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Prasanna Parthasarathy,

Syneos Health

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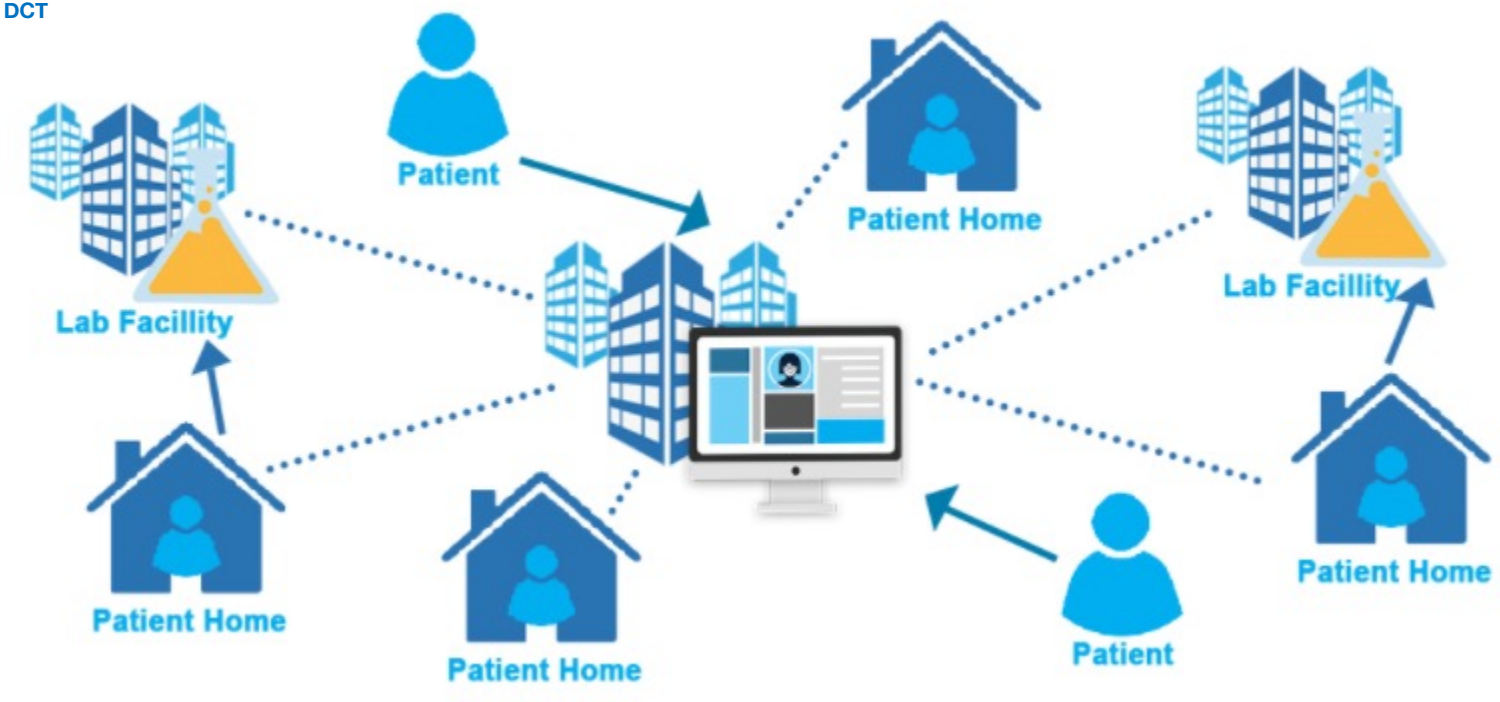
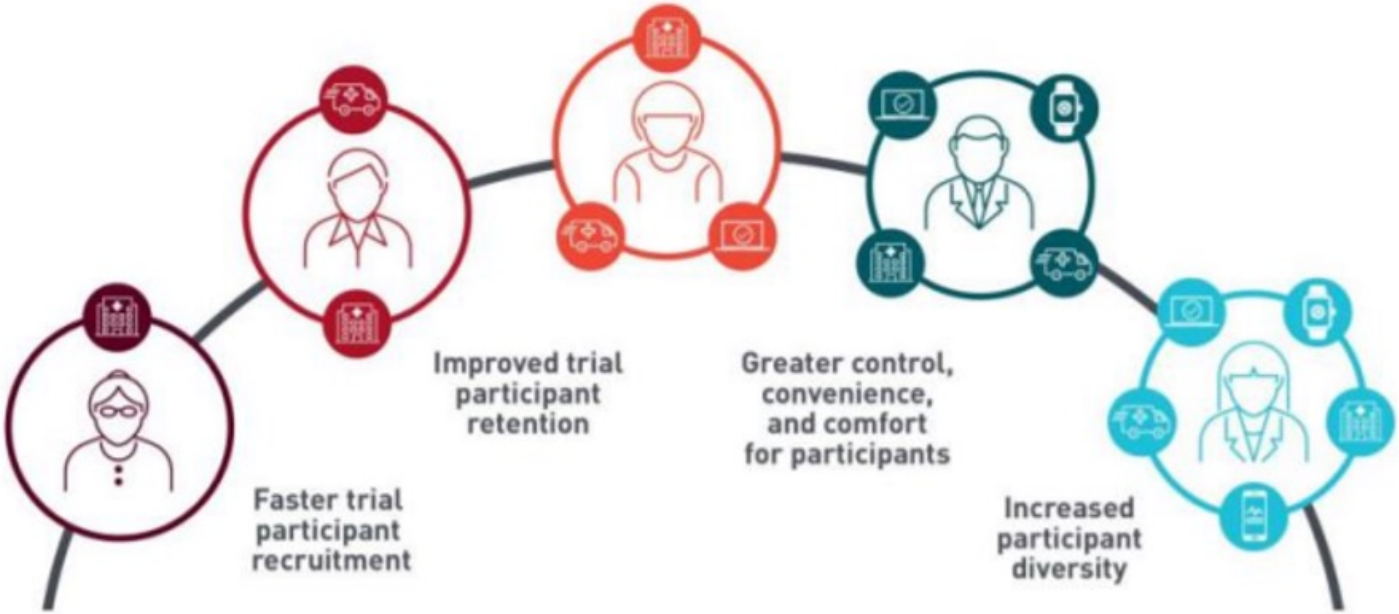
What is Decentralized Clinical Trial (DCT)

