Trial Innovation Network

Tackling the Critical Roadblocks in Clinical Trials

Monica R. Shah, MD
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May 6, 2017
Clinical Trials
The Road is Long and Slow
Clinical Trials
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Clinical Trials – Critical Roadblocks

- Recruitment Challenges
- High Costs
- Trial Start Up
- Lack of Engagement of Site Investigators, Providers, Participants
- Protocol Complexity

Expect Delays
Clinical Trials – Critical Roadblocks

- Fewer High Quality Trials
- Insufficient Evidence to Inform Clinical Care
- IRB Review – ~112 Days
- Contract Execution – ~91 Days
- Protocols often developed without input from key stakeholders
- ~170 study procedures
  ~1 million data points
  subject
- 25% of procedures not related to primary or secondary endpoints
- Lack of harmonization
- Duplication of infrastructure
- Variability in training
- Since 2000 – 50% decline in enrollment
- $160M to $2B
  Primary drivers – data collection, data management, study administration
- Fewer High Quality Trials
- Insufficient Evidence to Inform Clinical Care
Clinical Trials – Critical Roadblocks

- Recruitment Challenges
  - Lack of engagement of site investigators, providers, participants
- Fragmented site-based research
- High costs
  - Trial start-up
  - Protocol
  - Fewer high-quality trials
  - Insufficient evidence to inform clinical care
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Vision

Early Vision for the CTSA Program Trial Innovation Network: A Perspective from the National Center for Advancing Translational Sciences (NCATS)

Monica R. Shah, Michelle A. Culp, Kenneth R. Gersing, Patricia L. Jones, Mary E. Purucker, Tiina Urv, Todd M. Wilson, Petra Kaufmann

Accepted manuscript online: 8 March 2017  Full publication history

National Platform for Clinical Trials that Focuses on Operational Innovation, Operational Excellence, and Collaboration

Resource for NIH, Industry, and Other Partners
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Vision

Accelerate Translation
CTSA PROGRAM HUBS: Leading excellence and innovation locally

Collaborating regionally and nationally

Domain Task Forces

- Methods
- Processes
- Collaboration
- Engagement
- Understudied
- Populations
- Informatics
- Workforce
- Development

Consortium-wide programs

- Collaborative Innovation Awards
- Trial Innovation Network
- CTSA Program Data Harmonization
- Future Innovations & Partnerships
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CTSA Program

Hubs

Hub Liaison Teams

NIH Institutes
Industry Foundations

Partners
Participants
Providers
Public

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Trial Innovation Centers (TICs)

Recruitment Innovation Centers (RIC)

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Duke Clinical Research Institute

University of Utah Health Care

Vanderbilt University Medical Center

Johns Hopkins Medicine

Tufts Medical Center

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NIH National Institute on Aging

NIH NLM

NIH National Center for Advancing Translational Sciences

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Operational Excellence

**Trial Planning**

- Protocol Design
- Study and Budget Feasibility
- Statistical Analysis Plan
- Risk Assessment
- Engagement and Recruitment Plans
- Patient Engagement Studio
- Cohort Discovery Leveraging EHR
- Recruitment Training
- Access to unique populations – Rare Diseases
- Key Opinion Leader/Clinical Expertise

**Trial Execution**

- 3 Academic Central IRBs
- Standard Agreements Used Across Network (*FDP-CTSA*)
- CTSA Program Recruitment Sites with Trial Innovation Network Hub Liaison Teams
- Regulatory Support
- Project Management
- Consent Forms, CRFs
- Site Selection, Initiation, Training
- Performance Metrics
- Recruitment Plans and Tools
- Data Management
- DSMB
- Study Close Out, Statistical Analysis
- Publications
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Operational Excellence

What Makes the Trial Innovation Network Different?

Operational Innovation

- A living laboratory to study and innovate key elements of clinical trials
- Goal isn’t just to complete a trial – but to improve the clinical trials process
Harmonized Site Based Research System
Harmonized Data Standards
Harmonized Recruitment System
Harmonized Protocol System
Harmonized Contracting System
Harmonized CIRB System

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Innovating and Harmonizing to Clear Roadblocks

Delays in IRB Review
Delays in Contracting
Complex Protocols
Recruitment Challenges
Data not Fully Utilized
Fragmented Site Based Research
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Innovating and Harmonizing to Clear Roadblocks

Harmonized CIRB System
Harmonized Contracting System
Harmonized Protocol System
Harmonized Recruitment System
Harmonized Data Standards
Harmonized Site Based Research System
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Innovating and Harmonizing – IRB Review

