NIH Collaboratory

Health Care Systems Research Collaboratory

Dig if You Will the Picture . . . of the NIH Collaboratory

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Disclaimer

- This work is supported by the National Institutes of Health (NIH) Common Fund, through a cooperative agreement (U54 AT007748) from the Office of Strategic Coordination within the Office of the NIH Director.

- The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

Our Vision

Strengthen the national capacity to implement cost-effective large-scale research studies that engage healthcare delivery organizations as research partners

Today's Presentation

1. Collaboratory Year 4 Highlights
2. What are we working on now?
3. What should be next?

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Collaboratory Year 4 Highlights

Demonstration Projects Progress

Began Enrollment

TSOS Trial

A Policy-Relevant U.S. Trauma Care System Pragmatic Trial for PTSD and Comorbidity (Trauma Survivors Outcomes and Support)

PROVEN Trial

Pragmatic Trial of Video Education in Nursing Homes

ICD-Pieces Trial

Improving Chronic Disease Management with Pieces

Completed Enrollment

ABATE Trial

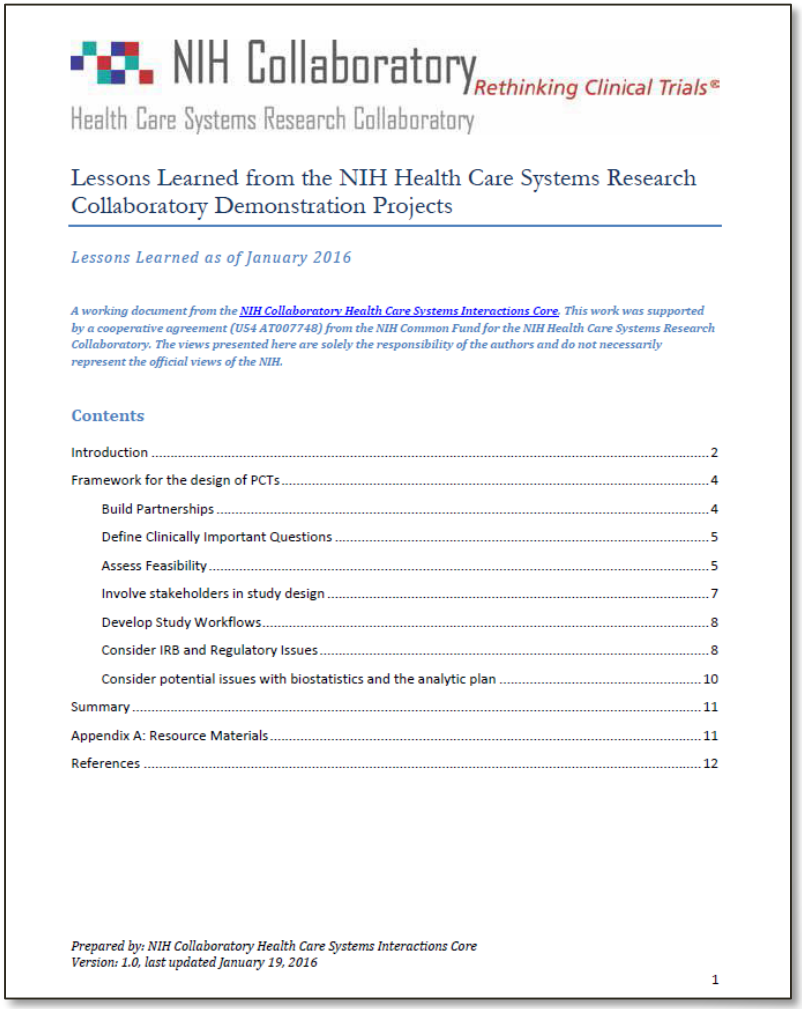
Active Bathing to Eliminate (ABATE) Infection

Enrollment Ongoing

5 Demonstration Projects: PPACT, SPOT, TiME, LIRE, STOP CRC

Lessons Learned From the Demonstration Projects

- Published on the Living Textbook January 2016
- Contains many case studies/examples
- Will be updated as new information learned



NIH Collaboratory Rethinking Clinical Trials®

Health Care Systems Research Collaboratory

Lessons Learned from the NIH Health Care Systems Research Collaboratory Demonstration Projects

Lessons Learned as of January 2016

A working document from the NIH Collaboratory Health Care Systems Interactions Core. This work was supported by a cooperative agreement (U54 AT007748) from the NIH Common Fund for the NIH Health Care Systems Research Collaboratory. The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

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Prepared by: NIH Collaboratory Health Care Systems Interactions Core
Version: 1.0, last updated January 19, 2016

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Manuscripts published or in press

Presentations and abstracts

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Presentations and abstracts

Dissemination of Ethics & Regulatory Approaches for PCTs

- Continue to discuss issues described in *Clinical Trials* October 2015 theme issue
- NIH hosted workshop **May 2016** for in-depth exploration
  - >180 attendees from 40 organizations, including NIH, FDA, OHRP
- Completed monthly special Grand Rounds series

VOLUME 12, NUMBER 5, OCTOBER 2015

CLINICAL TRIALS

Journal of the Society for Clinical Trials

Ethics of Research in Usual Care Settings

- *American Journal of Bioethics* special issue
  - Patients' views concerning research on medical practices: implications for consent (Weinfurt et al.)
  - Alternative consent models for comparative effectiveness studies: Views of patients from two institutions (Kass et al.)
  - Patient and physician views about protocolized dialysis treatment in randomized trials and clinical care (Kraybill et al.)
  - The patient's perspective on the need for informed consent for minimal risk studies: Development of a survey-based measure (Kaplan et al.)
  - Adrift in the gray zone: IRB perspectives on research in the learning health system (Soo Jin-Lee et al.)
- Summit meeting held April 2016
  - Analyzed synergies and inconsistencies across projects
  - Proceedings to be published

