NIH Collaboratory:
Research Transformation in Progress

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Today’s Presentation

1. Collaboratory story and highlights
2. What are we working on now?
3. What should be next?
Collaboratory Story and Highlights
Millions

Patients walk through the doors of hospitals and clinics each year with questions about their health and their care.

How do we study their experiences to find answers and create solutions that change care and improve outcomes?
The Collaboratory Story

Initiated through the NIH Common Fund in 2012

Goal: Strengthen the national capacity to implement cost-effective large-scale research studies that engage health care delivery organizations as research partners

Vision: Support the design and execution of innovative pragmatic clinical trial Demonstration Projects to establish best practices and proof of concept
Embedded PCTs Bridge Research into Clinical Care

- Study designed with input from health system stakeholders
- Intervention incorporated into routine clinical workflow
- Data collected through EHR in health care settings
- Diverse, representative study populations
- Outcomes important to decision makers
Collaboratory Opportunities

• Amazing opportunity to use new information and clinical learning to inform and change the system
• The Collaboratory effort provides a fascinating vantage point for the transformation
  • Tremendous progress and opportunity
  • Show how to overcome the hurdles or speed bumps
Flow of Information

Demonstration Projects

Core Working Groups
Teleconferences
Steering Committee Meetings
Partner Organizations

Lessons

Living Textbook & Knowledge Repository
Grand Rounds, Presentations & Social Media
Guidance Documents & Journal Publications
What’s been contributed

• Significant body of knowledge on ethical & regulatory issues in PCTs
  • Consulted with OHRP
  • Conducted research on clinician & participant attitudes
  • Published special journal issue on challenges & best practices
• Biostatistical guidance in area of cluster randomized trials
• Created functional distributed research network
• Established policies and culture for data sharing
• Developed resources and guidance to support re-use of EHR data, integration of patient-reported outcomes, and partnerships with healthcare systems
• Shared case studies from our Demonstration Projects
NIH Collaboratory Publications

80 total publications in peer-reviewed journals
NIH Collaboratory Presentations

>150 total conference presentations or symposia
NIH Collaboratory Presentations

>150 total conference presentations or symposia

Health Systems Partnerships

NIH Collaboratory

Health Care Systems Research Collaboratory

Rethinking Clinical Trials
The Living Textbook of Pragmatic Clinical Trials

www.rethinkingclinicaltrials.org
Distributed Research Network

Enables investigators to collaborate in the use of electronic health data while safeguarding protected health information.

Curated Distributed Data Using a Common Data Model

Baseline data to support planning of studies

Queries

Results

Clinical trials

Retrospective & prospective observational studies

Queries

Results
Demonstration Projects

- Collaboratory pragmatic trials conducted within health care systems to address questions of major public health importance
- Span multiple Institutes & Centers
- 1-year planning phase
- Implementation phase
What our projects contribute...

LESSONS LEARNED
Daily Chlorhexidine Bathing in General Hospital Units – Results of the ABATE Infection Trial (Active BAThing to Eliminate Infection)

Primary Results of the Time to Reduce Mortality in End-Stage Renal Disease (TiME) Trial: A Pragmatic Trial Demonstration Project of the NIH Health Care Systems Research Collaboratory
What are we working on now?
July 2018

NIH awards support for 6 new Demonstration Projects
ACP PEACE  Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly

- Cluster randomized trial testing whether clinician communication skills training and patient video decision aids will increase **advance care plan completion** in patients >65 with advanced cancer
- 4,500 patients in 36 oncology clinics across 3 systems
HiLo  Pragmatic Trial of Higher vs. Lower Serum Phosphate Targets in Patients Undergoing Hemodialysis

- Cluster randomized trial testing whether less stringent control of serum phosphate levels will yield non-inferior rates of all-cause hospitalization in patients with end-stage renal disease undergoing hemodialysis
- ~4,400 patients across >100 dialysis facilities
GGC4H  *Guiding Good Choices for Health*

- Cluster randomized trial testing whether an anticipatory guidance curriculum for parents of early adolescents will reduce **behavioral health problems and health service utilization**
- 72 pediatricians across 3 health systems; ~4,500 families
EMBED Pragmatic Trial of User-Centered Clinical Decision Support to Implement EMergency Department-Initiated BuprenorphinE for Opioid Use Disorder

• Cluster randomized trial testing the effect of user-centered computerized clinical decision support on rates of emergency department–initiated buprenorphine/naloxone and referral for ongoing medication-assisted treatment in patients with opioid use disorder
Nudge  Personalized Patient Data and Behavioral Nudges to Improve Adherence to Chronic Cardiovascular Medications

• Patient-level randomized pragmatic trial comparing the effects of digital interventions (text messages and chat bot) on medication adherence in patients with chronic CV conditions
• 3 health systems
PRIM-ER  Primary Palliative Care for Emergency Medicine

• Cluster randomized trial testing the effects of implementing primary palliative care in emergency medicine on healthcare utilization and survival
• 35 emergency departments across 18 health systems
## Summary of New Projects

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACP PEACE</td>
<td>Patients with advanced cancer</td>
<td>Clinician communication skills training and patient video decision aids for advanced care planning</td>
<td>Advance care plans completion; medical orders for resuscitation preferences; palliative care consultations; hospice use</td>
</tr>
<tr>
<td>HiLo</td>
<td>Patients undergoing hemodialysis</td>
<td>Liberalizing serum phosphate target</td>
<td>Rate of hospitalization</td>
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<td>Adherence to CV medications</td>
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<tr>
<td>PRIM-ER</td>
<td>Older adults (&gt;65 years)</td>
<td>Palliative care education; simulation-based workshops; clinical decision support; provider audit and feedback</td>
<td>Healthcare utilization and survival</td>
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Sharing Challenges & Solutions

