ATCOR

Advancing Patient Access, Anywhere

The Importance of the Patient in Decentralized Clinical Trials

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The impact of the COVID-19 disruption in clinical trials has stimulated innovative alternative approaches to the standard emphasis on clinic-based enrollment and assessment towards more efficient and effective models. Given the above, the decentralized clinical trial (DCT) model, has become widely adopted with early success.[1,2]

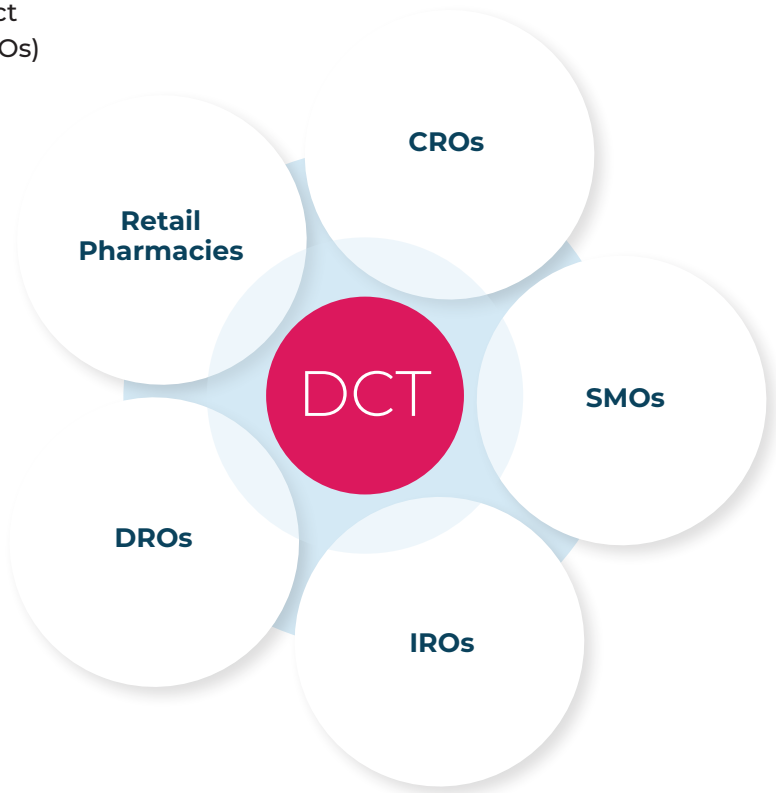
"Greater adoption of DCTs will facilitate drug development in areas of medical need, which means more treatment options and better outcomes for patients, the FDA added."[4]

"The FDA has long considered the benefits of decentralized clinical trials. Advancements in digital health technologies and the COVID-19 pandemic—when in-person visits were limited or unavailable for many trial participants—have accelerated the broader adoption of these activities," FDA Commissioner Robert Califf, M.D., said in a statement. "As we seek to improve our evidence generation system, decentralized clinical trials may enhance convenience for trial participants, reduce the burden on caregivers, expand access to more diverse populations, improve trial efficiencies, and facilitate research on rare diseases and diseases affecting populations with limited mobility."[3]

The DCT model encompasses innovations across recruitment, data capture technologies, clinically validated medical devices, home-based visits and telehealth, automation, real-world data, and artificial intelligence. An unexpected impact of DCT is the market expansion of trial site partners supporting pharmaceutical and biotechnology companies with wider reaching trial services in an effort to expedite trial timelines, reduce costs, and increase participant reach with diversity[5,6].

The vast list of clinical trial site partners may include:

- Clinical Research Organizations (CROs) & Contract Development Management Organizations (CDMOs)
- Site Management Organizations (SMOs)
- Decentralized Research Organizations (DROs)
- Integrated Research Organizations (IROs)
- Pharmacies & Distributor Partners
- Hospitals & Integrated Delivery Networks (IDNs)
- Digital Health Technologies (DHTs)



The recent release of the FDA's draft guidance focuses on patient safety within decentralized clinical trials. When coupled with the final FDA guidance on enhancing diversity in clinical trials[7], the anticipated impact is a heightened awareness and drive to include appropriate trial populations in protocol designs where therapeutic outcomes are reflective of a wider underrepresented population.