Guidance on ICD-10 Transition: Impact for PCTs

- "Preparing for ICD-10-CM transition: automated methods for translating ICD codes in clinical phenotype definitions" published in eGEMS April 2016

Biostatistical Guidance for PCTs

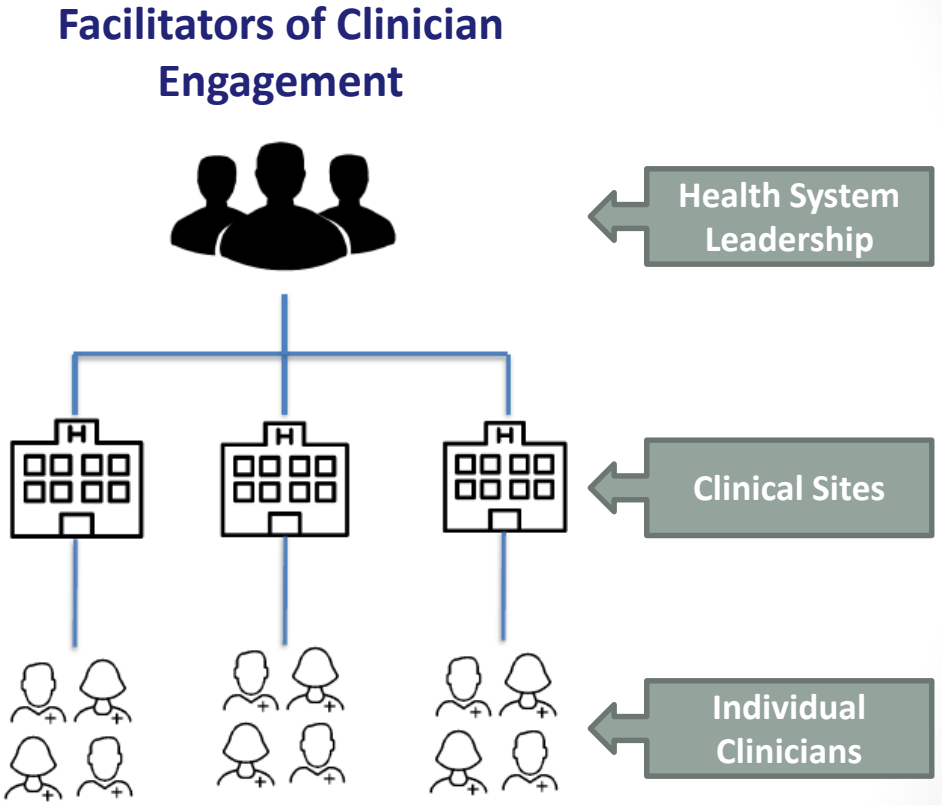
- Analytical challenges from the STOP CRC trial published in *eGEMS* December 2015
- Evaluation of constrained randomization for group-randomized trials published in *Statistics in Medicine* May 2016
- Statistical lessons learned for designing cluster randomized PCTs published in *Clinical Trials* October 2016

DRN Queries and Results

- Test cases assessed in 3 data organizations, representing ~1/3 of the total DRN data
  - Assess recruitment feasibility of replicating the Trial to Assess Chelation Therapy
  - Characterize statin users >age 75 with regard to CVD and diabetes status
  - Characterize frequency of abnormal breast, colorectal, and cervical cancer screening test results and follow-up care
- Informative of iterative process needed to refine queries and types of queries that are readily addressed vs. those requiring a more iterative process over time
- DRN user's manual updated based on this experience
- Revised processes and timelines for future test cases
- Results being prepared for publication

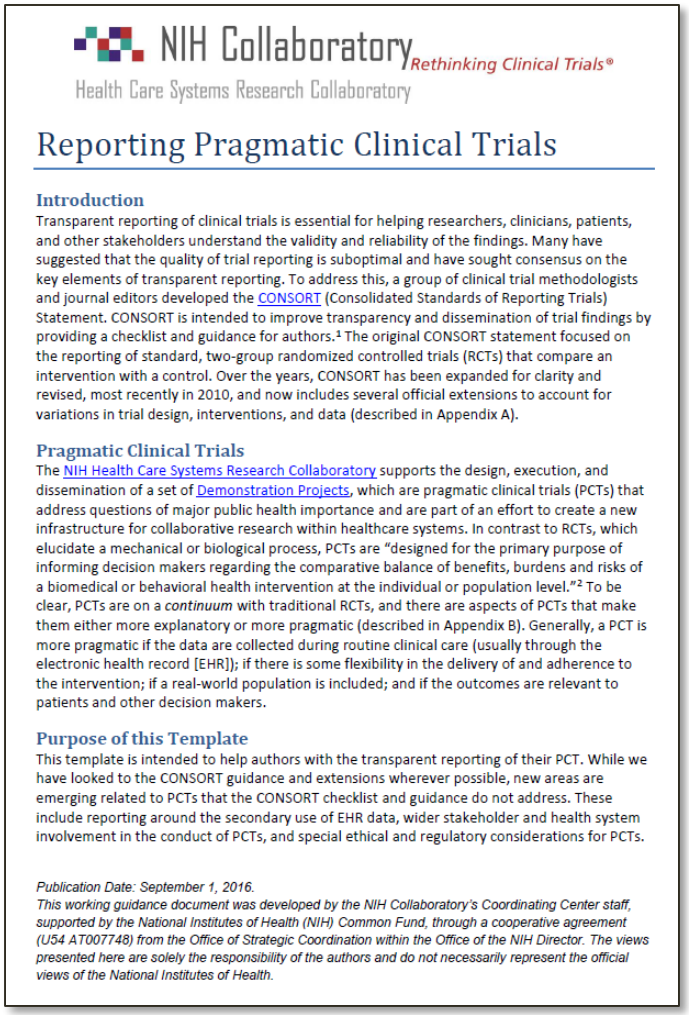
Stakeholder Engagement

- Patient and clinician support for the learning healthcare system: recommendations for enhancing value (Moloney et al. *J Comp Eff Res*. 2016)
- Preliminary results on clinician engagement interviews presented
  - ISPOR May 2016
  - Academy Health June 2016



