

Collaboratory Coordinating Center Overview and Goals

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Duke Clinical Research Institute



Agenda

1. What is the Collaboratory Coordinating Center trying to do?
2. How are we doing it?
3. How do we share what we've learned?
4. Conclusions

1

What is the NIH
Collaboratory Coordinating
Center trying to do?



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**?

Increasing System-ness...

U.S. Hospitals & physicians in Health Systems

2000: **5810 Hospitals**

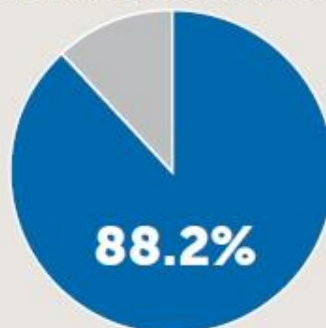
2016: 626 Health systems

2020: ??

By the end of 2016, there were **626 health systems*** in the United States.

U.S. hospitals and physicians in health systems

Percentage of U.S. hospital beds in systems

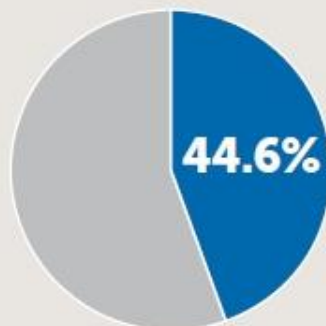


69.7% of U.S. hospitals are in health systems



91.6% of U.S. hospital discharges are from system hospitals

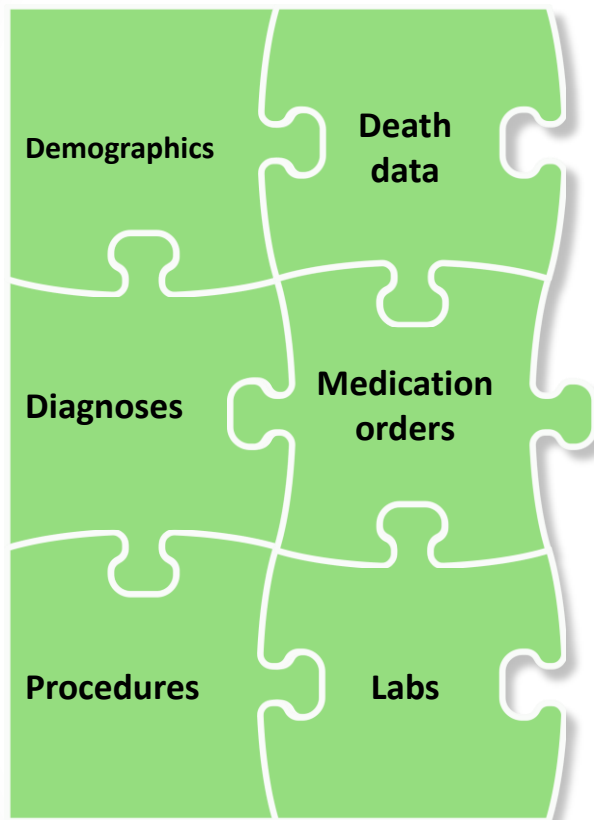
Percentage of U.S. physicians in health systems



42.7% of U.S. primary care physicians are in health systems

Note: The hospital figures represent all non-Federal general acute care hospitals in the United States.

Data Everywhere...



How do you include this disruptive technology...called randomization?

EFFECTIVENESS OF INTRAVENOUS THROMBOLYTIC TREATMENT IN ACUTE MYOCARDIAL INFARCTION

GRUPPO ITALIANO PER LO STUDIO DELLA STREPTOCHINASI NELL'INFARTO MIOCARDICO (GISSI)*

Summary In an unblinded trial of intravenous streptokinase (SK) in early acute myocardial infarction, 11 806 patients in one hundred and seventy-six coronary care units were enrolled over 17 months. Patients admitted within 12 h after the onset of symptoms and with no contraindications to SK were randomised to receive SK in addition to usual treatment and complete data were obtained in 11 712. At 21 days overall hospital mortality was 10·7% in SK recipients versus 13% in controls, an 18% reduction ($p=0\cdot0002$, relative risk 0·81). The extent of the beneficial effect appears to be a function of time from onset of pain to SK infusion (relative risks 0·74, 0·80, 0·87, and 1·19 for the 0–3, 3–6, 6–9, and 9–12 h subgroups). SK seems to be a safe drug for routine administration in acute myocardial infarction.

The Lancet · Saturday 22 February 1986



“It started with no funding and skepticism in some quarters but today GISSI is recognized as an Italian achievement that has changed cardiology treatment worldwide.”

 NIH Collaboratory

7 Health Care Systems Research Collaboratory

Rethinking Clinical Trials

<http://eurheartj.oxfordjournals.org/content/31/9/1023.full>

Re-engineering the Clinical Research Enterprise



Increasing Level of Difficulty

<p>Plan and start a few demonstration networks Simplify complex regulatory systems – demonstration projects Plan for networks in place for all institutes</p>	<p>Funding mechanism to sustain national system through consensus of all constituents (“1% solution”) Simplified regulatory system in place for networks</p>	<p>National Clinical Research System creates effectiveness data that moves rapidly into the community AND data on outcomes and quality of care; sustained efficient infrastructure to rapidly initiate large clinical trials; scientific information for patients, families, advocacy groups</p>
<p>Establish repositories of biological specimens and standards for collection Standardize nomenclature, data standards, core data, forms for most major diseases Start a library of these elements shared between institutes and NLM Develop efficient network administration infrastructure at NIH Develop standards for capturing images for research</p>	<p>Data standards shared across NIH institutes Funding mechanisms evaluated to determine which are most efficient</p>	<p>ONE medical nomenclature with national data standards (agreed to by NIH, CMS, FDA, DOD, CDC) Data standards updated “in real time” through networks National repository of images and samples Critical national “problem list” Most efficient network funding mechanisms in place across NIH</p>
<p>Create NIH standards to provide “safe haven” for clinical research Inventory and evaluate existing public-private partnerships, networks, CR institutions, and regulatory systems Establish FORUM(S) of <u>all</u> stakeholders Establish standards for and pilot creation of a National Clinical Research Corps Demonstration/planning grants to enhance/evaluate/develop model networks</p>	<p>NIH standards for safe haven in place Regulations and ethics harmonized with FDA, CMS Public private partnership mechanisms in place 100,000 members of certified “Clinical Research Corps” Standards shared across NIH</p>	<p>Participation in research is a professional standard (taught in all health professions schools) Study, evaluation and training regarding clinical research a part of every medical school, nursing school, pharmacy school Clinical research practices documented and updated regularly to maintain safe haven Networks provide detailed training about network specific issues</p>

