



NIH Collaboratory

Health Care Systems Research Collaboratory

# Rethinking Clinical Trials

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# Communications Goals

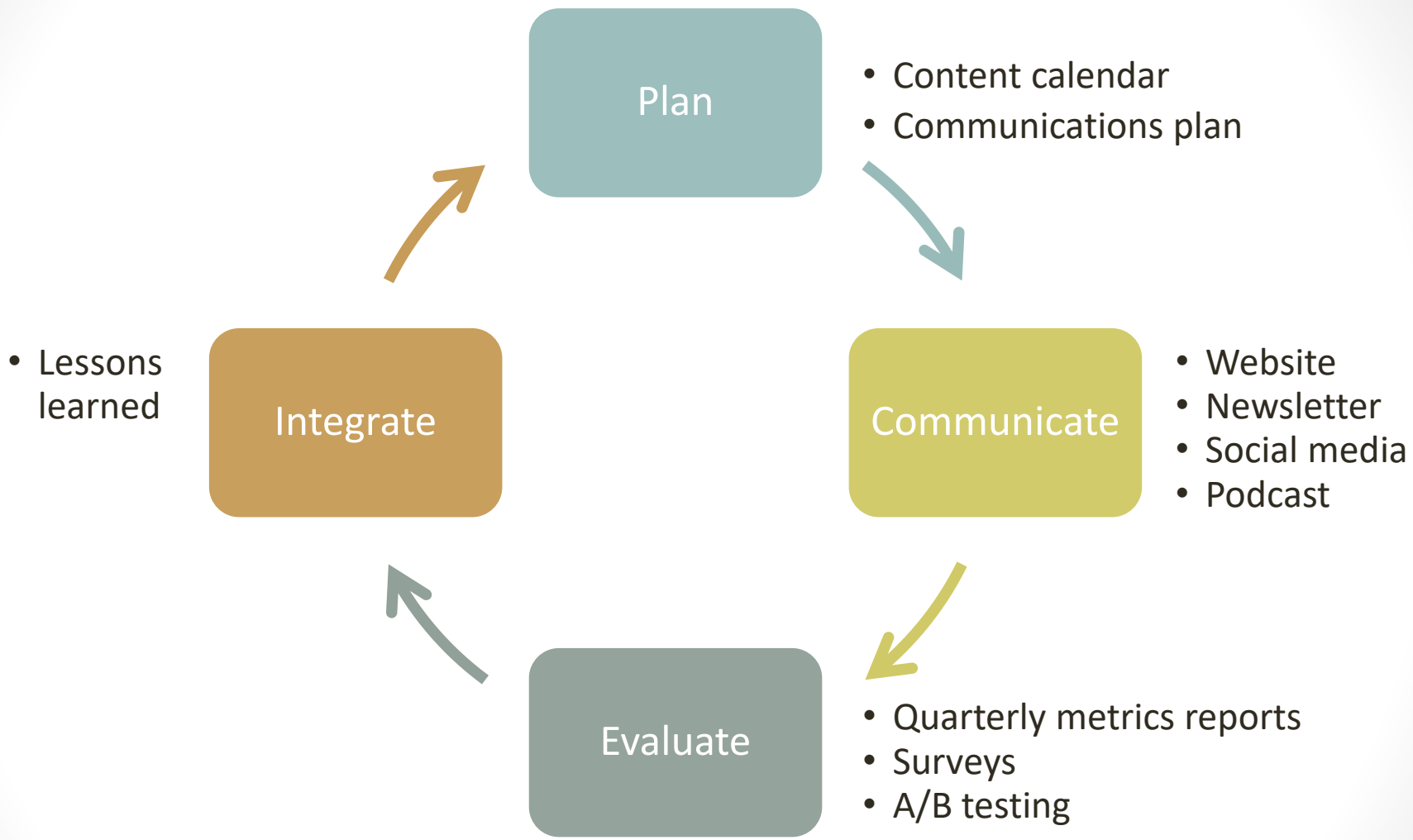
Maintain and strengthen the position of the NIH Collaboratory as a trusted and leading source of information on conducting pragmatic clinical trials

Support understanding of concepts and best practices for conducting pragmatic clinical trials

Support stakeholder understanding of and engagement with the NIH Collaboratory program

Inform key stakeholders about NIH Collaboratory educational resources and events

- Audiences:
  - Primary: Investigators and health system partners
  - Secondary: Research funders, healthcare providers, ethical oversight bodies
  - Tertiary: Patients, insurance payers & purchasers, congress, press, public



# The Living Textbook *of Pragmatic Clinical Trials*

The screenshot shows the top navigation bar with a hamburger menu icon on the left and a search icon on the right. The menu items are HOME, WELCOME, GRAND ROUNDS, and NEWS. Below the navigation bar are three main content areas, each with an icon and a title:

- DESIGN** (Icon: Sun-like symbol):
  - Experimental Designs and Randomization Schemes
  - Endpoints and Outcomes
  - Analysis Plan
- CONDUCT** (Icon: Cluster of arrows):
  - Consent, Disclosure, and Non-disclosure
  - Using Electronic Health Record Data
  - Data and Safety Monitoring
- DISSEMINATION** (Icon: Flowchart with people icons):
  - Designing With Implementation and Dissemination in Mind
  - Assessing Feasibility

