NIH Collaboratory: 
Looking Back, Looking Forward

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Today’s Presentation

- NIH Collaboratory Story and Highlights
- Completed Demonstration Projects
- HEAL Initiative and PRISM Awards
- Transitioned Projects
- What Should Be Next?
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NIH Collaboratory Story and Highlights
Millions of 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 NIH 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 healthcare 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
- Intervention incorporated into routine clinical workflow
- Diverse, representative study populations
- Outcomes important to decision makers
Flow of Information

- **Demonstration Projects**
  - Core Working Groups
  - Teleconferences
  - Steering Committee Meetings
  - Partner Organizations

- **Lessons**
  - Living Textbook & Knowledge Repository
  - Grand Rounds, Presentations & Social Media
  - Guidance Documents & Journal Publications

- NIH Collaboratory
  - Rethinking Clinical Trials
  - Health Care Systems Research Collaboratory
Demonstration Projects

• Pragmatic trials embedded in healthcare systems to address questions of major public health importance

• Projects span multiple NIH Institutes, Centers, and Offices

• One-year planning phase followed by implementation phase
NIH Collaboratory Publications

Articles published in peer-reviewed journals

115 total
NIH Collaboratory Presentations

>300 total conference presentations or symposia
Living Textbook
Annual Content Update

Completed January 2019

- Refreshed and new content
- Thank you, contributors!

rethinkingclinicaltrials.org
New Living Textbook Content

- Developing a Compelling Grant Application
- Experimental Designs and Randomization Schemes
  - Designing to Avoid Identification Bias
- Choosing and Specifying Endpoints and Outcomes
  - Using Death as an Endpoint
- Analysis Plan
  - Alternative Cluster Randomized Designs
  - Case Study: STOP CRC Trial
- ePCT Team Composition

rethinkingclinicaltrials.org
Our Following

@Collaboratory1
1,415 followers

Email newsletter
877 subscribers
NIH Collaboratory Grand Rounds

312 total Grand Rounds presentations since inception

139 average attendees per week over the last year
2

Completed Projects
ABATE Infection  
Active Bathing to Eliminate Infection

- **PI:** Susan Huang, MD, MPH
- **NIH Institute:** NIAID

**THE LANCET**

Chlorhexidine versus routine bathing to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial

Susan S Huang, Edward Septimus, Ken Kleinman, Julia Moody, Jason Hickok, Lauren Heim, Adriana Gomboev, Taliser R Avery, Katherine Haffenreffer, Lauren Shimelman, Mary K Hayden, Robert A Weinstein, Caren Spencer-Smith, Rebecca E Kaganov, Michael V Murphy, Tyler Forehand, Julie Lankiewicz, Micaela H Coady, Lena Portillo, Jalpa Sarup-Patel, John A Jernigan, Jonathan B Perlin, Richard Platt, for the ABATE Infection trial team
ABATE Infection

- **Intervention**: Decolonization with universal chlorhexidine and targeted nasal mupirocin in non–critical-care units

- **Results**
  - No overall reduction in methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant enterococcus (VRE) clinical cultures
  - In post hoc analyses of patients with medical devices, significant reductions in all-cause bloodstream infections and MRSA/VRE clinical cultures
# ABATE Infection

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Solution</th>
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<tbody>
<tr>
<td>Concurrent QI initiatives competing with study intervention</td>
<td>Monthly tracking and review; encouragement to delay, limit competing initiatives</td>
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<td>Changes in site leadership, trial unit names for identifying site locations</td>
<td>Study champions asked to disclose changes during monthly coaching calls</td>
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<tr>
<td>Need for data cleaning, standardization greater than anticipated</td>
<td>Increased programming effort budgeted for data cleaning and standardization</td>
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<tr>
<td>Requirement for dedicated ethical oversight for any prisoner admitted to non-ICU area during trial</td>
<td>Identification of participating site with prisoner on IRB to provide oversight</td>
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PPACT Collaborative Care for Chronic Pain in Primary Care