PCT Reporting Template

- Published on the Living Textbook September 2016
- Describes reporting elements based on CONSORT guidance and expertise from the NIH Collaboratory Demonstration Projects and Cores



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Health Care Systems Research Collaboratory

Reporting Pragmatic Clinical Trials

Introduction

Transparent reporting of clinical trials is essential for helping researchers, clinicians, patients, and other stakeholders understand the validity and reliability of the findings. Many have suggested that the quality of trial reporting is suboptimal and have sought consensus on the key elements of transparent reporting. To address this, a group of clinical trial methodologists and journal editors developed the CONSORT (Consolidated Standards of Reporting Trials) Statement. CONSORT is intended to improve transparency and dissemination of trial findings by providing a checklist and guidance for authors.[1] The original CONSORT statement focused on the reporting of standard, two-group randomized controlled trials (RCTs) that compare an intervention with a control. Over the years, CONSORT has been expanded for clarity and revised, most recently in 2010, and now includes several official extensions to account for variations in trial design, interventions, and data (described in Appendix A).

Pragmatic Clinical Trials

The NIH Health Care Systems Research Collaboratory supports the design, execution, and dissemination of a set of Demonstration Projects, which are pragmatic clinical trials (PCTs) that address questions of major public health importance and are part of an effort to create a new infrastructure for collaborative research within healthcare systems. In contrast to RCTs, which elucidate a mechanical or biological process, PCTs are "designed for the primary purpose of informing decision makers regarding the comparative balance of benefits, burdens and risks of a biomedical or behavioral health intervention at the individual or population level."[2] To be clear, PCTs are on a *continuum* with traditional RCTs, and there are aspects of PCTs that make them either more explanatory or more pragmatic (described in Appendix B). Generally, a PCT is more pragmatic if the data are collected during routine clinical care (usually through the electronic health record [EHR]); if there is some flexibility in the delivery of and adherence to the intervention; if a real-world population is included; and if the outcomes are relevant to patients and other decision makers.

Purpose of this Template

This template is intended to help authors with the transparent reporting of their PCT. While we have looked to the CONSORT guidance and extensions wherever possible, new areas are emerging related to PCTs that the CONSORT checklist and guidance do not address. These include reporting around the secondary use of EHR data, wider stakeholder and health system involvement in the conduct of PCTs, and special ethical and regulatory considerations for PCTs.

Publication Date: September 1, 2016.
This working guidance document was developed by the NIH Collaboratory's Coordinating Center staff, supported by the National Institutes of Health (NIH) Common Fund, through a cooperative agreement (U54 AT007748) from the Office of Strategic Coordination within the Office of the NIH Director. The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

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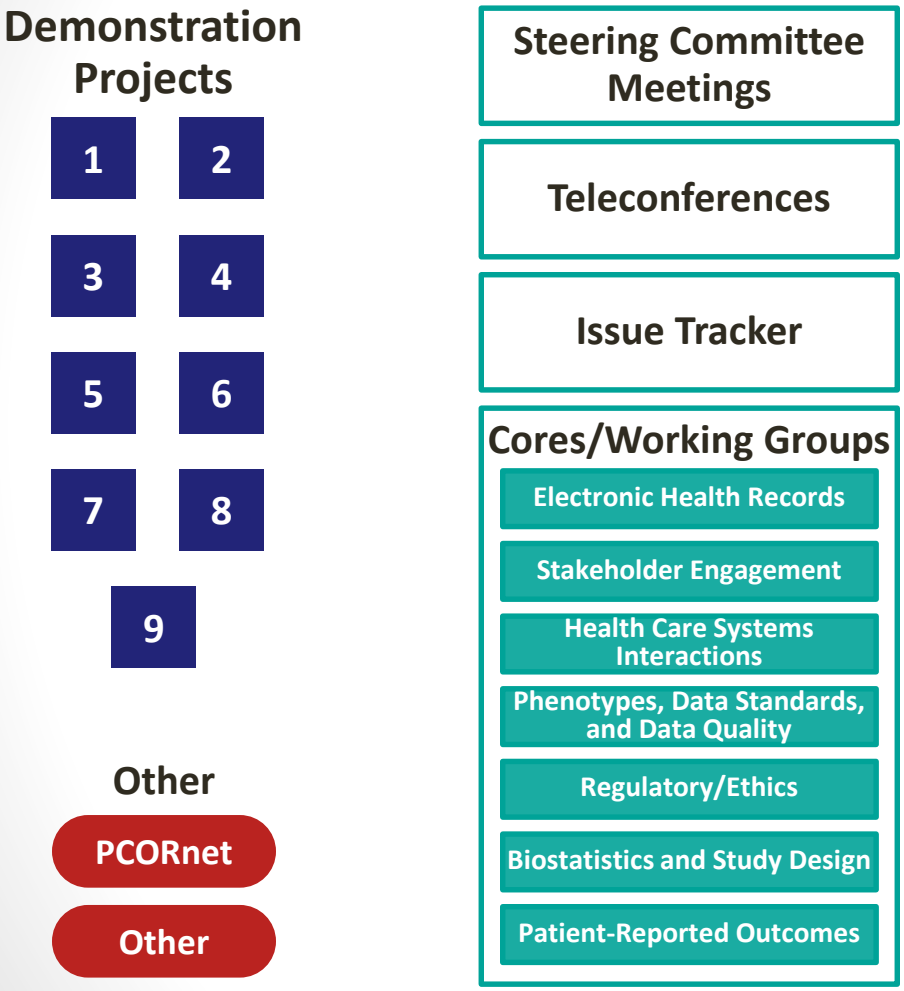
What are we working on now?

