NIH Collaboratory *Rethinking Clinical Trials®*

Health Care Systems Research Collaboratory

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

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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**?

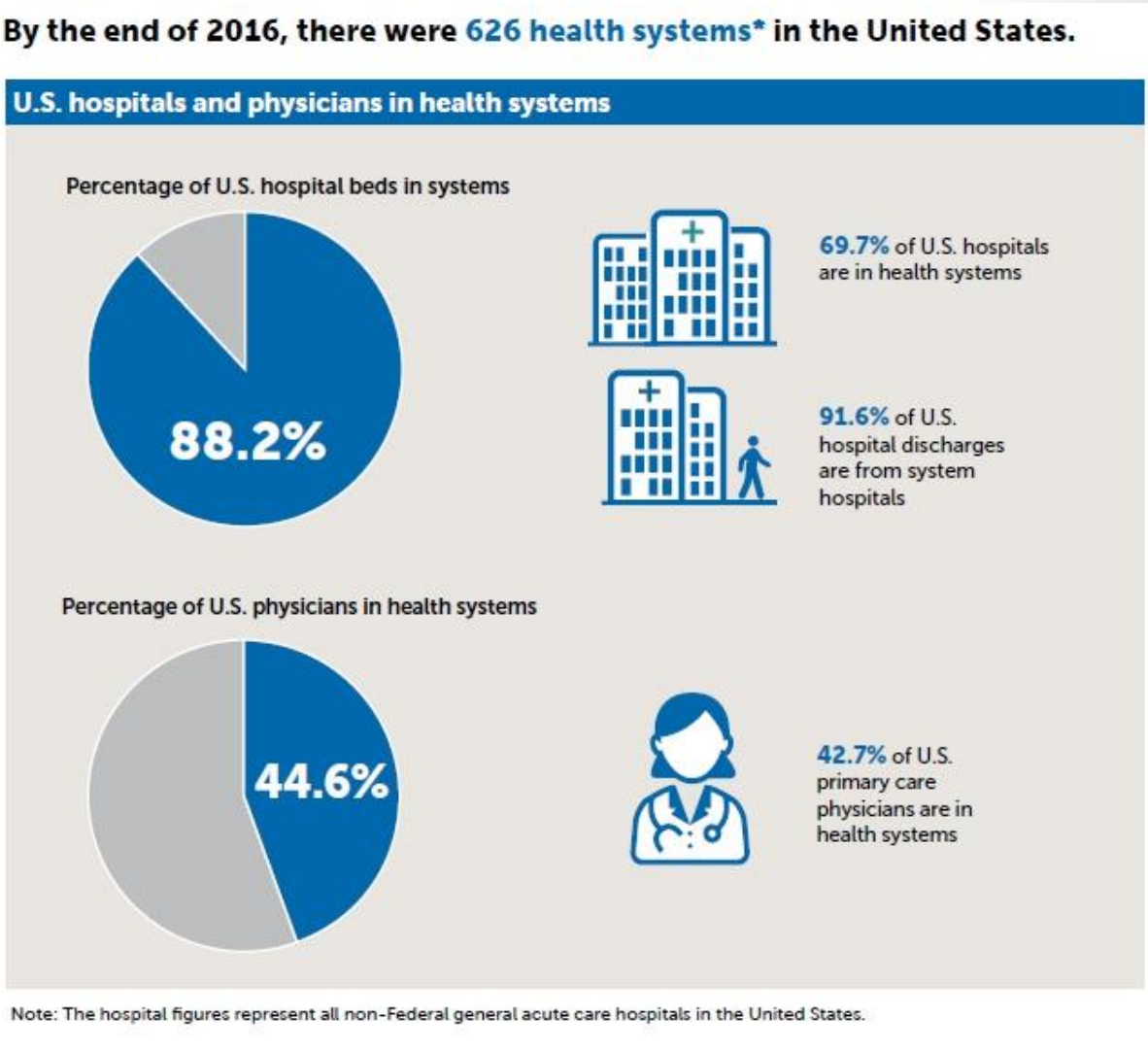
Increasing System-ness…

U.S. Hospitals & physicians in Health Systems

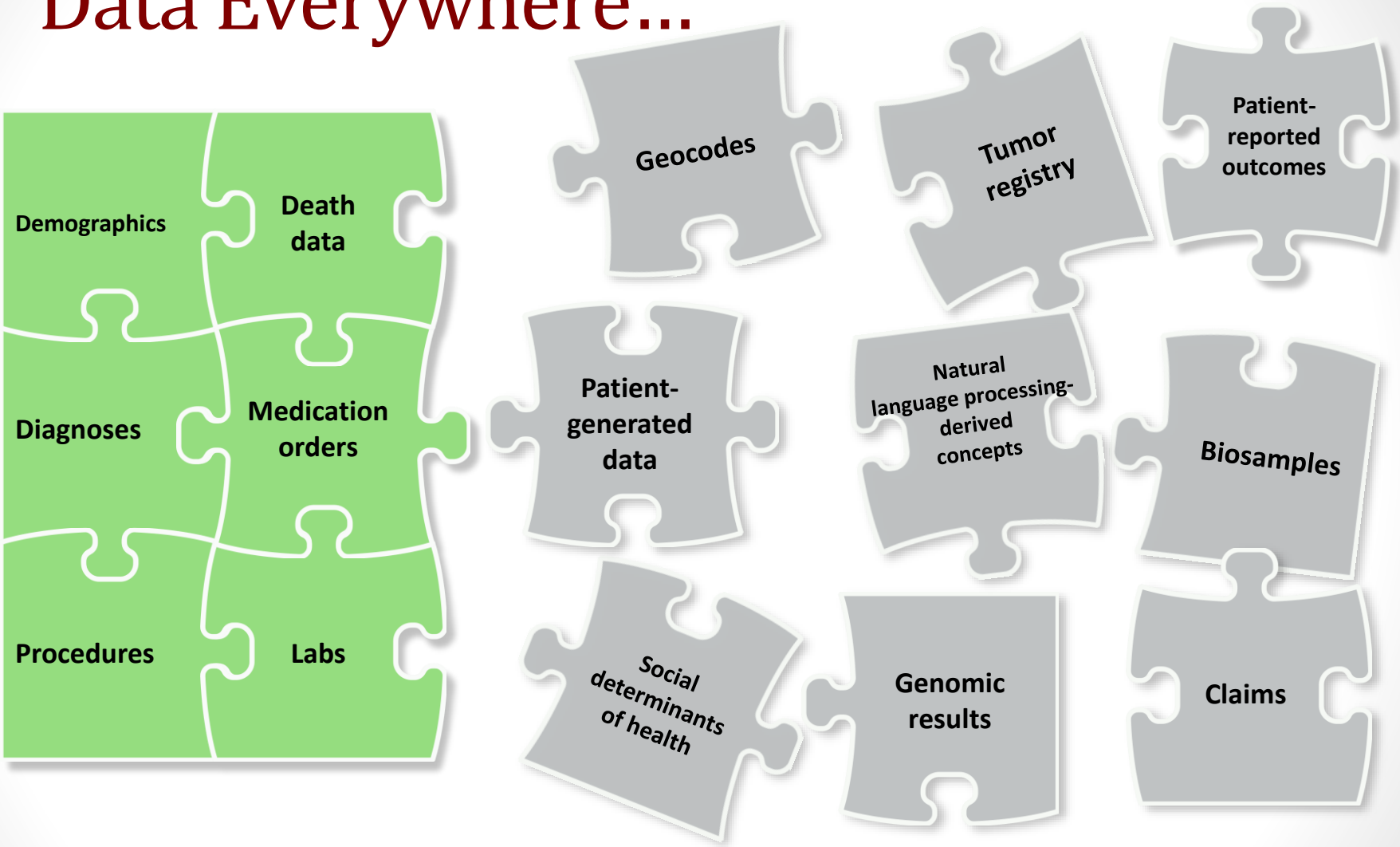
2000: 5810 Hospitals

2016: 626 Health systems

2020: ??



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=0·0002, 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."

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