Below these sections, there is a paragraph of text starting with "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"

Below the paragraph, there are two more sections:

- ENGAGING STAKEHOLDERS** (with a right-pointing arrow icon) and building partnerships to ensure a successful trial
- What is the **NIH COLLABORATORY?** (with a right-pointing arrow icon)

[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)



# New Living Textbook Is Born

- Launched August 25, 2017
- Updated design
- Improved navigation
- New educational content
  - 13 textbook chapters available



# NIH Collaboratory Living Textbook

- Comprehensive resource
  - Guidance on special considerations at each step of the PCT research process
  - Draws on experiences from NIH Collaboratory PCTs & community of experts
  - Details on the importance of PCTs & their impact on healthcare
  - Information about the NIH Collaboratory program
- Continuously expanded & updated

# NIH Collaboratory Living Textbook Content Generation

## Coordinating Center PI Oversight + NIH Input

>50 Subject Matter Experts



Coordinating Center Editors





# NIH Collaboratory Living Textbook

## Available Content

### PCT Design

Experimental Designs and Randomization Schemes

Endpoints and Outcomes

Analysis Plan

Consent, Disclosure, and Non-disclosure

Using Electronic Health Record Data

Data and Safety Monitoring

Designing With Implementation and Dissemination in Mind

Assessing Feasibility

### PCT Conduct

Study Startup

Participant Recruitment

### PCT Dissemination

Data Sharing and Embedded Research

Dissemination and Implementation

Dissemination Approaches for Different Stakeholders



# Resources available from the NIH Collaboratory Knowledge Repository archive

The screenshot shows a website interface with a navigation bar containing 'DESIGN', 'CONDUCT', and 'DISSEMINATION'. The main content area is titled 'EXPERIMENTAL DESIGNS AND RANDOMIZATION SCHEMES SECTION 6' and 'Randomization Methods'. It lists a contributor, Elizabeth R. DeLong, PhD, and a contributing editor, Jonathan McCall, MS. The text describes the simplest forms of individually randomized RCTs and discusses pair-matching and stratification. A 'SECTIONS' list on the right includes: 1. Introduction, 2. Statistical Design Considerations, 3. Cluster-Randomized Trials, 4. Choosing Between Cluster and Individual Randomization, 5. Concealment and Blinding, 6. Randomization Methods, and 7. Additional Resources. A 'RESOURCES' section at the bottom lists: 'Pair-Matching vs Stratification in Cluster-Randomized Trials' and 'Advanced Methods for Primary Care Research: The Stepped Wedge Design'.

## RESOURCES

### [Pair-Matching vs Stratification in Cluster-Randomized Trials](#)


A guidance document from the Biostatistics and Study Design Core

### [Advanced Methods for Primary Care Research: The Stepped Wedge Design](#)

Presentation from the Agency for Healthcare Research and Quality (AHRQ) provides a technical overview of applications of the stepped-wedge design in clinical research

# Other Web Resources

- Core Working Group Pages



**DESIGN**      **CONDUCT**      **DISSEMINATION**

### Core Working Groups

Active Cores

Core	Description
<a href="#">Biostatistics and Study Design</a>	Create guidance and technical documents regarding study design and biostatistical issues; develop case studies; and ally with collaborators, Demonstration Project investigators, and academic institutions to gather input into key methodological issues.
<a href="#">Electronic Health Records</a>	Created the <a href="#">NIH Collaboratory Distributed Research Network</a> to enable distributed remote analysis of research datasets across health systems and act as the key repository for the tools and infrastructure we create to leverage EHRs to support

# Other Web Resources

- Demonstration Pages



## Demonstration Projects

The NIH Collaboratory is designed in part to support the design and rapid execution of several pragmatic clinical trial Demonstration Projects. These projects address questions of major public health importance and engage healthcare delivery systems in research partnerships. The data, tools, and resources produced by the Demonstration Projects will be made available to the greater research community to facilitate a broadened base of partnerships with healthcare systems. A UH2 is a cooperative agreement that supports the development of exploratory or innovative research activities (considered a pilot phase for feasibility assessment), and a UH3 award provides support for the second phase of research activities initiated with the UH2.

## Active Projects

Title	Principal Investigator	Sponsoring Institution	Phase
<a href="#">A Policy-Relevant U.S. Trauma Care System Pragmatic</a>	Zatzick, Douglas	University of Washington	UH3

# Other Web Resources

- Distributed Research Network



## NIH Collaboratory Distributed Research Network (DRN)

Millions of people. Strong collaborations. Privacy first.

**Co-Chairs:** Jeffrey Brown, Richard Platt, and Lesley Curtis

**Project Manager:** [Sarah Malek](#)

[Publications and Supplementary Material](#) | [Presentations](#)

Established by the [Electronic Health Records \(EHR\) Core](#), the NIH Collaboratory Distributed Research Network (DRN) enables investigators to collaborate with each other in the use of electronic health data, while also safeguarding protected health information and proprietary data. It supports both single- and multisite research programs.



