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!

Agenda

Time (EST)	Content	Presenter
8:30 AM	Welcome Remarks and Introduction to CTTI	Sally Okun (CTTI)
8:40 AM	Opening Comments	Janet Woodcock (FDA)
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)

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CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

September 21, 2022

Introduction to CTTI

Sally Okun, CTTI Executive Director

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

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

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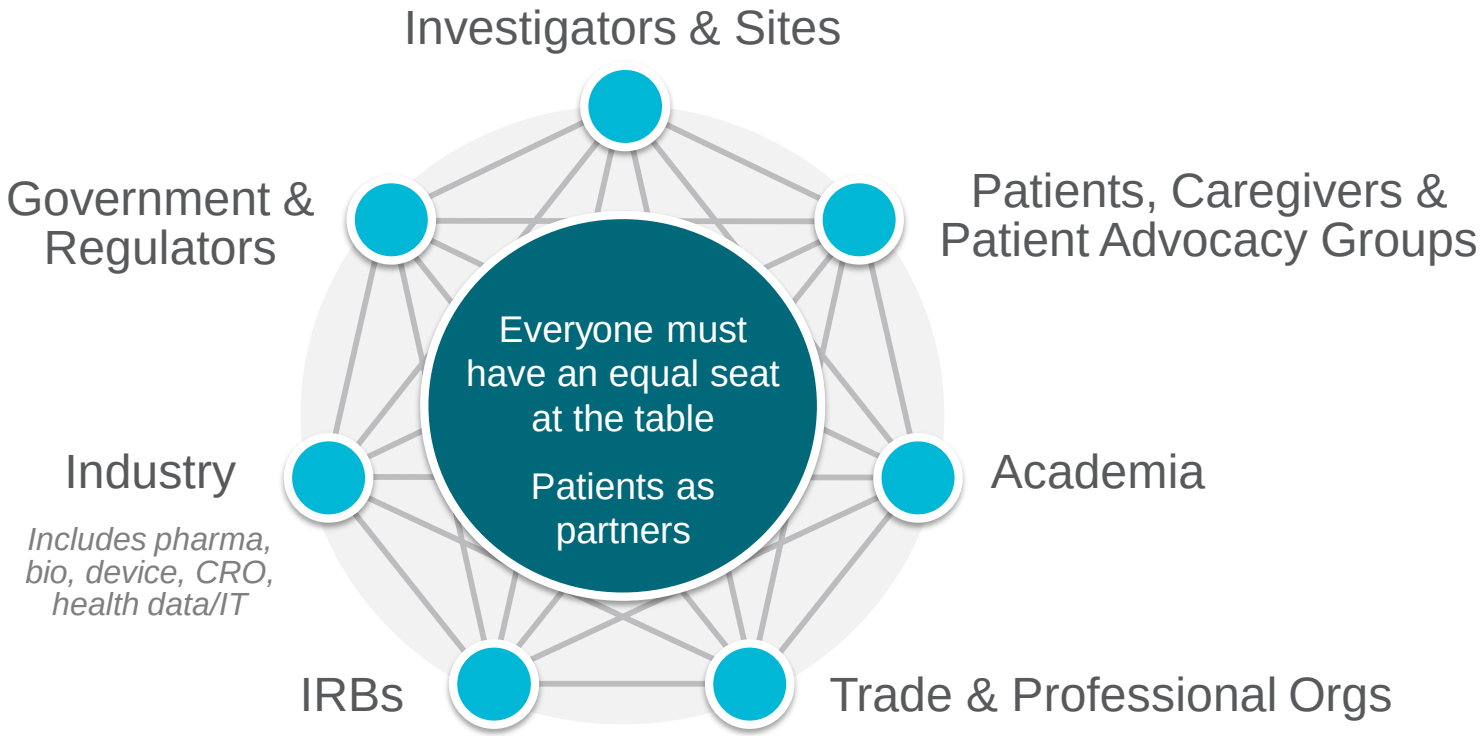
Multi-Stakeholder

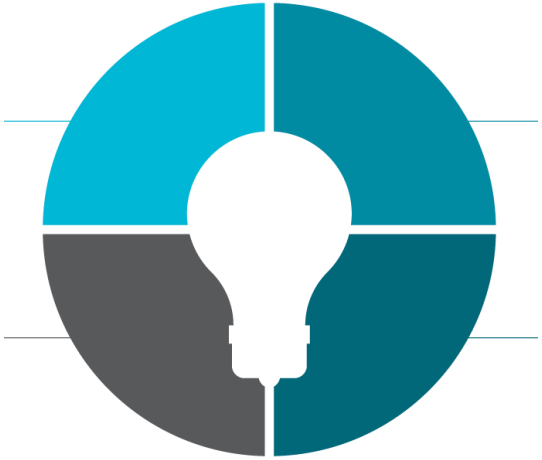


CTTI Recommendations

- 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

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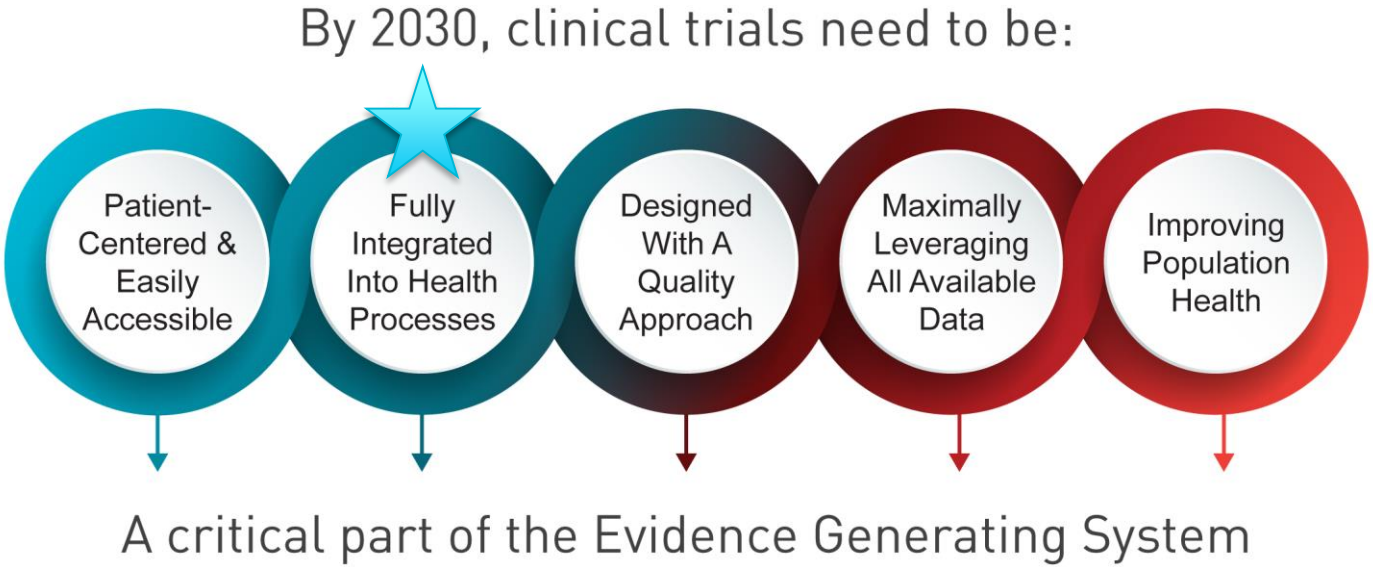
TRANSFORMING TRIALS 2030



https://ctti-clinicaltrials.org/who_we_are/strategic-vision/

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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

