Sharpe knows his way around a clinical trial. He says he has paid his dues, estimating he has participated in about 15 research studies. Sharpe is COO of Savvy Cooperative, a patient-owned co-op that connects people with opportunities to share their health experiences with companies, researchers, and innovators. He co-founded the co-op with Jen Horonjeff, who grew up with juvenile arthritis.

Sharpe has cystic fibrosis. He lives in Phoenix, and the most recent study he participated in was in Tucson, about a two-hour drive away. Initially, he had to make that trek every two weeks, then every 30 to 45 days. This went on for over four years.

“When COVID hit, I wasn’t thinking about COVID. … What I was thinking was, how is this going to impact the trial? This drug was definitely saving my life.”

That’s when the clinical trial switched from a traditional to a decentralized model. Sharpe says a medicine-grade scale was sent to his house. Nurses drew blood samples

from him on his front porch, taking up only about a half hour of his time. Everything that had been done at the trial site, except for EKGs, was now done at his home. The trial coordinator checked in with him by phone or text every three to four weeks.


Ronnie Sharpe

"I absolutely loved the DCT setup," says Sharpe. Previously, in addition to traveling two hours each way, he spent four hours on site for a total of eight hours. "I work full time. It wasn't easy," he says, explaining that DCTs are a more lifestyle-friendly trial design.

Teonna Woolford, who has sickle cell disease, was only 19 when she participated in her first clinical trial, a traditional design. The trial involved a bone marrow transplant; her mother was the donor. Treatment included chemotherapy and radiation, which Teonna knew could possibly cause infertility. But her doctor dismissed it and she was willing to take the risk.

As she researched her options for fertility preservation, she found little information and no resources to help pay for the costly procedure. While there were foundations awarding grant money to people undergoing chemo and radiation due to cancer, there were none for sickle cell patients. In the end, her body rejected the transplant, she still has sickle cell disease, and she's infertile.

That did not discourage Woolford from participating in future clinical trials. Like Sharpe, during the pandemic she participated in a trial that started out as a traditional design but switched to a DCT. She says it was important the study designers had the flexibility to change up their approach. "That's why I have a unique perspective," she says, "because I've done both" traditional and DCT studies. Her initial experience,

though, did lead her to co-found, with Drs. Kim Smith-Whitley and Lydia Pecker, the Sickle Cell Reproductive Health Education Directive (SCRed), which advocates for high-quality sexual reproductive healthcare for individuals living with sickle cell disease.

The goal of the second trial was to assess pain in individuals with sickle cell disease. Some patients experience daily, chronic pain. The trial involved a drug designed to reduce the stickiness of red blood cells, which can become hard and rigid due to sickle cell disease.

Teonna Woolford

To track their pain without medication, participants were required to complete daily surveys. For Woolford, the constant text message reminders were very disruptive to her day. “The questions every day were the same, so I found it annoying… I don’t have pain every day.” There was no option to explain that, so about a month into the two-month study, she dropped out of the trial.

“I was just starting a business at the time,” says Woolford, CEO of SCRed, in its second year of operation. “When you hear DCT, you automatically think it’s going to be more convenient.” And, in many ways, it is. “I don’t have to pay for child care, find parking.”

Based on her experience, however, she says, “There shouldn’t be a one-size-fits-all.” She notes that some people are too private, others see their home as sacred. “That’s the one place they can escape” from their disease. Woolford recommends more of a hybrid approach “to meet the patient where they are.”

Savvy Cooperative’s Sharpe is sold on DCTs. “If we want to talk about patients, DCTs are where it’s at.”

What's on the Horizon for DCTs?

"We're already starting to see this future come to light," says Lipset. More expansive locations include in-home testing, retail pharmacies, pop-up sites, mobile sites such as retrofitted ambulances and RVs.

"These are research sites. They just happen to have wheels."

"There is potential to significantly reduce our [drug] cycle time. Every single new medication that's on the market goes through a clinical trial, and only about 10 percent of the population participates in a clinical trial," says Sanofi's Hawkins. With DCTs, she adds, "There's opportunity to have clinical trials be a choice for more people."

In addition to improved cost savings, increased efficiency, patient access, recruitment, diversity, and retention, Lipset says many sponsors — mostly in Europe — are looking at DCTs through the lens of corporate responsibility. One focus of the Sustainable Healthcare Coalition is reducing the carbon footprint of clinical trials. In terms of sustainability and environmental impact, DCTs outperform their traditional counterparts.

However, industry stakeholders agree that patients should be the motivating factor in conducting DCTs. Lipset cautions: "With decentralized clinical trials, patients should feel more connected to the investigator, not less."

Savvy Cooperative's Sharpe sees DCTs as a launchpad for what's next, what's truly pro-patient. He's optimistic yet skeptical as he asks: "What else is being held back because of bureaucracy, the healthcare apparatus in the U.S.?"

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