NIH Collaboratory Rethinking Clinical Trials®

Health Care Systems Research Collaboratory

NIH Collaboratory: Research Transformation in Progress

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Today's Presentation

Collaboratory story and highlights
 What are we working on now?
 What should be next?



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Collaboratory Story and Highlights



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



National Institute of Health 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

Data collected through EHR in health care settings

Outcomes important to decision makers

Intervention incorporated into routine clinical workflow

Diverse, representative study populations

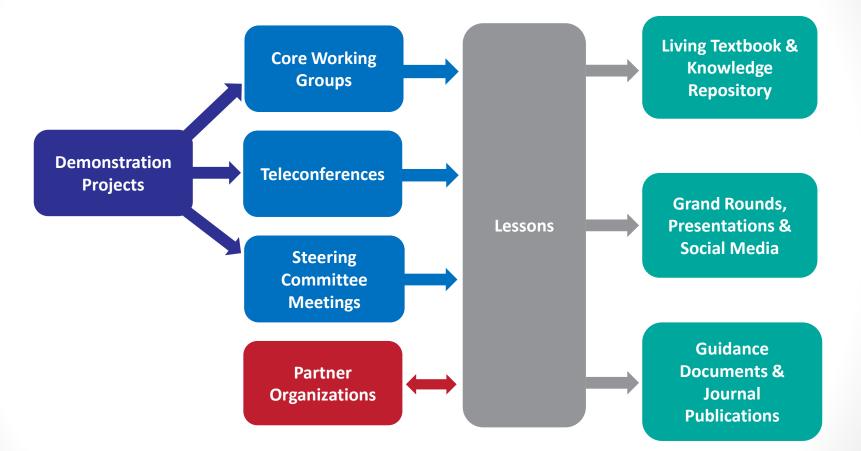
Collaboratory Opportunities

- 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











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

Statistical Issues in Clinical Trials **Academy Health OHA Transformation Center PMI Am Society Bioethics** Seattle Symposium on Data Analytics >150 NIH **NCURA ASCP** Natl Advisory Council for Nursing Home Research PRIM&R total conference **ISPOR HMORN ENAR** IOM presentations ACOS **AMWA** or symposia **RSA ASNR** Health Systems Partnerships **PMR Sports Medicine Joint Summits** AMIA NIH Collaboratory Rethinking Clinical Trials® Health Care Systems Research Collaboratory

The Living Textbook of Pragmatic Clinical Trials



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

ENGAGING STAKEHOLDERS >>

and building partnerships to ensure a successful trial

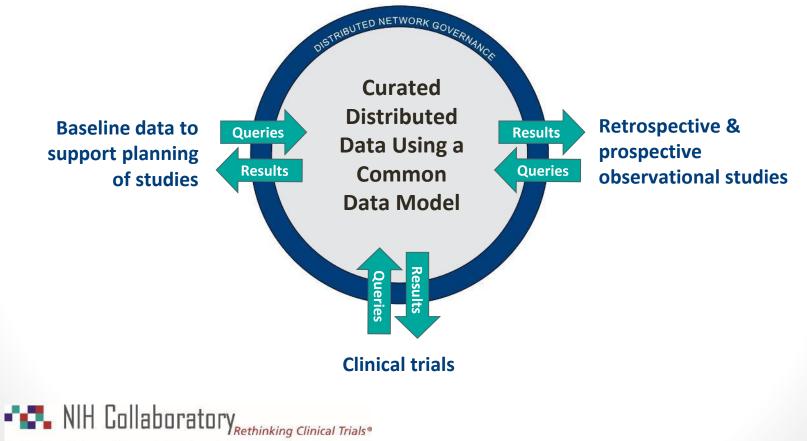
What is the NIH COLLABORATORY? (>)

www.rethinkingclinicaltrials.org



Distributed Research Network

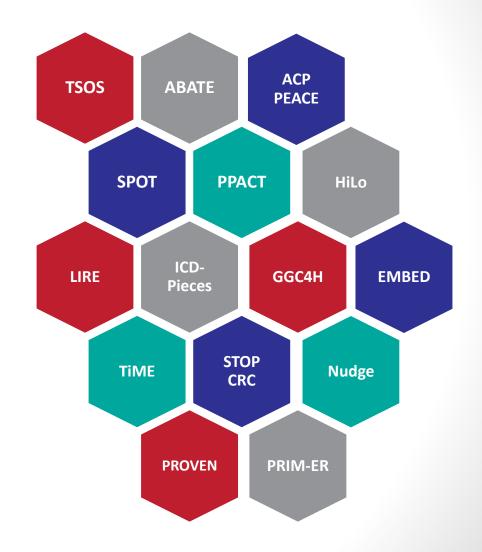
Enables investigators to collaborate in the use of electronic health data while safeguarding protected health information



