

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



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



National Institutes
of Health

Initiated through the NIH Common Fund in 2012

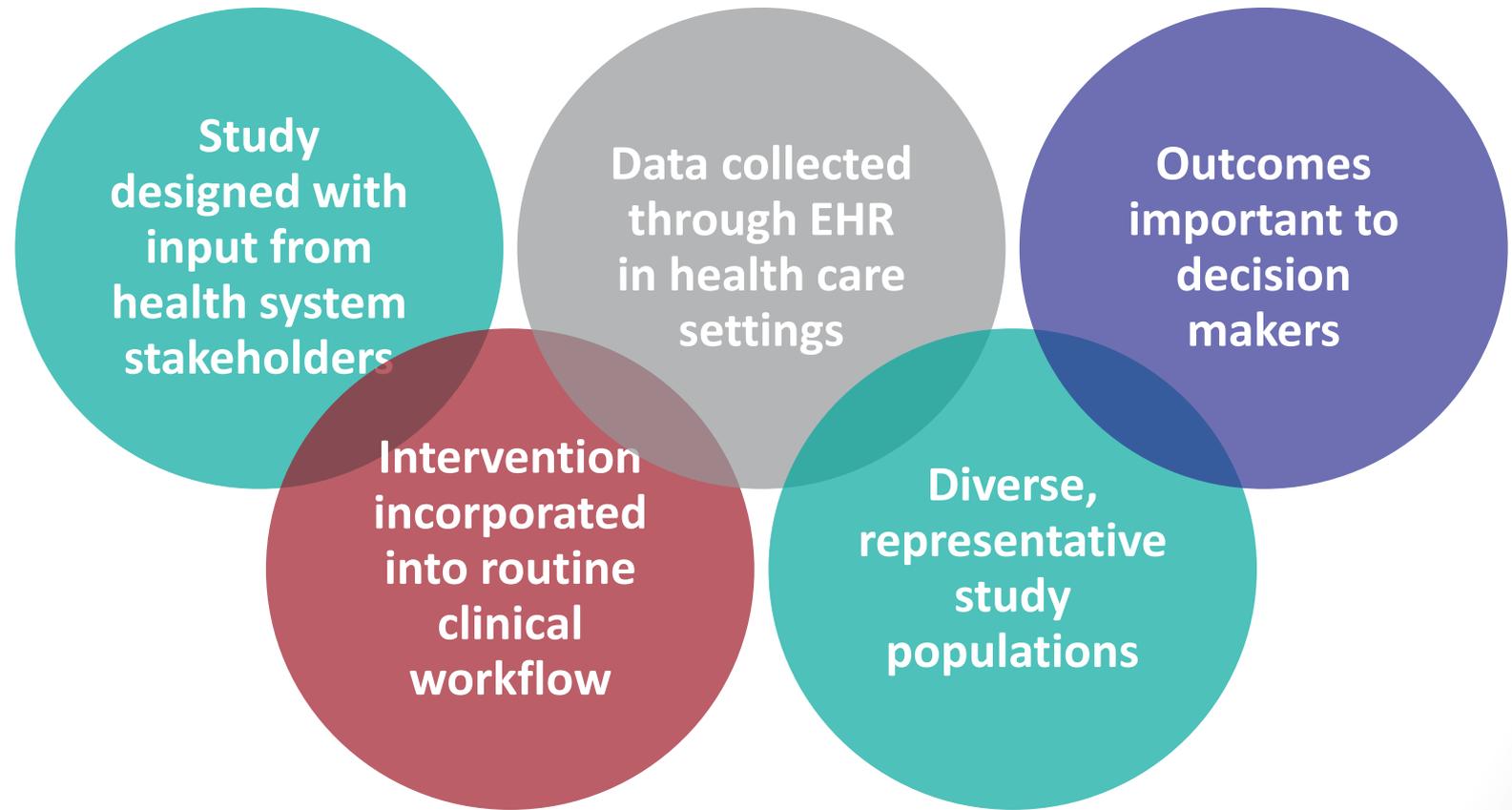


Goal: Strengthen the national capacity to implement cost-effective large-scale research studies that engage healthcare delivery organizations as research partners