Collaboratory videos & interviews

Advice to New Pragmatic Trial Investigators
from NIH Research Collaboratory

An Interview with Dr. Jerry Jarvik
Principal Investigator, LUMBAR Imaging with Reporting of Etiology and Etiology of Low Back Pain

AN INTERVIEW WITH DR. JERRY JARVIK
Principal Investigator, Lumbar Imaging with Reporting of Etiology (LIRE) Trial

Background
Over 15 years ago, Dr. Jarvik was involved in a Veterans Affairs (VA) study in which they obtained lumbar spine magnetic resonance imaging (MRI) to assess the impact of anatomic abnormalities on back pain and followed them longitudinally to see who developed back pain. They generated, in essence, a "normal range" of MRI findings in patients without back pain. Shortly thereafter, a paper was published by Martin Roland and colleagues in the Journal of Bone & Joint Surgery that questioned the clinical importance of MRI spine imaging findings and noted radiologists had consistently described abnormalities in the imaging reports of the lumbar spine. Surprised by the paper, Dr. Jarvik reabstracted the information from the previous report and normal range imaging and created a large database of imaging results from patients with normal findings. Using these results, he generated a "normal range" of MRI findings in patients without back pain. The study confirmed that MRI findings were not predictive of back pain and could not be used to identify patients with back pain.

Design
LIRE II is a cluster-randomized trial with a stepped-wedge crossover design. The primary unit of randomization is the clinic cluster, rather than the primary care provider or the patient. The trial was designed to test the effectiveness of a multidisciplinary intervention that includes education about back pain, physical therapy, and medication management. The study was conducted at 100 clinics in 4 health systems: Kaiser Permanente Northern California, Henry Ford Health Systems, Group Health in Seattle, and the University of North Carolina. The baseline data were collected before the intervention began, and the intervention was then rolled out to all clinics. The study was designed using a stepped-wedge crossover design, where clusters receive the intervention during the study period. At the end of the study, all clinics will have received the intervention and will be assessed for changes in clinical outcomes.
Rethinking Clinical Trials: A Living Textbook of Pragmatic Clinical Trials

Welcome to the Living Textbook of pragmatic clinical trials, a collection of knowledge from the NIH Health Care Systems Research Collaboratory. Pragmatic clinical trials are performed in real-world clinical settings with highly generalizable populations to generate actionable clinical evidence at a fraction of the typical cost and time needed to conduct a traditional clinical trial. They present an opportunity to efficiently address critical knowledge gaps and generate high-quality evidence to inform medical decision-making. However, these trials pose different challenges than are typically encountered with traditional clinical trials. The Living Textbook reflects a collection of expert consensus regarding special considerations, standard approaches, and best practices in the design, conduct, and reporting of pragmatic clinical trials. Given the rapid pace of change in this field, this electronic textbook will continue to be added to and updated.

GET STARTED

What is the NIH COLLABORATORY?

What is a PRAGMATIC CLINICAL TRIAL?

ENGAGING STAKEHOLDERS and building partnerships to ensure a successful trial

TRAINING RESOURCES
Partner Organizations

Grand Rounds
- Shared PCORnet/Collaboratory forum
- Frequent presentations by partner organizations

Collaboration on
- Workshops
- Regulatory/ethics publications

Shared tools & resources
- Links to external resources in Living Textbook
What should be next?
Value of Pragmatic Clinical Trials

- Embedded Research Leverages Health Systems
  - What are the fixed costs being leveraged?
    - Large?
  - What are the variable costs?
    - Small?
- What’s the net value?
  - Potential return of investment
- What’s the ideal state for economies of scale?
  - Multiple trials can achieve highest value
Expanded Education and Training

• Training for new investigators/NIH Staff on PCT methods
• Publicly available training materials, such as handouts, slides, videos, Living Textbook chapters/additions, or other content to be made available on the Collaboratory website.
Regulatory & Ethics

- Ethical and practical issues associated with incidental findings
  - Planned Administrative Supplement application
- Data safety and monitoring
- Nested Studies
Stakeholder Engagement

- Further stakeholder engagement
  - Empirical studies
  - How to build relationships with health systems
  - Address barriers with health system leaders
  - Healthcare plans
  - Clinicians
Sustainability for embedded PCTs

- Define what’s needed
  - What will it take for health systems to make this routine as opposed to the exception?
- Establishing a roadmap for eliminating barriers
  - Regulatory/Ethics
  - Engagement
  - Costs
  - Data silos
  - Others....
Conclusions
Conclusions

• Take advantage of continued interest in real world evidence and learning health systems
• Multiple lessons learned from rethinking research integrated with practice
• Cost-effective, large-scale research is possible and we have the charge to scale it...
  • By learning, sharing, and helping the ecosystem evolve
For More Information

- **Living Textbook**
  - Comprehensive, searchable information on design, conduct & dissemination of embedded PCTs
  - [www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)

- **Knowledge Repository**
  - Archives for the Living Textbook including presentations, videos, stakeholder interviews, guidance documents & more

- **Twitter**
  - @Collaboratory1
  - @PCTGrandRounds