The Impact of ADAPTABLE: The Industry's First and Largest Fully Decentralized Clinical Megatrial

Enhancing Site and Patient Engagement

For over half a century, millions of Americans living with heart disease have relied on a daily dose of aspirin to help prevent a heart attack or stroke. While commonly prescribed dosages had been 81 or 325 mg, the ADAPTABLE study was designed to determine the dosage that maximized results while minimizing side effects. Because of its deep industry expertise and technology offerings, Medidata was selected to provide eClinical solution support for this groundbreaking study, conducted from 2016-2021.

Whereas a traditional trial of this magnitude would have cost more than $100 million, a decentralized design significantly decreased the cost to less than $20 million. A virtual study of this size made it the industry's first and largest decentralized clinical megatrial.

The ADAPTABLE study team applied innovative decentralized clinical trial (DCT) concepts to enroll a large, widespread population. The trial protocol was designed to engage patients who would not otherwise participate because of their location or lack of desire to travel to a central site. Clinical technology and professional services were needed to support DCT functions at the patient, site, and sponsor levels. While DCT components were not commonplace in 2016, they have become more mainstream today - in part due to the success of the ADAPTABLE study.

"ADAPTABLE was designed to support more representative inclusion of patients, enhance engagement while reducing the burden on patients to participate in a clinical trial, and decrease many of the costs associated with traditional site-based studies," said Holly Robertson, PhD, project leader at the Duke Clinical Research Institute from 2015 to 2020.

Industry-Leading Trial Components

Working collaboratively with the client, Medidata provided key DCT components to ensure robust trial technology, engagement, and results:

The original **electronic virtual trial platform** was provided by Mytrus and its Engage service, acquired by Medidata in 2017. This early-generation DCT technology set the foundation for today's myMedidata portal. This intuitive portal allowed participants to easily access information and report health outcomes – using their own devices from the comfort of their homes. Behind the scenes, the platform provided the interface allowing sites to manage the trial and enter study data into EDC.

Medidata provided a **novel recruitment** approach, generating a series of "golden tickets" that enabled clinical research sites to invite eligible patients into the ADAPTABLE study. Potential participants were identified via an EHR search external to Medidata; sites created a common data model, searched patient matches, and invited candidates to join the study via the golden tickets. The tickets provided a unique, one-time-use alphanumeric access code to protect the identities of qualified patients and allow them to register for the study. Operationally, the golden tickets enabled sites to track eligible patients through identification, recruitment, enrollment, and follow-up. This approach evolved into best practice for present-day patient recruitment.

ABOUT THE STUDY

The Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-term Effectiveness (ADAPTABLE) study was funded through a Patient-Centered Outcomes Research Institute (PCORI) Award. The study was led by researchers at the Duke Clinical Research Institute (DCRI), the world's largest academic clinical research organization and a part of the Duke School of Medicine. ADAPTABLE was the first demonstration project to be conducted through PCORnet®, the National Patient-Centered Clinical Research Network.

Medidata's remote **eConsent** service helped engage participants and educate them regarding the trial. Patients could view pertinent videos and documents and then answer knowledge-review questions. This eConsent feature allowed participants to make informed decisions and sign consent forms digitally as part of a convenient, compliant, trackable process.

The platform also supported remote **eSource data capture** for the study. Patients logged into the myMedidata portal to complete forms at the appropriate times while getting information about taking their medication. Meanwhile, the platform gave sites centralized patient management capabilities, including reports for compliance and visits.

Patients accessed **adverse event (AE)** information and reported any AEs via myMedidata. The study team watched for primary safety endpoints through the portal – mainly reported hospitalizations. This ability was revolutionary at the time but paved the way for patient-reported AEs, commonplace today.

Next, the Medidata platform supported **patient self-dosing** and **supply management**. As the study protocol called for randomized patient groups to purchase OTC aspirin in 81 or 325 mg doses, the portal tracked compliance from the patient perspective. The goal was to ensure that participants were using the correct dose and taking it regularly according to the study protocol.

> **"Compared with traditional cardiovascular trials that engage hundreds or thousands of sites, this technology allowed us to enroll 15,000 participants from 40 centers."**
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> **Dr. Schuyler Jones**
> **ADAPTABLE Co-Principal Investigator, Associate Professor of Medicine , Duke University Medical Center**

Driving Patient-Centricity

Over 650,000 patients were identified as matching the inclusion criteria for the study; 450,000 were issued golden tickets and invited to review ADAPTABLE materials. More than 30,000 people used their unique access code to enter the myMedidata portal. The golden tickets ensured that the correct informed consent and site information were presented to the right patient. In the end, over half of the 30,000 patients who used their golden tickets enrolled in ADAPTABLE, making it the first and largest 100% virtual clinical megatrial.

When a virtual visit was due, the system automatically notified patients with a text or email reminder to visit the study portal. Patients could complete the scheduled electronic patient-reported outcomes, fill out case report forms, and update their health status via myMedidata. The system provided additional reminders if a patient did not complete the virtual visit and alerted the study's call center staff in cases of patient noncompliance.

The call center also accommodated patients having limited Internet access or needing additional follow-up. As necessary, patients requiring physician follow-up were referred to study sites. This approach reduced the administrative burden at the site and increased patient compliance.