Learning and Disseminating



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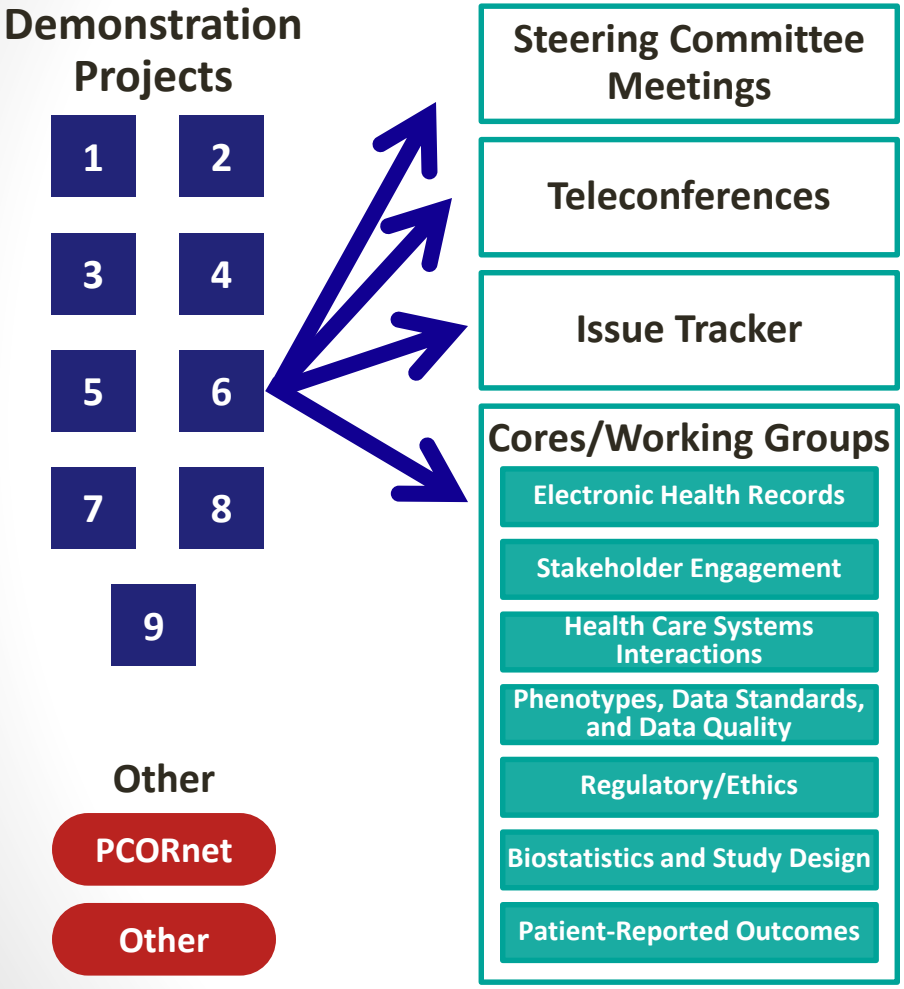

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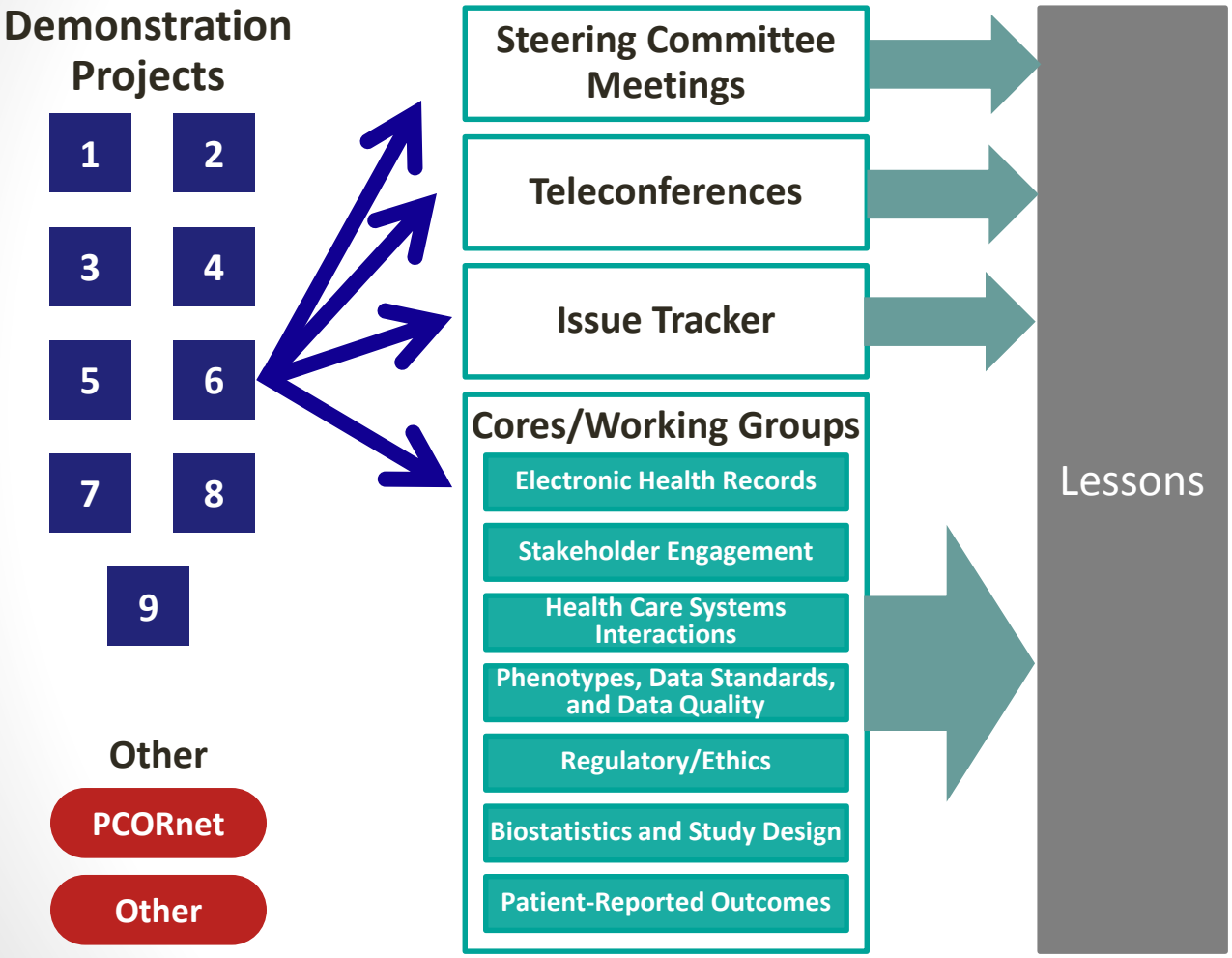