Re-engineering the Clinical Research Enterprise

Increasing Level of Difficulty

1-3 years	4-7 years	8-10 years
Plan and start a few demonstration networks Simplify complex regulatory systems – demonstration projects Plan for networks in place for all institutes	Funding mechanism to sustain national system through consensus of all constituents ("1% solution") Simplified regulatory system in place for networks	**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**
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	Data standards shared across NIH institutes Funding mechanisms evaluated to determine which are most efficient	**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**
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 all stakeholders Establish standards for and pilot creation of a National Clinical Research Corps Demonstration/planning grants to enhance/evaluate/develop model networks	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	**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**

The Collaboratory Story

NIH
National Institutes 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

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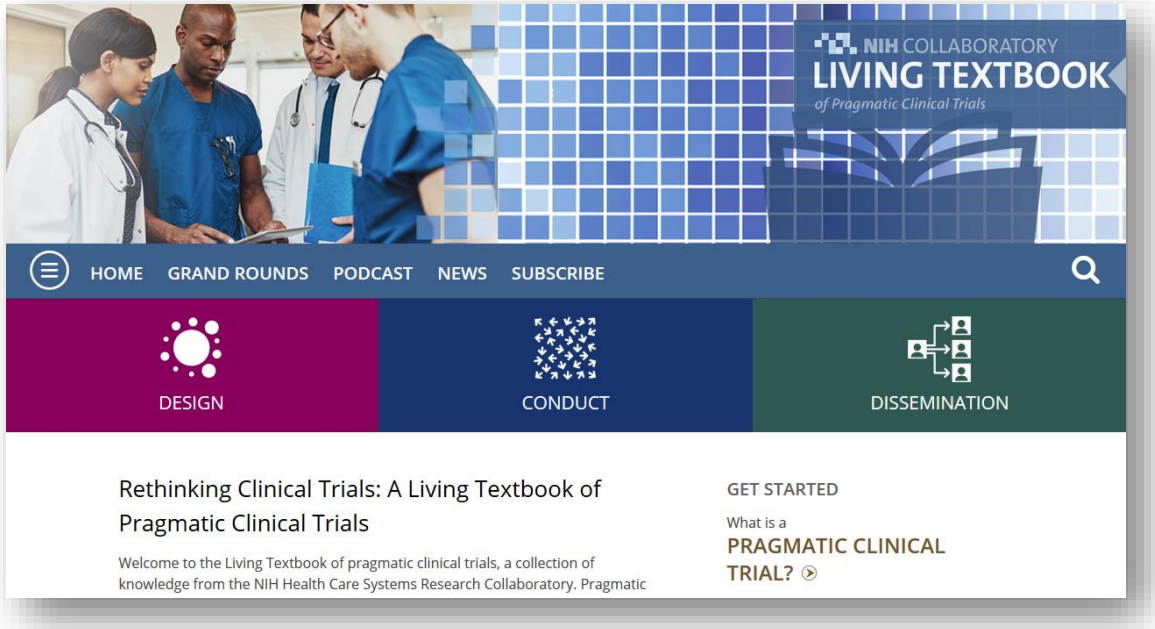
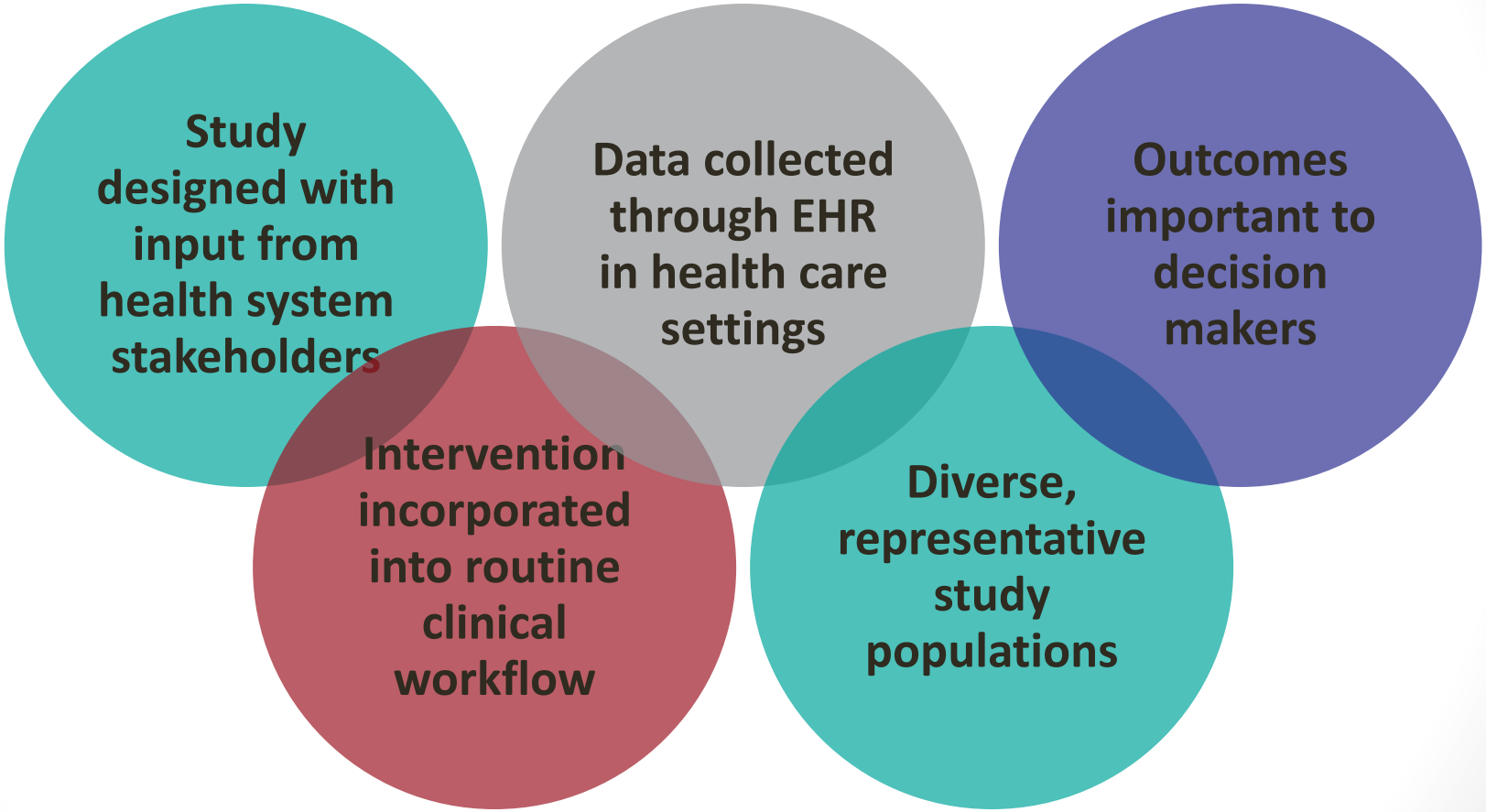
Evolving
Health Care Systems Research Collaboratory



