Developing Technology-Derived Novel Endpoints for Use in Clinical Trials: CTTI Recommendations & Case Examples

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Will Herrington, MD, MRCP, MBBS, MA | University of Oxford
Webinar Outline

- The need for recommendations
- CTTI recommendations and resources on the selection, development, and inclusion of technology-derived novel endpoints in clinical trials
- Where is our field right now with regards to adopting these novel endpoints and how will CTTI’s work continue to drive advancement?
- Why is CTTI so committed to driving the adoption of technology-derived novel endpoints in clinical trials and what other work are they doing to drive their adoption?
Clinical trials appear to be behind other industries in adopting mobile technologies to improve quality and efficiency.
Benefits of Technology-Derived Endpoints

Potential scientific and efficiency benefits of mobile technology-derived endpoints:

- Prospective
- Objective
- Sensitive
- Patient-centric
- Real-world
- Prolonged measurements
- Minimal interference with trial participant’s daily lives
- May increase the pool of people willing to volunteer
Recommendations: Summary

- Foster collaboration among key stakeholders

- Optimize novel endpoint selection
  - Focus on measures that are meaningful to patients
  - Select the device after selecting an outcome assessment
  - Use a systematic approach to identify key novel endpoints

- Approach novel endpoint development process practically
  - Create technical standards for mobile technology-derived assessments
  - Engage regulators throughout the process
  - Include novel endpoints as exploratory endpoints in existing clinical trials and observational cohort studies
  - Critically position novel endpoints in interventional trials
Multi-Stakeholder Collaboration

1. Patients and patient groups
2. Clinical academic groups
3. Technology developers
4. Regulators
5. Industries developing interventions (sponsors)
CTTI Strengths

Public-Private Partnership
Co-founded by Duke University & the FDA
Involves all stakeholders
80+ members

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials
Mobile Clinical Trials (MCT) Program

PURPOSE:

Develop evidence-based recommendations that affect the widespread adoption and use of mobile technology in clinical trials for regulatory submission.

ANTICIPATED IMPACT:

Increased number of clinical trials leveraging mobile technologies.

4 PROJECTS

- Novel Endpoints
- Mobile Technologies
- Stakeholder Perceptions
- Decentralized Clinical Trials

*Scope: FDA-regulated clinical trials after the time of initial research volunteer consent*
# The MCT Novel Endpoints Project Team

<table>
<thead>
<tr>
<th>Team Leaders</th>
<th>Team Members</th>
<th>Project Manager</th>
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<tr>
<td>Lauren Bataille (MJFF)</td>
<td>Ashish Naryan (Northwell)</td>
<td>Jen Goldsack (CTTI)</td>
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<td>Rob DiCicco (GSK)</td>
<td>Elektra Papodopoulous (FDA)</td>
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<td>Cheryl Grandinetti (FDA)</td>
<td>Theresa Strong (FPWR)</td>
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<td>Will Herrington (Oxford)</td>
<td>Komathi Stem (monARC Bionetworks)</td>
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<td>Martin Landray (Oxford)</td>
<td>Ken Skodacek (FDA)</td>
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<td>Kaveeta Vasisht (FDA)</td>
<td>Nirav 'Rav' Sheth (MC10)</td>
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Download the Recommendations & Resources

Visit https://www.ctti-clinicaltrials.org/projects/novel-endpoints to access and download the full suite of CTTI’s MCT Novel Endpoints Recommendations and Resources
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  - Include novel endpoints as exploratory endpoints in existing clinical trials and observational cohort studies
  - Critically position novel endpoints in interventional trials
Steps for Novel Endpoint Development

1. Identify an **aspect of health** affected by the disease that the patient cares about

2. Identify the **scope of assessment**: the aspect of an individual’s clinical, biological, physical, or functional state, or experience that the assessment is intended to capture

3. Select the **specific measurement** to report that is a good representation of the aspect of the patient’s medical status

4. Select **suitable mobile device** for data capture

5. Set or develop standards

6. Describe the study population for whom the endpoint will be targeted
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Are you developing a novel endpoint that is generated using data captured using a mobile device?

