Welcome to CTTI’s Trials in Clinical Practice Expert Meeting

- This meeting is being recorded for note taking purposes only.
- Masks are recommended if you are experiencing cold-like symptoms.
- Open discussion is encouraged and fostered by respect and collaboration.

Here’s to a great meeting... Your contributions will make this a productive one!
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<thead>
<tr>
<th>Time (EST)</th>
<th>Content</th>
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<tr>
<td>8:30 AM</td>
<td>Welcome Remarks and Introduction to CTTI</td>
<td>Sally Okun (CTTI)</td>
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<tr>
<td>8:40 AM</td>
<td>Opening Comments</td>
<td>Janet Woodcock (FDA)</td>
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</table>
| 9:00 AM   | Integrating Clinical Research and Practice: Perspectives from Groups Paving the Way | Adrian Hernandez (Duke)  
            |                                                                           | Martin Landray (University of Oxford)  
            |                                                                           | Mark McClellan (Duke Margolis)  
            |                                                                           | Neely Williams (Community Partners’ Linked Network) |
| 9:55 AM   | Trials in Clinical Practice Project Overview (Break to follow)          | Lindsay Kehoe (CTTI)                                                      |
| 10:30 PM  | Implementation Workshop: Break Out Groups (Lunch to follow)             | Matthew Roe (AstraZeneca) & Attendees                                     |
| 1:00 PM   | Workshop Debrief                                                        | Matthew Roe (AstraZeneca) & Attendees                                     |
| 1:35 PM   | Metrics Development: Break Out Groups                                  | Morgan Hanger (CTTI) & Attendees                                         |
| 2:25 PM   | Gaining Momentum: Open discussion                                       | Morgan Hanger (CTTI) & Attendees                                         |
| 3:25 PM   | Closing Comments and Adjourn                                            | Lindsay Kehoe (CTTI)                                                      |
Introduction to CTTI

Sally Okun, CTTI Executive Director
Multi-stakeholder, public-private partnership co-founded by Duke University & FDA

Participation of 500+ more orgs and + 80 member organizations

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials
Everyone must have an equal seat at the table

Patients as partners

Multi-Stakeholder

Investigators & Sites

Patients, Caregivers & Patient Advocacy Groups

Government & Regulators

Academia

Industry

Includes pharma, bio, device, CRO, health data/IT

IRBs

Trade & Professional Orgs
CTTI projects focus on streamlining and accelerating clinical trials, while ensuring the highest standards of quality and human subjects protection. We provide actionable, evidence-based, consensus-driven recommendations designed to:

- Accelerate study start-up times & streamline protocols
- Leverage new technologies to improve efficiency of clinical trials
- Enhance the quality of clinical trials without adding undue burden
- Identify streamlined strategies to meet regulatory requirements
TRANSFORMING TRIALS 2030

By 2030, clinical trials need to be:

- Patient-Centered & Easily Accessible
- Fully Integrated Into Health Processes
- Designed With A Quality Approach
- Maximally Leveraging All Available Data
- Improving Population Health

A critical part of the Evidence Generating System

https://ctti-clinicaltrials.org/who_we_are/strategic-vision/
Today’s Meeting Objectives

- Develop strategies for implementing at least 2 of CTTI’s new recommendations into the planning of trials, including trials intended for regulatory review.
- Identify 3 implementation barriers that trial designers and health systems have the power to mitigate.
- Brainstorm relevant metrics to monitor and evaluate implementation of the selected recommendations.
Janet Woodcock
Principal Deputy Commissioner,
U.S. Food & Drug Administration
Session I: Paving the Way

Adrian Hernandez  
DCRI

Mark McClellan  
Duke Margolis

Martin Landray  
University of Oxford

Neely Williams  
Community Partners’ Linked Network

Moderator: Lindsay Kehoe, CTTI, Project Manager
RWD into RWA(action): @home @ clinic

Adrian F. Hernandez, MD
Executive Director, Duke Clinical Research Institute
Going from Pre-Covid to Post COVID Clinical Trial Visits

Pre-COVID-19:
Site based visits & care

Possibilities:
Home based visits & care

Key clinical questions

How to help someone *feel better faster* with newly diagnosed mild-moderate COVID-19?

How to *prevent hospitalizations or death* in someone with newly diagnosed mild-moderate COVID-19?
What is ACTIV-6?

ACTIV-6 is part of the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership, which was created to speed the development of effective treatments and vaccines for COVID-19.

How do we share what we are learning?

Visit activ6study.org for study results and the latest news.

What are we trying to find out together?

How can we help people with COVID-19 feel better faster? How can we prevent people with COVID-19 from going to the hospital?
What makes ACTIV-6 different?

ACTIV-6 is testing several medications that are approved to treat conditions other than COVID-19 and can be found at your local pharmacy. This provides options to participants and helps generate results faster.

Participate from home — study medication is mailed directly to participants who can sign up and complete surveys online or over the phone.
How does the study work?