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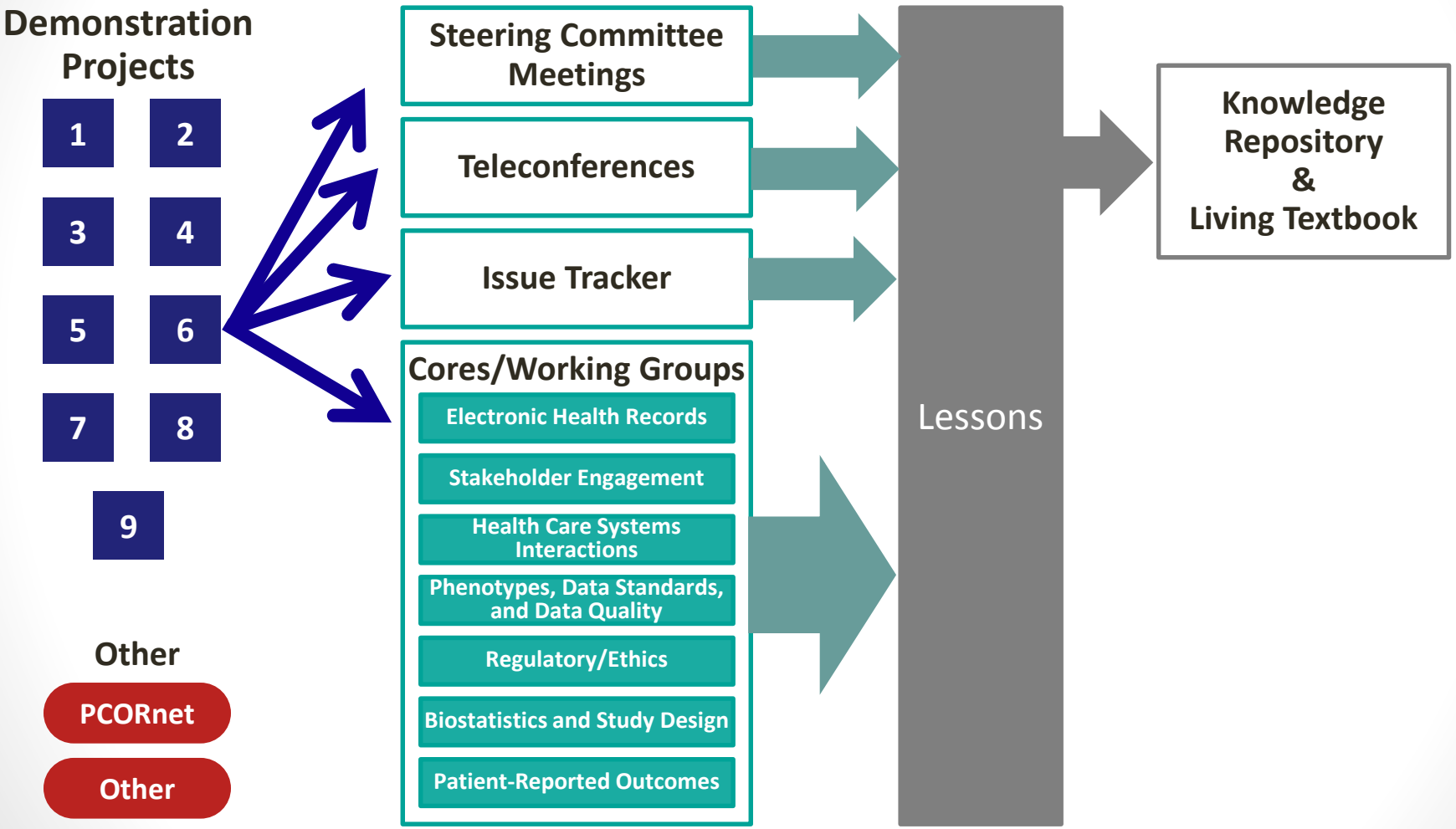