- YES
- NO
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Steps for Novel Endpoint Development

1. Determine measurement approaches
2. Evaluate the extent to which the measure reflects the intended scope of assessment
3. Ensure the absence of systematic measurement error
4. Demonstrate that the assessment is measuring what it claims to be measuring
5. Define meaningful change that can be interpreted as treatment benefit
6. Demonstrate that the measures is effective in detecting change
7. Develop a user manual that is appropriate for use with the intended study population
8. NOVEL ENDPOINT READY FOR USE
Steps for Novel Endpoint Development

1. Define meaningful change that can be interpreted as treatment benefit
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MCT Novel Endpoints Products

**Recommendations** for selecting, developing, and incorporating novel endpoints using mobile technologies for use in clinical trials

**Selection tool** to support decisions between viable novel endpoints for development

**Quick reference guide** to interacting with FDA regarding novel endpoint development
MCT Novel Endpoints Products

- **Flowchart** is supported by *detailed description* of novel endpoint development
  - Approaches to executing each step
  - Considerations at each step
  - Links to tangible examples demonstrating each step

- *Four use cases* providing tangible examples
  - Parkinson’s disease
  - Diabetes
  - Heart failure
  - Duchenne’s muscular dystrophy
Download the Recommendations & Resource

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Where is our Field Right Now?
How is CTTI Driving Adoption of its Work?

Rob DiCicco
TransCelerate BioPharma Inc.
How Should We Think about Mobile?

- Real World Evidence
- Registration Programs
- Patient Centricity
Multi-Stakeholder Collaboration is Needed

- Mobile devices are widely used in clinical research
- Utility in interventional trials to assess therapeutic benefit has been limited
- Consolidation of evidence supporting clinically meaningful specific outcomes
- Standardization of use
  - Data capture
  - Placement
# A Systematic Review: The Use of Mobile Technologies

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<th>Observational studies N=66 n(%)</th>
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<tr>
<td>Nutrition</td>
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<td>1(2)</td>
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Where Are We on the Journey?

2011 - Pfizer Launches 1st Virtual Trial

2015 - Apple Research Kit Launched
- NEJM (Redfield) publishes Heart Failure Study Using Accelerometry as Primary

2016 - mPower Results Published
- GSK Launches PARADE

2017 - CTTI Releases Novel Endpoints Recommendations
- Digital Biomarkers Journal

2018 - CTTI Releases Mobile Technologies Recommendations
Moving From What the Device Measures to Clinically Meaningful Endpoints

CTTI describes 4 use cases
- Heart failure
- Parkinson’s disease
- Duchenne’s Muscular Dystrophy
- Hypoglycemia

Digital Biomarkers Launched
- Pilot study in patients with PD and Huntington’s Disease
- Significantly more time spent lying down
- Differences in sleep patterns described
- Data collected passively and actively
- *Digit Biomark* 2017;1:52–63

https://www.karger.com/Article/FullText/479018
What Are We Learning?

- Value of Early Work
- Limitations of virtual
- Need for more sophisticated analytical methods
- How to develop an app
- How do we get the data from the device
- How do patients interact with their technology
The Way We Discover & Develop New Medicines is being Disrupted

Verily, Stanford and Duke kick off Project Baseline study to develop broad reference of human health

By Heather Mack | April 20, 2017

Alphabet-owned Verily has launched the Project Baseline Study, a collaborative effort with Stanford Medicine and Duke University School of Medicine to amass a large collection of broad phenotypic health data in hopes of developing a well-defined reference of human health.

Project Baseline aims to gather data from around 10,000 participants, each of whom will be followed for four years, and will use that data to develop a “baseline” map of human health as well as to gain insights about the transitions from health to disease. Data will come in a number of forms, including clinical, imaging, self-reported, behavioral, and that from sensors and biospecimen samples. The study’s data repository will be built on Google computing infrastructure and hosted on Google Cloud Platform.
How Can We Accelerate the Use of Mobile?

- Data sharing
  - MJF mobile tech advisory council, Vivli, TransCelerate?