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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

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CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

September 21, 2022

RWD into RWA(action): @home @ clinic

Adrian F. Hernandez, MD

Executive Director, Duke Clinical Research Institute

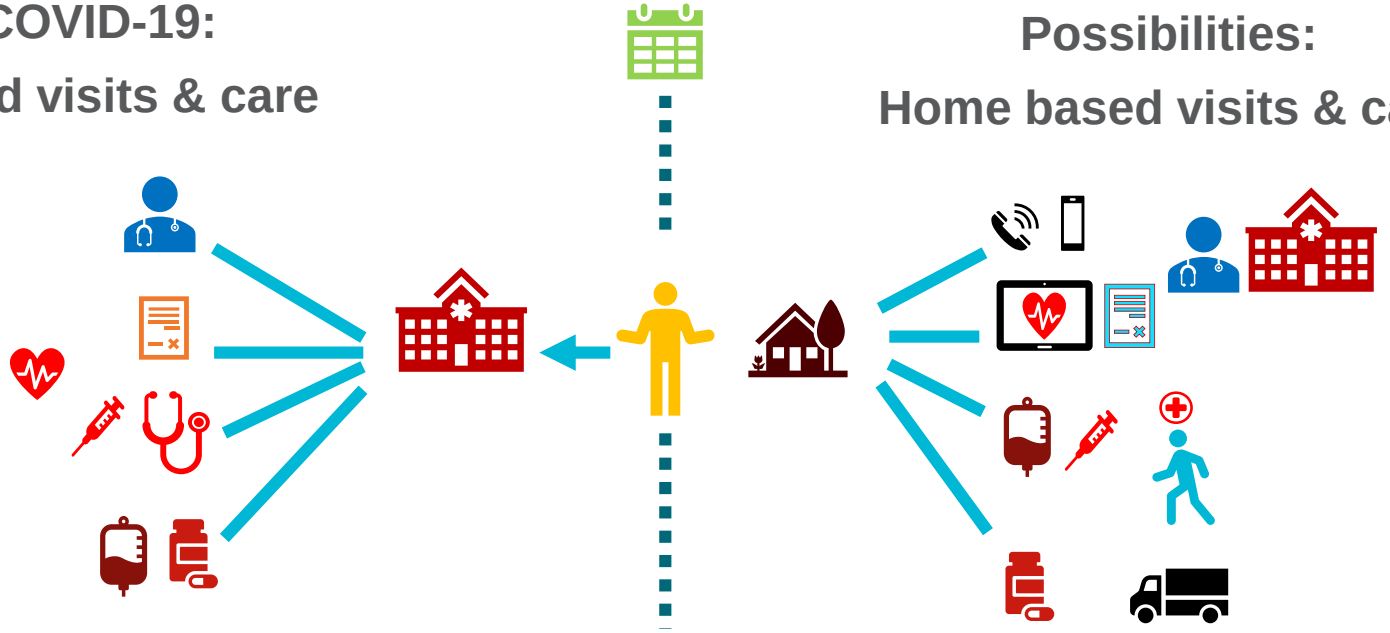
Going from Pre- Covid to Post COVID Clinical Trial Visits

Pre-COVID-19:

Site based visits & care

Possibilities:

Home based visits & care



https://ctti-clinicaltrials.org/our-work/digital-health-trials/running-a-decentralized-trial/

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Key clinical questions

ACTIV-6

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?

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What is ACTIV-6?

A STUDY TO HELP PEOPLE WITH MILD-TO-MODERATE COVID-19 FEEL BETTER FASTER

@ACTIV6study

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.

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?

How do we share what we are learning?

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

ACTIV-6

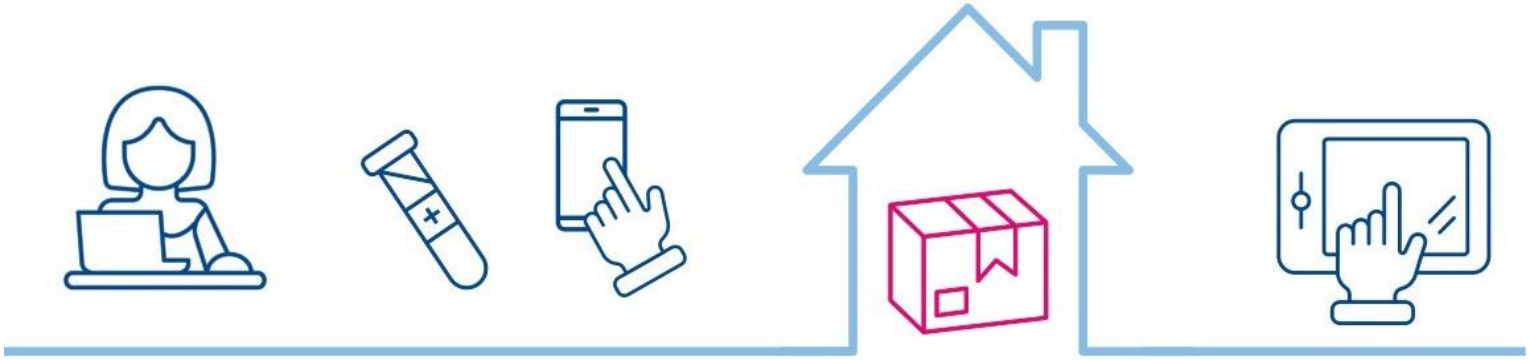
CTTI

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.

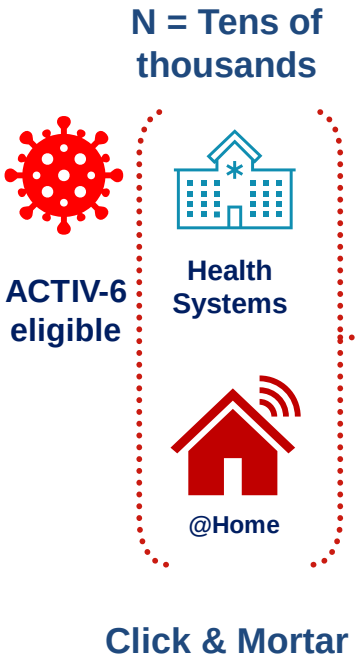
Test positive for COVID-19.