- 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



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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

Advisory Panel

NIH Project Officers

Demonstration Projects

Steering Committee

Core Workgroups

Coordinating Center

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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

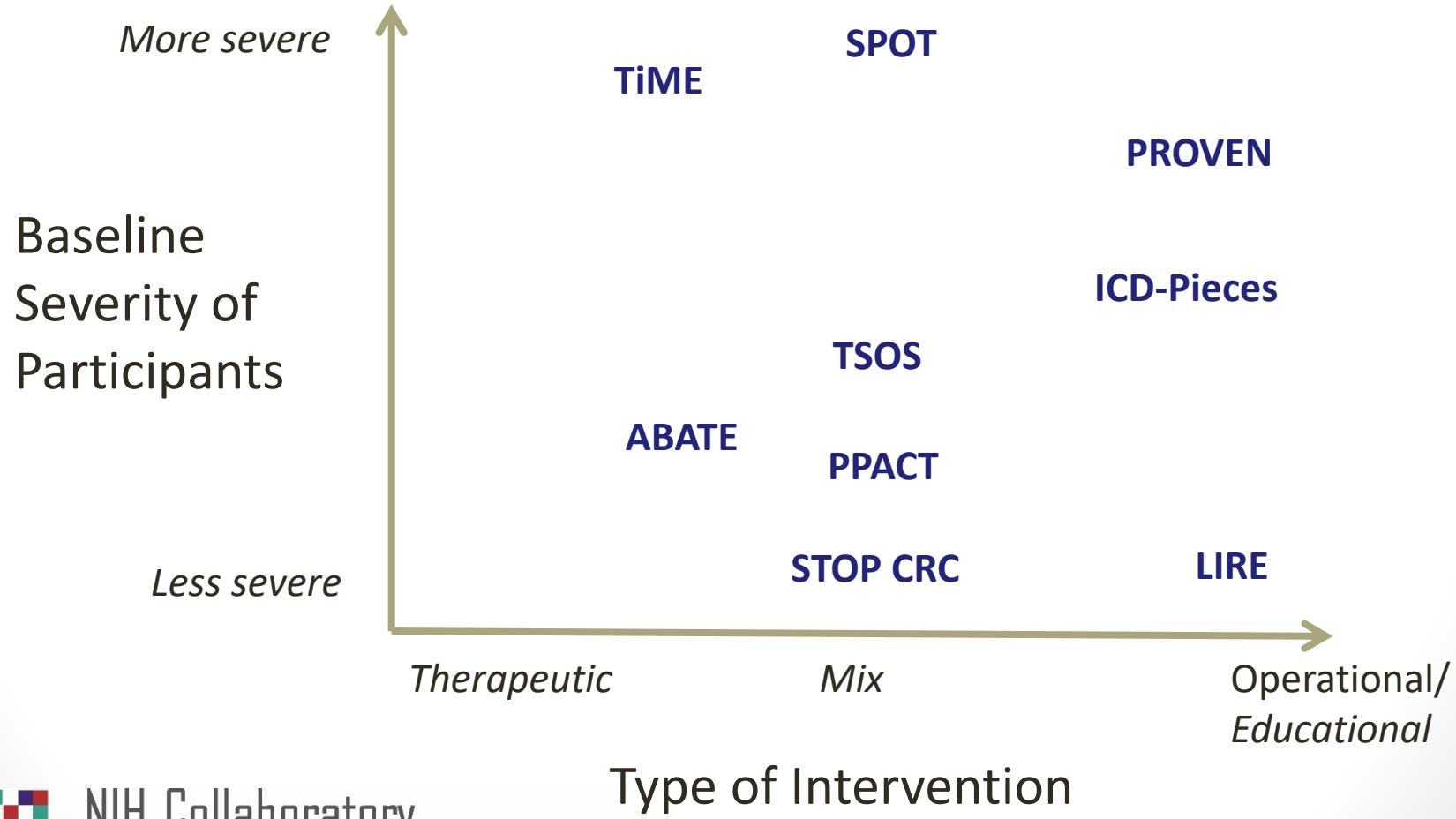
Demonstration Projects

- 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

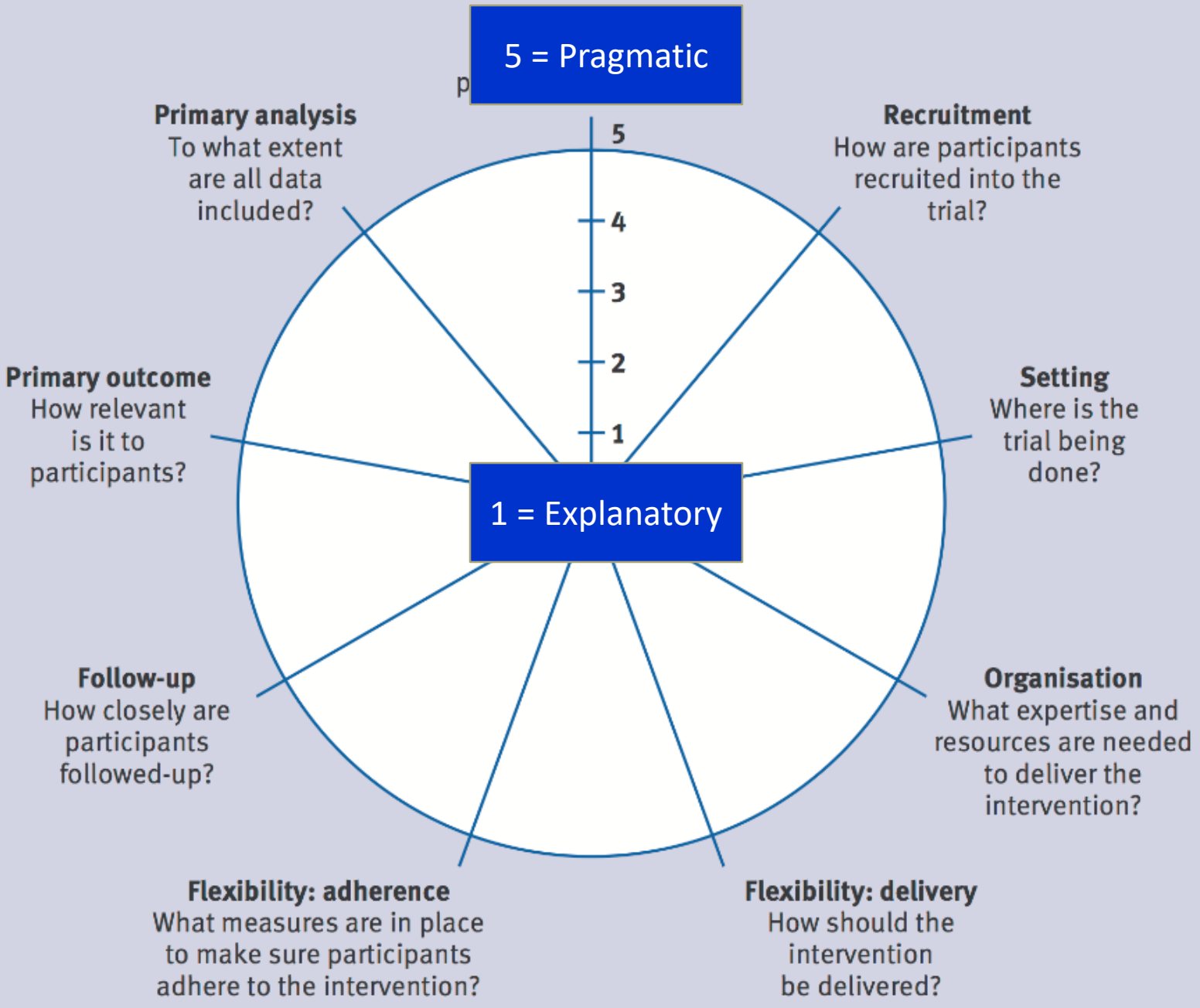


Pragmatic Trial	Target N	Health Care Systems
Ma		ters
M		S
D		CS
S		CS
C		IN
N		rp.
Bac		HCS
Hospital Infections	285,000	50 Hospitals in HCA

~ Cost/Patient

Average = $1,500

Range = $25 - $7,300



The PRagmatic-Explanatory Continuum Index Summary 2 (PRECIS-2) wheel.
Adapted from BMJ 2015;350:h2147