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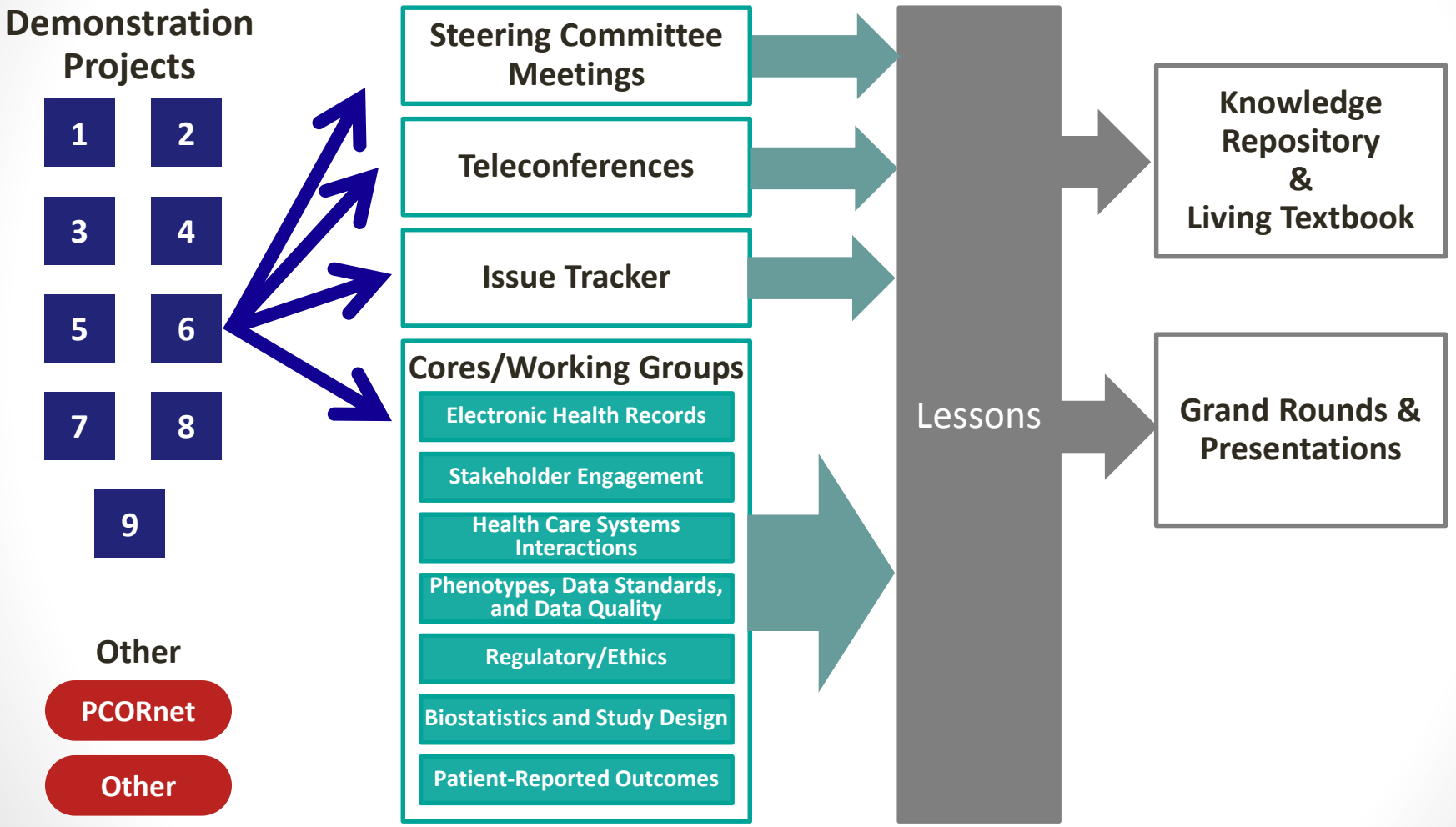

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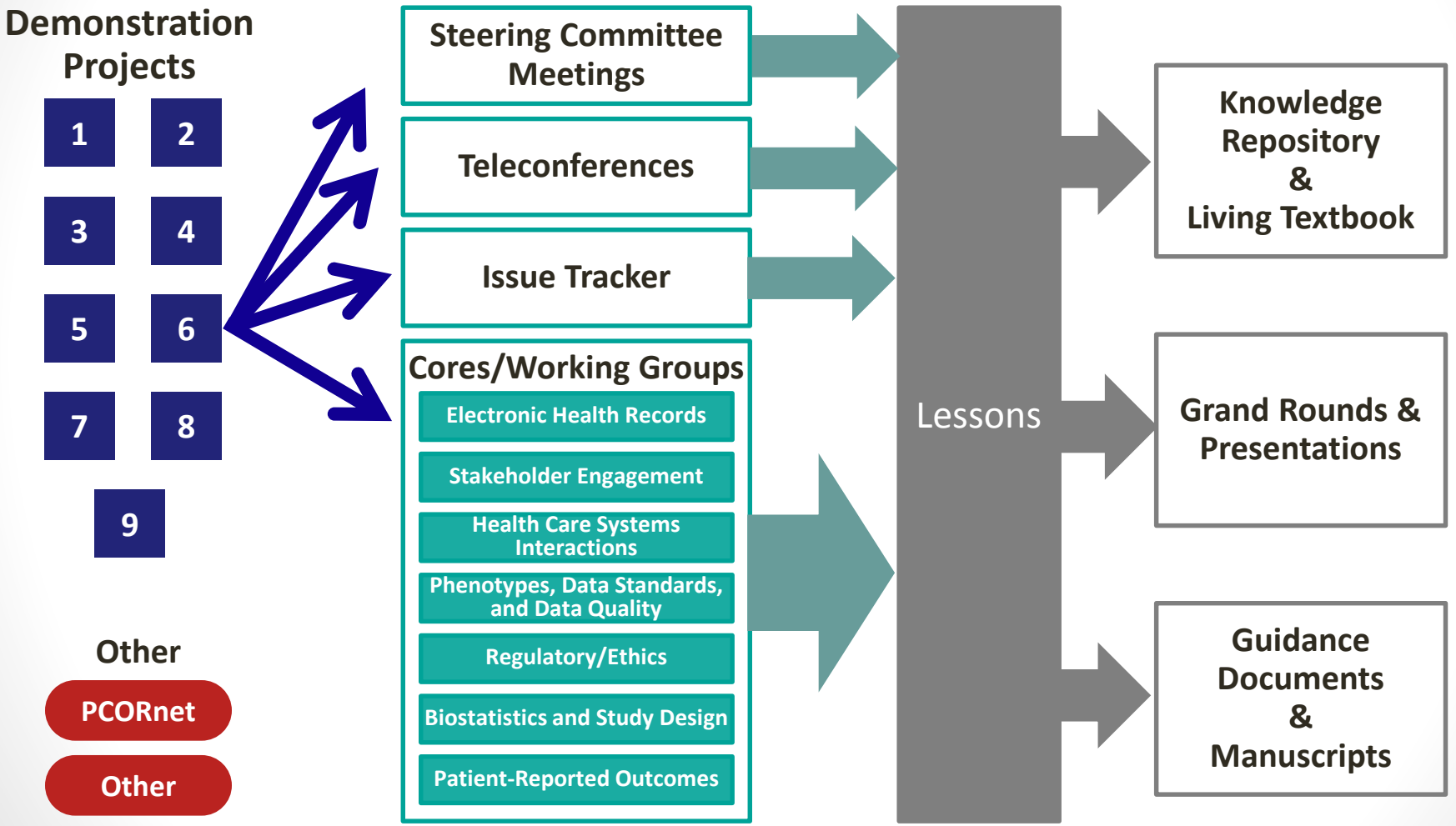