Enroll online or over the phone. activ6study.org

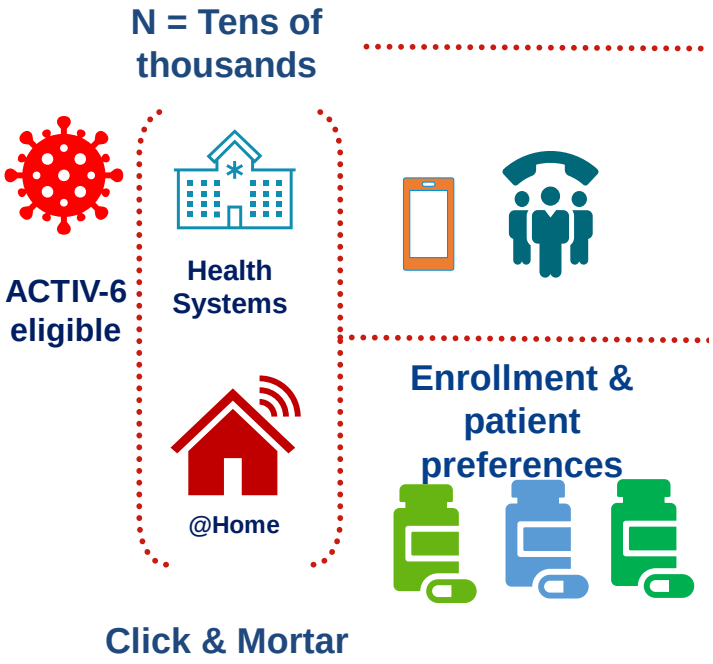
Receive assigned study medication and directions at home. **Take** the study medication as directed.

Complete surveys about how you feel online or over the phone.