Even with early DCT success, clinical trial designs still need improvement:

- Inconsistent collection of essential vital signs
- Slow patient and diversity population enrollment
- Patient drop-outs from adverse events
- Changes to vital signs relevant to drug risks are not reliably detected
- Patient monitoring uses minimal vital signs data for inclusion/exclusion screening

Many trials designs are now implementing a hybrid CT/DCT approach to enhance patient enrollment in communities where qualified clinical trial patients were previously unreachable.

30 YEARS

ATCOR addresses the challenges in clinical trial designs and improves patient outcomes

ATCOR Advances Clinical Trials & Real-World Evidence Using Digital Vascular Biomarkers

30-year history of developing non-invasive medical devices

Clinically validated & FDA-Cleared

Capture expanded vitals (digital biomarkers) in 3-5 minutes

Accuracy comparable to an intravascular catheter

ATCOR Focuses on the Patient

- Identify the right patient for the right trial
- Monitor expanded vital signs, anywhere
- Identify and mitigate adverse events
- Personalize the patient healthcare journey
- Improve patient outcomes, everywhere

Consistently simple to measure

Implement across therapeutic areas

CPT code 93050 for reimbursements

ISO 13485:2016 & EN ISO 13485:2016 certified

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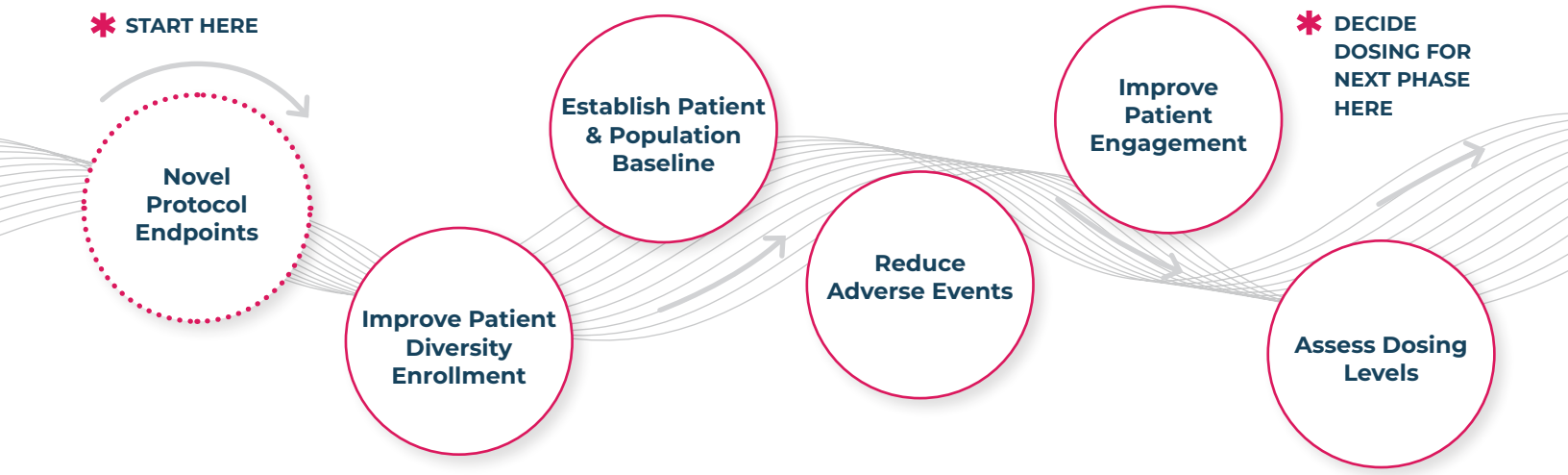
Expanding patient access is a known benefit of DCT, and as a result, a broader popultion integrated in clinical trial designs provides a more complete picture of drug efficacy within our neighborhoods[8]. The simplicity of ATCOR's remote collection of non-invasive digital vascular biomarkers (i.e. expanded vital signs) eliminates an industry gap of collecting patient safety data, anywhere. Capturing expanded vital signs data during screening establishes each patient's baseline to assess enrollment eligibility. **A patient's baseline is unique and personalized, just like a fingerprint.** Following identification of the right patient for the right trial, ATCOR monitors early risk personalized to each patient's original baseline biomarkers and signals alerts to intervene prior to an adverse event.