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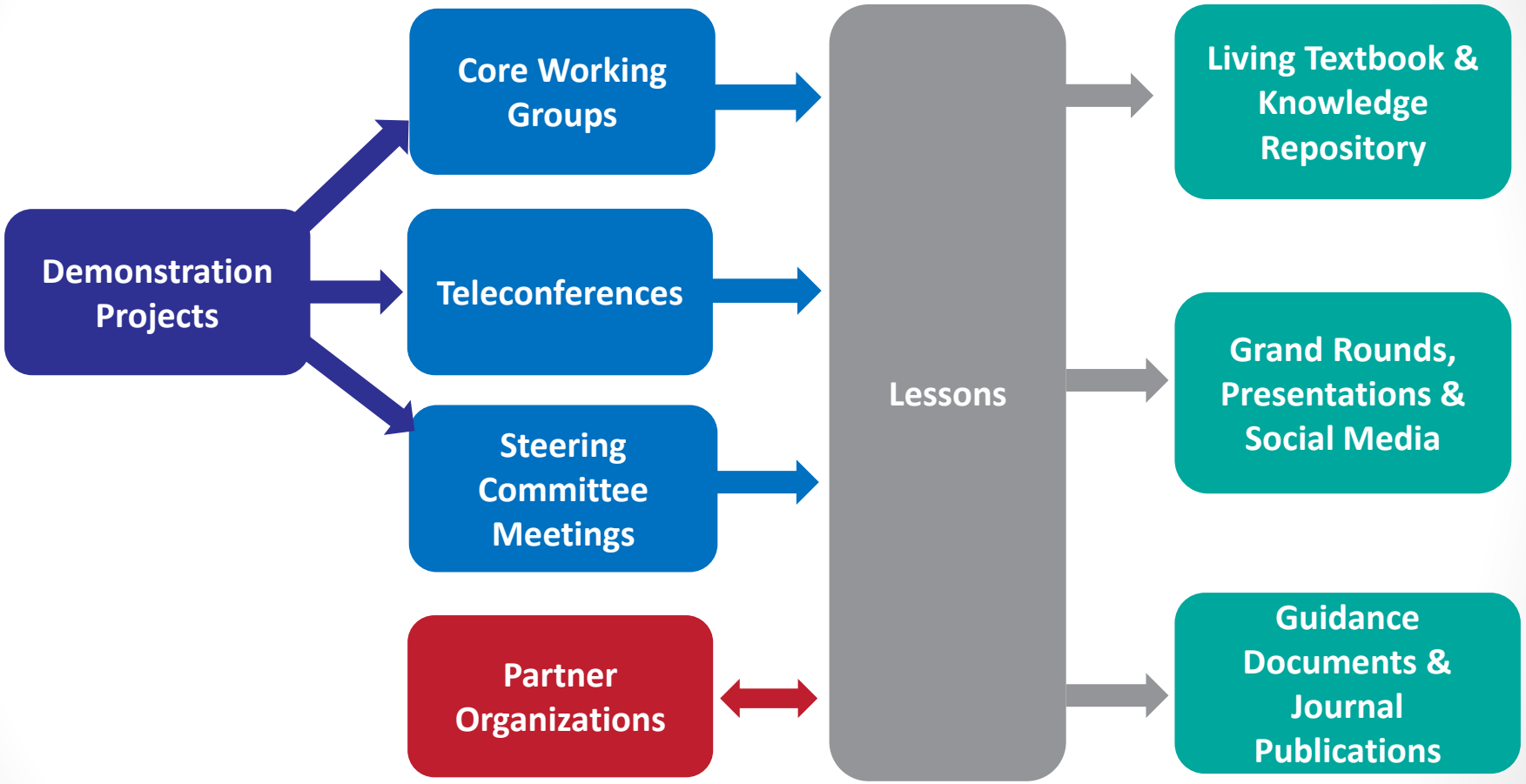
How are we doing it?

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	Engage-ment	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
● SPOT
● TiME
● LIRE
● PPACT
● ABATE

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Sharing Challenges & Solutions

Teleconferences, SC Meetings,
Collaboratory Videos & Interviews

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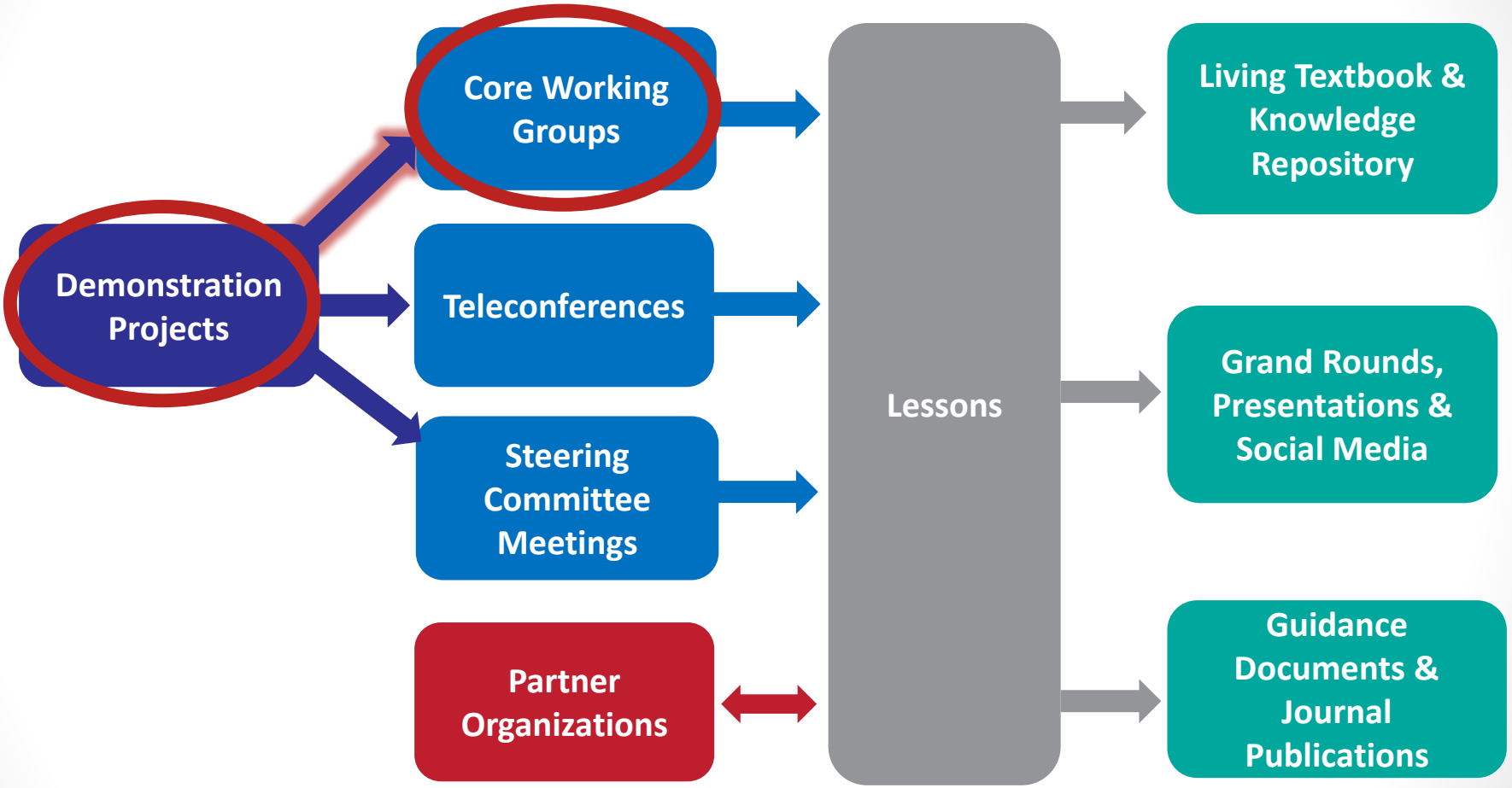
How do we share what we learn?