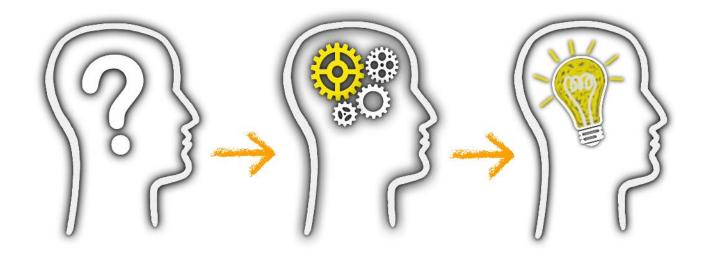
Demonstration Projects

- 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

• NIH Collaboratory Rethinking Clinical Trials®

JAMA Internal Medicine | Original Investigation

Effectiveness of a Mailed Colorectal Cancer Screening Outreach Program in Community Health Clinics The STOP CRC Cluster Randomized Clinical Trial

Gloria D. Coronado, PhD; Amanda F. Petrik, MS; William M. Vollmer, PhD; Stephen H. Taplin, MD, MPH; Erin M. Keast, MPH; Scott Fields, MD; Beverly B. Green, MD, MPH



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

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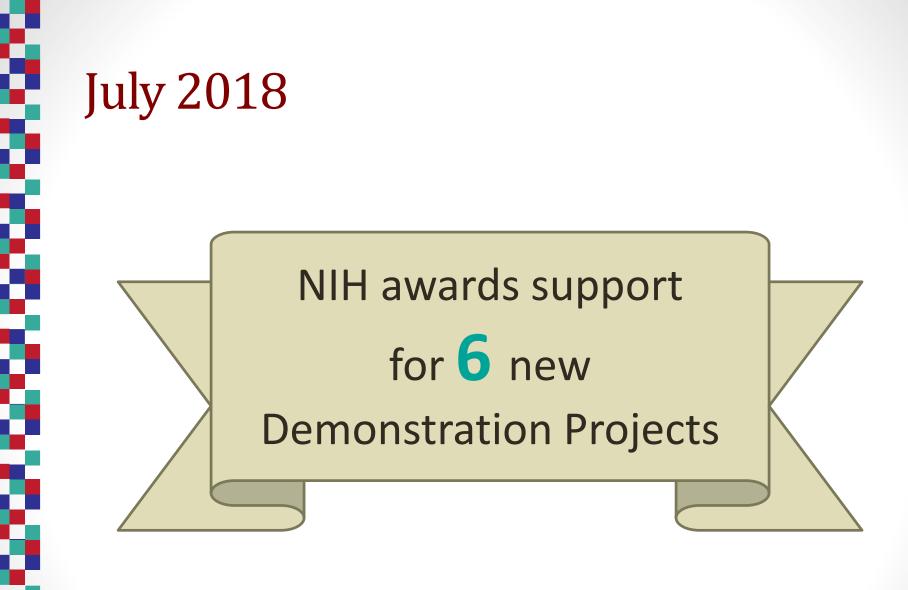
Primary Results of the Time to Reduce Mortality in End-Stage Renal Disease (TiME) Trial: A Pragmatic Trial Demonstration Project of the NIH Health Care Systems Research Collaboratory



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What are we working on now?





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

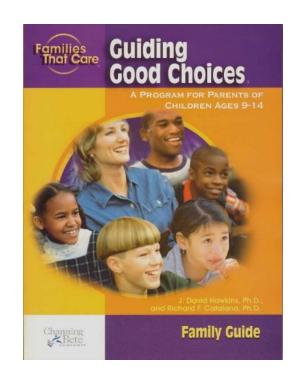




GGC4H Guiding Good Choices for Health

- 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 usercentered 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