1-3 years

4-7 years

8-10 years

The Collaboratory Story



Initiated through the NIH Common Fund in 2012

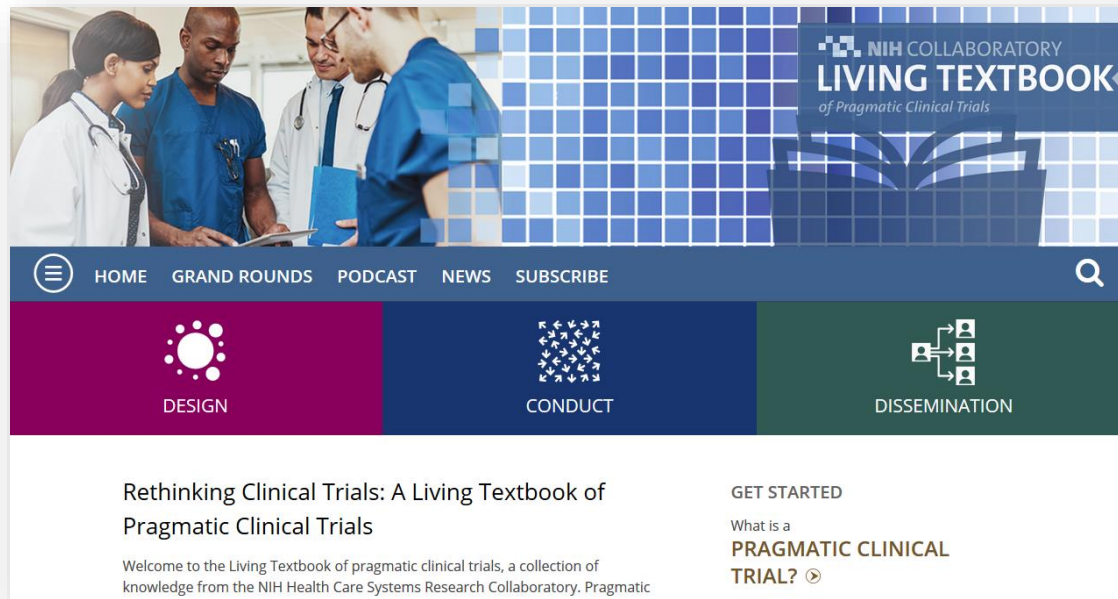


Goal: Strengthen the national capacity to implement cost-effective large-scale research studies that engage health care delivery organizations as research partners



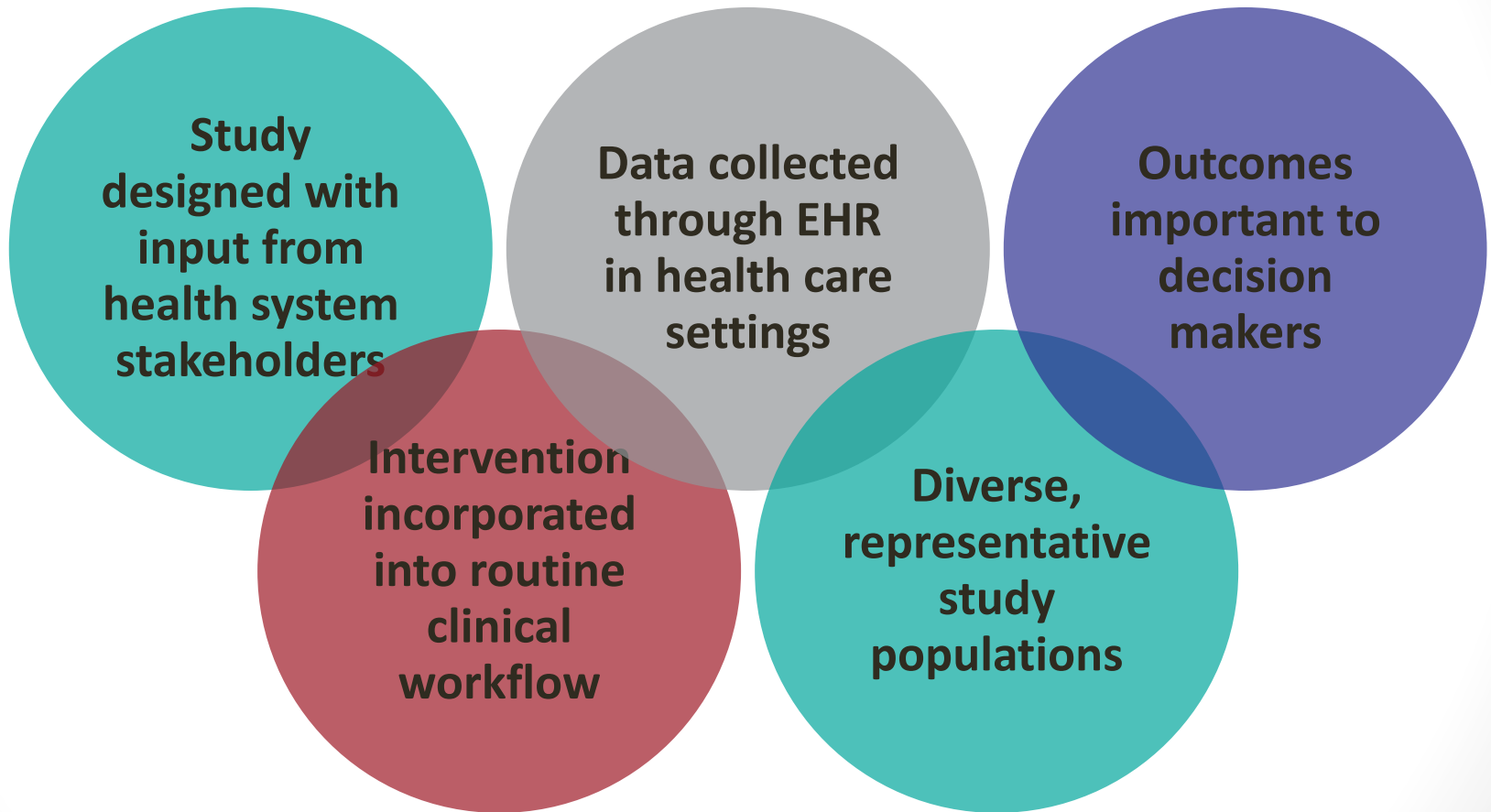
Vision: Support the design and execution of innovative pragmatic clinical trial Demonstration Projects to establish best practices and proof of concept