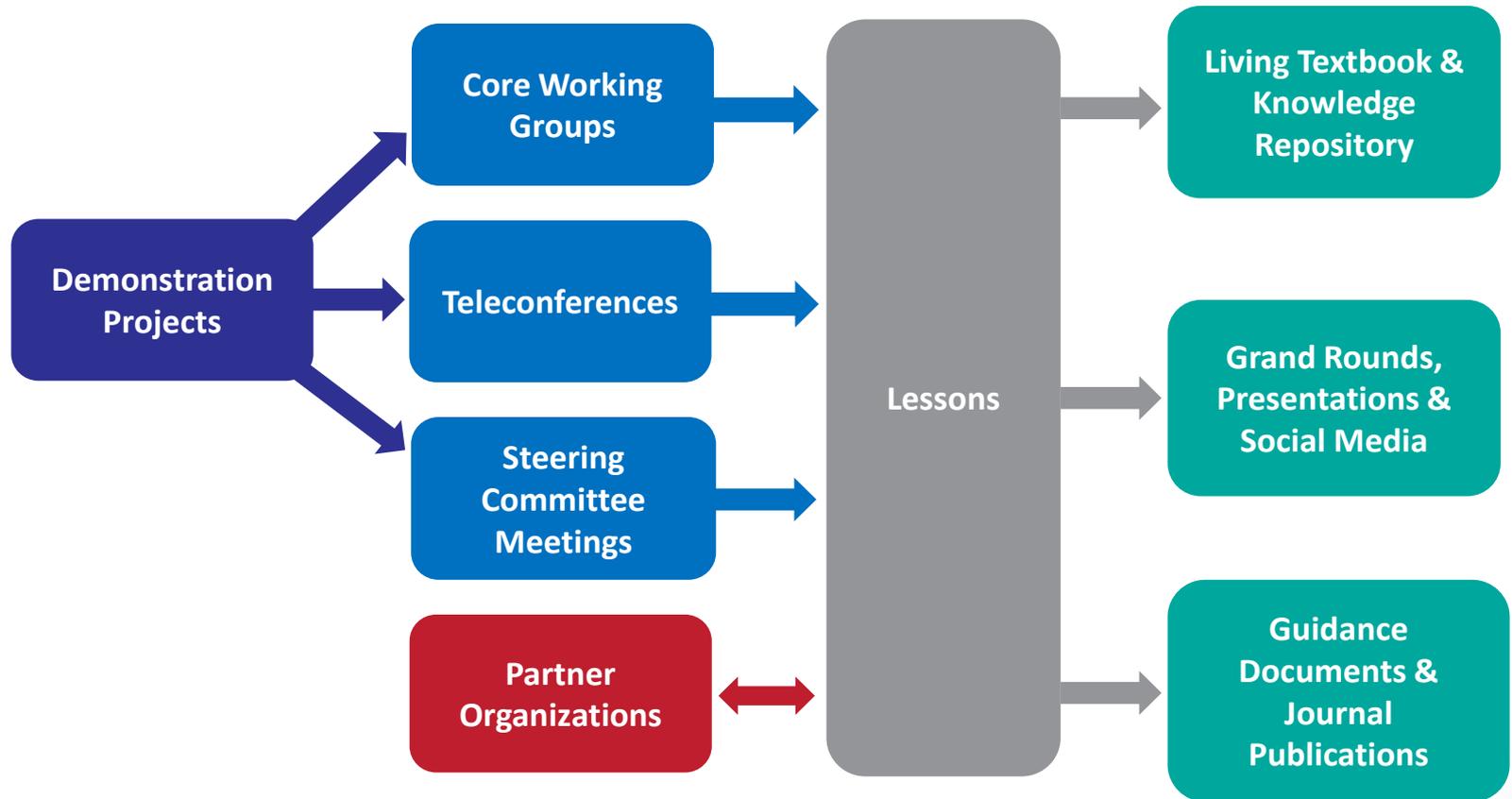


Vision: Support the design and execution of innovative pragmatic clinical trial Demonstration Projects to establish best practices and proof of concept