Study	Population	Intervention	Outcome
ACP PEACE	Patients with advanced cancer	Clinician communication skills training and patient video decision aids for advanced care planning	Advance care plans completion; medical orders for resuscitation preferences; palliative care consultations; hospice use
HiLo	Patients undergoing hemodialysis	Liberalizing serum phosphate target	Rate of hospitalization
GGC4H	Parents of early adolescents	Anticipatory guidance curriculum	Behavioral health problems; health service utilization
EMBED	Patients with opioid use disorder	User-centered computerized clinical decision support	Rate of emergency department—initiated buprenorphine/naloxone; referral for ongoing medication assisted treatment
Nudge	Patients with chronic CV conditions	Text messages and chat bot	Adherence to CV medications
PRIM-ER	Older adults (>65 years)	Palliative care education; simulation- based workshops; clinical decision support; provider audit and feedback	Healthcare utilization and survival



Sharing Challenges & Solutions

Collaboratory videos & interviews



Advice to New Pragmatic Trial Investigators from NIH Research Collaboratory PRO 1 month ago

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AN INTERVIEW WITH DR. JERRY JARVIK

Principal Investigator, Lumbar Imaging with Reporting of Epidemiology (LIRE) Trial concorno April 20, 2015

Background update on the Lumbar Over 15 years ago, Dr. Jarvik was Imaging with Reporting of involved in a Veteran's Attains (VA) study in which they obtained lumbar Foidemiology (LIRF) Trial at the April 2015 Collaboratory spine magnetic resonance image (MRI) ring Committee Meet reports of 148 asymptomatic patients (ricw slides). The LIRE trial ino back pain) and followed them is about halfway through iongitudinally to see who developed back pain. They generated, in essence, a "normal range" of MRI findings in its initial enrollment period with over \$2,000 patients patients without back pain. Shortly thereafter, a paper was published by Martin Roland and Maurits van Tulder that ourstioned the clinical importance of MRI spine imaging findings and urged radiologists to include prevalence information in their imaging reports of Even the simplest the lumbar spine ideas are complex Inspired by the paper, Dr. Jarvik to implement and incorporated the information from the rigorously study. VA cohort study--the normal range-into the routine imaging at the University of Washington Medical center This information was available as a template that could be inserted into the radiologist report. As it turned out, only a few of the radiologists used this template, giving Dr. Jarvik the opportunity to investigate the data to - NIH Collaboratory determine if epidemiologic information

had any effect on patient outcomes. He was ourprised by the results. Even shough they had relavely small numbers, there was evidence that the inclusion of the epidemiological information decreased utilization of spine-related interventions, and even more importantly, decreased opioid prescription rates.

That was the spark of the LIRE trial, a pragmatic trial to answer this question: Does inserting prevalence information decrease downstream spine-related utilization or opioid prescribing rates by primary care physicians?

Design

LIRE 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. They are randomizing 100 clinics in 4 health systems (Kaiser Permanente Northen California, Henry Ford Health Systems Group Health in Seattle, and the Mayo Clinici. For the stepped wedge design, they have five waves (steps) of randomization: a fifth of the 100 clinics are exposed to the intervention during each wave (see Figure 1). By the end of the study, all 100 clinics will have had the intervention - hence a "crossover design; all clinics eventually crossover from the control arm (no intervention)

Training Resources for Investigators

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	DESIGN	к	

Rethinking Clinical Trials: A Living Textbook of Pragmatic Clinical Trials



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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? ③

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









NIH Collaboratory Newsletter

Subscribe to this convenient monthly wrap-up: www.rethinkingclinical trials.org/newslettersubscribe/



The newsletter is intended to provide a convenient monthly wrap-up of NIH Collaboratory news, along with featured stories and a look at what's coming in the month ahead. We hope you'll find it useful, and we'd love to hear your feedback. Please let us know what you think.

Living Textbook

Grand Rounds Hub

Recent News

Reflections From the Patient-Reported Outcomes

Core: Dr. Kevin Weinfurt, chair of the Patient-Reported Outcomes (PRO) Core, shares the successes of the first 5 years of the Core and looks ahead to the coming years. "We need to determine when PROs are essential, supporting, or not at all informative for the clinical questions. This gets at the value proposition: When are they of value and to whom?"



NCI Announces Training Institute in Dissemination

and Implementation Research in Cancer: The National Cancer Institute is accepting applications for a Training Institute in Dissemination and Implementation Research in Cancer (TIDIRC). Designed for investigators at all levels, this cancerfocused training program will consist of a 4-month online course and a 2-day in-person training. The application window will close on February 9.





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What should be next?

Value of Pragmatic Clinical Trials

Value

- 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.



- 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....





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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

Knowledge Repository

• Archives for the Living Textbook including presentations, videos, stakeholder interviews, guidance documents & more

Twitter

- @Collaboratory1
- @PCTGrandRounds

