Ten Years of the Pragmatic Trial Collaboratory: Beginning, Present, Future

Josie Briggs, Wendy Weber, Cathy Meyers

April 20, 2022

NIH PRAGMATIC TRIALS COLLABORATORY

Rethinking Clinical Trials®

Overview:

In the beginning…

Presented by Dr. Josie Briggs

Learning as we go…

Presented by Dr. Wendy Weber

Shaping future evidence generation with pragmatic trials…

Presented by Dr. Cathy Meyers

Themes

1. Health care systems partnerships
   Research embedded in care – how to make it work

2. Ethics, Patient engagement
   Keeping the Patient's Interest in the center

3. Data Quality and Study Designs
   Learning what works and what doesn't

In the Beginning

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Starting points:

Goal:
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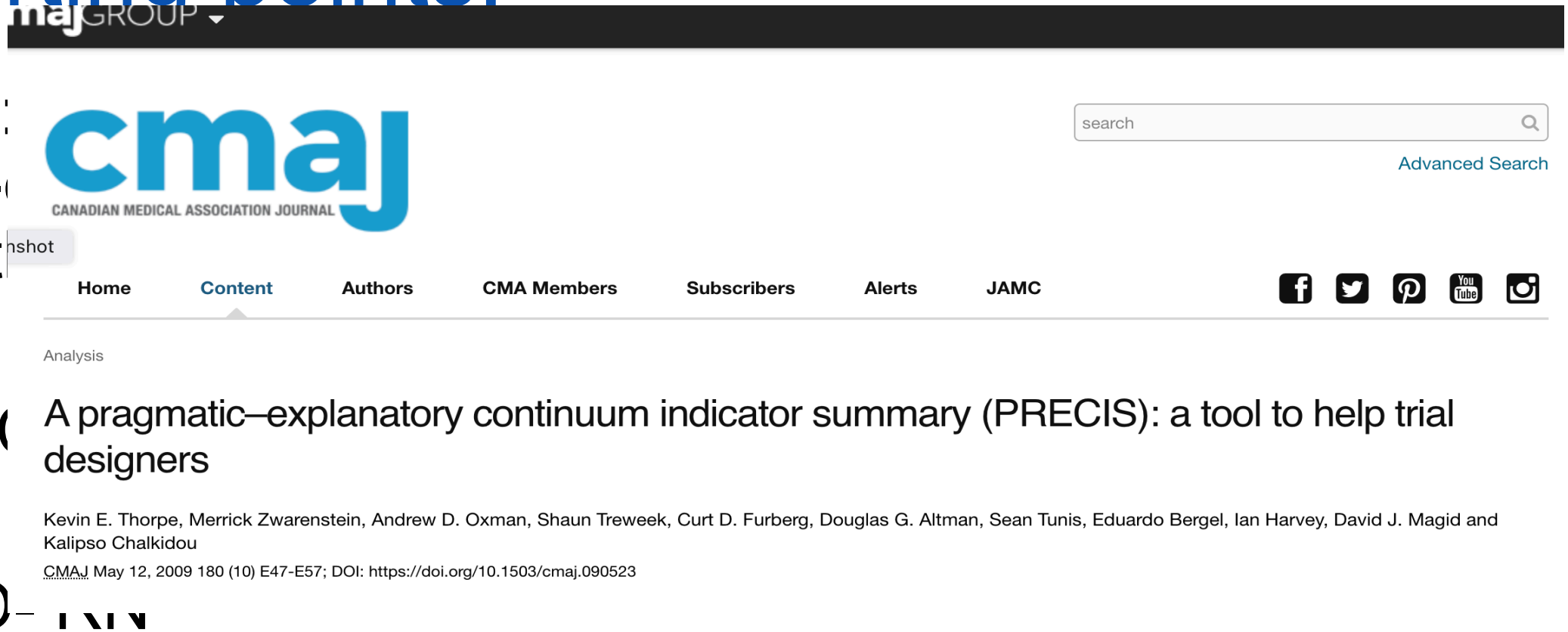

1. Health care system partnerships

Debated:

Model 1: Fund implementation network of HCS. Compete and fund projects separately

Model 2: Fund individual projects. Applicant builds the partnerships.

1. Health Care System Partnerships cont.

From the RFA:

The question should be of major public health importance – and one that will engage partnership with health care delivery systems.