Evolving Health Care Systems Research Collaboratory



- Pragmatic trial designs
- Electronic health records as core data collection instrument
- Collaboration of ≥ 2 integrated health systems
 - 7 funded for planning phase in 1st round
 - 3 funded in 2nd round
 - 6 funded in 3rd round

Embedded PCTs Bridge Research into Clinical Care



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



Accelerating Progress

- If we reach a common understanding of key issues, supported by the Core Working Groups, the learning health system will accelerate through policy, process and practice



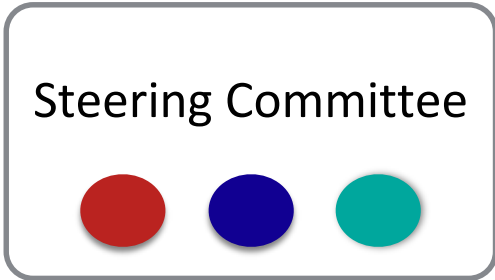


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How are we doing it?

*Structure of the
Coordinating Center*

Collaboratory Structure



Coordinating Center Members

- **Duke Clinical Research Institute**
 - Principal Investigators: Adrian Hernandez, MD, MHS; Lesley Curtis, PhD; Kevin Weinfurt, PhD
- **Harvard Pilgrim Health Care Institute**
 - Principal Investigator: Richard Platt, MD, MSc
- **Group Health Research Institute**
 - Principal Investigator: Eric Larson, MD, MPH, MACP
- **Johns Hopkins Berman Institute of Bioethics**
 - Principal Investigator: Jeremy Sugarman, MD, MPH, MA

Core Working Groups

- Guide and support Demonstration Projects
- Disseminate knowledge
- Chair from Coordinating Center and representatives from NIH and Demonstration Projects

Biostatistics and Study Design

Electronic Health Records

Health Care Systems
Interactions

Patient-Reported Outcomes

Regulatory/Ethics



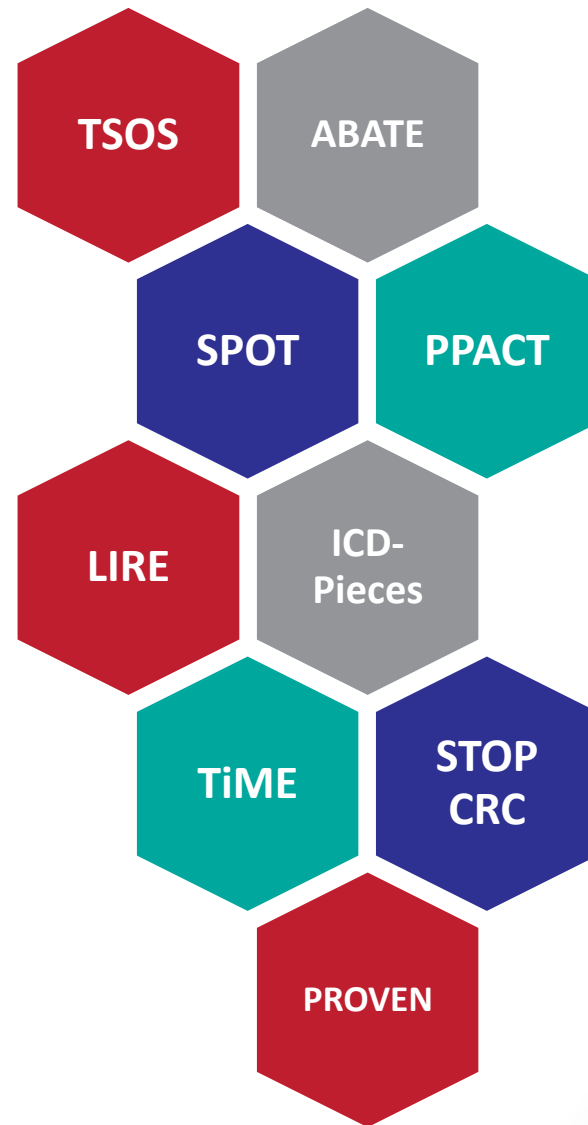
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How are we doing it?

Demonstration Projects

Demonstration Projects

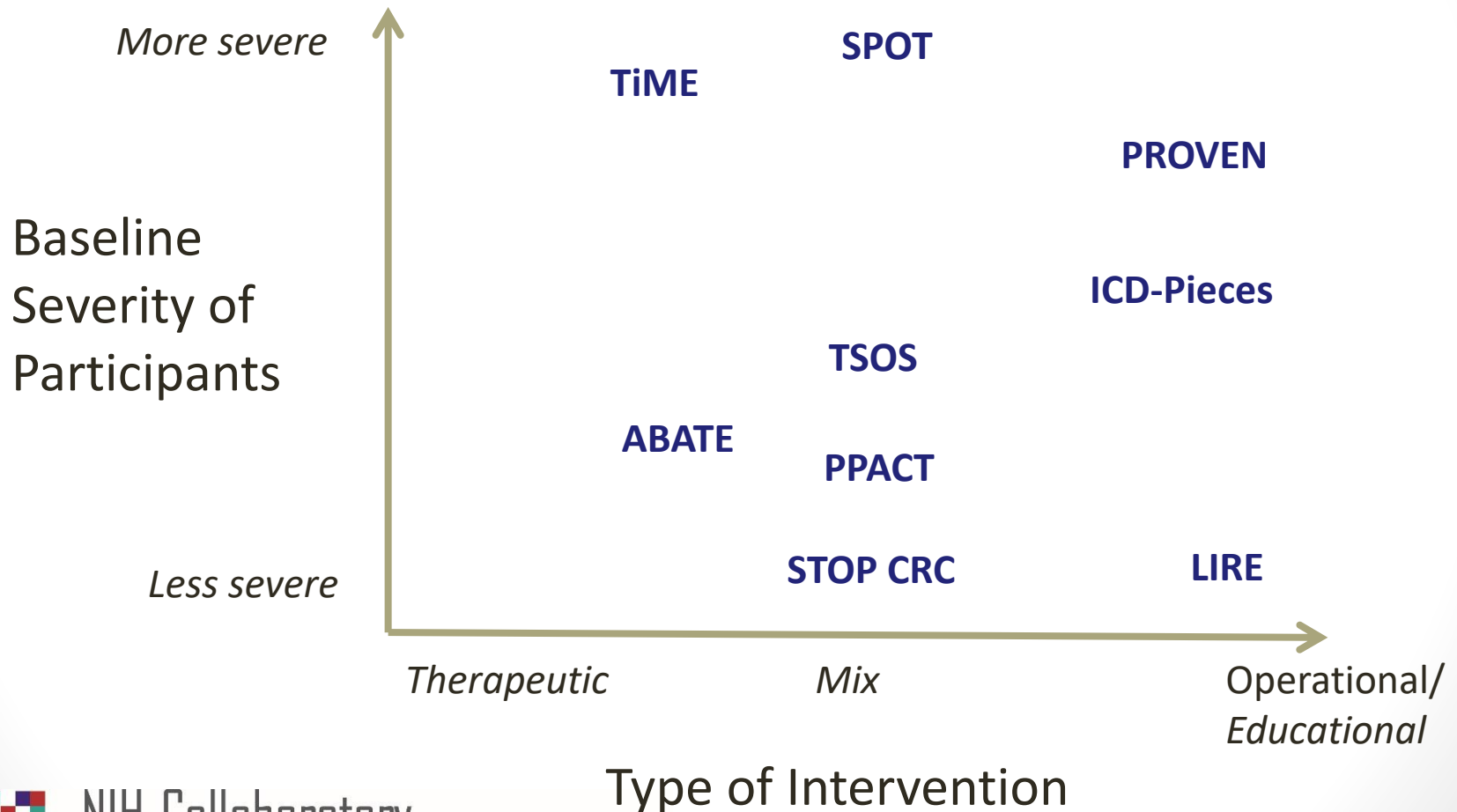
- Collaboratory pragmatic trials conducted within health care systems to address questions of major public health importance
- Spanning 12 NIH Institutes & Centers
- 1-year planning phase
- Implementation phase