Drs. Jeffrey Brown and Lesley Curtis explain the NIH Collaboratory Distributed Research Network.

# Other Web Resources

- About Us



## About NIH Collaboratory

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

Supported by the [Common Fund](#) at the National Institutes of Health (NIH), the NIH Health Care Systems Research Collaboratory aims to improve the way clinical trials are conducted by creating a new infrastructure for collaborative research with healthcare systems. The ultimate goal is to ensure that healthcare providers and patients can make decisions based on the best available clinical evidence.



Dr. Thomas Insel explains the NIH Collaboratory.

# Other Web Resources

- News



## News

- [May 5, 2018: New Article Explores Opportunities for Funding the Training of Future Health Services Researchers](#) In a new article, Dr. Vincent Mor, an NIH Collaboratory investigator, and Dr. Paul Wallace describe the history, current status, and opportunities for funding training in health services research (HSR). While the number of organizations seeking to solve problems with health services research has been expanding, direct government support for HSR is declining. The authors ...
- [May 1, 2018: Proposal for 6-month Delay for Implementation of Revised Common Rule](#) On April 20, 2018, the Department of Health and Human Services and 15 other federal departments and agencies proposed a rule to delay both the effective and compliance dates for the revisions to the “Federal Policy for the Protection of Human Subjects” (also known as the Common Rule). The Interim Final Rule initially announced a ...

RSS Feed

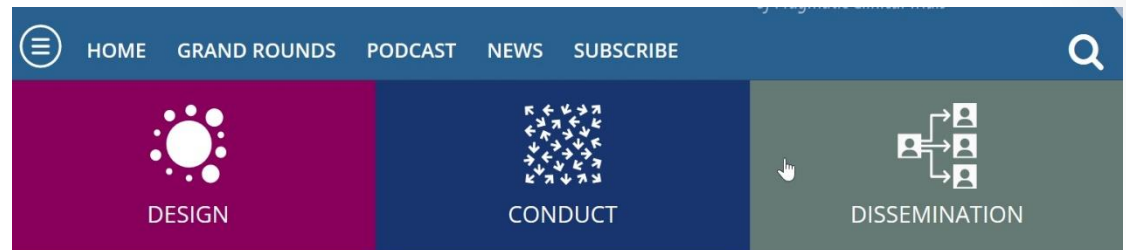
Subscribe for news updates from the NIH Collaboratory!

Tweets by @Collaboratory1



# Other Web Resources

- Training Resources



**NIH Collaboratory  
ePCT Training  
Workshop  
February 20-21, 2018**





# Other Web Resources

The screenshot shows the NIH Collaboratory website. At the top is a dark blue navigation bar with the following links: HOME, GRAND ROUNDS, PODCAST, NEWS, and SUBSCRIBE. Below the navigation bar is a dark grey sidebar menu with the following items: How to Use This Site, About Living Textbook, About NIH Collaboratory, Demonstration Projects, Core Working Groups, Distributed Research Network, and Calendar. The main content area features a large blue banner with the word "CONDUCT" and a cluster of white arrows pointing outwards. To the right of the banner is a dark green banner with the word "DISSEMINATION" and an icon of three people connected by arrows. Below the banners, the text "Pragmatic Clinical Trials: A Living Textbook of" is visible. Further down, there are several sections with titles and descriptions, each followed by a right-pointing arrow icon: "GET STARTED", "What is a PRAGMATIC CLINICAL TRIAL?", "ENGAGING STAKEHOLDERS", "and building partnerships to ensure a successful trial", "What is the NIH COLLABORATORY?", and "TRAINING RESOURCES".



## Demonstration Projects

The NIH Collaboratory is designed in part to support the design and rapid execution of several pragmatic clinical trial Demonstration Projects. These projects address questions of major public health importance and engage healthcare delivery systems in research partnerships. The data, tools, and resources produced by the Demonstration Projects will be made available to the greater research community to facilitate a broadened base of partnerships with healthcare systems. A UH2 is a cooperative agreement that supports the development of exploratory or innovative research activities (considered a pilot phase for feasibility assessment), and a UH3 award provides support for the second phase of research activities initiated with the UH2.

## Active Projects

Title	Principal Investigator	Sponsoring Institution	Phase
<a href="#">A Policy-Relevant U.S. Trauma Care System Pragmatic Trial for PTSD and Comorbidity (Trauma Survivors Outcomes and Support [TSOS])</a>	Zatzick, Douglas	University of Washington	UH3
<a href="#">Active Bathing to Eliminate (ABATE) Infection</a>	Huang, Susan	University of California, Irvine	UH3
<a href="#">Collaborative Care for Chronic Pain in Primary Care (PPACT)</a>	DeBar, Lynn	Kaiser Foundation	UH3
<a href="#">Improving Chronic Disease Management with Pieces (ICD-Pieces)</a>	Vazquez, Miguel	UT Southwestern Medical Center	UH3
<a href="#">Lumbar Imaging with Reporting of Epidemiology (LIRE)</a>	Jarvik, Jeffrey	University of Washington	UH3