Embedded PCTs Bridge Research Into Clinical Care

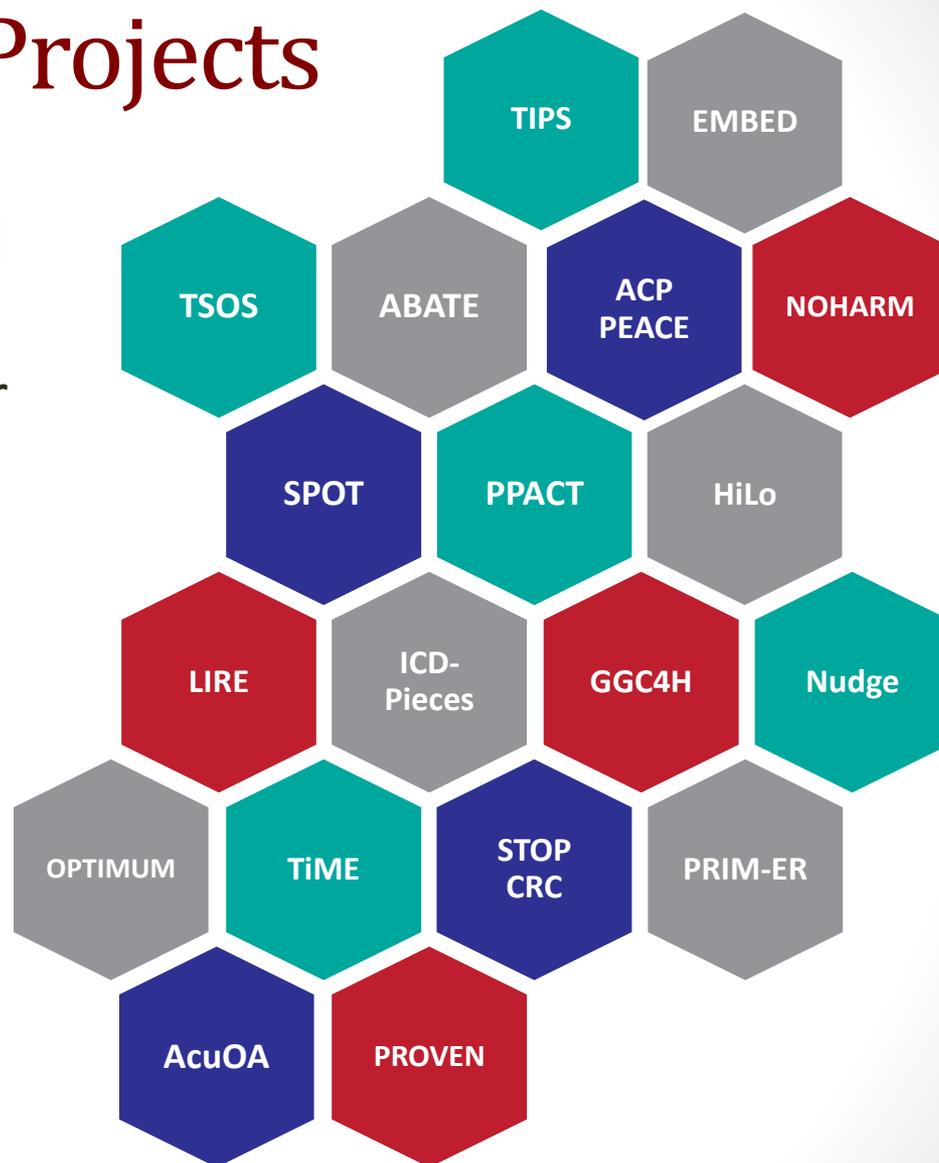


Flow of Information

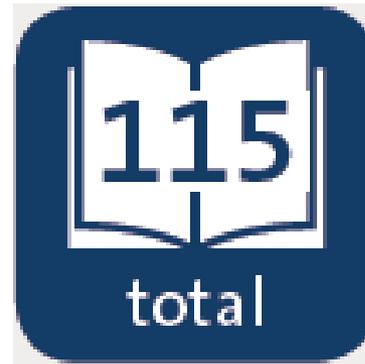


Demonstration Projects

- 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

NIH Collaboratory Presentations

>300

total conference
presentations
or symposia



Living Textbook Annual Content Update

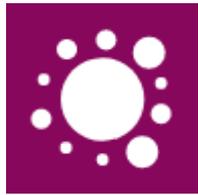
Completed January 2019



- Refreshed and new content
- Thank you, contributors!