Roadblock

• Individual IRB reviews take too long

Innovation

• SMART IRB Authorization Agreement
• 163 institutions have signed, including all 64 CTSA Hubs
• Workflows, SOPs, Metrics
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Innovating and Harmonizing – IRB Review

Harmonization

- 3 Harmonized Central IRBs
- All use same reliance agreement, standard procedures, and IT platform
- Metrics – time, cost, quality

Johns Hopkins

Harmonized CIRB Processes
SMART IRB Agreement

Vanderbilt

Utah
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Innovating and Harmonizing – IRB Review

Harmonized CIRB Processes

- SMART IRB Agreement
- 3 Harmonized Central IRBs
- All use same reliance agreement, standard procedures, and IT platform
- Metrics – time, cost, quality

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Operational Innovation

- Does a harmonized IRB system increase the quality and efficiency of IRB review?
- Does a harmonized IRB system decrease burden on research staff?
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Innovating and Harmonizing – IRB Review

National IRB System

- Harmonized Central IRBs
- All use same reliance agreement, standard procedures, and IT platform
- Metrics – time, cost, quality

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Operational Innovation

- Does a harmonized IRB system increase the quality and efficiency of IRB review?
- Does a harmonized IRB system decrease burden on research staff?

Other Stakeholders

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SMART IRB Agreement
Harmonized Workflows and SOPs
Harmonized Definitions and Metrics

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Innovation and Harmonization

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Innovating and Harmonizing – Contracts

Roadblock

- Contract negotiations are top reason for study delay

Innovation and Harmonization

- FDP-CTSA Master Contract
  - Addresses Indemnification, Confidentiality, Publication, Intellectual Property
- Harmonized Contracting System
- Metrics

Kiriakis, Clin & Transl Science, 2013; www.ara4us.org
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Innovating and Harmonizing – Contracts

Roadblock

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Operational Innovation

• Does a master contracting system decrease start up times for a clinical trial?

TIN will use FDP-CTSA Master Contract

• Metrics

Kiriakis, Clin & Transl Science, 2013; www.ara4us.org
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Innovating and Harmonizing – Protocols

- Suboptimal Protocols
- Limited Secondary Use Of Data
- Reactive Recruitment Planning
- Exclusive Focus on Science

Roadblock
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Innovating and Harmonizing – Protocols

Trial Design
• Novel Study Designs
• Quality by Design
  • Compelling Scientific Endpoints
  • Feasibility
• Limit Complexity
• Optimize Data Collection
• Metrics/Milestones
• Develop Realistic Budgets

Recruitment Planning
• Engage Stakeholders
• Tailored Messages and Recruitment Material
  • Pre-specified Recruitment Budgets
  • Monitor Recruitment Process, Metrics

Data Driven Approaches
• EHR Based Cohort Discovery and Site Selection
• Recruitment modeling to minimize amendments

Strategically Designed Protocols

Innovation

Analytics

Execution

Proactive Recruitment Planning

TIC and RIC Collaboration
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Innovating and Harmonizing - Protocols

THE NIH DIRECTOR

NIH Reaches Another Milestone Toward Clinical Trial Stewardship Reforms

Clinical e-Protocol Writing Tool

NIH > FDA

May 2, 2017

Harmonization

• Vanguard for NIH-FDA Protocol Template

• Harmonized approach to comply with national requirements for registration of trials and reporting of results

• Metrics

ClinicalTrials.gov
A service of the U.S. National Institutes of Health
FDAAA 801 Requirements

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Innovating and Harmonizing - Protocols

- Vanguard for NIH - FDA Protocol Template
- Harmonized approach to comply with national requirements for registration of trials and reporting of results
- Metrics

*Does using a standard protocol template increase the efficiency of a study and quality of data?*
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Innovating and Harmonizing - Recruitment

Roadblock

Poor recruitment is a top reason for trial delays

Recruitment often addressed after problems occur

Recruitment approaches often disorganized

Research staff often not trained to implement interventions

Adapted from a slide by R. Kost, Rockefeller Univ.
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Innovating and Harmonizing - Recruitment

**Innovation and Harmonization**

- Research Team
- Protocol Design
- Proactive Systematic Recruitment
- Recruitment Workflows
- Engagement/Recruitment Plans
- Outreach
- Advertising & Social Media

**Entry Criteria**
Minimize Barriers
- Stringency of Entry Criteria
- Time/Risks
- Adverse Events
- Pain/Invasiveness
- Procedures
- Lost Wages
- Language Barriers
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Innovating and Harmonizing - Recruitment