ADVANTAGES OF MEDIDATA'S PLATFORM

- Reduction in number of sites
- Faster enrollment
- Reduced patient burden
- Lower trial costs

STUDY DEDICATION

The ADAPTABLE study has been dedicated to one of its nine Adaptors, Bill Larsen, who passed away before the study was completed. A citizen scientist who previously worked on the OneFlorida Citizen Scientist Program, he brought his passion for improving the quality of health care to ADAPTABLE. Bill provided the patient's voice by noting his concerns and asking what average people would want to know about research.

Delivering Results beyond the Science

Researchers concluded that the 325 mg aspirin dose was likely fine for patients doing well on it, but the 81 mg dose probably was best for most heart patients. "ADAPTABLE has given clinicians confidence that low-dose aspirin is the best choice for most patients," noted Dr. Schuyler Jones, associate professor of medicine/cardiology at Duke University Medical Center and ADAPTABLE's co-principal investigator.

This scientific finding reassured millions of patients and physicians, but the study's impact went far beyond the science. ADAPTABLE's patient-centric design – with an emphasis on extensive patient input, recruitment of diverse participants, and use of novel technologies – reduced costs by 5x while ensuring reliable results. The study proved the many benefits DCTs could provide to study sponsors, researchers, and patients.

Medidata technology met the research team's needs for a centralized eClinical data source. The platform made it easy for patients to remain compliant with protocol objectives and provide updates to the clinical team for key study data, such as hospitalizations, aspirin usage, etc., without in-person study visits. It also supported regulatory and compliance requirements for clinical research, such as 21CFR Part 11, 21CFR50.20, and GCP.

Award-Winning Innovation

The ADAPTABLE Megatrial drew the attention of the medical research community. Its success led the Clinical Research Forum to name the study a Top Ten Clinical Achievement Awardee for 2022 – partly for the impact its methodology is likely to have on future medical research. Because the innovative project combined the expertise of academic and industry partners, nascent technology provided by Medidata, and a patient-centered research network, it proved that DCTs could produce value for doctors, patients, and their caregivers.

"ADAPTABLE has become the cornerstone trial for many pharmaceutical companies wanting to move to DCTs," said Robertson, now senior director, Advisory and Enablement Services at Medidata, a division of Medidata's Professional Services team.

Applying Lessons Learned

ADAPTABLE proved that patients could participate in a fully virtual trial design. It also demonstrated that older populations were adept at participating in clinical trials using well-designed technologies and their own devices. With an average age of 67, the ADAPTABLE patient base included many patients in their 70s, 80s, and several in their 90s, with a very low support call history around using the technology.

Incorporating the patient voice in trial design enhanced the patient experience and led to higher engagement and retention rates. ADAPTABLE included nine patient advocates or "Adaptors" in all phases of planning, operation, and follow-up. Their input ensured a study design that lowered the patient burden in trial participation by moving to a virtual setting.

Traditionally, the burden of travel to a trial site with multiple site visits throughout the duration would preclude some patients from participating. By removing this barrier, ADAPTABLE engaged with patients in rural areas who were naive to clinical trials and could represent a larger segment of the population. ADAPTABLE's results were shared directly with the study participants via an online town hall, simultaneously with a traditional medical conference presentation – another first for a clinical trial.

BENEFITS OF MEDIDATA'S PLATFORM

- Single source of data
- Improved engagement and compliance
- Trial Dial™ – Enabling fully virtual, hybrid, and traditional clinical trials

"Medidata allowed us to reach patients who wouldn't normally participate in a clinical trial because of location or convenience."

Dr. Holly Robertson, PhD
Project Leader
Duke Clinical Research Institute

Engaging patients pre-trial and post-trial allowed patient perspectives to be integrated into the trial process. Post-trial engagement helped to create an "alumni network," a registry of people more likely to join future studies. DCRI researchers began sharing information on ADAPTABLE's methodology and learnings even before the study was completed. The Institute and the study team published several papers on lessons learned as they developed best practices to drive widespread DCT adoption.

Finally, ADAPTABLE highlighted a successful shift to a DCT model for sponsors and sites using Medidata technology and support. Operational strategies were designed for successful implementation, while training ensured that study team members were comfortable with the technology. To date, Medidata has supported more than 1,000 DCT studies that have included some level of decentralization, involving some 400 sponsors and 1 million participants.

Moving Forward

> **"The fact that ADAPTABLE was identified as one of the Top Ten influential clinical trials is recognition that its many lessons learned have had an impact on decentralized trial design"**
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> **Dr. Schuyler Jones**
> **ADAPTABLE Co-Principal Investigator, Associate Professor of Medicine , Duke University Medical Center**

Several years after ADAPTABLE began, the COVID-19 pandemic significantly boosted interest in DCTs and remote patient participation. ADAPTABLE's trial methodology, supported by Medidata technology and guidance, will help future studies increase patient-centricity, efficiency, and cost-effectiveness.

Robertson added, "While many trials will not be a fit for a fully virtual design like ADAPTABLE, most trials can adopt a hybrid approach, embracing many of the study's elements to achieve a more patient-focused design. Technology such as Medidata's platform is crucial to optimizing the patient experience."

ABOUT MEDIDATA

Medidata offers technology and professional services to help lead 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 2,000+ customers and partners access the world's most trusted platform for clinical development, commercial, and real-world data.

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> **"I have great hope that this will be the model of the futre for answering questions of critical importantance to patients, families, clinicans & health systems more quickly and with high quality at a lower cost** @DukeForge"

Robert M. Califf M.D.
MACC Commissioner of Food and Drugs,
Food and Drug Administration

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