Early recognition:

Complexities that results from multiple proprietary interests of HCS

2. Ethics and Patient Engagement

Debated:

Did the regulatory framework for clinical trials - allow for a new paradigm of evidence generation – trials embedded in care?

Would other stakeholders - patients and clinicians agree/understand?

When would waiver of individual consent be considered ethical and appropriate?
Would cluster or group randomization be acceptable?

Would randomization of providers be ethical– and who needs to consent?

How will OHRP and IRBs respond?

Debated:

Patient engagement – not so much

3. Data and Trial Designs

Data

The HCSs partnership must facilitate access to all data sources relevant to the project, which may include inpatient, outpatient, imaging, clinical laboratory and pharmacy data.

The trial should… make use of primary endpoint events that can be captured by passive follow-up such as electronic health records, and with minimal adjudication.

3. Data and Trial Designs cont.

Debated: Randomization – required?

The trial design should incorporate rigorous controls, prospectively identified, preferably by randomization. The design may incorporate novel randomization approaches, such as by cluster or timing of implementation. If another method is used to generate the comparison group, perhaps by staged assignment or staged implementation of the intervention, **it should provide comparable rigor.**

Learning As We Go

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Key Learning Activities of the Coordinating Center

- Provide technical support and pragmatic trial expertise for Collaboratory trials and initiatives via 5 Core Working Groups
- Produce data, tools, and resources that are made available to the greater research community to promote partnerships with healthcare systems and propel a transformation in how clinical research is conducted.
- Disseminate new knowledge widely, including through the Collaboratory's Knowledge Repository, Living Textbook, and Grand Rounds.
- Train a new generation of investigators in pragmatic clinical trial methods.

Theme 1: Health care system partnerships

Understand the priorities of the health care systems – want answers quickly, return on investment, cost to implement

Engagement needed at multiple levels of the health care system

Importance of planning for implementation to conduct trial and post-trial dissemination of effective interventions

NIH Collaboratory *Rethinking Clinical Trials®*

Health Care Systems Research Collaboratory

EPCT QUICK START GUIDE FOR RESE ARCHER AND HEALTHCARE SYSTEMS LEADER PARTNERSHIPS

This Quick Start Guide is designed to help clinical inv
pragmatic clinical trial (ePCT) within their healthcar
essential content in the *Living Textbook* regarding pa

Considerations for Tr
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Healthcare

Contents lists ava

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ELSEVIER

journal homepage: www.elsevier.com/locate/healthcare

Healthcare 4 (2016) 138–141

Contents lists available at ScienceDirect

Healthcare

journal homepage: www.elsevier.com/locate/hjdsi

Perspectives

Trials without tribulations: Minimizing the burden of pragmatic research on healthcare systems

Eric B. Larson [a], Chris Tachibana [a], Ella Thompson [a], Gloria D. Coronado [b], Lynn DeBar [b], Laura M. Dember [c], Stacey Honda [d], Susan S. Huang [e], Jeffrey G. Jarvik [f], Christine Nelson [g], Edward Septimus [h], Greg Simon [a], Karin E. Johnson [a,*]

Review article

Pragmatic clinical trials offer unique opportunities for disseminating, implementing, and sustaining evidence-based practices into clinical care: Proceedings of a workshop

Leah Tuzzio*, Eric B. Larson, David A. Chambers, Gloria D. Coronado, Lesley H. Curtis, Wendy J. Weber, Douglas F. Zatzick, Catherine M. Meyers

Theme 2: Ethics and Patient Engagement

Discussions with each project on ethics and regulatory issues posted

Ethics Jamboree – set of 11 academic articles on ethic and regulatory issues related to pragmatic trials: Clinical Trials 2015 12:5.

Opportunity for Empirical Ethics Research

- Patient, provider views about disclosure, research participation
- Collateral Findings - patient and provider reactions

Healthcare 9 (2021) 100586

Contents lists available at ScienceDirect

Healthcare

journal homepage: www.elsevier.com/locate/healthcare

Identification and management of pragmatic clinical trial collater findings: A current understanding and directions for future resear

Stephanie R. Morain [a,b,*], Debra J.H. Mathews [b,c], Gail Geller [b,d], Juli Bollinger [b], Kevin Weinfurt [e], Jeffrey G. Jarvik [f], Elizabeth May [b], Jeremy Sugarman [b,d]

Contemporary Clinical Trials 115 (2022) 106703

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Ethical and epistemic issues in the design and conduct of pragmatic stepped-wedge cluster randomized clinical trials