New Tools and Guidances in the Works

- Case studies for incorporating PROs into healthcare systems
- A methods framework for clinician engagement in PCTs
- Sample DMC charter
- Alternative data monitoring approaches for PCTs
- Data sharing for completed PCTs
- Additional biostatistics topics related to PCTs

Continued Collaborations

- Biostatistical methods work funded by PCORI
- Collaboration on PCORI-funded work to advance use of PROs in EHRs
- Exploring synergies with CTSA Trial Innovation Network, MDEpiNet
- Stakeholder engagement

Approaches to Dissemination and Implementation of PCT Evidence

How do you design a PCT with dissemination and implementation in mind?

- Interviews completed
- Preparing publication of results
- Gathering lessons learned related to dissemination and implementation

Stakeholder	If/When to do a PCT	How to Do a PCT				How to Evaluate PCTs	How to Implement Evidence from PCTs
		Design	Assessing Likelihood of Success/ Impact	Conduct	Reporting		
Creators of Research							
Funders							
Currently fund PCTs							
Do not currently fund PCTs							
Investigators							
Consumers of Research							
Regulators (FDA)							
MS/Grant reviewers							
HCS administrators							
Providers							
DSMB/IRB/OHRP							
Payers							
Purchasers							
Patients							
Congress							
Press							
The public							

Note: **Bold font** denotes highest priority stakeholders for this round of Collaboratory funding.

