National Center for Advancing Translational Science (NCATS)

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NCATS
NCATS MISSION

• To catalyze the generation of *innovative methods and technologies* that will *enhance the development, testing and implementation of diagnostics and therapeutics* across a wide range of human diseases and conditions
What is translation?

Translation is the process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public — from diagnostics and therapeutics to medical procedures and behavioral changes.
What is Translational Science?

Translational Science is the field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process.

NCATS studies translation on a system-wide level as a scientific and operational problem.
Translational Science Spectrum

- Public Health
- General Research
- Pre-Clinical Research
- Clinical Research
- Clinical Implementation
- Patient Involvement
- Demonstrate Their Usefulness
- Develop New Approaches
- Disseminate the Findings
NCATS Stakeholders

- Patients and members of the health advocacy community
- Basic, translational and clinical scientists at universities and research institutions
- Health care providers
- Biotechnology, venture capital and pharmaceutical industry members
- Colleagues at other NIH Institutes, Centers and Offices
- Partners at other government agencies (e.g. FDA, other agencies of DHHS, EPA and DoD)
- Policy makers and funders
- General public
NCATS Organizational Chart

COUNCIL - CAN BOARD

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(Director)
CTSA PROGRAM
Clinical and Translational Science Awards Program (CTSA)

- The CTSA Program addresses the development and implementation of national standards and best practices for translation, from basic discovery to clinical and community-engaged research.
- >60 sites
NCATS CTSA Resources

- **Accrual to Clinical Trials (ACT)** to develop a nationwide network of sites that share electronic health record data to identify and enroll participants who meet criteria for a given clinical study. ncats.nih.gov/pubs/features/ctsa-act

- **Collaborative Innovation Awards** that provide incentives for multiple CTSA Program sites to work together on translational research projects.

- **Recruitment Innovation Centers** to improve clinical trial participant retention rates and improve trial success.

- **REDCap**, an easy-to-use, freely available tool for clinical study management and data capture, enabling investigators to build and manage online surveys and databases. project-redcap.org

- **ResearchMatch**, a secure online volunteer recruitment registry that connects people who are trying to find research studies with researchers who are seeking people to participate in their research studies, including clinical trials. researchmatch.org

- **Scientific project review templates** designed to assure the scientific feasibility of human research protocols in addition to standard ethical and regulatory review.

- **Single institutional review board** agreement to streamline ethical review and oversight of clinical trials.

- **Streamlined contracting** designed with government, industry and nonprofit partners to accelerate clinical trial start-up. ara4us.org

- **Training** based on network-wide standards. ctsa-gcp.org

- **Trial Innovation Centers** to facilitate multisite clinical trial implementation and improve its quality and efficiency.
Challenges in Clinical Trials

Multiple IRB Review

- Time consuming
- Expensive
- May not provide optimal human subjects protection

The Paradoxical Problem with Multiple-IRB Review

Jerry Menikoff, M.D., J.D.

Multiple IRB Review

Median Review Time

112 Days

The goal is to provide flexible resources that investigators nationwide can use to harmonize and streamline IRB review for their own multisite studies.

The NCATS SMART IRB Reliance Platform involves two steps:

- The first step is signing on to the NCATS SMART IRB Reliance Platform authorization agreement. Institutions sign the joinder, which documents their agreement with the roles established in the authorization agreement. This is done once.

- The second step is designating an IRB to be the single IRB (the reviewing IRB) and identifying the participating sites that will rely on the IRB for the review of a multisite study. The platform is flexible and can be used for one investigator-initiated multisite study or for a network conducting many multisite studies.

https://ncats.nih.gov/expertise/clinical/smartirb

NCATS SMART IRB Reliance Platform = Flexible platform
Challenges in Clinical Trials

- High Costs
- Prolonged Time Frames
- Suboptimal Recruitment
- Disconnect – Research & Medical Care

Fewer High Quality Trials
Insufficient Evidence to Inform Clinical Care
Negative Impact on Public Health
The Impact

Fewer High Quality Trials

Review of Clinical Trials.gov

- > 40,000 trials
- ~62% enrolled ≤100 subjects
- ~96% enrolled <1000 subjects
- 66% were single center
- Variability in use of DSMB, randomization, & blinding

The Impact

- <15% of US clinical guidelines informed by high quality evidence – adequately powered randomized clinical trials

Challenges in Clinical Trials
High Costs

**TABLE 3-2** Breakdown of the Costs for a Large, Global Clinical Trial (14,000 patients, 300 sites)

<table>
<thead>
<tr>
<th>Expense</th>
<th>Cost (in millions of $)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site payments</td>
<td>150.0</td>
</tr>
<tr>
<td>Monitoring</td>
<td>90.0</td>
</tr>
<tr>
<td>Data management and statistics</td>
<td>12.0</td>
</tr>
<tr>
<td>Project and clinical leadership</td>
<td>12.0</td>
</tr>
<tr>
<td>Interactive voice response systems (IVRS) and drug distribution</td>
<td>10.8</td>
</tr>
<tr>
<td>Publications</td>
<td>.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>~300</td>
</tr>
</tbody>
</table>