- Recruitment training
  - Training for specific populations
- Entry Criteria
  - Maximize Incentives
  - Engagement/Partnership
  - Direct Benefits
  - Access to Novel Treatment
  - Free Testing
  - Access to Test Results
  - Education/Learning
  - Compensation
  - EHR to identify participants and sites
  - Recruitment models
- Participant Experience
  - Assess experience of participation
  - Return of results
- Workflows
  - Metrics
- Proactive Systematic Recruitment
  - Target audience, patient pathways, messaging, recruitment approaches
  - Engagement studios, focus groups
- Recruitment Workflows
- Research Team
- Protocol Design
- Data Driven Cohort Discovery and Site Selection
- Engagement/Recruitment Plans
  - Outreach
  - Advertising & Social Media
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Innovating and Harmonizing - Recruitment

Optimized Recruitment and Retention
Accelerate Trials

- Participant Experience
- Proactive Systematic Recruitment
- Recruitment Workflows
- Engagement/Recruitment Plans Outreach Advertising & Social Media
- Data Driven Cohort Discovery and Site Selection
- Protocol Design
- Research Team

Accelerate Trials
Poor recruitment is a top reason for trial delays

Recruitment is often addressed after problems occur

Recruitment approaches are often disorganized

Research staff are often not trained to implement interventions

Roadblock

Proactive
Systematic
Recruitment

Research
Team

Protocol
Design

Data Driven
Cohort
Discovery
and Site
Selection

Engagement/
Recruitment
Plans

Outreach

Advertising &
Social Media

Proactive
Systematic
Recruitment

Participant
Experience

Recruitment
Workflows

Entry Criteria

Maximized Barriers

Minimized Barriers

• Direct Benefits

• Access to Novel Treatment

• Free Testing

• Access to Test Results

• Education/Learning

• Compensation

• EHR to identify participants and sites

• Recruitment models

• Target audience, patient pathways, messaging, recruitment approaches

• Engagement studios, focus groups

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Innovating and Harmonizing – Recruitment

Recruitment Toolkit

Systematic Recruitment Plan

Systematic Enrollment Workflows

Pipeline to Enrollment

As of right now there are:

Difficult diseases have met their match.

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Innovating and Harmonizing – Data Standards

Roadblock

- Different “languages” used to describe the same data
- Difficult to combine data and generate new insights
- Limits collaboration across organizations
- Decreases efficiency and quality of data collection

Tower of Babel, Pieter Bruegel
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Innovating and Harmonizing – Data Standards

Data Standards
Agreed upon rules that allow information to be shared in a uniform and consistent manner

Innovation and Harmonization

• CDISC/CDASH
• Harmonized data collection
• Harmonized adverse event reporting
• Harmonized risk-based monitoring
• Harmonized data reporting to Trial Innovation Network Data Safety and Monitoring Boards
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Innovating and Harmonizing – Data Standards

- CDISC/CDASH
- Harmonized data collection
- Harmonized adverse event reporting
- Harmonized risk-based monitoring
- Harmonized data reporting to Trial Innovation Network

Data Safety and Monitoring Boards

Agreed upon rules that allow information to be shared in a uniform and consistent manner

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Operational Innovation

- Do harmonized data standards produce lower data entry error rates?
- Is data quality related to the amount of data collected?
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Innovating and Harmonizing – Site Based Research

Clinical Research Sites—The Underappreciated Component of the Clinical Research System

Roadblock

- Workload, time, research a “secondary job”
- Complex institutional systems
- Regulatory and bureaucratic burdens
- Lack of harmonization of processes
- Variability in training and expertise of local study teams
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Innovating and Harmonizing – Site Based Research

Innovation and Harmonization

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TICs

RIC

Hub Liaison Team

CTSA Program Hub
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**Innovating and Harmonizing – Site Based Research**

- **Hub Investigators**
  - Encourage Ideas
  - Assist with Developing TIN Proposals
  - Identify Investigators for TIN Studies

- **Hub IRB Office**
  - Operationalize TIN CIRB

- **Hub Contracts Office**
  - Operationalize Standard Agreements

- **Hub Recruitment**
  - Cohort Discovery
  - Training
  - Community Engagement

- **Hub Research Teams**
  - Assist with Operationalizing TIN Studies

**Dedicated Clinical Trial Catalyst Team**

**NIH Industry Other Partners**

**Trial Innovation Network**

**TICs**

**RIC**

**Hub Liaison Team**
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New Treatments to Patients Faster

Decrease Complexity

Increase Efficiency and Productivity

Accelerate Timelines

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www.trialinnovationnetwork.org