Collaboratory Trials

Study	Population	Intervention	Outcome
ABATE	Non-ICU patients	Decolonization strategies	MRSA & VRE clinical cultures
ICD-Pieces	Comorbid diabetes, CKD & hypertension	Collaborative primary care program	All-cause hospitalizations for 3 conditions
LIRE	Low back pain	Insertion of epidemiologic benchmarks in lumbar spine imaging reports	Relative value unit for spine-related interventions
PPACT	Non-malignant chronic pain	Multidisciplinary behavioral care management	Brief pain inventory scale
PROVEN	Nursing home patients	Advance care planning video (behavioral program)	Hospitalizations; Presence of advance directives
SPOT	Suicidal ideation or depression	Collaborative care behavioral program (care management & skills training)	Suicide attempts
STOP CRC	Adults aged 50-75	Direct mail CRC screening program (FIT kit)	Increased CRC screening rates
TIME	Dialysis patients	Dialysis session of at least 4.25 hours	All-cause mortality; Hospitalization
TSOS	Traumatic injury	Collaborative care management program	PTSD checklist; PHQ-9 scale; Alcohol use disorders; SF-12/36

UH2s/UH3s by Severity and Intervention



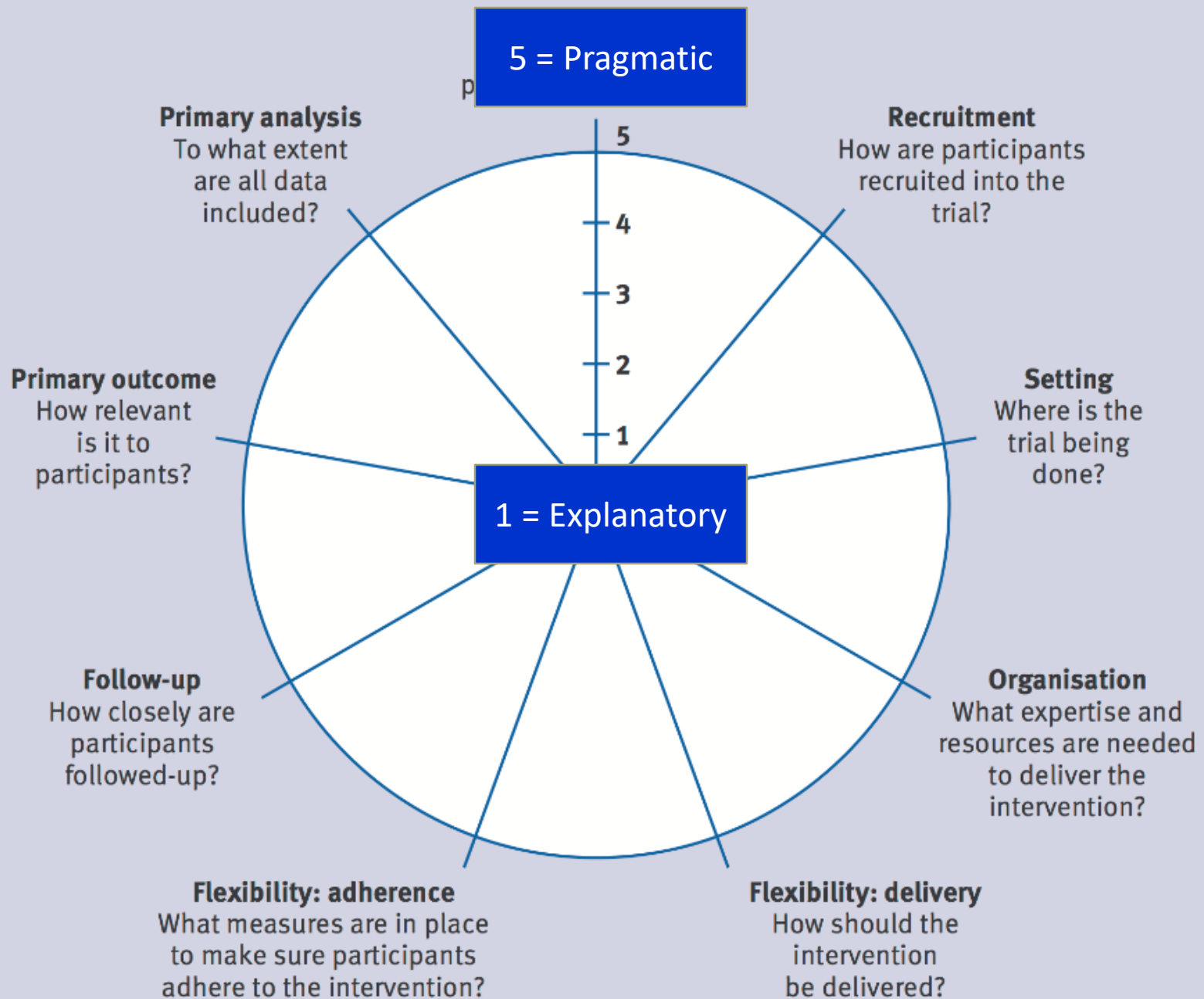


Pragmatic Trial	Target N	Health Care Systems
Ma		ters
M		S
D		CS
S		CS
C		IN
M		rp.
Ba		HCS
Hospital Infections	285,000	50 Hospitals in HCA