• PI: Lynn L. DeBar, PhD

• NIH Institutes: NINDS, NIDA
PPACT

• **Intervention**: Primary care–based interdisciplinary behavioral intervention among patients receiving long-term opioid therapy for chronic pain

• **Results**
  
  • Modest but significant and sustained reductions in pain impact, pain-related disability, and benzodiazepine use
  
  • Primary results manuscript under review
### PPACT

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Lesson</th>
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<tr>
<td>Competing change initiatives and quality improvement efforts</td>
<td>Adopt systems and processes native to the healthcare system, and partner with quality improvement managers</td>
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<td>Patient-reported outcomes not embedded into system in a way that enabled pulling data from EHR</td>
<td>Build infrastructure, processes, and additional resources into system ahead of time to gather this information</td>
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<tr>
<td>Intervention was challenging because it required different clinical skill set to harmonize support of patients’ self-care efforts with traditional treatments</td>
<td>Close work with clinicians and other stakeholders to sustain healthcare system investment in intervention</td>
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STOP CRC  Strategies and Opportunities to Stop Colorectal Cancer in Priority Populations

- **PIs**: Gloria D. Coronado, PhD; and Beverly B. Green, MD, MPH
- **NIH Institute**: NCI

**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
STOP CRC

- **Intervention**: EHR-embedded tool to identify patients overdue for colorectal cancer screening and mail a fecal immunochemical test (FIT) kit to them

- **Results**
  - Higher screening rates overall in intervention clinics compared with control clinics
  - Low and highly variable implementation rates among participating clinics
# STOP CRC

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<tr>
<td>Inadequate capacity at some clinics to immediately activate EHR tool</td>
<td>Regular teleconferences with clinic and data coordinating center representatives</td>
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<tr>
<td>Analysis challenges due to system-level HER upgrades and clinic-level delays</td>
<td>Consultation with Biostatistics and Study Design Core to modify statistical analysis and develop secondary analysis</td>
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<td>Lack of reliable data on colonoscopies</td>
<td>Validation of available colonoscopy codes and chart audits</td>
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<tr>
<td>Difficulty motivating clinic staff to learn new technology and process</td>
<td>Frequent contact with clinics; offers of training and support; advisory board of clinic staff with quarterly conference calls, annual meetings</td>
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TiME to Reduce Mortality in End-Stage Renal Disease

- **PI:** Laura Dember, MD
- **NIH Institute:** NIDDK

**The TiME Trial: A Fully Embedded, Cluster-Randomized, Pragmatic Trial of Hemodialysis Session Duration**

Laura M. Dember,¹,² Eduardo Lacson, Jr.,³ Steven M. Brunelli,⁴ Jesse Y. Hsu,⁵ Alfred K. Cheung,⁶ John T. Daugirdas,⁷ Tom Greene,⁸ Csaba P. Kovesdy,⁹ Dana C. Miskulin,¹⁰ Ravi I. Thadhani,¹¹,¹² Wolfgang Winkelmayer,¹³ Susan S. Ellenberg,⁵ Denise Cifelli,¹⁴ Rosemary Madigan,¹⁴ Amy Young,⁴ Michael Angeletti,³ Rebecca L. Wingard,³ Christina Kahn,³ Allen R. Nissenson,¹⁵,¹⁶ Franklin W. Maddux,³ Kevin C. Abbott,¹⁷ and J. Richard Landis⁵
**TiME**

- **Intervention**: Minimum hemodialysis session duration of 4.25 hours for patients with end-stage renal disease beginning maintenance hemodialysis