- **Learn** about ACTIV-6 online, on the radio, or from health systems, pharmacies, testing centers, or community partners.
- **Test** positive for COVID-19.
- **Enroll** online or over the phone. [activ6study.org](http://activ6study.org)
- **Receive** assigned study medication and directions at home. **Take** the study medication as directed.
- **Complete** surveys about how you feel online or over the phone.
ACTIV-6 Hybrid Approach: Click & Mortar

N = Tens of thousands

- ACTIV-6 eligible
- Health Systems
- @Home

Click & Mortar

Site Follow-up (as needed)

- Direct to Participant Portal
  - Daily Symptoms
  - Patient-reported hospitalizations
  - Medication use
  - Health outcomes

- DCRI call center
  - Patients who miss 2 contacts
  - Patients without internet access
  - Validated coding algorithms for endpoints

Baseline data
ACTIV-6 Hybrid Approach: Engagement

N = Tens of thousands

ACTIV-6 eligible

Health Systems

Enrollment & patient preferences

@Home

Click & Mortar

Site Follow-up (as needed)

Direct to Participant Portal

• Daily Symptoms
• Patient-reported hospitalizations
• Medication use
• Health outcomes

DCRI call center

• Patients who miss 2 contacts
• Patients without internet access
• Validated coding algorithms for endpoints

Baseline data

N = 15,000
ACTIV-6 Hybrid Approach: Recruitment

N = Tens of thousands

ACTIV-6 eligible

Health Systems

@Home

Enrollment & patient preferences

Baseline data & Randomization

Click & Mortar

ACTIV-6
ACTIV-6 Hybrid Approach: Follow-up

N = Tens of thousands

ACTIV-6 eligible

Health Systems

@Home

Enrollment & patient preferences

Baseline data & Randomization

Direct to Participant Portal

- Daily Symptoms
- Patient-reported hospitalizations
- Medication use
- Health outcomes

DCRI call center

- Patients who miss 2 contacts
- Patients without internet access
- Validated coding algorithms for endpoints

Site Follow-up (as needed)

N = 15,000

Click & Mortar

N = 15,000
Who is participating?

- All 50 US States
- 93 sites
- 5141 randomized
- 4 Arms Completed
- 1 Arm Ongoing
  (Fluvoxamine 100mg)
- 1 Arm in prep
Turning Real World Data into Action

From Evidence Generation to Implementation
Our Focus: Creating better value from research to care

Establish a health system Alliance with engaged clinicians, data scientists, healthcare leaders to develop new care-pathways and real-world data to action platform …

- Cardiovascular disease
- Renal disease
- Metabolic disease

And in so doing, position the consortium to:

- Establish a reusable real-world data platform to rapidly answer clinical questions
- Shorten implementation of evidence into practice
- Generate real-world evidence to inform stakeholders
- Establish an alliance to address value of care through policy
Key Health System Requirements

- Vision to shift from *reactive* to *proactive* care
- Engaged leadership
- Clinical champions
- Ability to leverage healthcare data into action
  - Population health
  - Implementation science
  - Embedded clinical trials
- An integrated clinical, research, operational, and technical team
  - Clinical, clinical-investigator, data scientists, informatics, healthcare operations, healthcare leadership
The Alliance

Founding members
- Amgen
- Bayer
- Novartis
- SomaLogic
- TBA
- TBA

Future members
- Allina
- Duke
- Intermountain
- Ochsner
- Stanford
- UPMC
- Vanderbilt
- TBA
- TBA

Map showing locations of member institutions.
Changing the Map of ASCVD

What’s the problem?
REVEAL: EHR based population study characterizing gaps

What’s the solution?
CHAMPIONS: A cluster randomized of multi-disciplinary teams with augmented pophealth tools

Total Cardiovascular Death 2018-2020
https://nccd.cdc.gov/DHDSPAtlas/
Conclusions:

- Moving RWData to RWEvidence to RWAction is possible
  - Meeting people where they are
  - Getting closer to home and clinic and back
  - Filling in clinical trial deserts
  - Addressing major public health questions
  - Accelerating trustworthy, high-quality evidence

- But need to ensure it fits the purpose!
Building on the RECOVERY trial experience

Sir Martin Landray
Professor of Medicine & Epidemiology, Oxford University
Chief Executive, Protas
Need for reliable evidence from randomized trials

- Essential for making appropriate decisions concerning the benefits and harms associated with clinical interventions.

- Decisions made in the absence of reliable evidence (either because relevant trials have never been performed or because those that have been performed were inadequately designed, conducted, analyzed, or reported) may harm individual patients and public health.
Re-inventing Randomized Controlled Trials

Smart design & delivery

PLUS

Integrated with routine healthcare & data systems

SUPPORTED BY

Proportionate trial regulations & guidance

FOR THE BENEFIT OF

Better patient care and public health
RECOVERY trial

Timeline
- Rapid initiation: 9 days from protocol to first participant
- Rapid recruitment: 100 days from protocol to first results
- Rapid impact: 4 hours from first results to policy implementation

Population:
- 48,000 participants at 200 hospitals
- Age <1 to >100 years
- 18% non-White; 40% female

16 treatments evaluated
- 4 life-saving treatments
- 7 ineffective or harmful treatments
- 4 ongoing
Lessons from RECOVERY

- Arbitrary use of unproven treatments is damaging to patient care & public health
- Randomized trials are a critical component of high quality clinical care
- Compelling results change practice