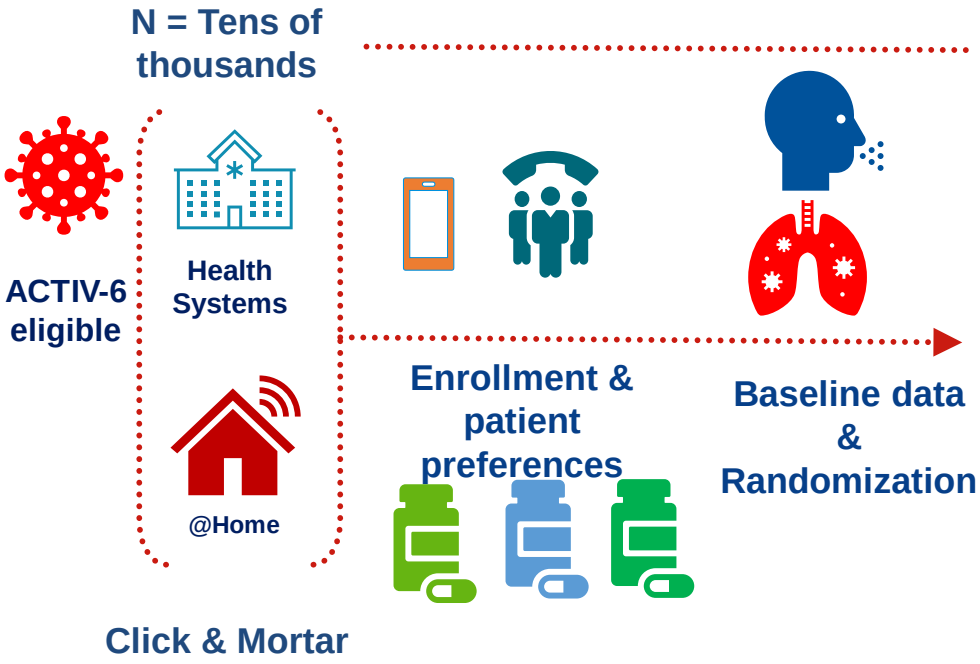
ACTIV-6 Hybrid Approach: Click & Mortar



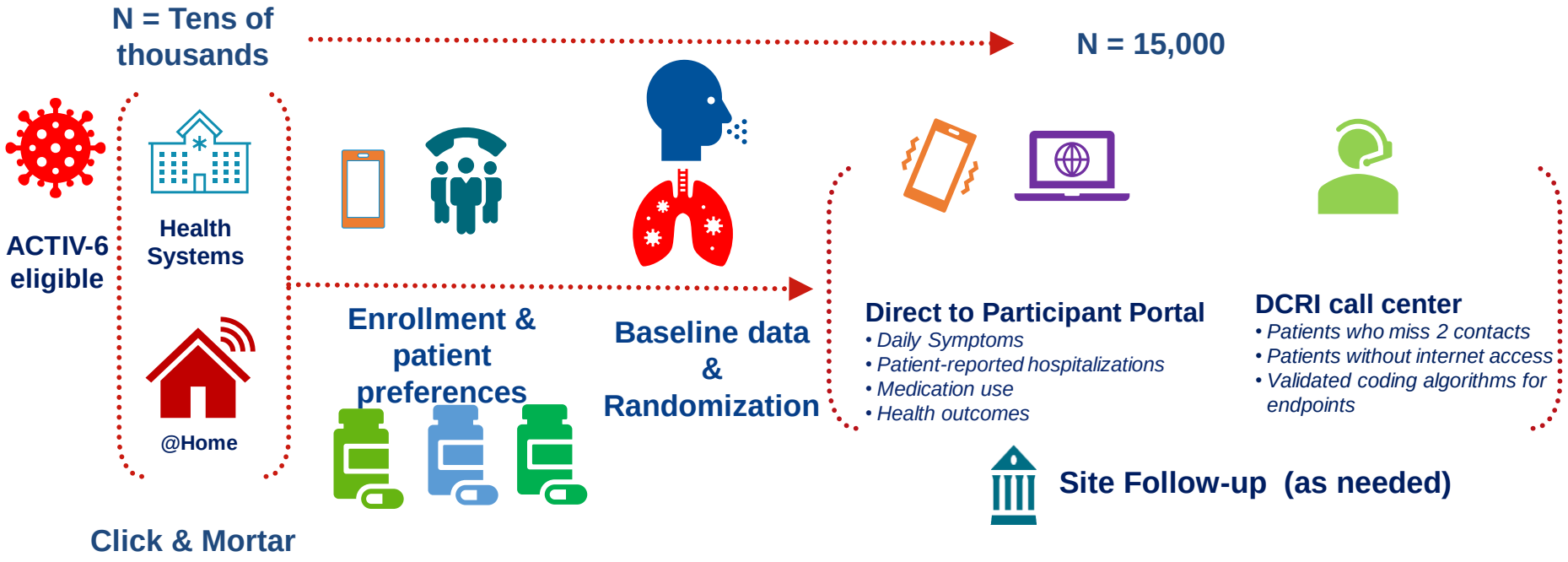
ACTIV-6 Hybrid Approach: Engagement



ACTIV-6 Hybrid Approach: Recruitment

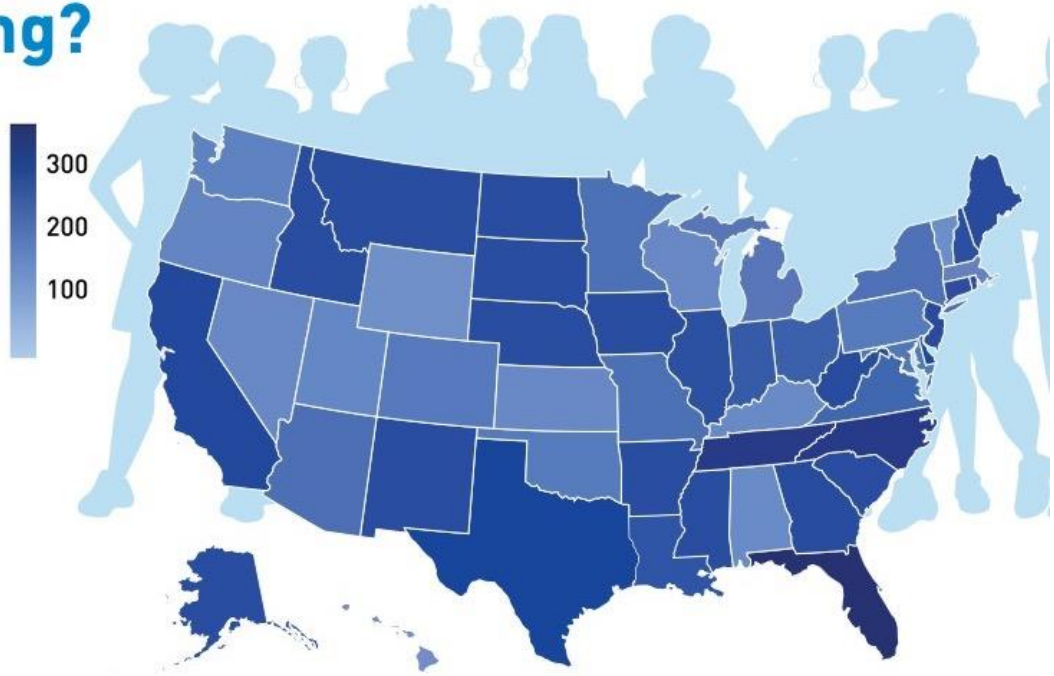


ACTIV-6 Hybrid Approach: Follow-up



Who is participating?

- All 50 US States
- 93 sites
- 5141 randomized
- 4 Arms Completed
- 1 Arm Ongoing (Fluvoxamine 100mg)
- 1 Arm in prep



ACTIV-6

@ACTIV6study

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Turning Real World Data into Action

From Evidence Generation to Implementation

CardioHealth Alliance

CTTI

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:

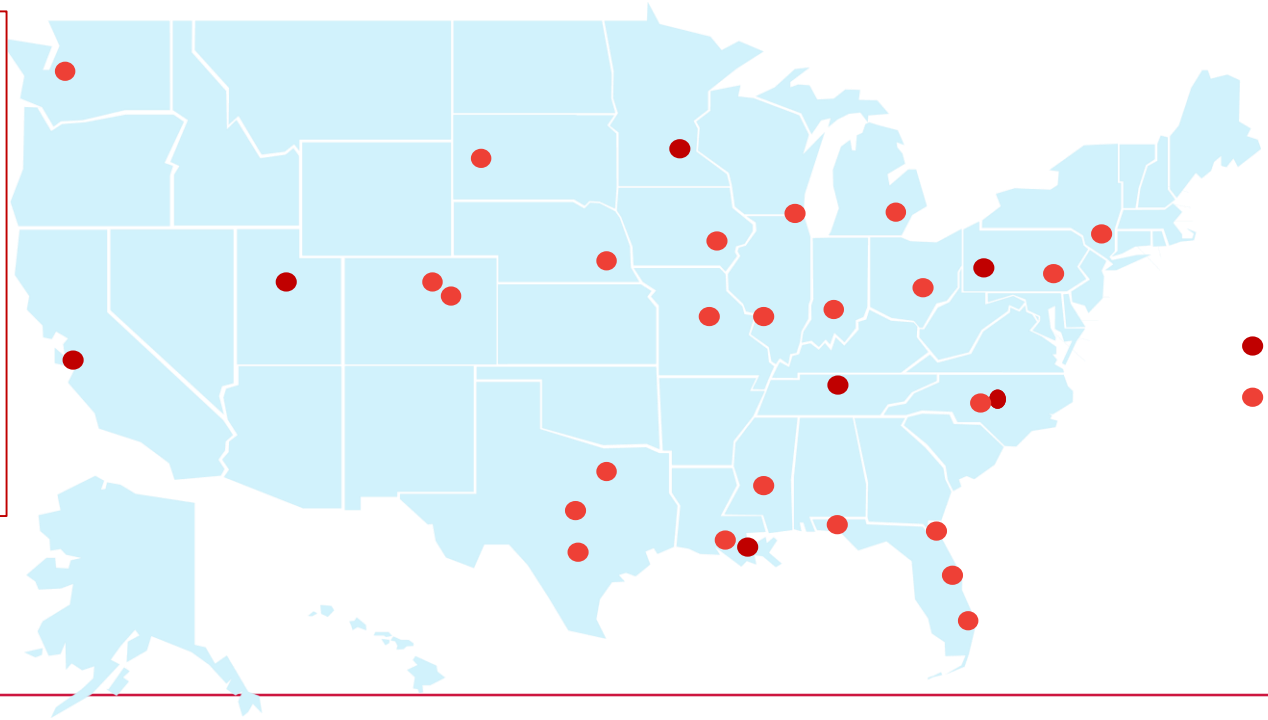
- Establish a reusable real-world data platform to rapidly answer clinical questions
- Shorten implementation of evidence into practice
- Generate real-world evidence to inform stakeholders
- Establish an alliance to address value of care through policy