## UH3 Project: Strategies and Opportunities to Stop Colorectal Cancer in Priority Populations (STOP CRC)



**Principal Investigator:** [Gloria D. Coronado, PhD](#)

**Co-Principal Investigator:** [Beverly B. Green, MD, MPH](#)

**Sponsoring Institution:** Kaiser Permanente Center for Health Research

**Collaborators:**

- Federally qualified health centers in the Oregon Community Health Information Network (OCHIN)
- Kaiser Permanente Washington Health Research Institute
- The National Center for Complementary and Integrative Health (NCCIH)

**NIH Institute Providing Oversight:** [National Cancer Institute \(NCI\)](#)

**Program Official:** Erica Breslau (NCI)

**Project Scientist:** Jerry Suls (NCI)

**ClinicalTrials.gov Identifier:** [NCT01742065](#)

**Study Locations:** [Affiliated clinics in California and Oregon](#)

**Trial Status:** Currently recruiting participants

Study Snapshot

## Presentation



## Interviews

[2/7/2018: In a video interview, Drs. Susan Huang and Gloria Coronado give advice to pragmatic trial investigators](#)

[4/20/2015: Drs. Coronado and Green Discuss Lessons Learned in the STOP CRC UH3 Demonstration Project](#)

[10/23/2012: Dr. Coronado Discusses the STOP CRC Project](#)



DESIGN

CONDUCT

DISSEMINATION

## Core Working Groups

### Active Cores

Core	Description
<a href="#">Biostatistics and Study Design</a>	Create guidance and technical documents regarding study design and biostatistical issues; develop case studies; and ally with collaborators, Demonstration Project investigators, and academic institutions to gather input into key methodological issues.
<a href="#">Electronic Health Records</a>	Created the <a href="#">NIH Collaboratory Distributed Research Network</a> to enable distributed remote analysis of research datasets across health systems and act as the key repository for the tools and infrastructure we create to leverage EHRs to support clinical research across multiple health systems.
<a href="#">Health Care Systems Interactions</a>	Engages those involved in healthcare delivery systems to participate in research, facilitate the design and conduct of research protocols attractive to practitioners, lower administrative barriers, and communicate results to all parties.

## Biostatistics and Study Design

**Chair:** Elizabeth DeLong

**NIH Representative:** David Murray

**Members:** Chul Ahn, Bryan Comstock, Andrea Cook, Constantine Gatsonis, Dan Gillen, Roei Gutman, Patrick Heagerty, Jesse Hsu, Ken Kleinman, J. Richard Landis, Michael Leo, Qian Li, Joan Russo, Susan Shortreed, Liz Turner, William Vollmer, Jin Wang, Rui Wang, Song Zhang

**Project Manager:** [Darcy Louzao](#)

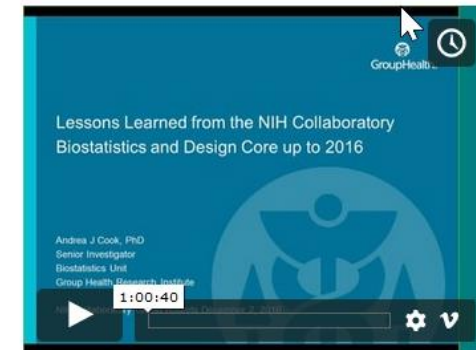
[Products and Publications](#) | [Presentations](#)

Pragmatic clinical trials, including cluster-randomized trials, present biostatistical and study design issues in addition to those typically encountered with traditional clinical trials. The Biostatistics and Study Design Core works with the NIH and [Demonstration Project](#) teams to create guidance and technical documents regarding study design and biostatistical issues relevant to pragmatic clinical trials.

For example, when randomizing clusters rather than individuals, several issues need attention. These include the trade-off between sample size and potential contamination, the intra-class correlation at different levels, varying cluster size, and the need for stratification or matching.

Additionally, special consideration must be given to [handling informative missing follow-up data](#) when using electronic health records as the basis for follow-up data collection. Individuals who are less healthy and have more chronic conditions will have more healthcare visits, so even if an intervention is effective in improving general

## Presentation



Andrea J. Cook, PhD, of the University of Washington and Group Health Research Institute discusses biostatistics and study design challenges for pragmatic clinical trials.

## Interviews

[6/11/2015: Dr. Liz DeLong Discusses Lessons](#)



# Resources available for Core Working Groups

## Products and Publications

- [Richesson RL, et al. J AM Med Inform Assoc 2017](#)
- [Zozus MN, et al. AMIA Jt Summits Transl Sci Proc 2016](#)
- [EHR Data FAQs](#)
- [PopMedNet-i2b2 Integration Proof of Concept Video](#)
- [Richesson RL, et al. eGEMs 2016](#)
- [Richesson R, et al. Artif Intell Med 2016](#)
- [Acquiring and Using Electronic Health Record Data](#)