But trials must be:

- Focused to answer a question that matters
- Designed to deliver actionable results
- Inclusive of relevant patient groups
- Feasible for patients and clinical staff
- Optimised to build on the existing strengths of their setting
Lessons for the future

Requires:

- Health systems to recognise & embrace their role in finding solutions
- Ongoing education & communication with professional & lay audiences
- Smart use of technology (relevant, reliable, inter-connected, usable)
Lessons for the future

Requires:

- Health systems to recognise & embrace their role in finding solutions
- Ongoing education & communication with professional & lay audiences
- Smart use of technology (relevant, reliable, inter-connected, usable)
- Substantial transformation of clinical trial regulation & guidance
  
  (both what is written & manner with which it is applied)

  to focus on the fundamental principles of Good Randomized Clinical Trials
Protas
a not-for-profit organisation
Smarter trials for better health
Our approach

- **Smart design – efficient delivery**
  - focus on delivering compelling answers to key questions

- **Methodological innovation**
  - timely integration of routine healthcare data for planning, recruitment, and follow-up
  - software engineering to drive clinical, scientific & operational quality & efficiency
  - central & statistical approaches to performance monitoring

- **Collaboration & partnership**
  - patients, clinicians, healthcare system
  - pharma, device & medtech

- **Shaping policy & advocacy**
  - regulatory/GCP, privacy, funding, training, publishing
Good Clinical Trials Collaborative

Supported by:
Wellcome Trust
Bill & Melinda Gates Foundation

The GCTC was set up to develop guidance to promote and enable good Randomised Controlled Trials

The guidance has been developed with the involvement of hundreds of individuals & organizations with an interest in Good Clinical Trials

www.goodtrials.org
What does good guidance look like?

Good science & ethics
Focused on issues that materially influence the well-being of trial participants & reliability of the results

Clear and concise
Promotes critical thinking and application through accessibility and decision-making support.

Inclusively developed
Co-developed with regulators, funders, commercial & academic trialists, clinicians, patients & public.

Progressive & durable
Forward looking and applicable across disease areas, intervention types, development phases, trial designs, geographies & time

www.goodtrials.org
Produce a scientifically sound answer to a relevant question

Good Randomized Controlled Trials

Manage quality effectively & efficiently
Respect the rights & well-being

Designed to be feasible for their context
Be collaborative & transparent
Transform the approach to clinical trial regulation, shortening the time to authorise trials and streamlining the requirements and guidelines relating to trial conduct.

We should refocus regulatory guidelines on the fundamental scientific and ethical principles that underpin randomised trials, whilst embracing flexibility and innovation across a range of health threats and technologies...

The Good Clinical Practice for clinical trials guidance should be revised to focus on what matters for the generation of actionable information about effects of an intervention, rather than what is easy to check but less relevant, placing an emphasis on principles and purpose rather than process.

https://www.g7uk.org/g7-discuss-100-days-mission-to-improve-readiness-for-future-pandemics/
ICH E6 Principles

(Draft Version: March 2021)

Clinical trials are a fundamental part of clinical research that support the development of new medicines or uses of existing medicines. Well designed and conducted clinical trials help answer key questions in health care and drug development. Their results are essential for evidence-based healthcare decisions. Trials with inadequate design and/or poorly conducted trials may place participant safety at risk and yield inadequate or unreliable evidence. They waste resources and the efforts and time of investigators and participants.

The principles of GCP are designed to be flexible and applicable to a broad range of clinical trials. This guideline, along with ICH E8, encourages thoughtful consideration and planning to address specific and potentially unique aspects of an individual clinical trial. This includes evaluation of trial characteristics, such as the design elements, the investigational product being evaluated, the medical condition being addressed, characteristics of the participants, the setting in which the clinical trial is being conducted, and the type of data being collected. Careful consideration of factors relevant to ensuring trial quality is needed for each clinical trial.
For more information

- RECOVERY trial: [www.recoverytrial.net](http://www.recoverytrial.net)
- Protas: [www.protas.co.uk](http://www.protas.co.uk)
- Good Clinical Trials Collaborative: [www.goodtrials.org](http://www.goodtrials.org)

- Prof Sir Martin Landray
  - BBC Life Scientific podcast
  - Twitter
  - LinkedIn
Advancing Clinical Trials at the Point of Care Coalition

Mark McClellan, MD, PhD
Director, Duke-Margolis Center for Health Policy
Disclaimer

The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

The presenter is an Employee of Duke University. Duke-Margolis receives funding from cooperative agreements with the Food and Drug Administration

Independent director on the boards of Johnson & Johnson, Cigna, Alignment Healthcare, and PrognomIQ; Co-chair the Executive Forum of the Health Care Payment Learning and Action Network; advisor for Arsenal Capital Partners, Blackstone Life Sciences, and MITRE.
COVID-19 Experience: Big Gaps and High Costs for Developing Actionable Evidence