DCT



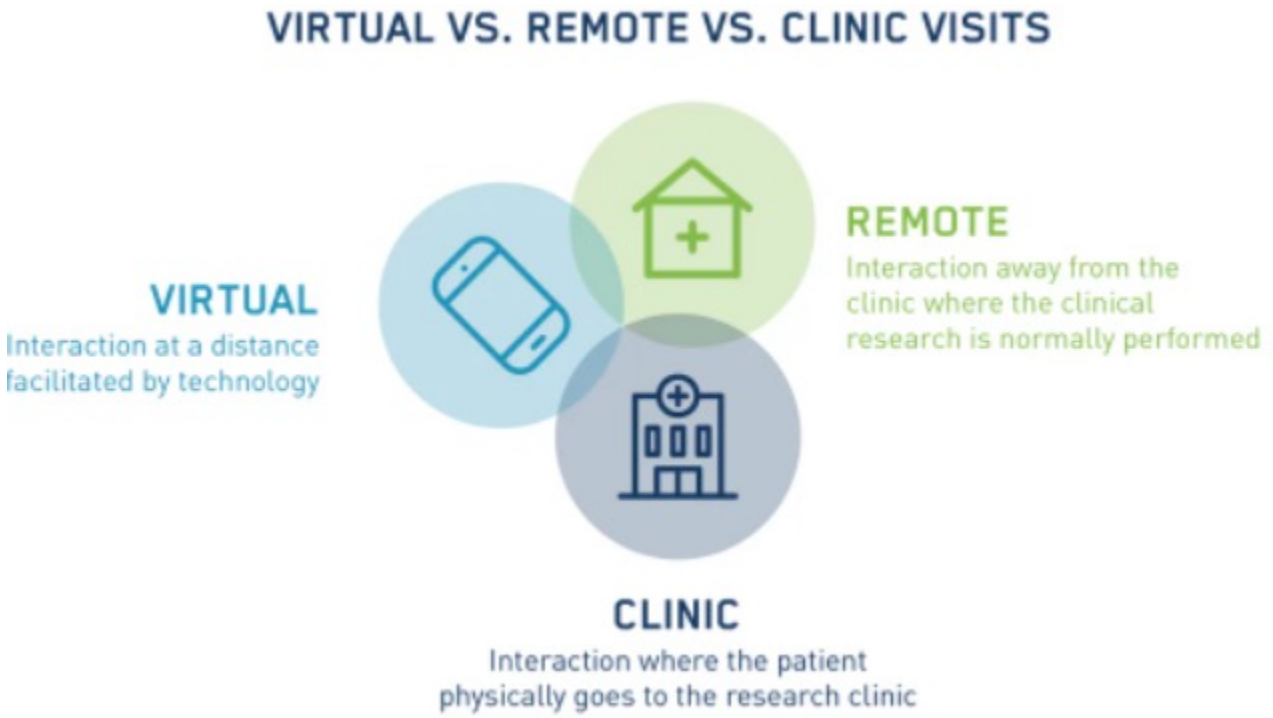
DCT – A Pioneering Approach



Challenge

There was no standard approach to how COVID-19 modifications to be identified in clinical trial datasets submitted to the US FDA.

Considerations from the US FDA for performing a DCT



US FDA Proposals on DCT

1) Creation of a COVIDMOD dataset that will document the timing of when REMOTE trial modifications to address COVID19 were permitted at the patient and site level.

COVIDMOD [PatientID], [Site], [ModType], [DateModStart], [DateModStop]

Purpose: Document the date that remote assessments were permitted at the patient and site level

Telemedicine visits, Remote labs, Remote imaging, Remote administration of investigational product (IP), Remote site monitoring, Other

US FDA Proposals on DCT

2) Flag individual assessments (clinic visits, laboratory assessments, imaging assessments, delivery of IP) as to whether they were conducted REMOTE or at the standard trial site

Separate column in the ADAE, ADLB, ADRS, and ADEX

Adding additional columns in SDTM.SUPPSV dataset

US FDA Proposals on DCT

3) Assess the data quality

- Adding Data quality Flag
- Compare missing data rates/ out of window rates
- Compare scan quality (interpretable vs uninterpretable)
- Compare missed doses, dose modifications
- Compare missed visits, out of window visits
- Compare dose mod rate, AE/SAE rate, hospitalization rate

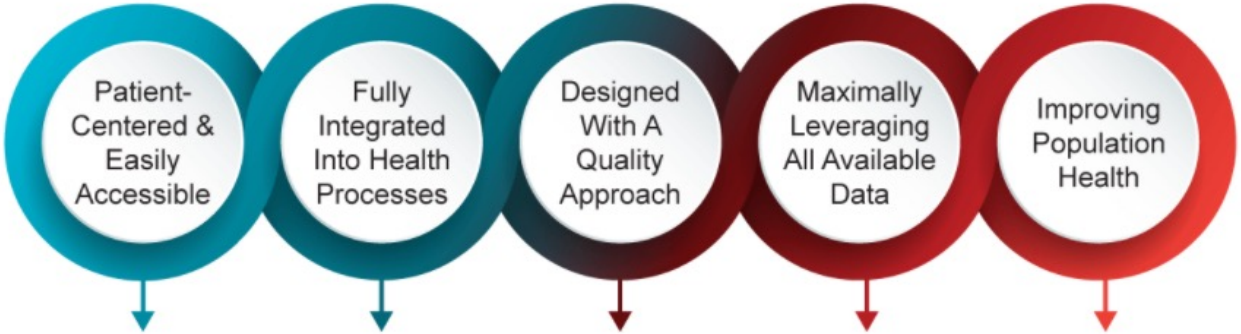
Considerations from the Clinical Trials Transformation Initiative (CTTI) for performing a DCT

Clinical Trials Transformation Initiative (CTTI), a public-private partnership co-founded by Duke University and the U.S. Food and Drug Administration, seeks to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials. CTTI has brought together more than 500 organizations across the clinical trials ecosystem to blend diverse perspectives representing academia, clinical investigators, government and regulatory agencies, industry, institutional review boards, patient advocacy groups, and other groups. Many regulatory agencies and organizations have applied CTTI's existing recommendations and associated resources to make better clinical trials a reality.