## Presentations

- [8/25/2017: Thoughts From the Phenotypes, Data Standards & Data Quality Core](#)
- 8/14/2015: Grand Rounds Presentation: ICD-10 Transition: Implications for Pragmatic Trials ([Video](#); [Slides](#))
- 11/14/2014: Grand Rounds Presentation: Using the NIH Collaboratory's and PCORnet's Distributed Data Networks for Clinical Trials and Observational Research: A Preview ([Video](#); [Slides](#))

DESIGN
CO

### Electronic Health Records

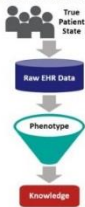
**Co-Chairs:** Rachel Richesson, Greg Simon  
**NIH Representatives:** Jerry Sheehan, Barbara Wells  
**Members:** Nick Anderson, Alan Bauck, Denise Cifelli, Lesley Curtis, Erik Van Essen, Pedro Gozalo, Beverly Green, Ed Hammond, Susan Huang, Michael Kahn, Rees Lewis, Rosemary Madigan, Meghan Mayhew, Tom Meehan, Vincent Moran, George "Holt" Oliver, Jon Puro, Jerry Sheehan, Kari Stephens, Ferdinand Tascas, Wolfgang Winkelmayr  
**Project Manager:** [Jesse Hickerson](#)

[Products and Publications](#) | [Presentations](#)

The ability to harness electronic health data is transforming the way clinical research is conducted. The Electronic Health Records (EHR) Core's goal is to facilitate multisite research collaborations between investigators and data stewards. Core members have expertise in data models, data standards and quality, algorithms, and approaches to define clinical phenotypes, extract information, define endpoints, and discover errors in data from healthcare systems.

The secondary use of electronic health record (EHR) data for clinical research requires not only an understanding of data representation, exchange standards, and the influence of workflows, but also the development and implementation of valid approaches for identifying cohorts with clinical conditions. This involves collaboration among clinicians, EHR experts, and informaticians to develop algorithms, or [computable phenotypes](#), for identifying patients with clinical conditions being studied by researchers.

There are many ways to identify patients who have been diagnosed with a specific condition, and understanding the pros and cons of the various approaches is essential for using EHRs effectively in pragmatic



**Update from the Phenotypes, Data Standards, Data Quality Core of the NIH HCS Research Collaboratory**

NIH Collaboratory Grand Rounds  
August 26, 2016

Rachel Richesson, PhD, MPH  
[@RachelRichesson](#)

Rachel Richesson, PhD, Duke University School of Nursing, describes recent updates from the Collaboratory's EHR Core (formerly the Phenotypes, Data Standards, and Data Quality Core).

**Special Topics**

- [Learning healthcare systems](#)
- [ICD-9 to ICD-10 Mapping](#)
- [Phenotype Case Study: LIBE Trial](#)
- [Phenotype Case Study: MURDOCK Trial](#)

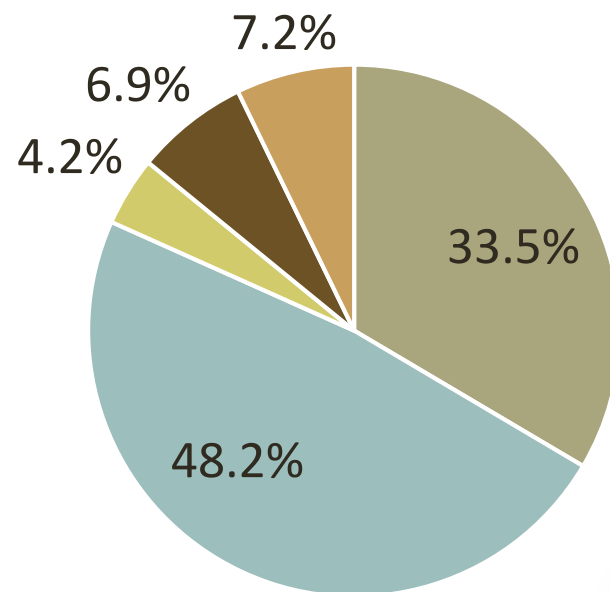
# How Is the Site Performing?

## Metrics After 6 months

Metric	Average per month
Sessions	2,823
Users	1,778
Pageviews	6,848
Pages/session	2.44
Session duration	2:52 min
Bounce rate	57%

### Traffic Sources

- Organic search
- Referral
- Email
- Direct
- Social



# Overall Metrics Analysis

- Large increases in traffic to site overall
- Modest increase in average time per session
  - Our 3:10 min remains well above industry average of 1:50 min
- Bounce rate decreased slightly, meaning fewer visitors left almost immediately (good)
  - Rate of 56% remains below 70% threshold considered concerning
- Slightly fewer page visits per session with the new site
  - Could mean people are finding information faster

# Most Visited Chapters

## Q4 2017

Chapter	Pageviews
What is a Pragmatic Clinical Trial?	414
Experimental Designs and Randomization Schemes	279
Resource Chapter: Electronic Health Records-Based Phenotyping	140
Study Startup	122
Engaging Stakeholders and Building Partnerships to Ensure a Successful Trial	110