~ Cost/Patient

Average = \$1,500

Range = \$25 - \$7,300



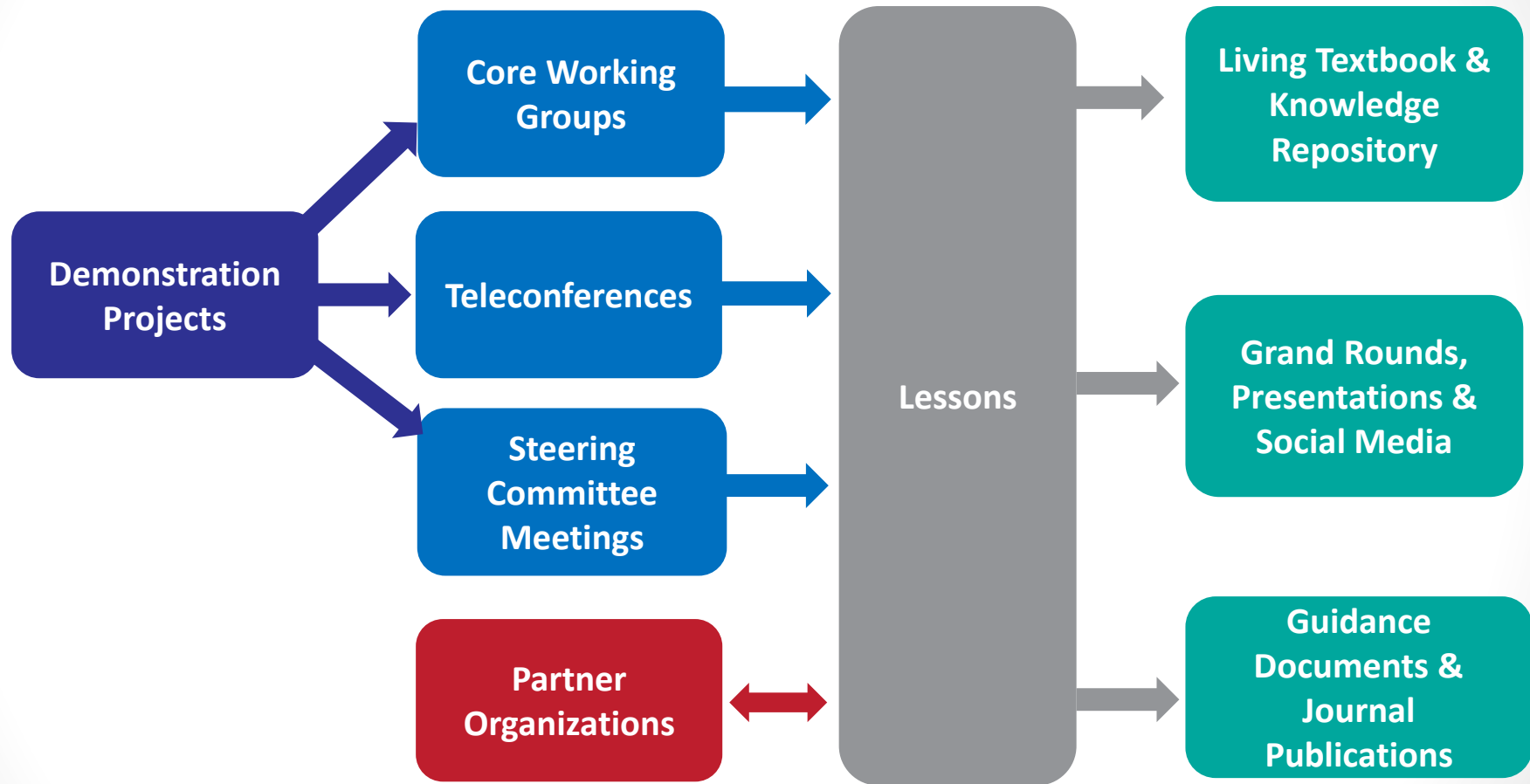


2

How are we doing it?

*Process for Identifying
and Responding to Issues*

Flow of Information



Issue Tracker

Challenge	Raised by (PI)	Category	Date Reported	Status Updated	Status at Last Check In
Culture: Beginning second set of site visits; culture change is needed around beliefs about infection control.	Huang	Practice norms & workflow	9/12/14	2/25/15	Ongoing – Investigators continuing follow up site visits for facilities struggling with compliance and overuse of CHG.
A radiologist unhappy with the intervention and how it changes the format of radiology reports. This might lead to a site withdrawing.	Jarvik	Engagement	4/24/15	4/24/15	New challenge: We're currently doing what we can to work through this issue.

Barriers as Reported by PIs

Barrier	Level of Difficulty				
	1	2	3	4	5
Enrollment and engagement of patients/subjects	● ● ●		●	● ● ●	
Engagement of clinicians and health systems		● ● ● ●	●		●
Data collection and merging datasets	●	● ●	● ● ●		
Regulatory issues (IRBs and consent)	● ● ●	●	●		●
Stability of control intervention		● ● ● ●	●		●

1 = Little difficulty
5 = Extreme difficulty

- STOP CRC
- LIRE
- SPOT
- PPACT
- TiME
- ABATE

Sharing Challenges & Solutions

Teleconferences, SC Meetings,
Collaboratory Videos & Interviews



Advice to New Pragmatic Trial Investigators

from NIH Research Collaboratory **PRO** 1 month ago

AN INTERVIEW WITH DR. JERRY JARVIK
Principal Investigator, Lumbar Imaging with Reporting of Epidemiology (LIRE) Trial
conducted April 20, 2015

Dr. Jarvik provided an update on the Lumbar Imaging with Reporting of Epidemiology (LIRE) Trial at the April 2015 Collaboratory Steering Committee Meeting (view slides). The LIRE trial is about halfway through its initial enrollment period with over 52,000 patients enrolled.