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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**

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Our Following



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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, Adrijana Gombosev, Taliser R Avery, Katherine Haffnerreffer, 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

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

PPACT Collaborative Care for Chronic Pain in Primary Care

- **PI:** Lynn L. DeBar, PhD
- **NIH Institutes:** NINDS, NIDA



Automating Collection of Pain-Related Patient-Reported Outcomes to Enhance Clinical Care and Research

Ashli Owen-Smith, PhD, SM^{1,2}, Meghan Mayhew, MPH³, Michael C. Leo, PhD³,
Alexandra Varga, MPH³, Lindsay Benes, PhD, RN, CNS^{3,4}, Allison Bonifay, MA, LPC³, and Lynn DeBar,
PhD, MPH⁵

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

Challenge	Lesson
Competing change initiatives and quality improvement efforts	Adopt systems and processes native to the healthcare system, and partner with quality improvement managers
Patient-reported outcomes not embedded into system in a way that enabled pulling data from EHR	Build infrastructure, processes, and additional resources into system ahead of time to gather this information
Intervention was challenging because it required different clinical skill set to harmonize support of patients' self-care efforts with traditional treatments	Close work with clinicians and other stakeholders to sustain healthcare system investment in intervention

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

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

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. Kovcsy ⁹, Dana C. Miskulin,¹⁰ Ravi I. Thadhani,^{11,12} Wolfgang Winkelmayr,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

TiME

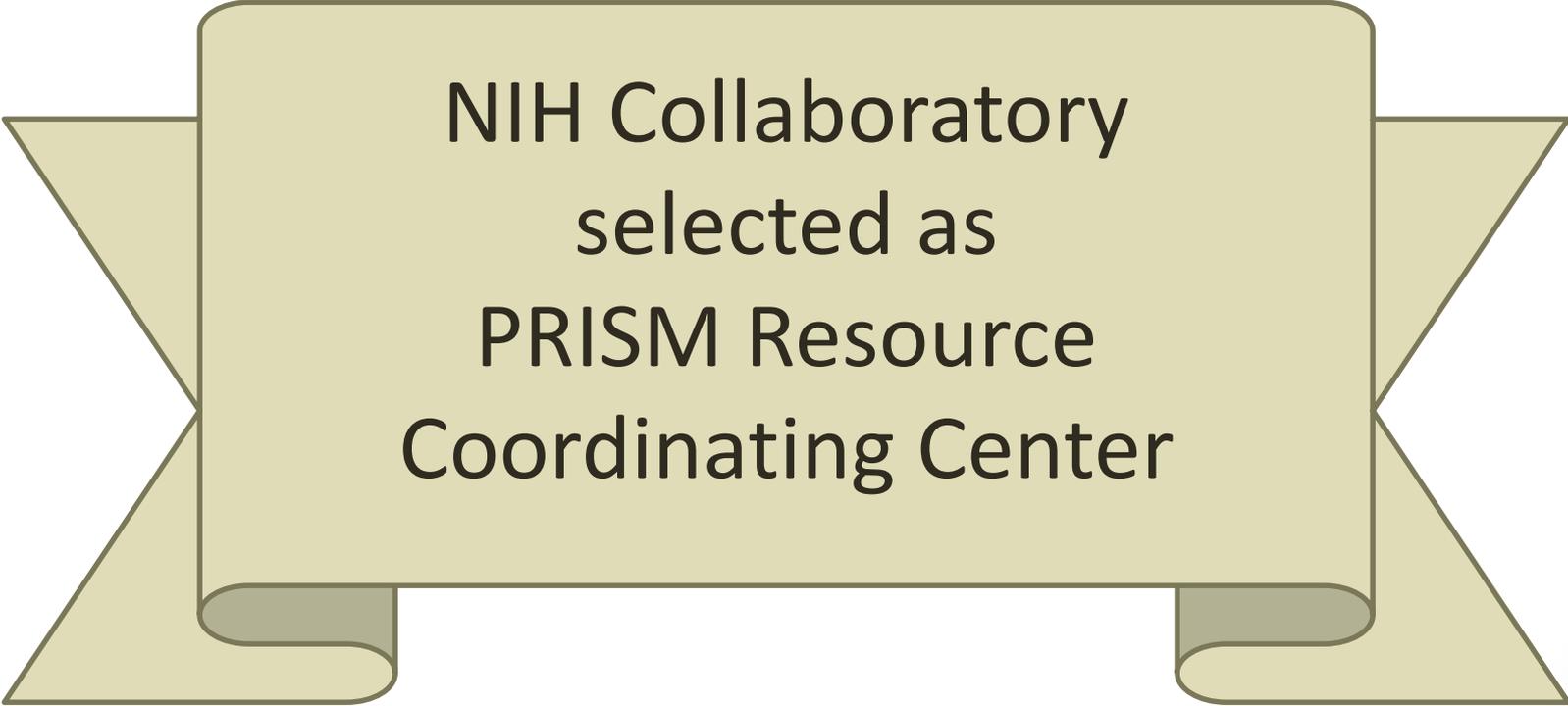
Challenge	Solution
Difficulty implementing intervention due to lack of on-site research staff, implementation by clinicians rather than researchers	Use of multiple approaches to engage facility personnel and participating patients during all stages of trial design and conduct
Incomplete ascertainment of patient-reported outcome already being used routinely in clinical practice	Adding processes to those already being used in clinical practice