Process for Dissemination

Flow of Information



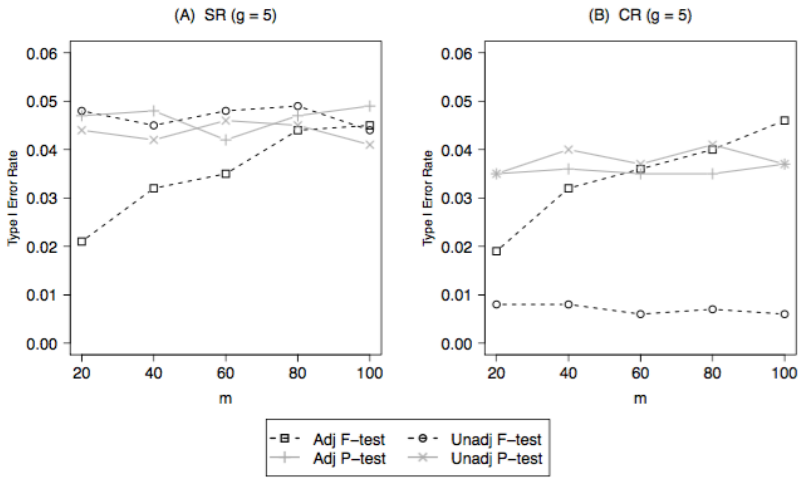
Biostatistics and Study Design Core

Elizabeth DeLong, PhD, MA

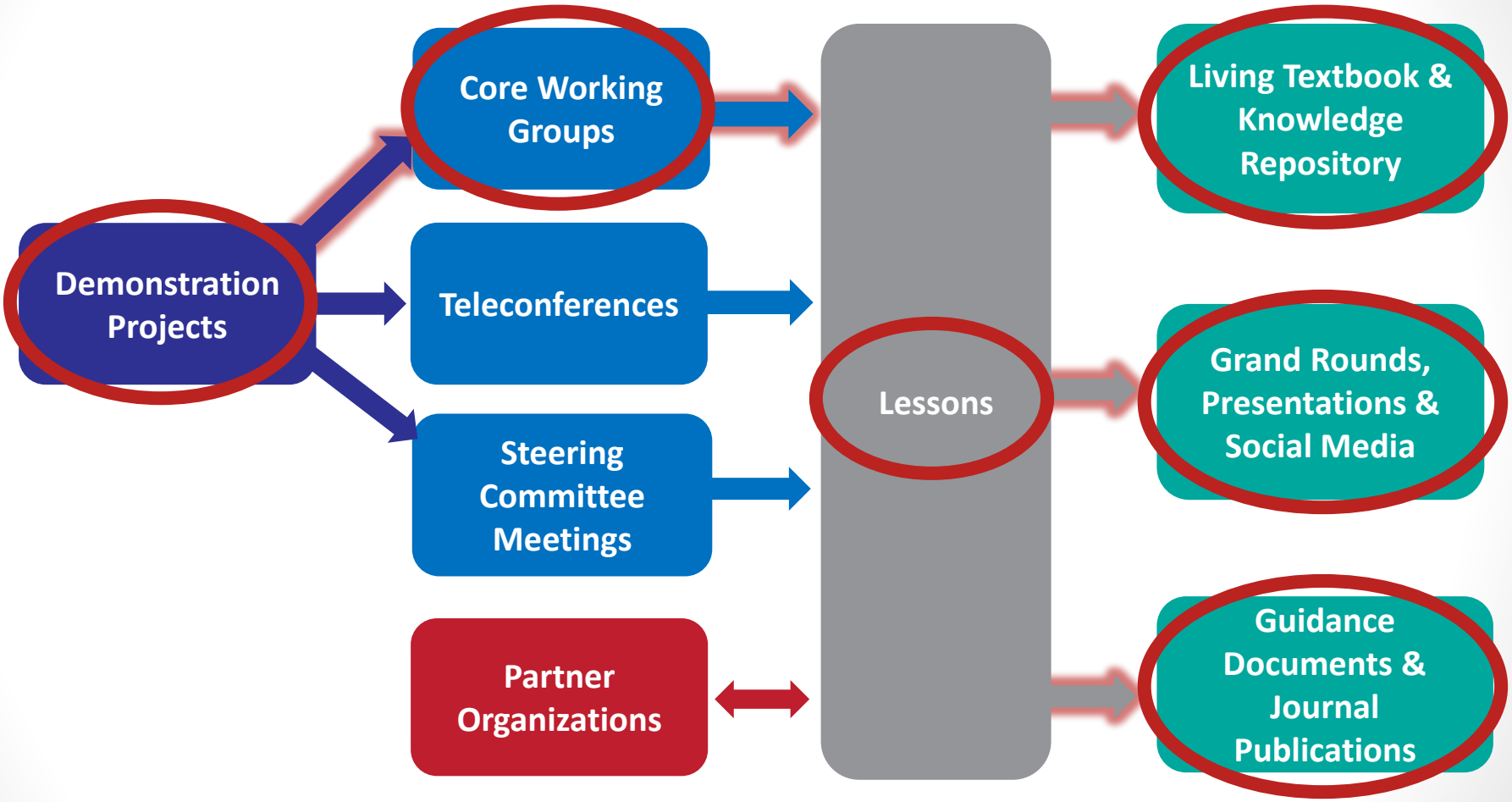
Duke Clinical Research Institute

Simulation Studies

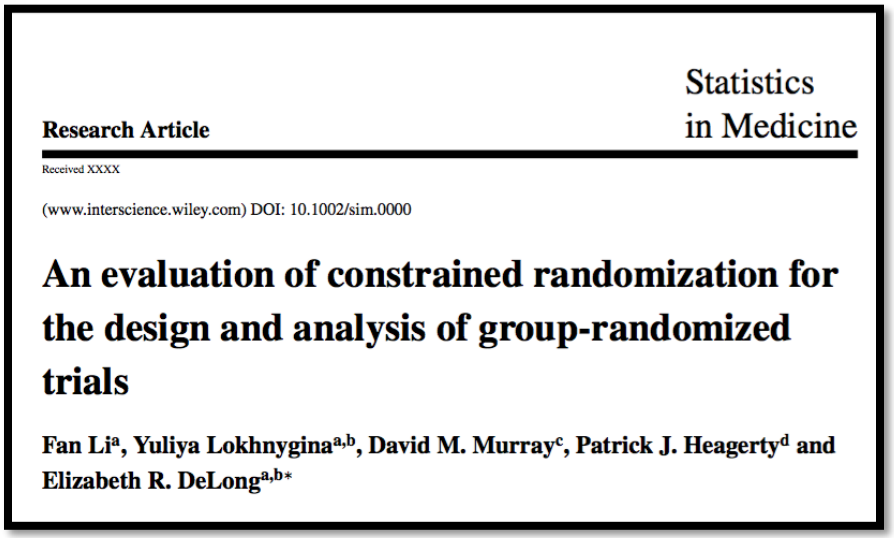