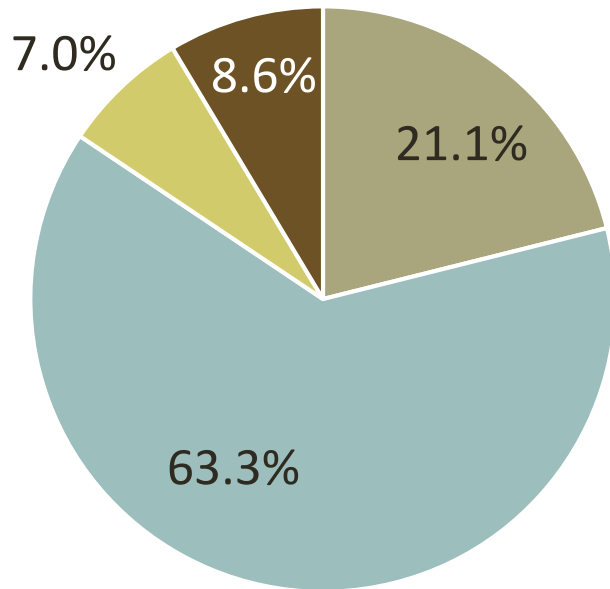
## Q1 2018

Chapter	Pageviews
What is a Pragmatic Clinical Trial?	1,586
Experimental Designs and Randomization Schemes	557
Using Electronic Health Record Data	351
Dissemination and Implementation	285
Analysis Plan	236

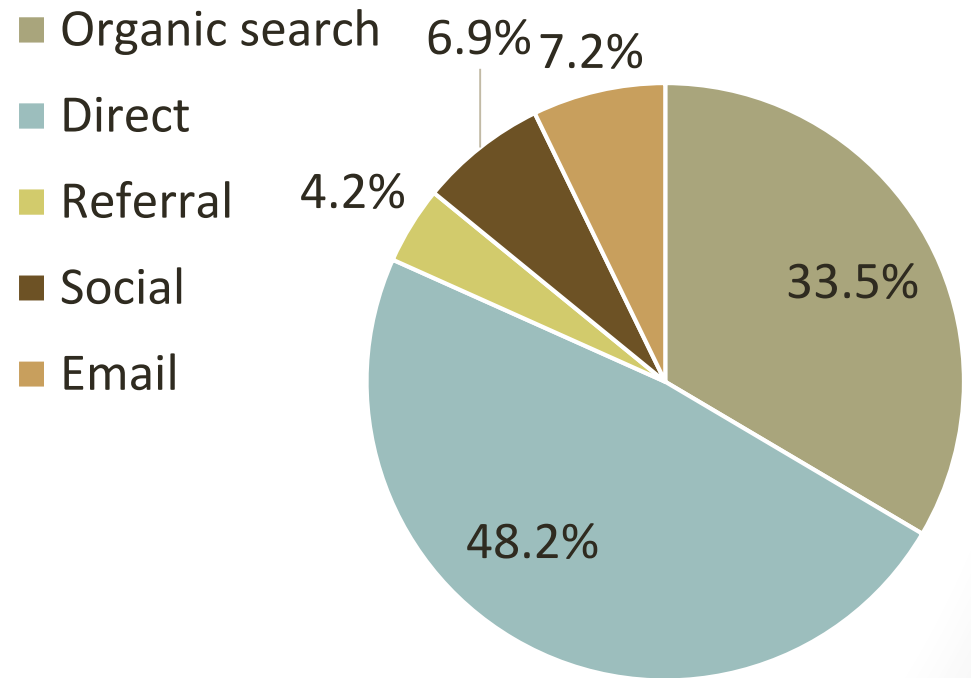


# Traffic Sources

## Q4 2017



## Q1 2018



- Organic search
- Direct
- Referral
- Social
- Email

# Visitors

- .gov, .edu, and .org traffic accounted for 23% of all sessions in Q1
- United States accounts for majority of visitors, with a scattering of others worldwide
- Homepage usage Q1
  - ~20% of users scroll at least 75% down homepage
  - “Featured Information” section least clicked (<1%)

## Desktop vs. Mobile vs. Tablet

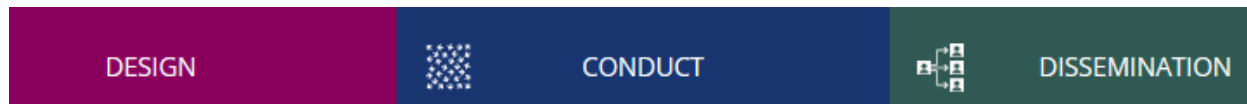
	Q4 2017	Q1 2018
Desktop	86.4%	86.5%
Mobile	10.2%	12%
Tablet	3.4%	3.5%

# Website Summary

- New website performing well
- Will continue to monitor metrics and make improvements as indicated
- Using other Collaboratory channels (e.g., Grand Rounds, Twitter, e-newsletter) to drive traffic to website
- Chapter content undergoes annual review and update
  - Ad hoc updates & additions also made as appropriate

# PCT Grand Rounds Presentations

- Weekly public webinars
- >250 presentations
- Avg. >161 attendees/wk
- Videos played >2000 times in 2017