Background
Over 15 years ago, Dr. Jarvik was involved in a Veteran's Affairs (VA) study in which they obtained lumbar spine magnetic resonance image (MRI) reports of 148 asymptomatic patients (no 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 Maurits van Tulder that questioned the clinical importance of MRI spine imaging findings and urged radiologists to include prevalence information in their imaging reports of the lumbar spine. Inspired by the paper, Dr. Jarvik incorporated the information from the 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 determine if epidemiologic information

had any effect on patient outcomes. He was surprised by the results. Even though they had relatively 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 Northern California, Henry Ford Health Systems, Group Health in Seattle, and the Mayo Clinic). 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)

Even the simplest ideas are complex to implement and rigorously study.

NIH Collaboratory
Health Care Systems Research Collaboratory

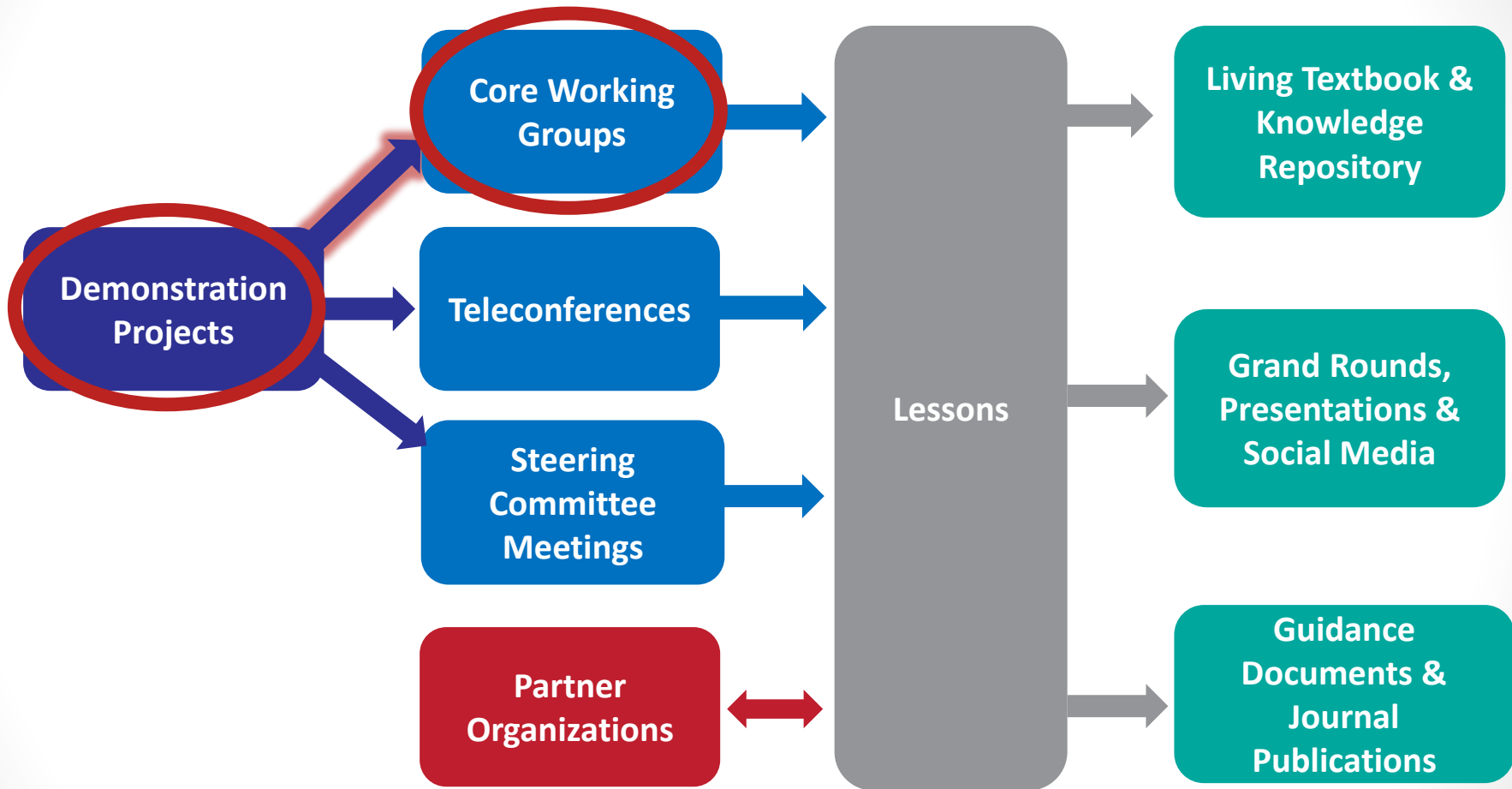


3

How do we share what we learn?