- Only 5% of COVID-19 trial arms have yielded actionable evidence
- Existing trial infrastructure not equipped to flex with local surges in COVID-19 cases
- COVID-19 therapeutic trials enrolled <1% of hospitalized patients
- Only 26% of patients who were enrolled in COVID-19 trials were enrolled in randomized, adequately powered trials
- Similar major gaps in evidence development exist for many other high-burden health conditions

https://www.nature.com/articles/d41573-021-00037-3
COVID-19 highlighted shortfalls in our clinical trial infrastructure

More health care systems in the US and globally are taking steps (and facing new accountability) for improving population health outcomes

There is an increasing need and opportunities for clinical trial transformation to support the generation of more practically relevant evidence

The Advancing Clinical Trials at the Point of Care (ACT@POC) Coalition is building new platforms to bridge the infrastructure gaps and better link clinical research to routine care by engaging

- Health system leadership
- Frontline clinicians
ACT@POC Coalition Members

- Duke-Margolis Center for Health Policy
- MITRE
- Mayo Clinic
- Ascension Health
- CVS Health
- Duke University Health System
- Intermountain Healthcare
- University of California, Irvine
- UMass Memorial Health
- Vanderbilt University Medical Center
- The Broad Institute

- CURE Drug Repurposing Collaboratory (C-Path + NCATS + FDA)
- Emory-Morningside Center for Innovative and Affordable Medicine
- Medable

Collaborating Organizations:
- Clinical Trials Transformation Initiative
- Ochsner Health
- University of Pittsburgh Medical Medical Center
ACT@POC Activities: Platform pilots

- Working with ACT@POC health systems to develop detailed trial POC platform protocol for initial research question(s)
  - Focusing primarily on chronic conditions with the potential for innovation in delivering frontline longitudinal care to diverse patient populations
  - Targeting research questions that matter to health care systems while also generating regulatory-grade evidence

- Pilot platform implementation will inform readiness assessment tool and contracting pathway for additional potential trial participants for implementation in ACT@POC networks beyond initial pilot efforts
ACT@POC Activities: Policy Reform

- Identification of policy issues that if addressed could increase participation and reduce cost of trials, alongside assessment of costs of such design reforms – as basis for engagement with regulatory agencies, payers, and other stakeholders

  - **Regulatory policy**
    - 1572 reform, GCP reform, minor adverse event and concomitant treatment reporting, and other issues where substantial frontline burden reduction is possible without compromising value of evidence

  - **Payer policy**
    - Leveraging quality improvement initiatives and opportunities for treatment cost coverage for studies of high relevance for CMS and other payers

  - **Health system policy**
    - Organization culture
    - Administrative and patient contact policy barriers
ACT@POC Activities:
Digital tool development

- Identify priority list of key areas for further digital tool development to support point of care trials
- Develop a point-of-care trial “digital toolbox”: providing trial sites and investigators with access to high-quality digital tools and resources to support point-of-care trial participation across multiple sites, platforms, and networks
For more information contact trevan.locke@duke.edu or visit actpoc.org
PCORnet® Coordinating Center

Engagement Core

Neely Williams
Community Partners’ Linked Network
Patient-Centered Outcome Research (PCOR)

- Focus on questions and outcomes that are important to patients and caregivers
- Patients have unique perspectives that can change and improve clinical questions

Patient-Centered Outcome Research Hypothesis:

- Stakeholder perspective and input
- Enhancement of relevant research for health decisions
- Increased likelihood that patients will achieve the health care desired
Aims to advance the shift from investigator-driven to patient-centered studies

Unites researchers, patients, clinicians and healthcare systems to create a nationwide data infrastructure to conduct patient-centered health research more efficiently
Patients are at the center of all PCORnet-enabled research

“Good studies consider all relevant evidence – and no evidence is more relevant than the patient experience.” – PCORnet Steering Committee Member

From the Researcher Perspective

• Patients offer important context, directly informing understanding of a condition, its effects, and the burden of illness
• Patients can identify processes or procedures that research participants may find too burdensome, allowing researchers to amend and potentially boost study enrollment
• Patients ensure endpoints are meaningful, helping researchers deliver results that will improve the patient experience
• Patients can mobilize patient groups for participation in clinical trials
• Patients are essential partners in helping to disseminate results in a way that is clear to diverse communities

From the Patient Perspective

• Partnering in research empowers patients and caregivers to set the research agenda, advocating for prioritization of questions that matter to their community
• Patient partners can influence meaningful changes to study designs, giving these projects the best chance of success
• Patient partners report positive experiences in participating in and contributing to research that leads to improved clinical answers
• Patients drive adoption of actionable findings and meaningful changes in clinical care
Patient Engagement in Research

Steps in Research Process

| Topic solicitation | Identify topics that are important to patients, caregivers, and the community
| | Propose topics to be investigated
| Prioritization | Solicit feedback on relevance and priority of topics
| | Discuss the urgency of addressing topics
| Framing the question | Ascertain questions’ relevance and usefulness
| | Assess “real-world” applicability
| Selection of comparators and outcomes | Identify comparator treatments of interest
| | Identify outcomes of interest
| | Incorporate other aspects of treatment
| Creation of conceptual framework | Provide a “reality check”
| | Verify logic of conceptual framework
| | Supplement with additional factors not documented in the literature
| Analysis plan | Verify importance of factors and variables
| | Ascertain whether there is a good proxy for a specific concept
| | Inquire about potential confounding factors
| Data collection | Determine best approaches for data collection (eg, trial, registry, medical charts)
| | Assist with selection of data sources
| Reviewing and interpreting results | Assess believability of results
| | Suggest alternative explanations or approaches
| | Provide input for sensitivity analysis
| Translation | Interpret results to be meaningful
| | Document which results are easy or difficult to understand
| | Indicate which results are counterintuitive
| Dissemination | Facilitate engagement of other patients
| | Help other patients to understand findings