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

Allina
Duke
Intermountain
Ochsner
Stanford
UPMC
Vanderbilt
TBA
TBA



Amgen
Bayer
Novartis
SomaLogic
TBA
TBA

Founding members
Future members

CardioHealth Alliance

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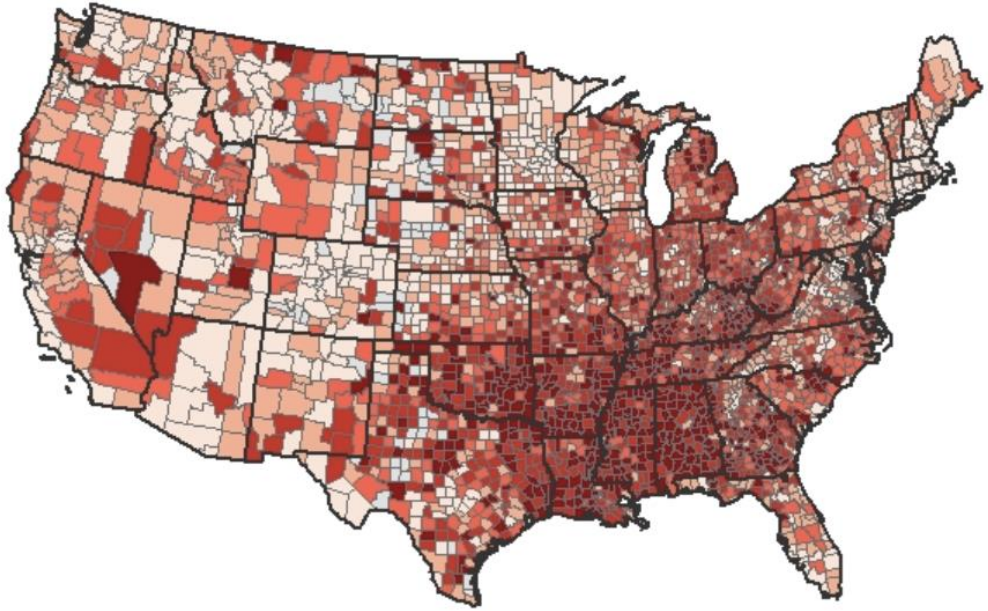
Changing the Map of ASCVD

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

CardioHealth Alliance

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

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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

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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.

OXFORD POPULATION HEALTH

protas

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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

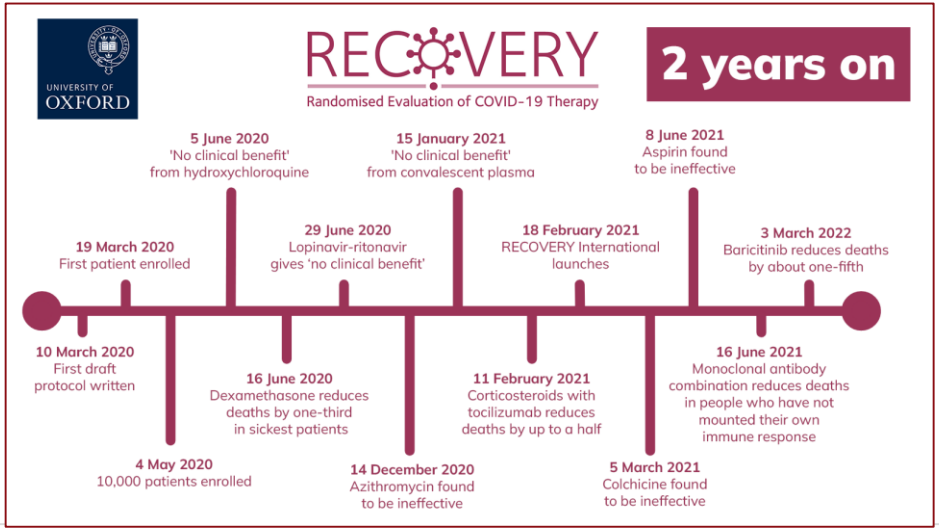
- Rapid initiation: 9 days from protocol to first participant
- Rapid recruitment: 100 days from protocol to first results
- Rapid impact: 4 hours from first results to policy implementation

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



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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

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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

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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

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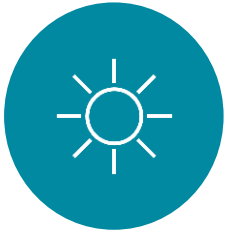
What does good guidance look like?

Good science & ethics

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

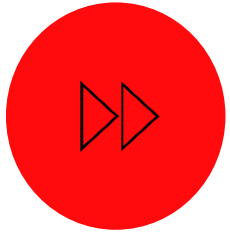


Clear and concise

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

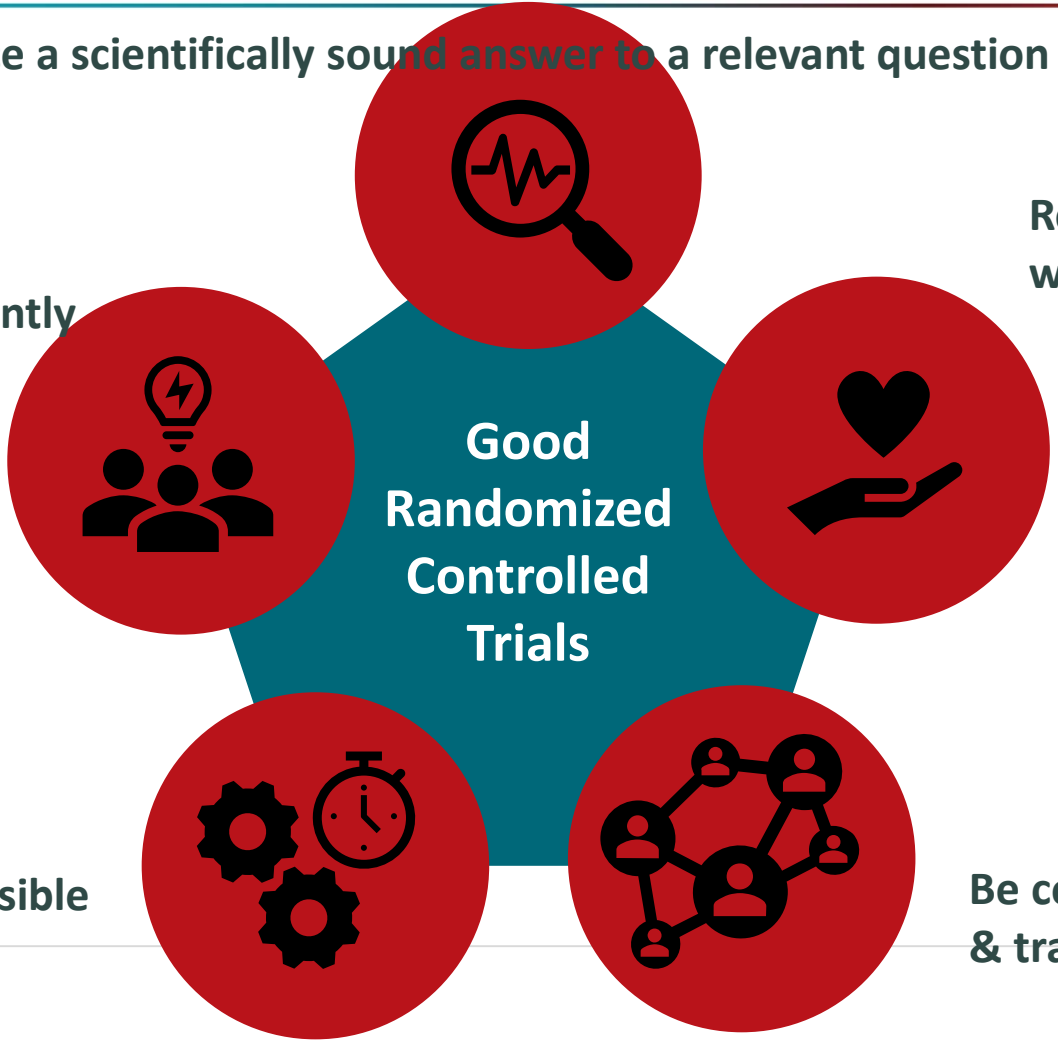
Forward looking and applicable across disease areas, intervention types, development phases, trial designs, geographies & time