Carole A. Federico [a], Patrick J. Heagerty [b], John Lantos [c], Pearl O'Rourke [d], Vasiliki Rahimzadeh [a], Jeremy Sugarman [e], Kevin Weinfurt [f], David Wendler [g], Benjamin S. Wilfond [h], David Magnus [a,*]

Ethics

CLINICAL TRIALS

Clinical Trials
2019, Vol. 16(6) 574–579

DOI: 10.1177/1740774519858917
journals.sagepub.com/home/ctj
SAGE

Public views regarding the responsibility of patients, clinicians, and institutions to participate in research in the United States

Kevin P Weinfurt[1], Li Lin[1] and Jeremy Sugarman[2]

Theme 3: Data and Trial Designs

Challenges of clustered and stepped wedge designs

EHR interventions or data capture needs monitoring and maintenance, not all data is there – need to augment data

Growing appreciation for challenges of implementing the intervention

Many things can disrupt trials – pandemic, updated guidelines, poor uptake of intervention, new EHR implementation, system updates…

Journal of the American Medical Informatics Association, 28(12), 2021, 2626–2640
doi: 10.1093/jamia/ocab202
Advance Access Publication Date: 1 October 2021
Research and Applications

Research and Applications

Enhancing the use of EHR systems for pragmatic embedded research: lessons from the NIH Health Care Systems Research Collaboratory

Rachel L. Richesson[1], Keith S. Marsolo[2], Brian J. Douthit[3,4], Karen Staman[5], P. Michael Ho[6], Dana Dailey[7], Andrew D. Boyd[8], Kathleen M. McTigue[9], Miriam O. Ezenwa[10], Judith M. Schlaeger[11], Crystal L. Patil[11], Keturah R. Faurot[12], Leah Tuzzio[13], Eric B. Larson[13], Emily C. O'Brien[2], Christina K. Zigler[2], Joshua R. Lakin[14], Alice R. Pressman[15], Jordan M. Braciszewski[16], Corita Grudzen[17] and Guilherme Del Fiol[18]

Article

CLINICAL TRIALS

Clinical Trials
2016, Vol. 13(5) 504–512

DOI: 10.1177/1740774516646578
ctj.sagepub.com
SAGE

Statistical lessons learned for designing cluster randomized pragmatic clinical trials from the NIH Health Care Systems Collaboratory Biostatistics and Design Core

Andrea J Cook[1,2], Elizabeth Delong[3,4], David M Murray[5], William M Vollmer[6] and Patrick J Heagerty[2]

Perspective

CLINICAL TRIALS

Clinical Trials
2019, Vol. 16(4) 431–437

DOI: 10.1177/1740774519845682
journals.sagepub.com/home/ctj
SAGE

Addressing guideline and policy changes during pragmatic clinical trials

Lesley H Curtis[1], Laura M Dember[2], Miguel A Vazquez[3], David Murray[4], Lynn DeBar[5], Karen L Staman[6], Edward Septimus[7], Vincent Mor[8], Angelo Volandes[9], Barbara L Wells[10], Susan S Huang[11], Beverly B Green[5], Gloria Coronado[12], Catherine M Meyers[13], Leah Tuzzio[5], Adrian F Hernandez[1] and Jeremy Sugarman[14]

Shaping Future Evidence Generation with Pragmatic Trials

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Theme 1: Health care system partnerships

Essential – engagement and incentives

Models for future trials – types of systems, types of costs, administrative burdens

Is Learning Worth the Trouble? — Improving Health Care System Participation in Embedded Research

Richard Platt, M.D., Gregory E. Simon, M.D., and Adrian F. Hernandez, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

Theme 2: Ethics and Patient Engagement

Ethical Framework that facilitates need for more randomized comparative effectiveness trials (A vs B) to address healthcare priorities

Engaging systems, communities and individual patients across the demographic spectrum, recognizing some patients are not connected to a system

Using PCT as test bed for implementation of intervention – whether it can reasonably be tested – expected many failures in early days….

Theme 3: Data and Trial Designs

EHR Systems – Rich source of information - Limitations and Solutions. Utility of Data Sharing

Design Strategies – Innovative Adaptive Approaches. Integrating Implementation Methods Essential

PCT – Evidence hierarchy from real-world use. Randomized A vs B trials

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“If You Build It, They Will Come”