Stakeholder Role

Continuous Patient Engagement, Mullins 2012
PCORnet Engagement Core Priorities

1. Build capacity to support engagement of patient stakeholders across the network.

2. Support patient stakeholder participation in PCORnet governance and leadership.

3. Consult with research teams on patient engagement.

4. Strengthen PCORnet’s policies and practices around patient engagement.
Challenges/Opportunities

- Preparing researchers for patient engagement
- Adequate funding to support engagement
- Disseminating research results to non-academic stakeholders
- Engaging diverse patient stakeholders
- Engaging clinicians
- Evaluating engagement
How can PCORnet help researchers?

PCORnet-enabled studies are answering critical research questions. What questions can PCORnet help answer for you?

While PCORnet is fit for a broad range of research types, research conducted using the Network’s resources has been focused on studies like:

- Real-world evidence studies
- Health systems research
- Population health research
- Pragmatic clinical trials
- Studies on how to best engage patients in research
PCORnet Resources

Resources developed within the PCORnet network are available to everyone through the PCORnet Resources page on PCORnet.org

Resources are sorted by Research, Data, and Engagement and are keyword searchable or can be filtered.

Examples include common data model code; a lay audience data glossary; press release templates; and engagement case studies.

Resources

Explore our resources for improving research through better practices

Research

Explore innovative tools and models that can be used throughout every stage of your research project - from generation of a hypothesis to disseminating results.

SEARCH RESEARCH

Data

Improve the quantity and quality of data used in your study with innovative resources and tools. Data resources should follow the principles of efficiency, interoperability, transparency, accessibility, security, and minimal use of stakeholders.

SEARCH DATA

Engagement

Search best practices for engaging a variety of stakeholders throughout the research process. Engagement means active involvement of all stakeholders.

SEARCH ENGAGEMENT

Search All Resources

Enter any keyword or phrase in the Search box, or use the drop-down options to narrow your search by category, network partner, resource type, and/or audience. Click Reset to view all resources in an unfiltered view.

Click Reset to view all resources in an unfiltered view.
THANK YOU

Work with PCORnet.

Visit us at www.pcornet.org to get the relationship started.
Q & A
Embedding Trials into Clinical Practice

Recommendations & Supporting Resources

Lindsay Kehoe, CTTI, Senior Project Manager
Paving the Way for Embedded Trials

- National Academy of Medicine, FDA RWE Framework, NIH Collaboratory, PCORI, Veteran’s Affairs, AHRQ...

- Existing CTTI work

**Quality by Design**
Recs that help focus resources on the errors that matter

**Registry Trials**
Recs for assessing & designing registries to meet FDA review expectations

**Sentinel**
1st randomized trial using FDA-Catalyst System, IMPACT-Afib

**RWD**
Recs for using RWD to evaluate trial eligibility criteria & enhance recruitment
# The Case for Embedding Clinical Trials into Practice

<table>
<thead>
<tr>
<th>Patients</th>
<th>Providers</th>
<th>Sponsors &amp; Investigators</th>
<th>Regulators</th>
<th>Payers</th>
<th>Health System Leaders</th>
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<tbody>
<tr>
<td>Research and care are better aligned</td>
<td>Potential to engage in research with minimal burden</td>
<td>Generalizable research populations and evidence</td>
<td>Sufficiently sized trials with diverse populations</td>
<td>More, diverse data for reimbursement decisions</td>
<td>A means to innovate and support quality care</td>
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<td>Less burden to participate in research</td>
<td></td>
<td>Insights into real-world implementation of interventions</td>
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<td>Greater trial diversity and inclusivity</td>
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<td>Potential for increased efficiency &amp; cost savings by reducing duplication of trial &amp; care activities</td>
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<tr>
<td>Uses health care data for research to represent more real life experiences</td>
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<td>Generalizable evidence</td>
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- Potential to engage in research with minimal burden
- Addresses clinically meaningful questions to improve care in a broad population
- Treatment optionality for patients
- ...
Embedded clinical trials have:

- Elements integrated into health care delivery
- Accessibility to patients at the point of care
- Close alignment with clinical workflows
- Ability to use clinical care data sources for research purposes

Ultimately, what is the trial purpose? What is the question to be answered?
Embedding Trials into Clinical Practice

Project Overview

**Purpose:** Facilitate the integration of clinical trials intended for, but not limited to, medical product review into clinical practice

**Focused on:**
- the operations of embedding elements of trials into clinical practice
- randomized trials with U.S. sites, global trials included

**Objectives:**
- Identify the barriers and potential solutions to incorporating interventional trials into clinical practice
- Identify when integration of clinical trial elements into clinical settings would be feasible and the associated benefits and risks
- Describe the operational approaches to incorporating interventional trials into clinical practice