Produce a scientifically sound answer to a relevant question

good clinical trials

Manage quality effectively & efficiently

Respect the rights & well-being



Designed to be feasible for their context

Be collaborative & transparent

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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
harmonisation for better health

19 April 2021

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.

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For more information

- RECOVERY trial: www.recoverytrial.net
- Protas: www.protas.co.uk
- Good Clinical Trials Collaborative: 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

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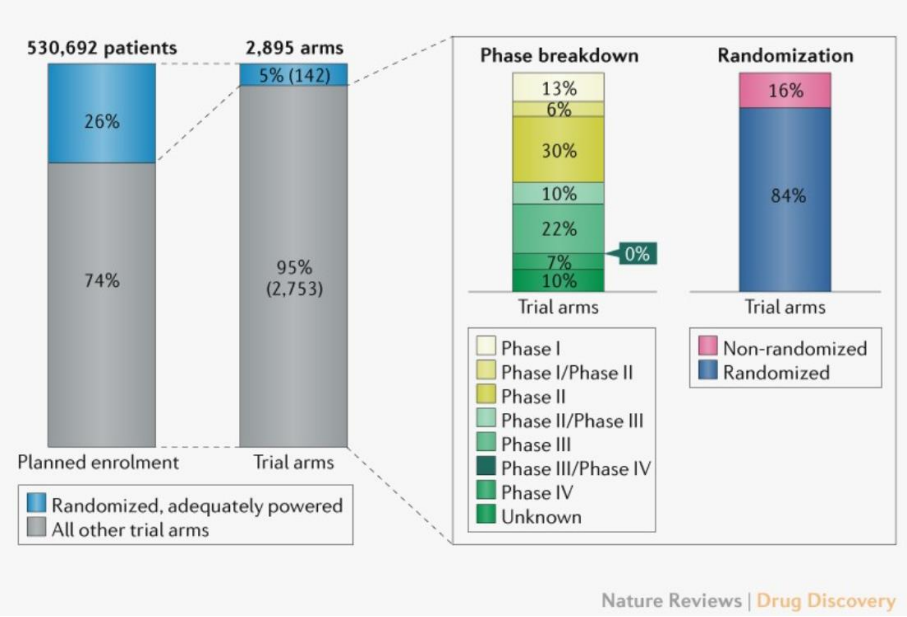
Disclaimer

- 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

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Frontline Trial Networks for Improving Evidence for Patient Care

- 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

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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 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

ACT@POC™

For more information

contact trevan.locke@duke.edu

or visit actpoc.org

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pcornet®

The National Patient-Centered Clinical Research Network

September 21, 2022

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

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PCORnet Purpose

- 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

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Patient Engagement in Research

	Steps in Research Process	Stakeholder Role
Research idea generation	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
Planning	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
Implementation	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
Returning findings to public	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

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:

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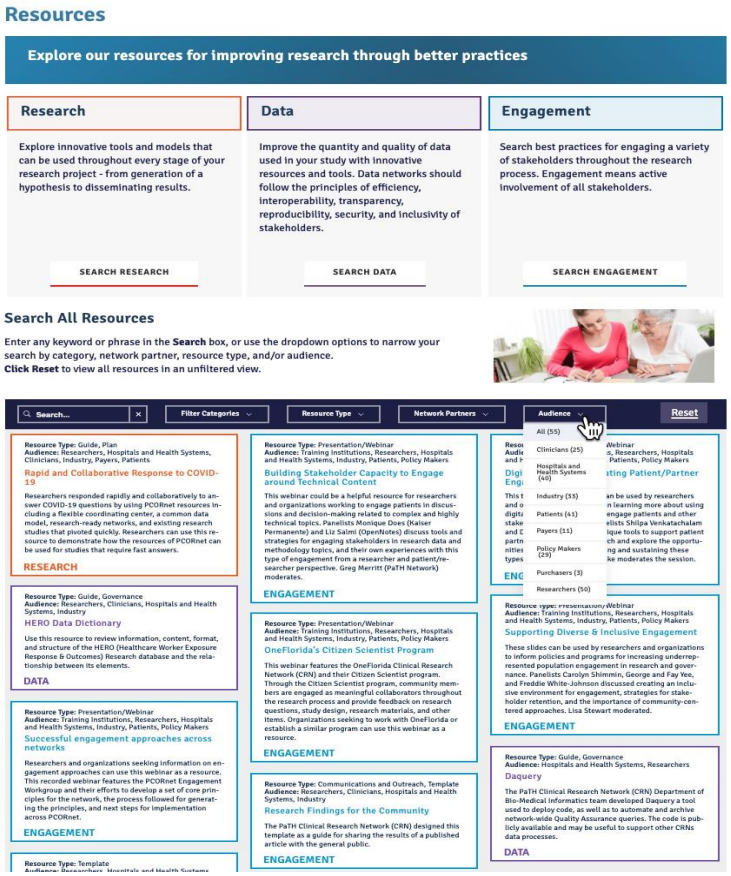
PCORnet Resources

- 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.



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The National Patient-Centered Clinical Research Network

THANK YOU

Work with PCORnet.

Visit us at www.pcornet.org to get the relationship started.