- Use existing paradigms for tissue biomarkers and patient reported outcomes
  - Engage regulators (and other stakeholders) early

- Define your mobile strategy along with the development plan for a medicine
  - What are the goals?
    - Facilitate enrolment, develop value evidence, measure disease burden, proof of principle, product labeling
CTTI’s Commitment to Driving the Adoption of Technology-Derived Novel Endpoints in Clinical Trials

Jen Goldsack
Clinical Trials Transformation Initiative
Alzheimer’s Disease

- Affects >5 million Americans today
- Projected to affect >16 million Americans by 2050
- Alzheimer’s and other dementias cost $259 billion in the U.S. in 2017
- Projected to cost up to $1.1 trillion in 2050
- Symptomatic treatments offer little relief
- No disease modifying interventions
- “Gold standard” endpoint is ADAS-cog, first used in 1984
Parkinson’s Disease

- Affects ~1 million Americans today
- Projected to affect >3.8 million Americans by 2050
- Direct and indirect costs were $25 billion in the U.S. in 2017
- Projected to cost up to $86.9 billion in 2050
- No disease modifying interventions
- UPDRS first used in 1987
  - Modified 2007 MDS-UPDRS
- PDQ-39 first used in 1995
Duchenne Muscular Dystrophy
Benefits of Technology-Derived Endpoints

**PATIENT CENTRICITY**
- High-quality, patient-centric endpoints
- Endpoints that matter to patients
- Reduced participation burden
- Fewer barriers to participation
- Better, more complete info

**EFFICACY**
- Improved predictability rates
- Increase in # of potentially successful treatments

**EFFICIENCY**
- Generation of data needed by payers to make coverage determinations
- Prevention of delays in coverage, payment, & use decisions
- Prevention of delays in patient access to meds

Potential Benefits of Using Mobile Technology in Clinical Trials
CTTI Mobile Clinical Trials (MCT) Program

PURPOSE:
Develop evidence-based recommendations that affect the widespread adoption and use of mobile technology in clinical trials for regulatory submission

ANTICIPATED IMPACT:
Increased number of clinical trials leveraging mobile technologies

4 PROJECTS

- Novel Endpoints
- Mobile Technologies
- Stakeholder Perceptions
- Decentralized Clinical Trials

*Scope: FDA-regulated clinical trials after the time of initial research volunteer consent
CTTI MCT Mobile Technologies Project

- Mobile Technology Selection
- Data Collection, Analysis, & Interpretation
- FDA Submission & Inspection
- Participant Engagement
- Protocol Design & Execution
- Data Management

Existing scientific principles

Data quality standards

Participant engagement

REMAIN CRITICAL
CTTI MCT Decentralized Trials Project

Focus is decentralized trials conducted through telemedicine and mobile healthcare providers in the U.S.

Federal and local U.S. state laws, regulations, and considerations come into play.

The recommendations will target industry sponsors and CROs, addressing the following topics:

- Protocol Design
- Telemedicine State Licensing Issues
- Drug Supply Chain
- Mobile Practitioners
- Considerations for Investigator Delegation and Oversight
- Safety Monitoring
CTTI MCT Stakeholder Perceptions Project

*Project recommendations and resources will address…*

- Engaging patient and site perspectives for study planning
- Maximizing value and minimizing burden for study participants
- Addressing barriers for investigative sites
Creating a Comprehensive Toolkit

- Developing an integrated, program-level offering
  - A “one-stop shop” for mobile clinical trials
  - Coming in 2019!
Take Action

Download published recommendations and resources


Go to [www.ctti-clinicaltrials.org](http://www.ctti-clinicaltrials.org) to sign up to receive CTTI’s monthly e-newsletter for updates on the rolling release of future recommendations

- Decentralized Trials, September 2018
- Stakeholder Perceptions, January 2019
- Additional Program level offerings
- Related Driving Adoption Activities
THANK YOU.

Rob DiCicco dicicco.ra@gmail.com

Jen Goldsack jennifer.Goldsack@duke.edu

Will Herrington will.herrington@ndph.ox.ac.uk

www.ctti-clinicaltrials.org