Lessons re: Design & Analysis



Flow of Information



Dissemination



Research Article

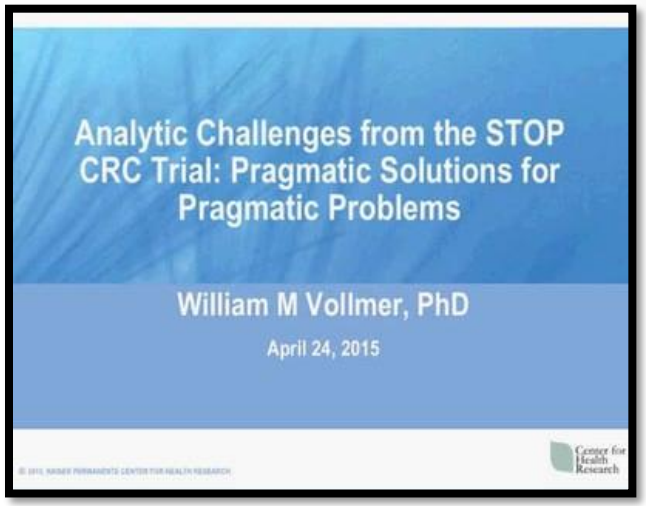
Statistics in Medicine

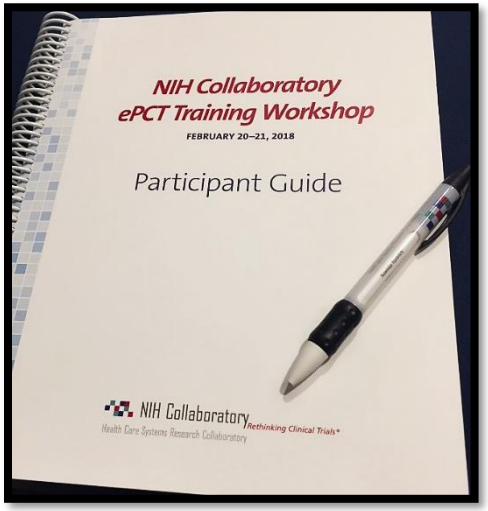
Received XXXX

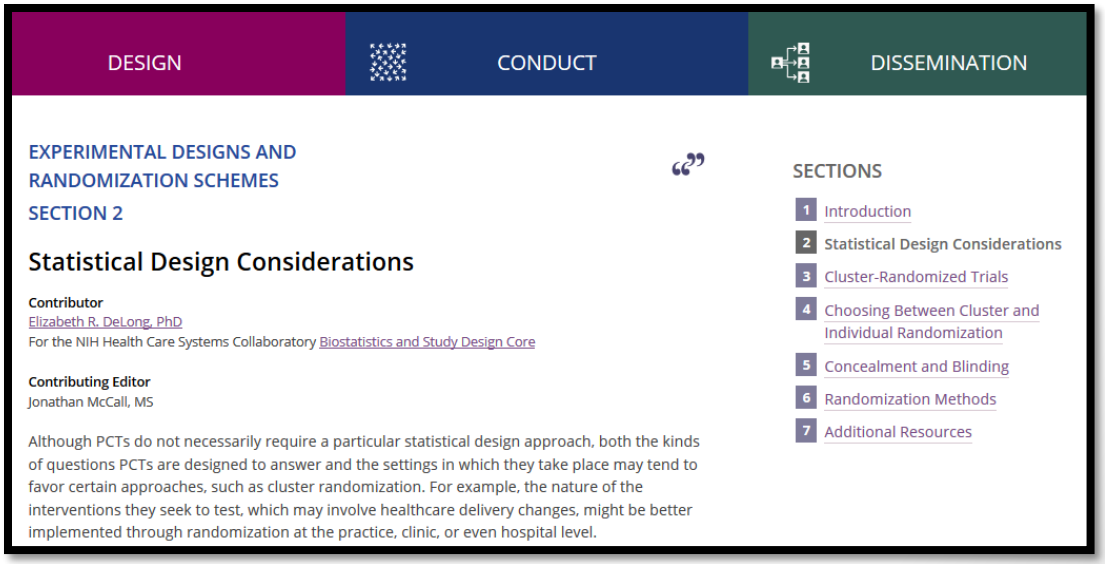
(www.interscience.wiley.com) DOI: 10.1002/sim.0000