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Q & A

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

September 21, 2022

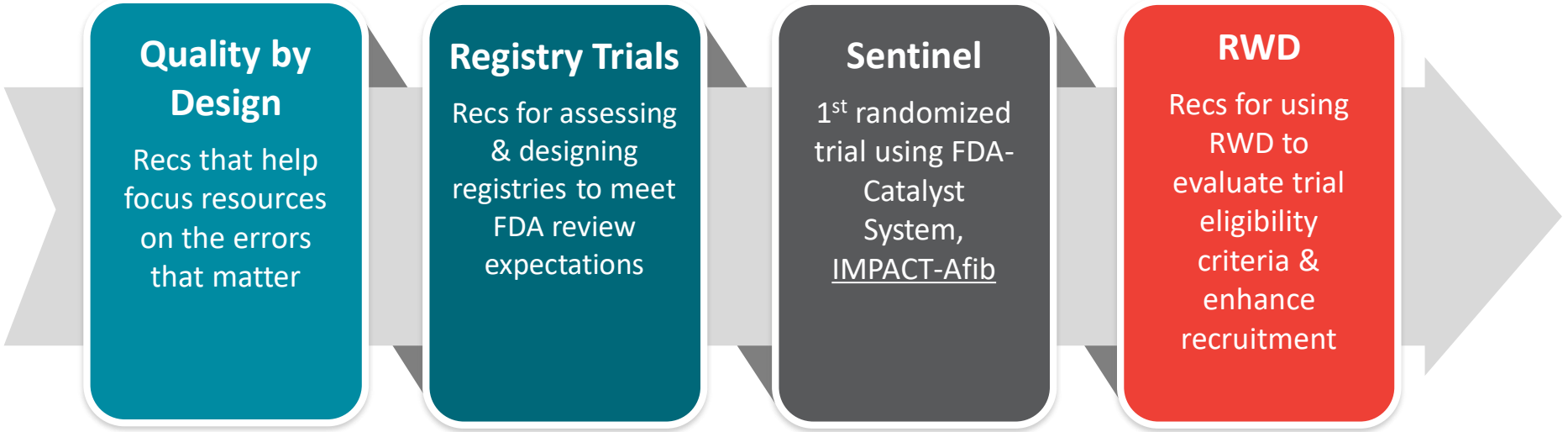
Embedding Trials into Clinical Practice

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



The Case for Embedding Clinical Trials into Practice

Patients

- Research and care are better aligned
- Less burden to participate in research
- Greater trial diversity and inclusivity
- Uses health care data for research to represent more real life experiences

Providers

- Potential to engage in research with minimal burden
- Addresses clinically meaningful questions to improve care in a broad population
- Treatment optionality for patients

Sponsors & Investigators

- Generalizable research populations and evidence
- Insights into real-world implementation of interventions
- Potential for increased efficiency & cost savings by reducing duplication of trial & care activities

Regulators

- Sufficiently sized trials with diverse populations
- Leverages power of randomization & RWD in the context of regulatory decision-making
- Generalizable evidence

Payers

- More, diverse data for reimbursement decisions
- Better understanding of the effectiveness and safety of medical product interventions

Health System Leaders

- A means to innovate and support quality care
- Potential to attract new patients with research opportunities

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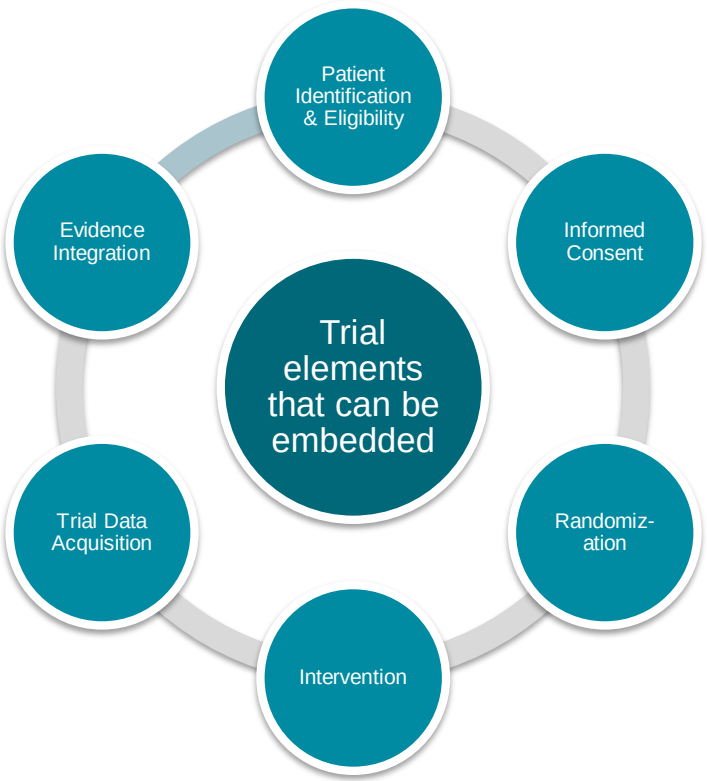
Embedded clinical trials have:

- 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?



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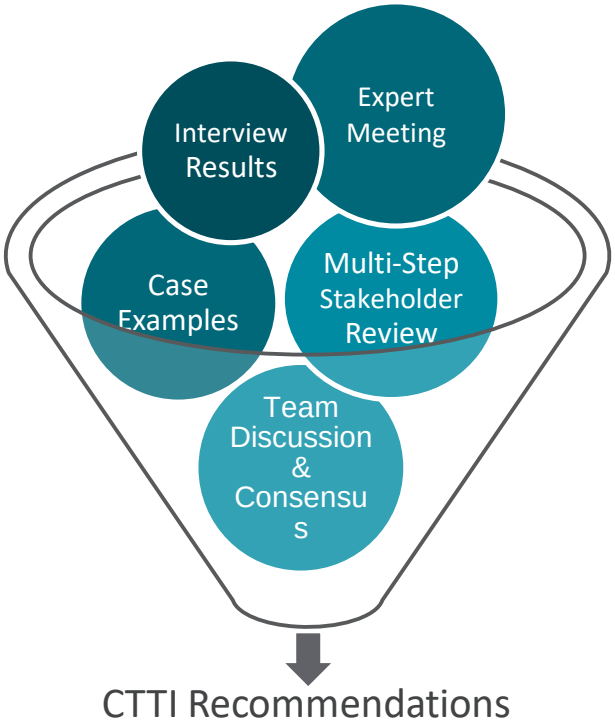
Embedding Trials into Clinical Practice

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

Trial Design/Methodology	Operational	Health Care & Research Culture
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	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	8. Recognize and invest in research activities 9. Promote the basis for and ways to embed trial elements into clinical practice
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.

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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)

Health Care & Research Culture Recommendations

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.