Process for Dissemination

Flow of Information



Biostatistics and Study Design Core

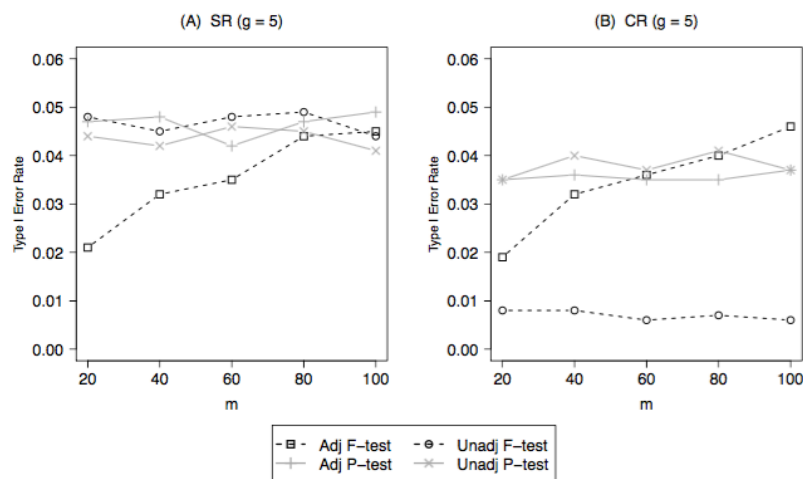


Elizabeth DeLong, PhD, MA
Duke Clinical Research Institute

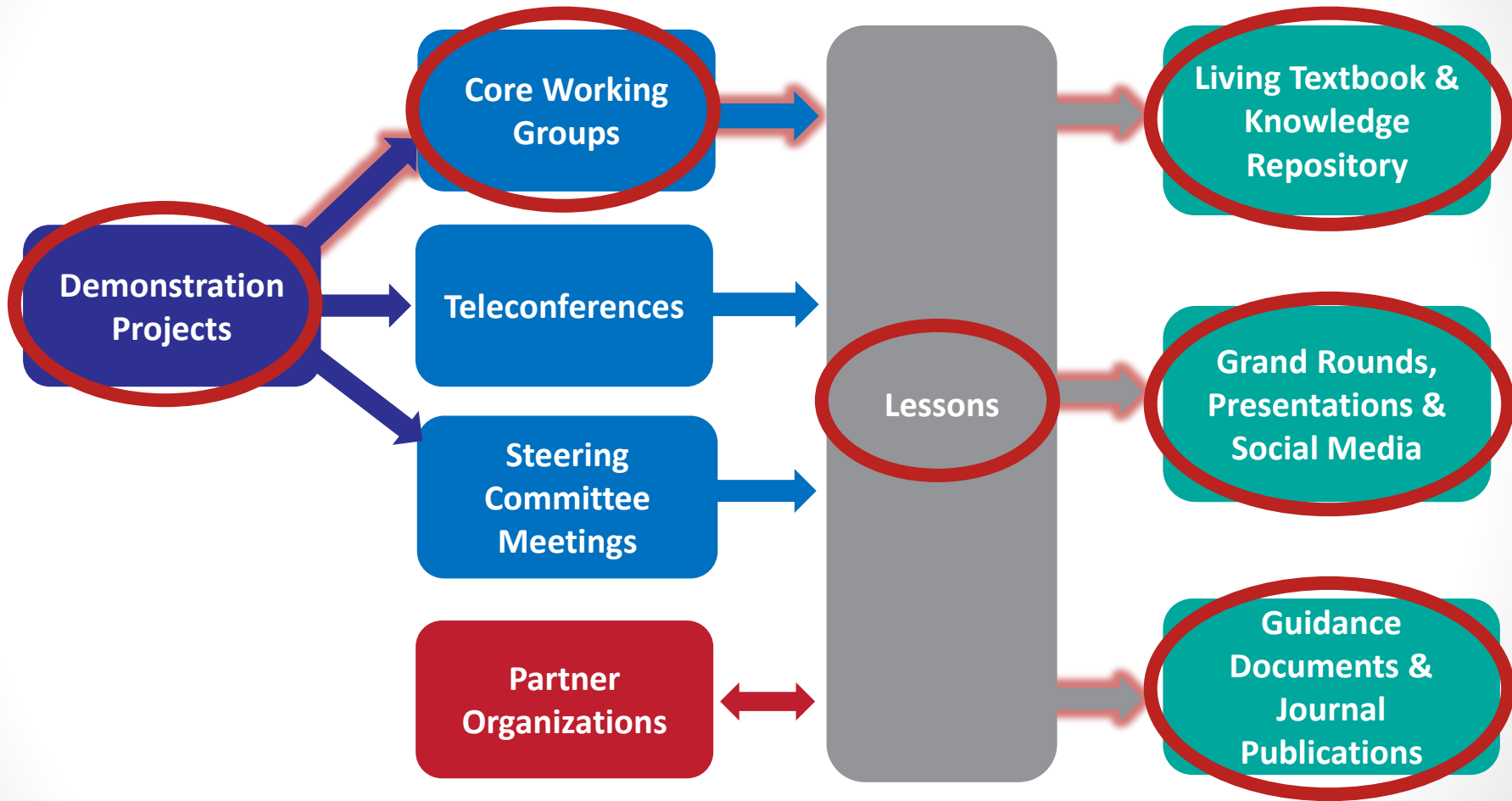
Simulation Studies



Lessons re: Design & Analysis



Flow of Information



Dissemination

Statistics
in Medicine

Research Article

Received XXXX

(www.interscience.wiley.com) DOI: 10.1002/sim.0000

An evaluation of constrained randomization for the design and analysis of group-randomized trials

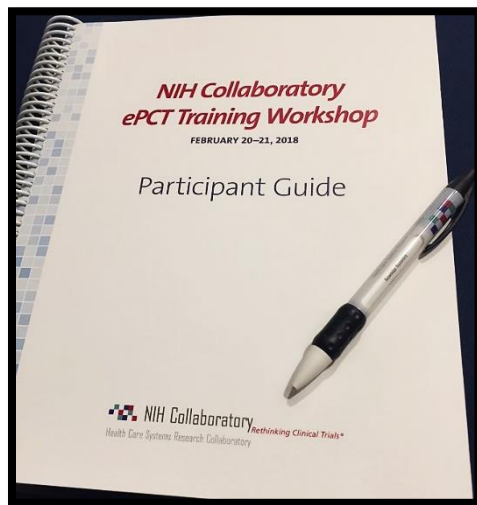
Fan Li^a, Yuliya Lokhnygina^{a,b}, David M. Murray^c, Patrick J. Heagerty^d and Elizabeth R. DeLong^{a,b*}

Analytic Challenges from the STOP CRC Trial: Pragmatic Solutions for Pragmatic Problems

William M Vollmer, PhD

April 24, 2015

Center for Health Research



DESIGN CONDUCT DISSEMINATION

EXPERIMENTAL DESIGNS AND RANDOMIZATION SCHEMES

SECTION 2

Statistical Design Considerations

Contributor
Elizabeth R. DeLong, PhD
For the NIH Health Care Systems Collaboratory [Biostatistics and Study Design Core](#)

Contributing Editor
Jonathan McCall, MS

Although PCTs do not necessarily require a particular statistical design approach, both the kinds of questions PCTs are designed to answer and the settings in which they take place may tend to favor certain approaches, such as cluster randomization. For example, the nature of the interventions they seek to test, which may involve healthcare delivery changes, might be better implemented through randomization at the practice, clinic, or even hospital level.