CTTI Recommendations
# CTTI Recommendations

<table>
<thead>
<tr>
<th><strong>Trial Design/Methodology</strong></th>
<th><strong>Operational</strong></th>
<th><strong>Health Care &amp; Research Culture</strong></th>
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<tr>
<td>1. Recognize that embedding a trial into clinical practice is not all or nothing</td>
<td>5. Ensure site readiness to embed trial elements</td>
<td>8. Recognize and invest in research activities</td>
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<td>2. Assess whether clinical trial elements should be embedded into clinical practice</td>
<td>6. Minimize participation burden for patients, providers, and research staff</td>
<td>9. Promote the basis for and ways to embed trial elements into clinical practice</td>
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<tr>
<td>3. Verify that data sources are fit for purpose – relevant and reliable</td>
<td>7. Validate the quality of the clinical data for research purposes</td>
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<tr>
<td>4. Streamline trial design to align with clinical workflows</td>
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Recommendations 1-7 are particularly relevant for: sponsors, clinicians interested in conducting research, CROs, funders, health care settings, technology providers, patients/caregivers/patient advocacy groups, payers, and regulatory bodies.

Recommendations 8 & 9 are particularly relevant for: health care system leaders, regulatory bodies, funders, patient advocacy groups, and policy makers.
Trial Design/Methodology Recommendations

1. Recognize that embedding a trial into clinical practice is not all or nothing

2. Assess whether clinical trial elements should be embedded into clinical practice

3. Verify that data sources are fit for purpose – relevant and reliable

4. Streamline trial design to align with clinical workflows

Key Points

- Components or elements of a trial can be embedded into clinical practice and benefits can be gained regardless of the # of elements integrated.
- Aim to lessen duplicate efforts already occurring in care.
- Determine which trial activities and data are essential and whether they align with clinical workflows.
- Validate the reliability of the clinical data through manual and automated data checks.
- Consult early and often with regulatory authorities on data quality questions.
- Develop processes conducive for future trials.
Operational Recommendations

5. Ensure site readiness to embed trial elements

6. Minimize participation burden for patients, providers, and research staff

7. Validate the quality of the clinical data for research purposes

**Key Points**

- **Assess** 1) resources and degree of training settings will require, 2) that GCP requirements for clinical staff participating are not compromised, and 3) sites current connections with the local community- help support efforts to engage community clinicians

- **Communicate** across health systems to determine how technology solutions can facilitate changes that meet both research and clinical needs

- **Train** clinical staff to be ready to complete research-related tasks

- **Provide** support staff so that HCPs feel assisted and not overwhelmed

- **Automate**: 1) what can be done before or during clinical care encounters, 2) quality assurance checks of clinical data (compare to a manual check)
8. Recognize and invest in research activities

9. Promote the basis for and ways to embed trial elements into clinical practice

**Health Care System Leadership can:**

- **Prioritize** research participation
- **Collaborate** to build stronger digital and financial infrastructures
- **Encourage** standardization
- **Develop** communication plans with sponsors

**Government and Policy Forums can:**

- **Promote** the rationale for embedded trials as a means to improve evidence generation
- **Encourage** regulatory, reimbursement, and policy changes
- **Develop** standards and acknowledge international opportunities to align
- **Support** the sharing of learnings
- **Recognize** that there is shared accountability across organizations to make the required changes

Leadership partnerships are needed across health care systems and the clinical trial enterprise (CTE) to embed trials.
Supporting Resources

- Five Case Examples that reflect, at an individual study level, embedding trial elements into care is possible.
- Coming soon- New Tool Embedding Trial Elements into Clinical Practice: Critical to Quality Considerations

<table>
<thead>
<tr>
<th>Trial</th>
<th>Includes U.S. sites?</th>
<th>Regulatory review of a medical product?</th>
<th>Type of Medical Product</th>
<th>Investigational Medical Product included?</th>
<th>Embedded Trial Elements</th>
<th>Health Care Data Source(s)</th>
<th># of Patients As of April 2022</th>
<th># of Sites As of April 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECOVERY</td>
<td>No</td>
<td>Yes</td>
<td>Drug, Biologic</td>
<td>Yes</td>
<td>Eligibility, Intervention, Data acquisition, Evidence Integration</td>
<td>National health care datasets</td>
<td>47,465</td>
<td>~200</td>
</tr>
<tr>
<td>I-SPY</td>
<td>Yes</td>
<td>Yes</td>
<td>Drug, Device, Biologic</td>
<td>Yes</td>
<td>Eligibility, Intervention, Data acquisition, Evidence Integration</td>
<td>EHR</td>
<td>2,000</td>
<td>30</td>
</tr>
<tr>
<td>VA Diuretic Comparison Project</td>
<td>Yes</td>
<td>No</td>
<td>Drug</td>
<td>No</td>
<td>Eligibility, Intervention, Data acquisition</td>
<td>National VA EHR, Medicare, NDI</td>
<td>13,523</td>
<td>72</td>
</tr>
<tr>
<td>TASTE (completed)</td>
<td>No</td>
<td>No</td>
<td>Device</td>
<td>No</td>
<td>Eligibility, Randomization, Intervention, Data acquisition</td>
<td>National registry database</td>
<td>7,244</td>
<td>29</td>
</tr>
<tr>
<td>REMAP-CAP</td>
<td>Yes</td>
<td>Yes</td>
<td>Drug, Biologic</td>
<td>Yes</td>
<td>Eligibility, Randomization, Intervention, Data acquisition, Evidence Integration</td>
<td>EHR</td>
<td>11,131</td>
<td>359</td>
</tr>
</tbody>
</table>
Next Steps: Dissemination & Implementation