ATCOR's Digital Vascular Biomarkers Improve Patient Outcomes



Improve Patient Diversity Enrollment

Set inclusion/exclusion criteria w/ digital vascular biomarkers

Selective screening for populations

Confirm white coat hypertension

Establish Patient & Population Baseline

Establish patient baseline prior to trial for adverse event monitoring

Create a population synthetic control arm

Reduce Adverse Events

Monitoring identifies early risk

Real-time data access

Alerts decrease patient risk

Improve Patient Engagement

Personalize safety monitoring

Reduce adverse events to improve retention

Assess Dosing Levels

Correlate adverse events to demographics

Identify population-based digital vascular biomarkers

Together, the FDA and industry are collaboratively building new DCT guidance with the goal to provide a framework for keeping patients at the center of trials and a focus on managing patient safety through the integration of new technologies that enhance the patient experience, collect real-time data for patient safety monitoring, and secure data transfer from remote environments.

How ATCOR's Solutions Align with FDA's DCT Guidance:

1 ATCOR Facilitates Improved Clinical Trial Design & Protocol Endpoints

Decentralized clinical trial designs and protocols should focus on ensuring patient safety through adverse event (AE) monitoring, technology monitoring, and investigational product (IP) monitoring. By integrating digital vascular biomarker protocol endpoints to facilitate remote patient monitoring of real-time data collection, early identification of adverse events may potentially be avoided. If not identified early, adverse events could progress to serious adverse events. In addition, early identification and intervention may lead to few patients discontinuing the trial prematurely.

ATCOR's non-invasive and FDA-cleared medical devices share an expanded profile of a patient's vital signs to provide personalized monitoring from a patient's baseline screening values. When used pre and post dose, monitored biomarker data may identify small changes and confirm a patient's self-administration of IP. In the example of pre and post dose biomarker levels showing early signs of patient risk, connected technologies send pre-programmed alerts to study team clinicians that a patient evaluation and biomarker assessment is needed. Remote monitoring can initiate a timely intervention through a number of methods using the power of today's technology, including a study team clinician deploying an unscheduled telemedicine visit following the alert on a patient's digital vascular biomarker levels.

	Adverse Event (AE) Monitoring	Technology for Patient Safety Monitoring	Investigational Product (IP) Monitoring
Design & Protocol	✓ Evaluation and management of AEs remotely ✓ Personalized response to AEs needing urgent attention	✓ Flexibility for remote visits: scheduled & unscheduled ✓ Integrating video for visibility of patient interaction	✓ IP administration monitoring based on drug profile ✓ Personalized patient monitoring to reduce risks

When used in the trial design, remote technology may further improve patient safety monitoring by expanding the data collected from both patient reported outcomes (PRO) and physiological data, such as digital vascular biomarkers. Protocols inclusive of digital vascular biomarkers as secondary and safety endpoints in DCT designs expand the depth of data collected with associated patient monitoring and patient reported outcomes, providing deeper insights into IP efficacy and safety.

2 ATCOR Enhances Patient Safety Monitoring Plans

Incorporating a safety monitoring plan is a core focus area in all models of clinical trials – conventional, hybrid, and decentralized. Data and safety monitoring is considered to be a standard practice across phase I through IV clinical trials. Decentralized trials may differ with the integration of a risk-based monitoring plan that integrates the use of multiple remote technologies, devices, data collection tools, and communication tools to enable accessible and virtual patient interaction.