SECTIONS

- 1 Introduction
- 2 Statistical Design Considerations
- 3 Cluster-Randomized Trials
- 4 Choosing Between Cluster and Individual Randomization
- 5 Concealment and Blinding
- 6 Randomization Methods
- 7 Additional Resources

The Living Textbook *of Pragmatic Clinical Trials*



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

ENGAGING STAKEHOLDERS ▶
and building partnerships to ensure a successful trial

What is the
NIH COLLABORATORY? ▶

www.rethinkingclinicaltrials.org

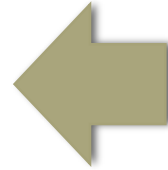
Embedded PCTs Training Workshop

- Goals
 - Provide training in ePCTs to mid/senior-level investigators
 - Pilot educational materials and collect feedback on quality & appropriateness
- Held February 20-21, 2018
- 27 investigators attended
 - Selected from >90 applicants
- Instructors included
 - NIH Collaboratory experts
 - Demonstration Project PIs
 - NIH staff

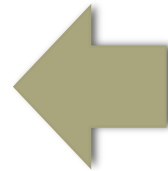


Training Workshop Content

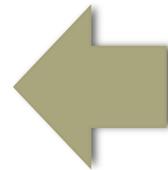
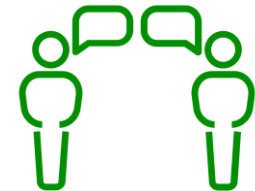
- What are ePCTs?
- Engaging All Stakeholders & Aligning With HCS Partners
- Designing With Implementation in Mind
- Design & Analytic Considerations
- Regulatory & Ethical Challenges
- Measuring Outcomes
- Pilot & Feasibility Testing
- Dissemination
- ePCT Team Composition
- Developing a Compelling Application



Case Studies



Interactive Exercises



Living Textbook Content



PCT Grand Rounds Presentations

- Weekly webinars on a wide range of research topics
- 250+ presentations since inception
- Podcasts of expert interviews available on iTunes



Grand Rounds

Join our **weekly webinars** on Fridays from 1-2 pm ET.
Open to the public; no registration required.

[Join our mailing list](#)

Upcoming Webinars

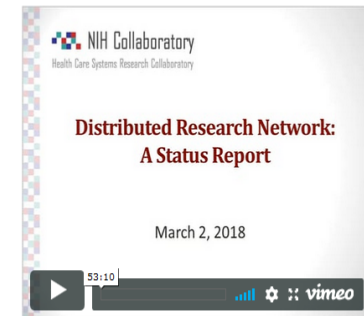
- Grand Rounds March 16: Straight from the Source: Clinicians' Views on Participating in CER/PCOR (Ellen Tambor, MA; Rachael Moloney, MHS; Sean Tunis, MD, MSc)
- Grand Rounds March 23: Data Science in the Era of Data Ubiquity (Robert M. Califf, MD)
- Grand Rounds March 30: HHS-DoD-VA Pain Management Collaboratory (Robert Kerns, PhD)

[View Calendar of All Events](#)

Podcasts

- [Podcast February 16, 2018: Considerations for the Return of Genomic Results](#)

Last Week's Grand Rounds



Jeff Brown, Lesley Curtis, and Richard Platt give a status report on the Distributed Research Network

Tweets by [@PCTGrandRounds](#)

NIH Collaboratory Newsletter

Subscribe to this convenient monthly wrap-up



The screenshot shows the top portion of an email newsletter. At the top is the NIH Collaboratory logo, which consists of a grid of colored squares (red, blue, green, white) to the left of the text "NIH Collaboratory" and "Health Care Systems Research Collaboratory". Below the logo is the tagline "Rethinking Clinical Trials®". A dark blue horizontal bar contains the text "News From the NIH Collaboratory" in white. Below this bar, the newsletter content is organized into two columns. The left column starts with a "Welcome to the NIH Collaboratory E-Newsletter!" followed by a paragraph about the newsletter's purpose and a link to provide feedback. The right column is titled "QUICK LINKS" and contains two links: "Living Textbook" and "Grand Rounds Hub". Below the welcome message is a section titled "Recent News" with a dotted line separator. It features two news items. The first is "Reflections From the Patient-Reported Outcomes Core" with a sub-link "Core" and a photo of Dr. Kevin Weinfurt. The second is "NCI Announces Training Institute in Dissemination and Implementation Research in Cancer" with a sub-link "and Implementation Research in Cancer".

NIH Collaboratory
Health Care Systems Research Collaboratory
Rethinking Clinical Trials®

News From the NIH Collaboratory

Welcome to the NIH Collaboratory E-Newsletter!
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.](#)

QUICK LINKS

- [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 cancer-focused 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.

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

What Have We Done So Far?

www.rethinkingclinicaltrials.org/about-nih-collaboratory/

QUICK LINKS

[Policies and Guidance](#)

[Documents](#)

[Steering Committee Meetings](#)

[Knowledge Repository](#)

[Milestone Timeline](#)

[Communication Channels Chart](#)



SEPTEMBER 1, 2012

NIH COLLABORATORY TIMELINE

This timeline presents a history of milestones for the NIH Health Care Systems Research Collaboratory, including events, achievements, leadership changes, publications, products, and presentations. Last updated August 2017. To learn more about the NIH Collaboratory, visit www.rethinkingclinicaltrials.org...



NIH
COLLABORATORY
GRANT AWARDED

Knowledge Exchange

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

Partner Organizations





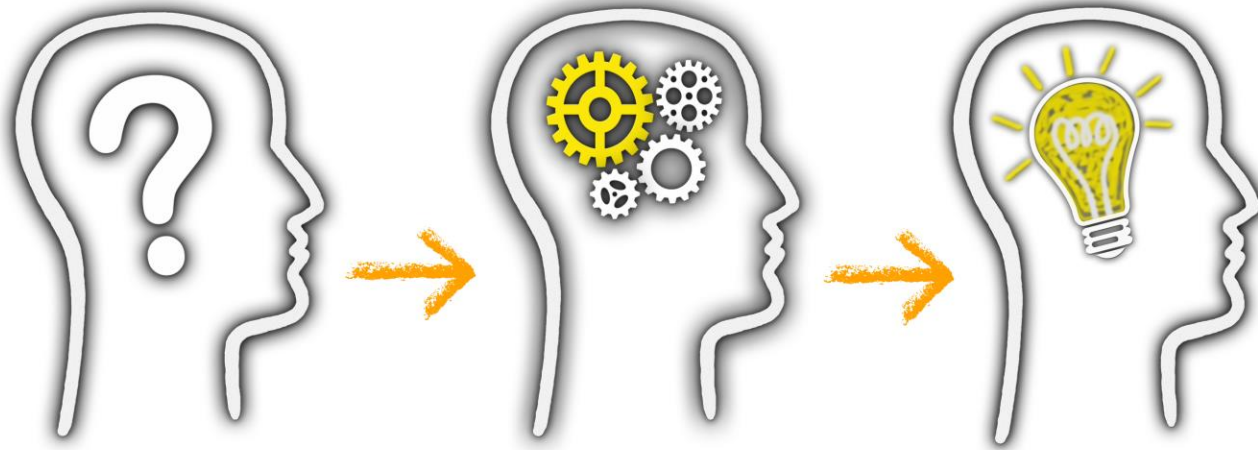
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Conclusions

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

What will you contribute...



LESSONS LEARNED

Conclusions

- Take advantage of growing interest in population health and “systemness” to do research
- 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