CTTI Vision – By 2030

TRANSFORMING
TRIALS 2030

By 2030, clinical trials need to be:



A critical part of the Evidence Generating System

DCT Approaches and Protocol Design – CTTI Recommendations

1) A DCT does not have to be an all-or-nothing approach.

Partially decentralized or hybrid approaches

- **Hybrid Model**
- **Assessments by Mobile HCPs**
- **Video Conferencing**
- **Local Labs**

CTTI - Clinical Trials Transformation Initiative

DCT Approaches and Protocol Design – CTTI Recommendations

2) Engage with all stakeholders during the protocol design stage

Stakeholder kick-off meeting

Stakeholders (e.g., patients, US FDA, IRBs, investigators, CROs, pharmacies, state medical boards, mobile HCPs)

US FDA's Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER)

US FDA's Center for Devices and Radiological Health (CDRH) and Investigational Device Exemption (IDE) approval

Meet Experienced Vendors (Mobile HCPs)

CTTI - Clinical Trials Transformation Initiative

DCT Approaches and Protocol Design – CTTI Recommendations

3) A DCT will need some fit-for-purpose protocol design, including the following:

- **Activities performed at Investigative site**
- **Activities Performed by Mobile HCPs/Local Labs**
- **Technological Support**
- **Protocol Compliance**
- **Site Management**

CTTI - Clinical Trials Transformation Initiative

DCT Approaches and Protocol Design – CTTI Recommendations

4) Proactively address and map data flow, data storage, and associated procedures :

Integrity and Reliability (CTTI's Mobile Technologies recommendations)

Data Privacy Laws and Regulations

Data Flow in Protocol/Data Management Plan

CTTI - Clinical Trials Transformation Initiative

DCT Approaches and Protocol Design – CTTI Recommendations

5) Drug Supply Chain:

Direct-to-trial participant shipping – State Law Requirements

Physician Dispensing Law Requirements

Tracking IMP

IMP Storage/Inventory
IMP Dispensation

Documentation of Supply Chain Logistics

CTTI - Clinical Trials Transformation Initiative

DCT Approaches and Protocol Design – CTTI Recommendations

6) Mobile Healthcare Providers:

- Credentials and Qualification
- Trained on SOPs like Human Subject Protection, GCP, Data Integrity and Protection, Clinical Trial Billing
- Local HCPs as Sub-Investigator List in US-FDA form 1572
- Trained on Sponsor Specific SOPs

DCT Approaches and Protocol Design – CTTI Recommendations

Responsibilities of local HCP:

- Blood Draws (Lab Samples/PK Samples)
- Biological sampling (e.g., pharyngeal and oral mucosal swabs, urine or fecal samples)
- IMP administration
- Training and education of the trial participant (e.g., IMP self-administration)
- Clinical assessments (e.g., vital signs, electrocardiograms, concomitant medications, adverse events)
- Administration of questionnaires or in-home compliance checks (e.g., timely completion of trial participant diaries, proper storage of IMP)

CTTI - Clinical Trials Transformation Initiative

DCT Approaches and Protocol Design – CTTI Recommendations

7) Safety Monitoring

Train investigative staff on processes that are unique to DCTs

Develop protocol-specific safety monitoring and communication escalation plans.

Frequent Patient Monitoring and Pre coordination between mobile HCPs and Investigative staffs

Trial participant at a remote location should be capable to address possible adverse events IMP administration.

Our Goal


Empowering digital health stakeholders to advance health care
INNOVATE
EMPOWER
CONNECT
SHARE

References

Regulatory/Governance:

https://www.fda.gov/about-fda/oncology-center-excellence/advancing-oncology-decentralized-trials

https://www.fda.gov/about-fda/fda-organization/center-biologics-evaluation-and-research-cber

https://www.fda.gov/about-fda/fda-organization/center-drug-evaluation-and-research-cder

CTTI:

https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_DCT_Recs.pdf

https://ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_Digital_Health_Technologies_Recs.pdf

Learning Resources:

https://www.law.cornell.edu/cfr/text/21/part-601/subpart-E

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=314&showFR=1&subpartNode=21:5.0.1.1.4.8

Community:

https://www.dtra.org/

The Global Healthcare Data Science Community

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