- **Results**
  - Trial discontinued early due to insufficient difference in mean hemodialysis session duration between intervention and usual care groups
  - No observed reduction in mortality or hospitalization rate in either group
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<td>Difficulty implementing intervention due to lack of on-site research staff, implementation by clinicians rather than researchers</td>
<td>Use of multiple approaches to engage facility personnel and participating patients during all stages of trial design and conduct</td>
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<tr>
<td>Incomplete ascertainment of patient-reported outcome already being used routinely in clinical practice</td>
<td>Adding processes to those already being used in clinical practice</td>
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HEAL Initiative and PRISM Awards
September 2019

NIH Collaboratory selected as PRISM Resource Coordinating Center
HEAL Initiative and PRISM Awards

- As part of HEAL Initiative, NIH awards funding for new Demonstration Projects:
  - Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM)
  - Pragmatic Randomized Controlled Trial of Acupuncture for Management of Chronic Low Back Pain in Older Adults
PRISM Resource Coordinating Center

- PRISM awards total $35.7 million
- 8 participating NIH Institutes, Centers, and Offices
- NIH Collaboratory added 4 new large-scale ePCTs to portfolio of innovative Demonstration Projects
  - Focus on effectiveness of non-opioid interventions for pain, assessing impact of interventions or guidelines to improve pain management and reduce reliance on opioids
  - Coordinating Center will provide technical support and pragmatic trial expertise
Welcome! New experts join the NIH Collaboratory

Joining the NIH Collaboratory Leadership

Steven Z. George, PT, PhD
Welcome! New experts join the NIH Collaboratory

Joining the Biostatistics and Study Design Core

Elizabeth L. Turner, PhD
Welcome! New experts join the NIH Collaboratory

Joining the Electronic Health Records Core

Keith A. Marsolo, PhD
Welcome! New experts join the NIH Collaboratory

Joining the Health Care Systems Interactions Core

Devon K. Check, PhD
Welcome! New experts join the NIH Collaboratory

Joining the Ethics and Regulatory Core

Joseph Ali, JD; and Stephanie Morain, PhD, MPH
Welcome! New experts join the NIH Collaboratory

Ethics and Regulatory Core – Panel of Experts

John D. Lantos, MD; David Magnus, MD; Pearl O’Rourke, MD; and Kayte Spector-Bagdady, JD, MBioethics
Welcome! New experts join the NIH Collaboratory

Joining the Patient-Centered Outcomes Core

William Maixner, DDS, PhD; Emily C. O’Brien, PhD; and Christina K. Zigler, PhD
PRISM Projects

• Research embedded in healthcare systems

• Studies to determine effectiveness of non-opioid interventions for treating pain, and assess impact of implementing interventions or guidelines to improve pain management and reduce reliance on opioids

• Pragmatic clinical trials aimed at improving availability of, effectiveness of, and adherence to evidence-based, nonpharmacological pain management
## PRISM Projects

<table>
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<tr>
<th>Study</th>
<th>PI/Co-PI</th>
<th>Program Official/Project Scientist</th>
<th>Institution</th>
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</table>
| **AcuOA**    | Lynn DeBar, PhD, MPH  
Karen J Sherman, PhD, MPH | PO: Robin Boineau, MD, MA (NCCIH)  
PS: Basil Eldadah, MD, PhD (NIA) | Kaiser Foundation Research Institute                     |
| Pragmatic trial of acupuncture for chronic low back pain in older adults | | | |
| **NOHARM**   | Andrea Cheville, MD  
Jon Tilburt, MD | PO: Marcel Salive, MD, MPH (NIA)  
PS: Jennie Conroy, PhD (NICHD) | Mayo Clinic Rochester                               |
| Non-pharmacological options in postoperative hospital-based and rehabilitation pain management | | | |
| **OPTIMUM**  | Natalia Morone, MD | PO: Wendy Weber, ND, PhD, MPH (NCCIH)  
PS: Luke Stoeckel, PhD (NIA) | Boston Medical Center                                      |
| Group-based mindfulness for patients with chronic low back pain in the primary care setting | | | |
| **TIPS**     | Kathleen Sluka, PT, PhD  
Leslie Crofford, MD | PO: James Witter, MD, PhD, FACR (NIAMS)  
PS: Martha Matocha, PHD (NINR) | University of Iowa                                           |
| Fibromyalgia TENS in physical therapy study: an embedded pragmatic clinical trial | | | |
AcuOA *Pragmatic Trial of Acupuncture for Chronic Low Back Pain in Older Adults*