**October 2022**

**Expert Meeting Summary**
- Key themes from meeting will be posted on CTTI Website in early October

**November 2022**

**New Tool**
- Embedding Trial Elements into Clinical Practice: Critical to Quality Considerations
- A framework to help assess which elements to embed into clinical practice during the design of a study
- To be informed by and developed after Expert Meeting

**December 2022**

**Manuscript**
- Summarizing in-depth interviews and recommendations
- Aiming for Publications Advisory Committee review December 2022
THANK YOU

Special shout out to the project team & team leads
BREAK

Return to Grand Ballroom at 10:30 am
Session II: Implementation Workshop

Matthew Roe, VP Head of Early Clinical Development for Cardiovascular, Renal, and Metabolic (CVRM), AstraZeneca, CTTI Team Lead
Welcome Back!

Session II Objectives

- Develop strategies for implementing at least 2 of CTTI’s new recommendations into the planning of trials intended for regulatory review
- Identify 3 implementation barriers that trial designers and health systems have the power to mitigate

Approach: Break Out Groups

- Discuss feasibility, pain points, and how CTTI recommendations can help to embed trial elements into different case scenarios
Break Out Group Overview

- **4 Break Out Groups** designated by colored dots on back of your name tag:
  - Group 1 = red
  - Group 2 = yellow
  - Group 3 = green
  - Group 4 = blue

- Grand Ballroom with Karen
- Grand Ballroom with Lindsay
- Freedom Room 1 with Sara
- Freedom Room 2 with Morgan

- Duration = 90 minutes (10:30am - 12:00pm) then break for Lunch
- Debrief (25 mins) post Lunch
# Break Out Group Questions

**Individual Exercise (11:00-11:30)**

For your trial scenario:

<table>
<thead>
<tr>
<th>Question</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>What elements of your trial are embedded into clinical practice and how feasible are they to embed?</td>
<td>On <strong>red</strong> post-it, assign a number and stick it on the element</td>
</tr>
<tr>
<td></td>
<td>• 1 not likely</td>
</tr>
<tr>
<td></td>
<td>• 3 likely</td>
</tr>
<tr>
<td></td>
<td>• 5 very likely</td>
</tr>
<tr>
<td>What are 2-3 pain points with embedding these elements?</td>
<td>On a <strong>blue</strong> post-it, write a pain point and stick it on the element</td>
</tr>
<tr>
<td>Which CTTI recommendation(s) help with embedding the trial elements?</td>
<td>On a <strong>green</strong> post-it, write the CTTI recommendation # and stick it on the element</td>
</tr>
</tbody>
</table>
## Break Out Group Questions

### Entire Group Exercise (11:30-12:00)

For your trial scenario:

<table>
<thead>
<tr>
<th>How do we overcome the pain points noted?</th>
<th>Who is responsible?</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Of the CTTI recommendations that help with embedding trials elements:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Why is the recommendation(s) helpful?</td>
<td></td>
</tr>
<tr>
<td>• How would you use the recommendation in planning a trial?</td>
<td></td>
</tr>
</tbody>
</table>

| Is there anything in your scenario that you’d change to make integrating elements of your trial more feasible? | Explain |

*Plan 5-10 mins at the end to identify themes, add to if needed, and prepare read out*
LUNCH

Return to Grand Ballroom at 1:00 pm ET
Session II Break Out Debrief

Recap

- Unique vs common pain points across the 4 scenarios
- Potential mitigation approaches and who is responsible

How can CTTI help?
Session III: Metrics of Implementation

Morgan Hanger, Director of Strategic Programs, CTTI
Breakouts = 35 minutes (1:35-2:10) then break

- 4 Break Out Groups designated by colored dots on back of your name tag:
  - Group 1 = red       Grand Ballroom with Karen       (Design & Ops)
  - Group 2 = yellow    Grand Ballroom with Lindsay     (Culture)
  - Group 3 = green     Freedom Room 1 with Sara         (Design & Ops)
  - Group 4 = blue      Freedom Room 2 with Morgan       (Culture)

Break = 15 minutes (2:10-2:25)

Discussion = 60 minutes (2:25-3:35)
Looking at CTTI’s Role in Adoption

CTTI & Clinical Trial Enterprise

CTTI Staff & Members

Clinical Trial Enterprise (including CTTI Members)
CTTI’s Evolving Role in Measurement

We are interested in assessment at the organizational scale:

- How does an individual adopter of CTTI recommendations assess their progress?