## 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 30: HHS-DoD-VA Pain Management Collaboratory (Robert Kerns, PhD)
- Grand Rounds April 6: Legal and Ethical Architecture for PCOR Data (Jane Hyatt Thorpe, JD; Lara Cartwright-Smith, JD, MPH; Elizabeth Gray, JD, MHA)
- Grand Rounds April 13: OHDSI: Drawing Reproducible Conclusions from Observational Clinical Data (George Hripcsak, MD, MS)

## Last Week's Grand Rounds

Duke **FORGE**

**DATA SCIENCE IN THE ERA OF DATA UBIQUITY**

Robert M. Califf, MD  
Vice Chancellor for Health Data Science  
Director, Duke Forge  
Duke University School of Medicine  
Advisor, Verily Life Sciences  
NIH HCS Collaboratory Grand Rounds  
March 23<sup>rd</sup>, 2018

1:00:22      vimeo

# Grand Rounds Podcast

- Monthly episodes
- Short format (~10-15 min)
- Launched September 2017
  - Avg. >75 listens/episode
  - >200 subscribers

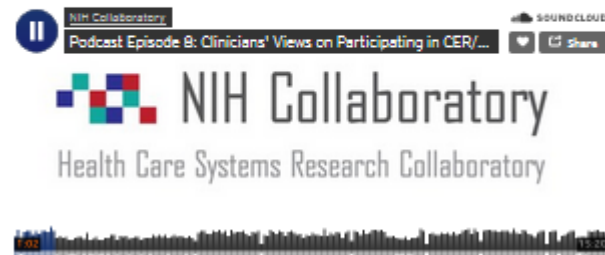


Podcast March 22: Straight from the Source:  
Clinicians' Views on Participating in CER/PCOR  
(Sean Tunis, MD, MSc; Ellen Tambor, MA)



In this episode of the NIH Collaboratory Grand Rounds podcast, Dr. Sean Tunis and Ellen Tambor of the Center for Medical Technology Policy (CMTF) speak with moderator Dr. Kevin Weinfurt about their findings on clinician attitudes on comparative effective research (CER) and patient-centered outcomes research (PCOR). The speakers discuss their findings on clinician attitudes towards research participation, and how and when to best engage them. They describe the need for involving clinicians in the planning of study design, and in closing feedback loops after studies are completed, in order to build clinicians' trust that research does lead to quality improvement for their patients.

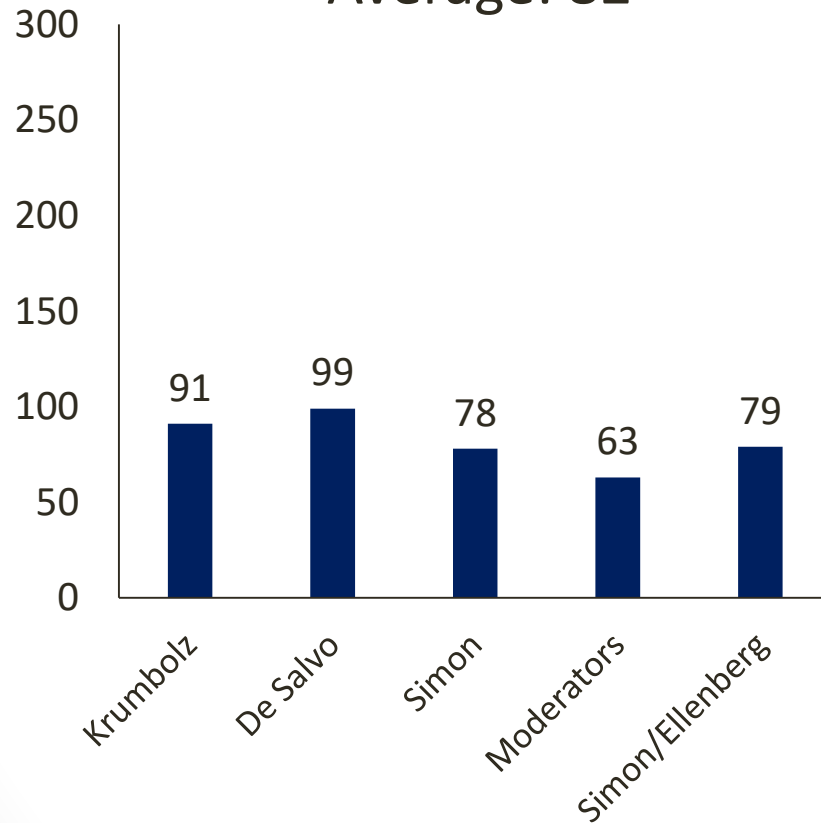
Click on the recording below to listen to the podcast.