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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*

CLINICAL TRIALS WITH EMBEDDED TRIAL ELEMENTS

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

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Next Steps: Dissemination & Implementation

Expert Meeting Summary

- Key themes from meeting will be posted on CTTI Website in early October

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

Manuscript

- Summarizing in-depth interviews and recommendations
- Aiming for Publications Advisory Committee review December 2022

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CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

@CTTI_Trials

THANK YOU

Special shout out to the project team & team leads

BREAK

Return to Grand Ballroom at 10:30 am

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

September 21, 2022

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  Grand Ballroom with Karen
  - Group 2 = yellow  Grand Ballroom with Lindsay
  - Group 3 = green  Freedom Room 1 with Sara
  - Group 4 = blue  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:

What elements of your trial are embedded into clinical practice and how feasible are they to embed?	On **red** post-it, assign a number and stick it on the element • 1 not likely • 3 likely • 5 very likely
What are 2-3 pain points with embedding these elements?	On a **blue** post-it, write a pain point and stick it on the element
Which CTTI recommendation(s) help with embedding the trial elements?	On a **green** post-it, write the CTTI recommendation # and stick it on the element

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Break Out Group Questions

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

For your trial scenario:

How do we overcome the pain points noted?	Who is responsible?
Of the CTTI recommendations that help with embedding trials elements:	• Why is the recommendation(s) helpful? • How would you use the recommendation in planning a trial?
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*

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LUNCH

Return to Grand Ballroom at 1:00 pm ET

Session II Break Out Debrief

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

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CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

September 21, 2022

Session III: Metrics of Implementation

Morgan Hanger, Director of Strategic Programs, CTTI

Session Overview

- 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)

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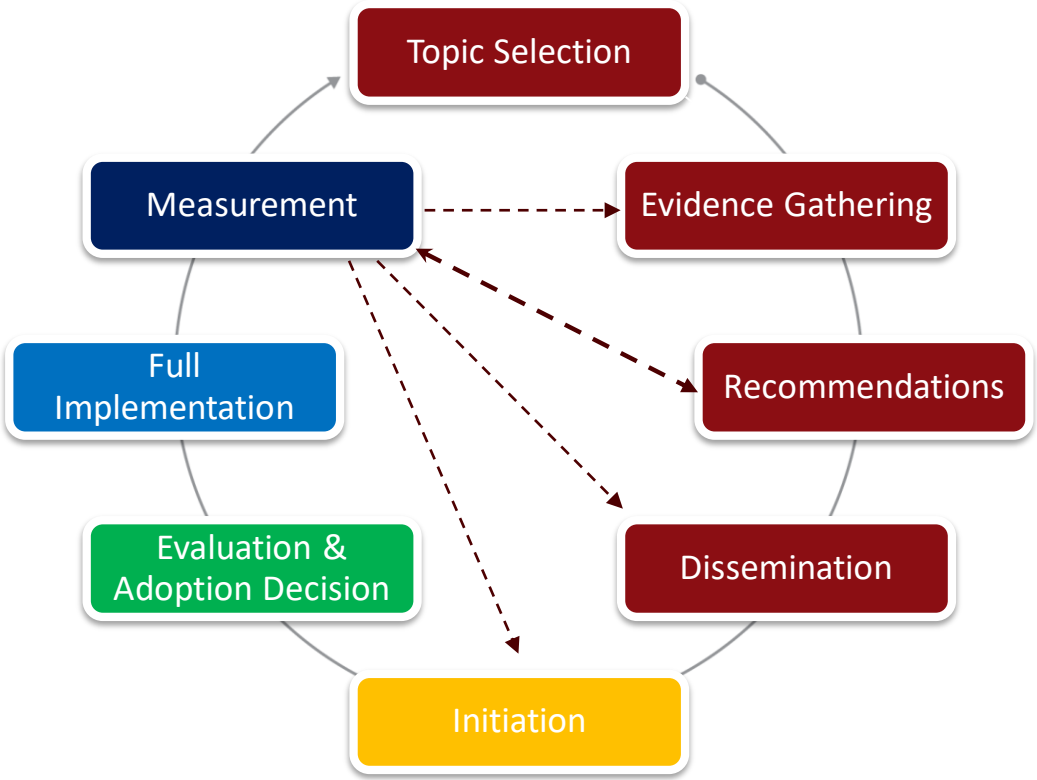
Looking at CTTI's Role in Adoption

CTTI & Clinical Trial Enterprise

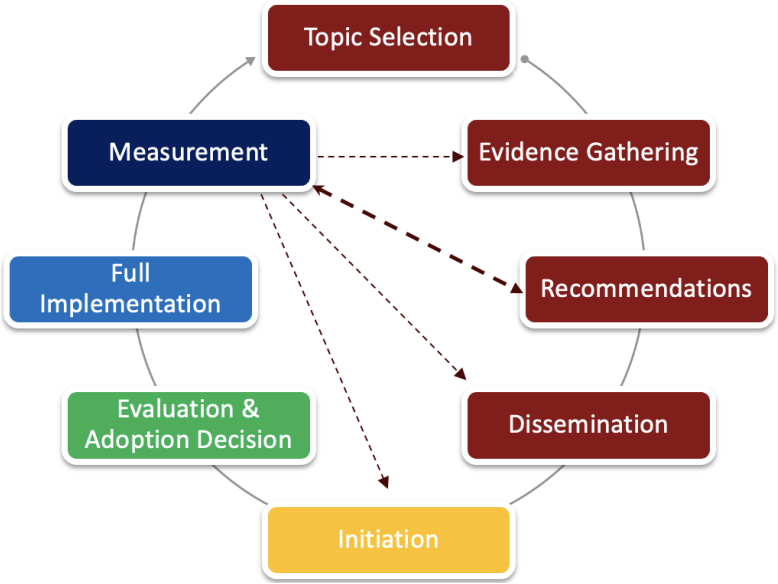


CTTI Staff & Members

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?

	Adopter	Enterprise	Outcomes
Design	How can we know whether change is happening at the organization level?	How can we quantify the way that change is happening across the entire trial enterprise?	How will we know if change is improving the quality and/or efficiency of clinical trials?
Operational			
Cultural			

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How Can We Observe Change?

	Adopter	Enterprise	Outcomes
Trial Design and Operational (Groups 1, 4)	• *% of trials that have any embedded elements*	• *% of healthcare systems (EHR, pharmacy, nurse, etc.) that have technology and people solutions that account for research needs*	• *More patients that have access to clinical care have access to clinical trials*

Health Care & Research Culture Recommendations

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How Can We Observe Change?

	Adopter	Enterprise	Outcomes
Healthcare and Research Culture (Group 3)	• *% of HC staff that view clinical trials as part of their job*	• *The proportion of the healthcare enterprise that is involved in running trials as a recognized, measured part of their work*	• *Clinical trial findings are integrated into practice more quickly*

Inspiration for Outcome Measures

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

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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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CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

@CTTI_Trials

"Without deviation from the norm, progress is not possible."

– Frank Zappa

THANK YOU

www.ctti-clinicaltrials.org