- **PIs:** Karen J. Sherman, PhD, MPH; and Lynn L. DeBar, PhD
- **NIH Institute:** NCCIH
- **Intervention:** Standard and enhanced 12-week courses of acupuncture
- **Outcomes:** Back-related function at 26 weeks; cost-effectiveness
NOHARM  Non-pharmacological Options in postoperative
Hospital-based And Rehabilitation pain Management

- **PIs**: Andrea Cheville, MD; and Jon Tilburt, MD
- **NIH Institute**: NIA
- **Intervention**: Patient- and clinician-facing EHR-embedded tools to aid shared decision making about postoperative pain management
- **Outcomes**: Postoperative opioid use, pain, and function
Optimizing Pain Treatment in Medical Settings Using Mindfulness

- **PI**: Natalia E. Morone
- **NIH Institute**: NCCIH
- **Intervention**: Group-based mindfulness in outpatient clinical settings
- **Outcomes**: Reduction in pain; improvements in physical and psychological function; and reduction in opioid prescriptions for chronic low back pain
TIPS Fibromyalgia TENS in Physical Therapy Study

• **PI**: Kathleen A. Sluka, PT, PhD; and Leslie Crofford, MD

• **NIH Institute**: NIAMS

• **Intervention**: Addition of transcutaneous electrical nerve stimulation to physical therapy for patients with fibromyalgia

• **Outcomes**: Improvement in fibromyalgia symptoms; adherence to physical therapy; likelihood of meeting therapeutic goals; and reduction in medication use
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Transitioned Projects

Congratulations
ACP PEACE  Advance Care Planning: Promoting Effective and Aligned Communication in the Elderly

- Cluster randomized trial of clinician communication skills training and patient video decision aids to increase advance care planning in patients older than 65 years with advanced cancer
- 4500 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 level yields noninferior rates of all-cause hospitalization in patients with end-stage renal disease undergoing hemodialysis

• 4400 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 reduces behavioral health problems and health service utilization

• 72 pediatricians across 3 health systems; 4500 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 user-centered computerized clinical decision support on rates of emergency department–initiated buprenorphine or 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 cardiovascular 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
What Should Be Next?
Expanded Knowledge

- Develop and disseminate guidelines and lessons learned from the PRISM projects
- Promote synergies with newer Collaboratory programs
  - NIA Imbedded Pragmatic AD/ADRD Clinical Trials (IMPACT) Collaboratory
  - NIH-DoD-VA Pain Management Collaboratory
- Advance the quality and impact of patient-centered outcome measures
  - Using patient engagement activities
  - By understanding and disseminating best practices for assessing pain and related constructs in the context of ePCTs
- Study innovative dissemination and implementation science approaches
Expanded Education and Training

- Training workshops for investigators, research community, and NIH staff on PCT methods
  - At scientific conferences
  - At NIH
- Additional publicly available training materials, such as handouts, slides, videos, Living Textbook chapters/additions, or other content to be made available on the NIH Collaboratory website
Regulatory and Ethics

- Ethical and practical issues associated with collateral findings
- Opting Out
- GCP training/PCT tensions
- Certificates of Confidentiality
- Postdoctoral fellowships at Johns Hopkins Berman Institute of Bioethics
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, and dissemination of embedded PCTs
  - rethinkingclinicaltrials.org

- Monthly Newsletter
  - Convenient monthly wrap-up of NIH Collaboratory news, Demonstration Project spotlights, and new Living Textbook content
  - rethinkingclinicaltrials.org/newsletter-subscribe

- Twitter
  - @Collaboratory1