**SOURCE:** Califf, 2009.

Challenges in Clinical Trials

High Costs

Impact of High Costs

• Cannot afford many adequately powered trials with clinical endpoints
• Key clinical questions answered with surrogate endpoints
• Suboptimal evidence
• Fewer new drugs
• Opportunity costs

DiMasi, Clinical Therapeutics, 2013
Challenges in Clinical Trials

Prolonged Timelines

Impact of Prolonged Timelines

- Scientific question no longer relevant
- Decreased recruitment & data quality
  - Decreased scientific impact
  - Decreased public health impact
- Decreased return on research investments

Time from start of clinical testing to marketing of new drug – 7.5 years

Tufts Center for the Study of Drug Development
Clinical Trials

Huge Challenges & Golden Opportunities

Opportunity for Operational Excellence

Execute trials better, faster, & more cost-effectively
Trial Innovation Network

• A Network that Accelerates Translation of Novel Interventions to Evidence Based Treatments
  • Single IRB Reliance Model
  • Master Contracts
  • Harmonized Data Collection
  • Streamlined Protocols
  • Larger Sample Sizes
  • Poised Research Teams
  • Patient Engagement
  • Safety Oversight
  • High Quality Evidence
Trial Innovation Network

What is the Vision?

• A clinical trials network that supports multi-center trials producing high quality evidence to inform clinical practice

• A Network focused on Operational Innovation, Operational Excellence, Quality & Collaboration
Trial Innovation Network

How Will We Turn Vision to Reality?

• **Strategy** - Focus on trials with patient-centered endpoints powered to answer clinical questions & inform clinical practice

• **Approach** - Optimize trials through quality by design, evidence-based recruitment strategies, patient engagement, & innovation

• **Collaborate** - Leverage the talent, expertise, & resources of the CTSA Program

• **Learn** - Create a national laboratory to study, understand, and improve multi-center clinical trials
Trial Innovation Network

- Duke Clinical Research Institute
- University of Utah Health Care
- Vanderbilt University Medical Center
- Johns Hopkins Medicine
- Tufts Medical Center
- CTSA Clinical & Translational Science Awards
- NIH National Institute on Aging
- NIH NLM
- NIH National Center for Advancing Translational Sciences

Partners:
- NIH ICs
- Federal
- Non-federal

Collaborative Strategic Management

Executive Committee

Evidence-based & innovative approaches to recruitment

Recruitment Innovation Centers (RICs)

Trial Innovation Centers (TICs)

Data Coordinating Centers

Patients
Active Initiatives

- **Limited Competition: Administrative Supplements to Enhance Network Capacity: Collaborative Opportunities for the CTSA Program (Admin Supp)**
  - PA-16-328
  - Expiration Date: March 2, 2019
  - The purpose of the administrative supplement is to enhance network capacity through implementing, assessing, and/or disseminating discoveries in methods, approaches, education, and training in clinical and translational science.
  - Funds will allow investigators from two or more different CTSA hubs to form collaborations within the CTSA network and/or with external partners to implement, assess, and/or disseminate discoveries across the network.

- **Limited Competition: Exploratory CTSA Collaborative Innovation Awards (R21) (link is external)**
  - PAR-16-343 ·
  - Expiration Dates July 31 2018
  - The purpose of this funding opportunity announcement (FOA) is to support highly innovative, exploratory collaborative research projects in the NCATS Clinical and Translational Science Award (CTSA) program, with the goal of assessing utility and feasibility of proposed innovation(s).
Office of Rare Diseases Research

• **Rare Diseases Clinical Research Network (RDCRN)**
  - 22 consortia at 250 institutions worldwide
  - Studying >200 diseases with 83 active protocols, and
  - More than 85 patient advocacy groups participating

• **Genetic and Rare Disease Information Center (GARD)**

• **Scientific Conferences Program**
  - Identify scientific opportunities and establish research agendas
  - Patients + NCATS + NIH ICs + FDA + Biopharma

• **Global Rare Disease Registry (GRDR)**
  - 15 GRDR patient registries + 19 existing registries
  - Ability to conduct cross-disease analysis and recruitment
TOOL KIT INITIATIVE

• To provide a single portal with resources that patient groups can readily access along with context.

• To convene partners across multiple sectors to create a central source for online educational and informational resources and tools.

• Rather than re-create existing resources, the goal is to facilitate coordination.

• To identify and fill gaps in online resources, and disseminate information to patient groups.

• To facilitate development of tools/resources for patient groups across the lifecycle of the drug development process.

• Keep it simple from a “how to” perspective
What is a “Tool”?  

**Approach:** If you were starting a patient advocacy group, what “how to” information would assist you?

**Examples:**

- References
  - Guidance
  - Policies
  - Scientific Papers
  - Position statements
  - Best practices
  - Data standards
  - Websites
  - White papers
- Instructional videos
- Software/Apps
- Collaborative interactions
With the goal of linking patient groups and communities to existing online tools and resources that are:

- Accessible
- User-friendly
- Functional and Interactive
- Searchable
- Part of a roadmap
- Other characteristics?

Discussion - What is the product?
Thank you

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