We also care about the full CTE:

- How can we quantify the uptake in embedding across the entire clinical trial enterprise?
- How will we know if adoption of TCP is improving the quality and/or efficiency of trials?
## Breakouts: How Can We Measure Progress in TCP?

<table>
<thead>
<tr>
<th>Design</th>
<th>Adopter</th>
<th>Enterprise</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Operational</strong></td>
<td>How can we know whether change is happening at the organization level?</td>
<td>How can we quantify the way that change is happening across the entire trial enterprise?</td>
<td>How will we know if change is improving the quality and/or efficiency of clinical trials?</td>
</tr>
<tr>
<td><strong>Cultural</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Trial Design/Methodology Recommendations

1. Recognize that embedding a trial into clinical practice is not all or nothing
2. Assess whether clinical trial elements should be embedded into clinical practice
3. Verify that data sources are fit for purpose – relevant and reliable
4. Streamline trial design to align with clinical workflows

Key Points

- Components or elements of a trial can be embedded into clinical practice and benefits can be gained regardless of the # of elements integrated.
- Aim to lessen duplicate efforts already occurring in care.
- Determine which trial activities and data are essential and whether they align with clinical workflows.
- Validate the reliability of the clinical data through manual and automated data checks.
- Consult early and often with regulatory authorities on data quality questions.
- Develop processes conducive for future trials.
Operational Recommendations

5. Ensure site readiness to embed trial elements

6. Minimize participation burden for patients, providers, and research staff

7. Validate the quality of the clinical data for research purposes

Key Points

- **Assess** 1) resources and degree of training settings will require, 2) that GCP requirements for clinical staff participating are not compromised, and 3) sites current connections with the local community- help support efforts to engage community clinicians

- **Communicate** across health systems to determine how technology solutions can facilitate changes that meet both research and clinical needs

- **Train** clinical staff to be ready to complete research-related tasks

- **Provide** support staff so that HCPs feel assisted and not overwhelmed

- **Automate**: 1) what can be done before or during clinical care encounters, 2) quality assurance checks of clinical data (compare to a manual check)
## How Can We Observe Change?

<table>
<thead>
<tr>
<th>Adopter</th>
<th>Enterprise</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Design and Operational (Groups 1, 4)</td>
<td>• % of trials that have any embedded elements</td>
<td>• % of healthcare systems (EHR, pharmacy, nurse, etc.) that have technology and people solutions that account for research needs</td>
</tr>
</tbody>
</table>
8. Recognize and invest in research activities

9. Promote the basis for and ways to embed trial elements into clinical practice

**Health Care System Leadership can:**

- **Prioritize** research participation
- **Collaborate** to build stronger digital and financial infrastructures
- **Encourage** standardization
- **Develop** communication plans with sponsors

**Government and Policy Forums can:**

- **Promote** the rationale for embedded trials as a means to improve evidence generation
- **Encourage** regulatory, reimbursement, and policy changes
- **Develop** standards and acknowledge international opportunities to align
- **Support** the sharing of learnings
- **Recognize** that there is shared accountability across organizations to make the required changes

Leadership partnerships are needed across health care systems and the clinical trial enterprise (CTE) to embed trials.
## How Can We Observe Change?

<table>
<thead>
<tr>
<th>Healthcare and Research Culture (Group 3)</th>
<th>Adopter</th>
<th>Enterprise</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% of HC staff that view clinical trials as part of their job</td>
<td>The proportion of the healthcare enterprise that is involved in running trials as a recognized, measured part of their work</td>
<td>Clinical trial findings are integrated into practice more quickly</td>
</tr>
</tbody>
</table>
## Inspiration for Outcome Measures

<table>
<thead>
<tr>
<th>Patients</th>
<th>Providers</th>
<th>Sponsors &amp; Investigators</th>
<th>Regulators</th>
<th>Payers</th>
<th>Health System Leaders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and care are better aligned</td>
<td>Potential to engage in research with minimal burden</td>
<td>Generalizable research populations and evidence</td>
<td>Sufficiently sized trials with diverse populations</td>
<td>More, diverse data for reimbursement decisions</td>
<td>A means to innovate and support quality care</td>
</tr>
<tr>
<td>Less burden to participate in research</td>
<td>Addresses clinically meaningful questions to improve care in a broad population</td>
<td>Insights into real-world implementation of interventions</td>
<td>Leverages power of randomization &amp; RWD in the context of regulatory decision-making</td>
<td>Better understanding of the effectiveness and safety of medical product interventions</td>
<td></td>
</tr>
<tr>
<td>Greater trial diversity and inclusivity</td>
<td>Treatment optionality for patients</td>
<td>Potential for increased efficiency &amp; cost savings by reducing duplication of trial &amp; care activities</td>
<td>Generalizable evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uses health care data for research to represent more real life experiences</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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CTTI
Gaining Momentum Questions

- What are the measure concepts that the break out groups identified?
- Beyond our recommendations, dissemination, and measurement efforts, how else can CTTI drive momentum for embedding trials into practice?
- Outside of CTTI, what are some other levers for change across the CTE?
- Who is responsible for those additional levers?
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“Without deviation from the norm, progress is not possible.”
– Frank Zappa

THANK YOU

www.ctti-clinicaltrials.org