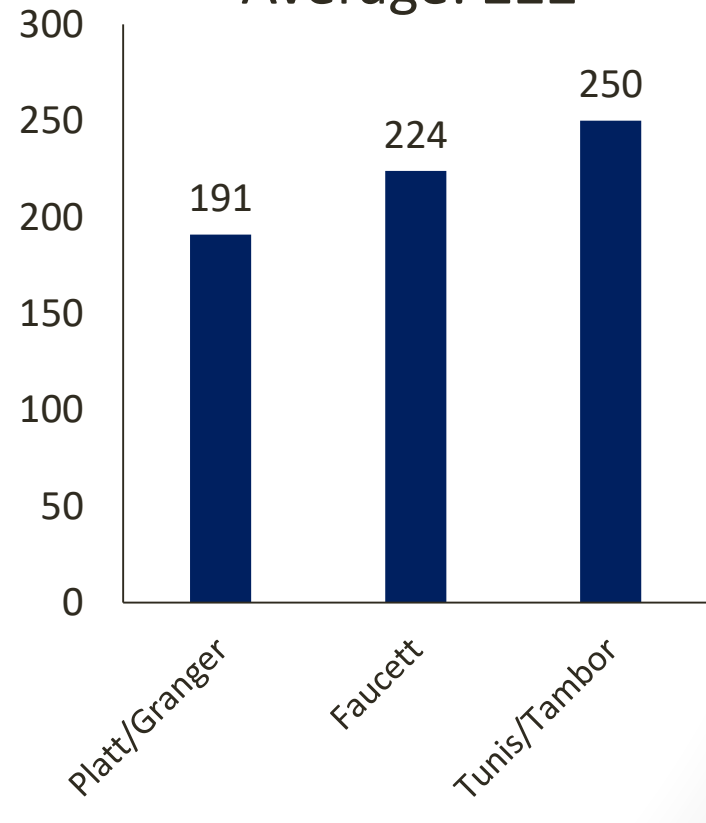
[rethinkingclinicaltrials.org/podcasts](http://rethinkingclinicaltrials.org/podcasts)

# Total Podcast Plays Per Episode

**Q4 2017**  
Average: 82



**Q1 2018**  
Average: 222



# Social Media

## @Collaboratory1

- >1000 followers
- ~8000 impressions/mo

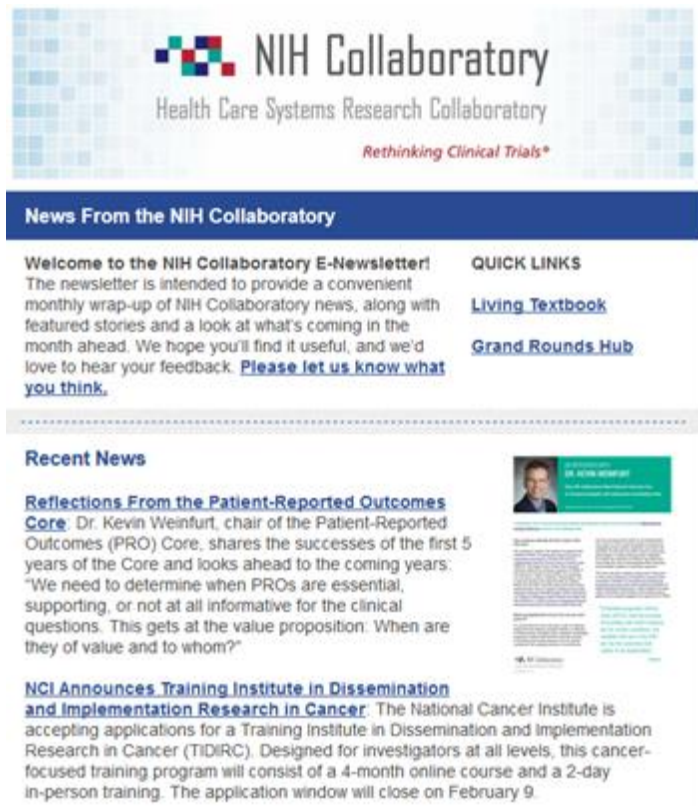
## @PCTGrandRounds

- >550 followers
- ~20,000 impressions/mo



8.4% of traffic to the  
Living Textbook comes  
from social media

# NIH Collaboratory Email Newsletter



- Convenient monthly wrap-up
  - NIH Collaboratory & PCT news
  - Feature stories
- Launched January 2018
  - >400 subscribers

[rethinkingclinicaltrials.org/newsletter-subscribe](https://rethinkingclinicaltrials.org/newsletter-subscribe)



# E-newsletter Metrics Q1 2018

Metric	January 2018	February 2018	March 2018
Day and time sent	Thu, 12:15 pm	Thu, 4:00 pm	Thu, 11:00 am
Total sent	377	403	418
Bounces	4	7	8
Open rate	163 (43.7%)	157 (39.6%)	159 (38.8%)
Desktop	145 (88.8%)	118 (75.4%)	133 (83.7%)
Mobile	18 (11.2%)	39 (24.6%)	26 (16.3%)
Click-through rate	44.8%	33.8%	34.0%
Unsubscribed	0	0	1

# 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





# An Open Invitation

- We welcome your contributions to the Living Textbook and other web-based resources:
  - Help author/revise Living Textbook chapters
  - Contribute to guidance documents & other resources
  - External resources of interest
  - News items of interest to the PCT community
  - Case studies/lessons learned from Demonstration Projects



Health Care Systems Research Collaboratory

Thank you.