Effective patient safety monitoring takes advantage of bi-directional communication, where either the clinician or the patient may initiate a request for medical communication. The simultaneous use of technologies encourages multifaceted data collection. For example, a patient may initiate a digital vascular biomarker assessment during a video visit call while the clinician initiates an evaluation of the biomarker results in real-time and simultaneously while recording observations of a patient's physical appearance and general behavior. **Both subjective data (i.e., observations) and objective data (i.e., peripheral blood pressure, central blood pressure, arterial stiffness, heart rate) provide complementary data to more thoroughly assess a patient's well-being.**

Safety Monitoring Plan	Ensure Safety and Welfare of Patients	Enable Patient Medical Communication	Digital Health Technologies
	✓ Capture and address AEs ✓ Visit technology or site for collecting safety data	✓ Technology for patient self-reporting of AEs ✓ Patient-requested unscheduled visit or assistance	✓ Plan for monitoring of collected patient data ✓ Action for abnormal or patient monitoring alerts

An unexpected benefit of remote patient monitoring is increased interaction from using multiple communication tools that facilitate patient engagement in a standardized and structured manner. Providing opportunities that conveniently allow a patient to report outcomes may be a key factor in retaining patients on a decentralized trial. Whether at the request of clinician during a scheduled visit or from a patient's request for an unscheduled visit, the ability to collect subjective data from different sources, in addition to objective data, provides valuable data and perspective to increase the engagement of a patient when face to face interaction time is limited.

Introduced into the safety monitoring plan, collected data from multiple sources can be used to confirm patient risk. A patient's request for assistance may correlate with the patient's digital vascular biomarker data collected a few minutes later. Remote technology offers decentralized trials multiple methods by which data can be obtained to both monitor and assess a patient's well-being.

3 ATCOR Partners with Digital Health Technologies to Secure Real-Time Data Capture

The wide array of technologies today only encourages additional opportunities to enhance the trial experience while capturing vast data that enhances remote monitoring of patients, improves engagement, and expands evidence to evaluate IP efficacy and safety. Decentralized clinical trials are rapidly expanding the volume of remote-based and real-time data being captured, elevating the risk of potential data errors. Enhancing data transfer using ATCOR's application programming interface (API) to automate digital vascular biomarker data transfer removes common errors associated with manual data transfer. Enhancing data security through the use of access control for authentication and authorization protects data sources and improves real-time data access.

Not typically considered a data risk is technology. If technology is deployed in a decentralized clinical trial, it should be intuitive and not introduce challenges or barriers that may impact data collection. Usability and fit-for-purpose technologies should be clinically validated and require assessment for the intended use within a remote setting where the only available support is virtual. The most common risk that technology introduces, if data is not automatically transferred, is the potential loss of real-time data collection by either the patient or a study team clinician.

A best practice when considering data capture tools is the integration of common or comfortable technology platforms used in our daily activities. De-risking the collection of data remotely relies on technology that is easily and consistently used. When training on a technology that will be deployed in a remote setting, multiple communication platforms and job aids should be provided to increase understanding and introduce feedback to encourage adoption. Technology used for data capture within a DCT should be teachable and usable for the intended population[9].

Data Capture

Common Technology Platforms

- ✓ Flexible for patient communication and data capture
- ✓ Convenient technology: cell phone, tablet, laptop

Usability of Digital Health Technologies

- ✓ Patient training to confirm use and understanding
- ✓ Clinician training to consistently perform data capture

Data Collection & Transfer

- ✓ 21 CFR Part 11
- ✓ Electronic transfer avoids manual risks

Data capture for a DCT should be supported by remote technologies that enhance the trial experience for the patient and de-risk the challenges that technologies may introduce in a remote setting. The robust evaluation prior to the deployment of common technologies typically reduces barriers to successful use for both patient and study team clinicians. The integration of automated data transfer reduces burden on clinicians, improves access to real-time data, and facilitates the real-time remote monitoring of patients.

ATCOR Aligns with FDA DCT Draft Guidance by:

- Improving patient access, anywhere
- Increasing patient retention and engagement
- Personalizing therapeutic programs
- Integrating expanded vital signs monitoring into any therapeutic trial design
- Enhancing protocol designs with digital endpoints to support drug efficacy and patient safety

ATCOR Advances Patient Access, Anywhere

Contact us! Learn more about using personalized digital vascular biomarkers in decentralized clinical trials.

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