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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

Study	PI/Co-PI	Program Official/Project Scientist	Institution
AcuOA Pragmatic trial of acupuncture for chronic low back pain in older adults	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
NOHARM Non-pharmacological options in postoperative hospital-based and rehabilitation pain management	Andrea Cheville, MD Jon Tilburt, MD	PO: Marcel Salive, MD, MPH (NIA) PS: Jennie Conroy, PhD (NICHD)	Mayo Clinic Rochester
OPTIMUM Group-based mindfulness for patients with chronic low back pain in the primary care setting	Natalia Morone, MD	PO: Wendy Weber, ND, PhD, MPH (NCCIH) PS: Luke Stoeckel, PhD (NIA)	Boston Medical Center
TIPS Fibromyalgia TENS in physical therapy study: an embedded pragmatic clinical trial	Kathleen Sluka, PT, PhD Leslie Crofford, MD	PO: James Witter, MD, PhD, FACR (NIAMS) PS: Martha Matocha, PHD (NINR)	University of Iowa

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



OPTIMUM *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

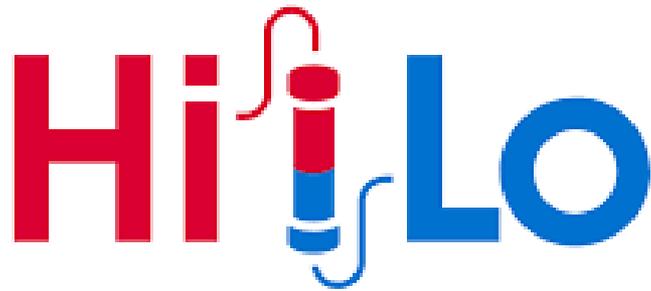
ACP PEACE

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

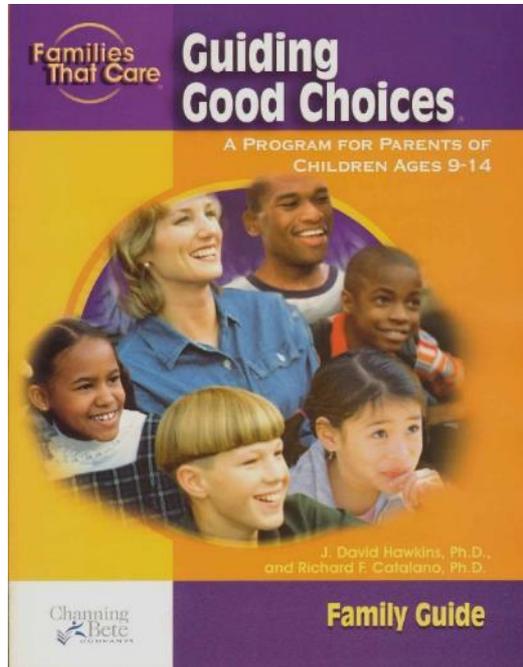
HiLo *Pragmatic Trial of Higher vs Lower Serum Phosphate Targets in Patients Undergoing Hemodialysis*



A Pragmatic Trial Sponsored by the
National Institutes of Health

- 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

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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

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- @Collaboratory1