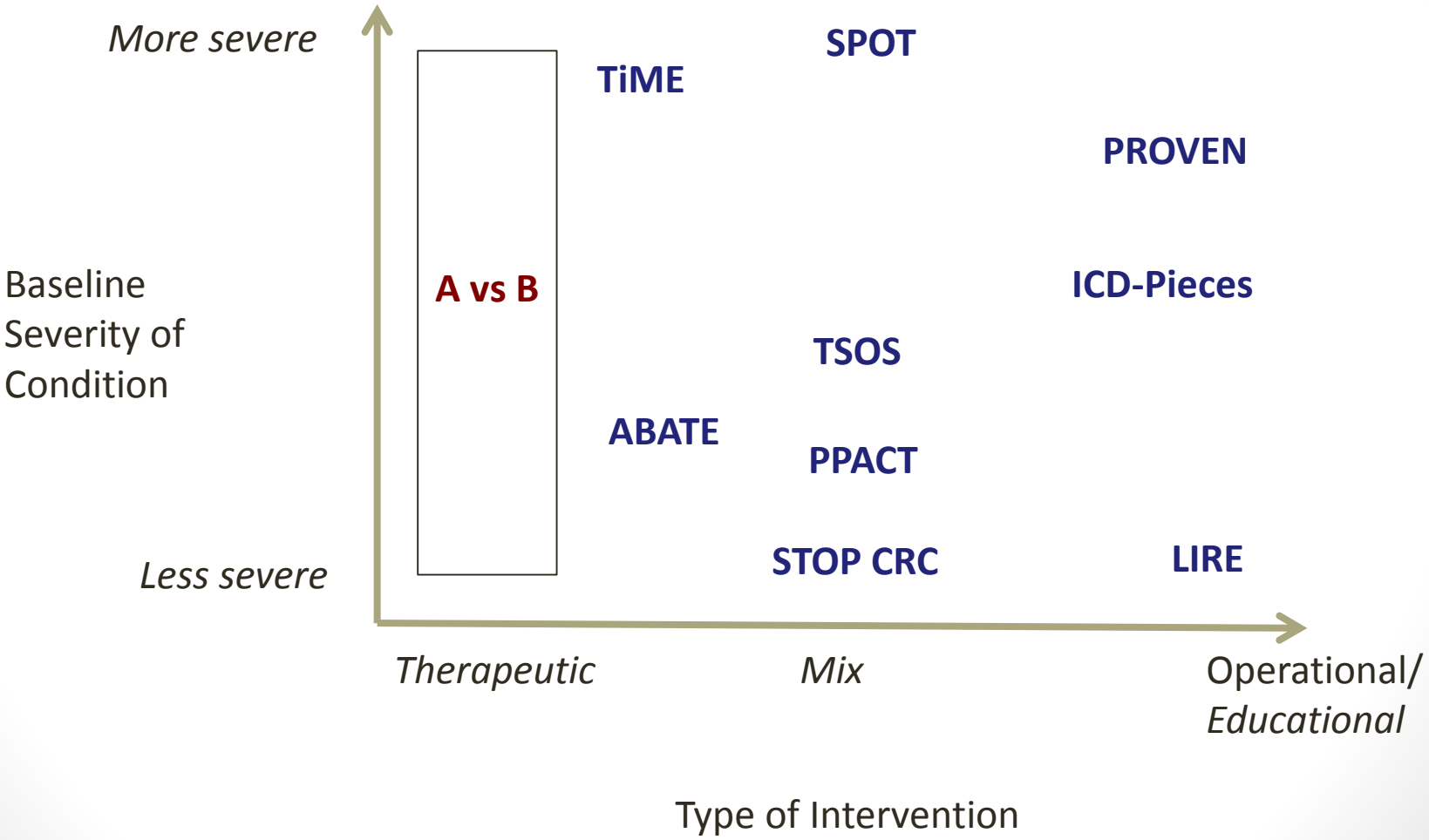
Restructuring the Living Textbook

Introduction	Design	Conduct	Reporting
What is a PCT?	Sample Definition & Selection	Startup	Special Considerations for Reporting PCTs
How to engage stakeholders	Intervention & Comparison Groups	Recruitment	Data Sharing & Promoting Transparency
	Experimental Designs & Randomization Schemes	Data Collection	Dissemination Strategies for Different Stakeholders
	Choosing and Specifying Endpoints & Outcomes	Data Analysis	
	Analysis Plan		
	Ethical & Regulatory Considerations in Identifying and Enrolling Patients		
	Data Access, Collection, and Storage		
	Planning for Data Safety and Monitoring		
	Pilot testing to assess feasibility		

3

What should be next?

UH2s/UH3s by Severity and Intervention



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

Stakeholder Engagement

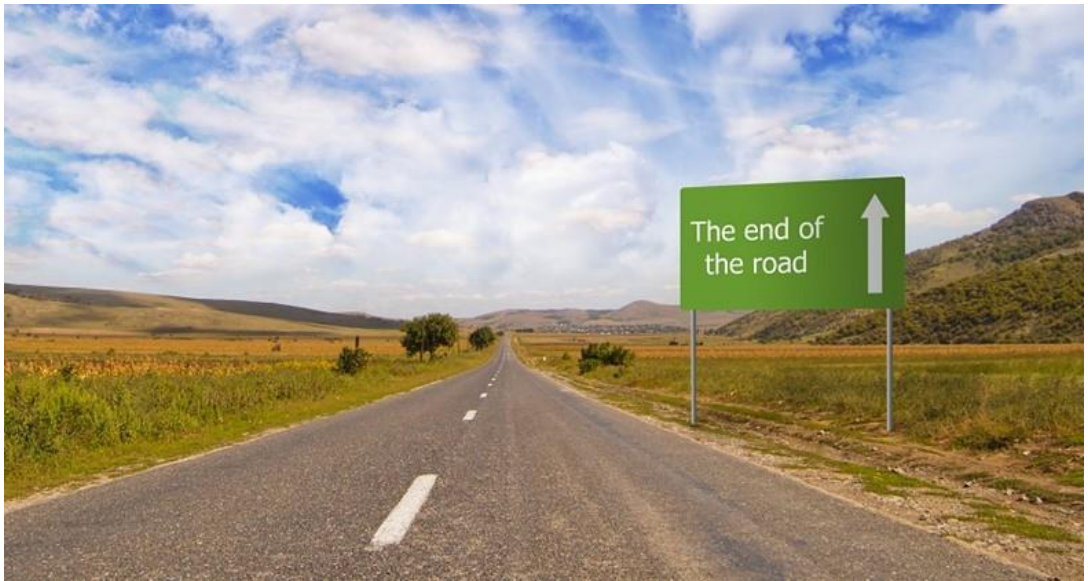
- Further stakeholder engagement
  - Empirical studies
  - How to build relationships with health systems
  - Address barriers with health system leaders
  - Healthcare plans
  - Clinicians

Regulatory & Ethics

- Generating Evidence
  - Nested Studies
- Addressing upcoming changes in the Common Rule

Implementation

- Results in a Boston-Based Journal ≠ Success
- What is successful implementation?
- How long to get evidence into practice? (<17 years)



Expanding the Capacity

- Improving research infrastructure
  - Re-thinking how health systems can be more fully leveraged
  - Expanding capacity for quality improvement with research
- Address methodological issues
  - Leveraging multiple health systems that aren't fully integrated
- Learning
  - Online training modules/course
  - How to sessions?
  - Academies or apprenticeships
  - Embedding researchers or 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….

Areas for Expansion

- Training for new investigators on PCT methods
  - In-person, online, apprenticeship
- Further stakeholder engagement
  - Empirical studies
  - How to build relationships with health systems
  - Address barriers with health system leaders
  - Healthcare plans
- How can we evaluate the quality and efficiencies of PCTs?
  - Tools and metrics
- What other issues do we want to tackle in depth?
  - Data sharing
  - Implementing PCT evidence
- How do we optimize dissemination and outreach?

4

Conclusions

Conclusions

- The Collaboratory: Still work to be done
  - To strengthen the national capacity to implement cost-effective large-scale research studies that engage healthcare delivery organizations as research partners
- Knowledge development continues to grow
  - Via project experiences
  - Via multidisciplinary teams
  - Via Cores
- Expanding embedded PCTs will need a few things….
  - Value equation
  - Unlocking barriers
  - Expanding capacity

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Thank you