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]*







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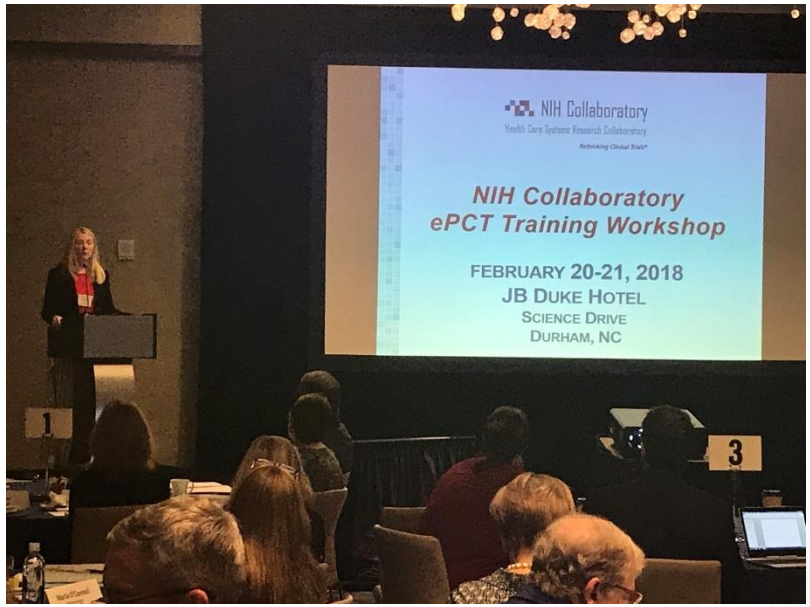
Rethinking Clinical Trials

The Living Textbook *of Pragmatic Clinical Trials*

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

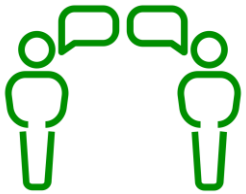


Training Workshop Content

- 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

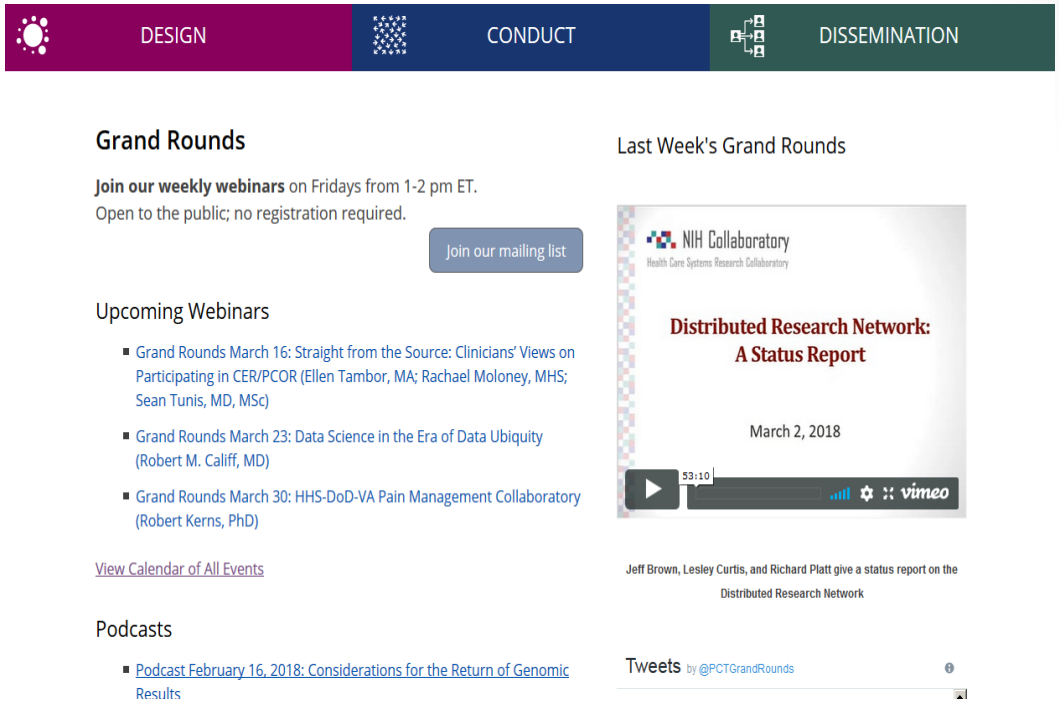
Interactive Exercises



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



NIH Collaboratory Newsletter

Subscribe to this convenient monthly wrap-up

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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

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

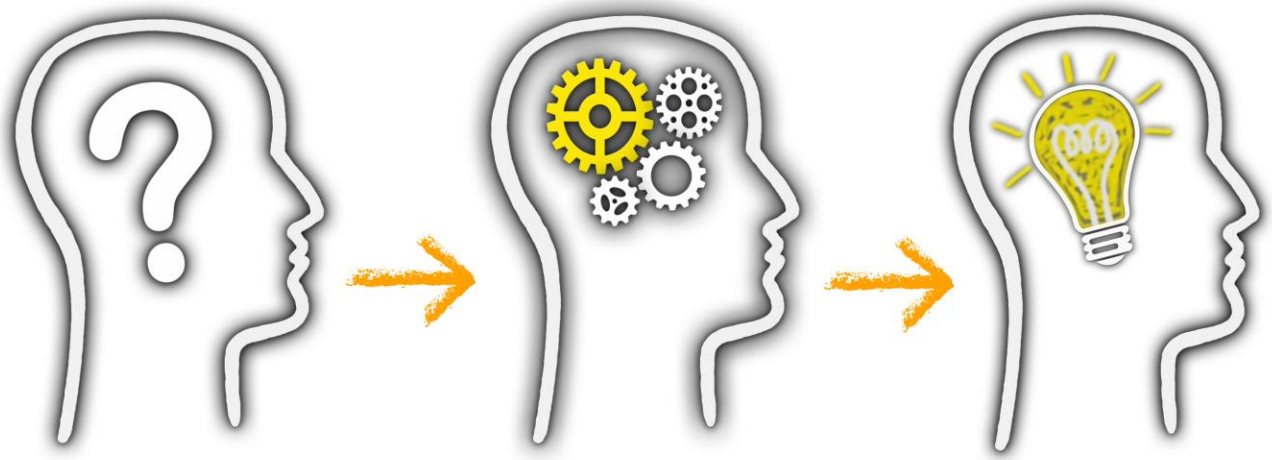
4

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