Emerging Topic of Interest: Pragmatic Clinical Trials

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Learning Objectives

By the end of this session, you will be able to:

• Describe the nature of Pragmatic Clinical Trials
• Recognize why communication plans are useful for PCTs
• Describe ethical and regulatory issues involved in conducting a PCT
Overview

Pragmatic Clinical Trials (PCTs)
- discuss several case studies using the PRECIS-2 tool

Communication plan
- discuss how you might develop communication plan for a case study

Regulatory/Ethical issues
- discuss regulatory and ethical issues posed by a case study
1. What is a pragmatic clinical trial?
“The purpose of **pragmatic trials** is to evaluate potential therapeutic benefits in real-world situations, to really look at clinical effectiveness rather than efficacy in idealized academic systems. Pragmatic trials can have a tremendous impact on what we all struggle with, which is translating our knowledge to clinical practice. Pragmatic trials give us insights into how we can do this in average clinical settings. The most important outcome is improving patient safety and saving lives.”

Edward J. Septimus, MD
Medical Director
Infection Prevention & Epidemiology Clinical Services
Hospital Corporation of America
and NIH Collaboratory PCT partner
What Can Different Types of Trials Tell Us?

- **Explanatory or traditional randomized clinical trials (RCTs)** confirm a physiological or clinical hypothesis. They test efficacy.

- **Pragmatic clinical trials (PCTs)** inform clinical practice and/or policy decisions by providing evidence for adoption of the intervention in real-world clinical settings. They test effectiveness.

- **Example:** Chronic pain research
# Key Differences Between RCTs and PCTs

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<tr>
<th></th>
<th><strong>Explanatory Trials/Traditional RCTs</strong></th>
<th><strong>Pragmatic Trials</strong></th>
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<tbody>
<tr>
<td><strong>Intent</strong></td>
<td>Test hypothesis, determine causes and</td>
<td>Inform practice and</td>
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<td></td>
<td>effects of treatment</td>
<td>policy by testing</td>
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<td></td>
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<td>effectiveness in situ</td>
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<td><strong>Design</strong></td>
<td>Test intervention against placebo with</td>
<td>Test two or more real-</td>
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<td>standard protocols</td>
<td>world treatments</td>
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<td></td>
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<td>using flexible</td>
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<td>protocols and local</td>
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<td></td>
<td></td>
<td>customization</td>
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<tr>
<td><strong>Setting</strong></td>
<td>Research clinics/specialized centers</td>
<td>Usual care settings</td>
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<tr>
<td><strong>Population</strong></td>
<td>Highly defined and carefully selected</td>
<td>Representative of</td>
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<td>patients in usual care</td>
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<td></td>
<td></td>
<td>setting</td>
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<td><strong>Measures</strong></td>
<td>Data collection outside routine usual</td>
<td>Brief and designed</td>
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<td></td>
<td>care</td>
<td>so data can be easily</td>
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<td>collected in clinical</td>
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<td>settings</td>
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**PRECIS-2: Explanatory or Pragmatic?**

The Pragmatic-Explanatory Continuum Indicator Summary 2 (PRECIS-2) wheel

1. Very explanatory
2. Rather explanatory
3. Equally pragmatic and explanatory
4. Rather pragmatic
5. Very pragmatic

Kirsty Loudon et al. BMJ 2015;350:bmj.h2147
Small Group Activity: Pragmatic or Explanatory?

Working in your small groups, use the PRECIS-2 tool to discuss and score each domain-based case study on the pragmatic <-> explanatory continuum.

Bonus (for fast groups): Use the PRECIS-2 tool to identify where your current and past project(s) fit on the pragmatic – explanatory continuum. Discuss.
2. Why have a communication plan?
Why Have a Communication Plan?

- Researchers, health care systems, clinicians, and often patients have to work together for a PCT to be successful.
- Different stakeholders have different goals and needs.
- Most pragmatic trials are multi-site.
- Pragmatic trials need to be flexible.

Lots of moving pieces means lots to keep track of!
Communication Plan?

- Someone on the study team “owns” a directory of contacts at each site (a list)
- Someone on the study team “owns” a directory with listed roles and responsibilities (a spreadsheet)
- A formalized agreement laying out study organization and delineating levels of governance and communication, including meeting days/times and requirements (a contract)
Formal Communication Plan

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Small Group Activity: PROUD Trial – Communication Plan

Introduction to the Primary Care Opioid Use Disorders Treatment (PROUD) Trial

• In your small groups you will discuss how you might approach developing a communication plan for PROUD
The PROUD Trial: Objective

Primary Objective

Evaluate whether implementation of the Massachusetts Model of collaborative care for management of Opioid Use Disorders (OUDs) increases OUD treatment with buprenorphine or injectable naltrexone, documented in EHR over 2-year follow-up compared to usual primary care.

The MA Model is a team-based, collaborative care approach that uses a fulltime clinic-based nurse care manager (NCM) to integrate medication treatment for OUDs into PC.

Main Features

• Pragmatic, cluster-randomized, quality improvement trial—mixed effectiveness and implementation trial
• 6-health systems across the US, each with two PC clinics
• The QI intervention is owned by the healthcare delivery systems, implementation and research evaluation is owned by research teams
• Data collection, minimum necessary from EHR
PROUD Trial: Eligibility

Table 1. Eligibility of Sites & Clinics for the PROUD Trial

- Regulatory and data sharing requirements
- Availability of required secondary EHR data
- Leadership support for the trial in the health system
- Leaders of 2 PC clinics support participation
- 3 willing PC prescribers in each participating PC clinic
- Adequately sized clinics with low cross-over of patients
- Desirable: geographic, demographic, site diversity
PROUD Trial: Cluster Randomization

**Period 1 (~4 months)**
- Start-up Prior to Kickoff
  - Contracts, DUAR/DTA
  - Central IRB and ceding
  - Programming for baseline data
  - Describe Usual Care
  - Randomization
  - DSMR Review

**Period 2 (6 months)**
- PROUD Intervention Implementation
  - Kickoff
  - NCM hiring and training
  - NCM technical assistance (TA)
  - Start treating OUD in PC
  - Begin formative evaluation
  - Obtain baseline data

**Period 3 (18 months)**
- Ongoing TA & Data Collection
  - Ongoing NCM TA
  - Ongoing formative evaluation
  - Preliminary baseline analyses
  - Statistical Analysis Plan finalized
  - Data collection every 6 months
  - Programming; clean/coded data

**Period 4 (12 months)**
- Analyses and Dissemination
  - Two sites join observational analyses of exemplar clinics
  - Final 6-month data collection
  - Main and secondary analyses
  - Final locked dataset to DSC
  - Manuscripts

*or cluster  IRB – Institutional review board;  DUAR – Data use agreement;  DTA – Data transfer agreement;  NCM – Nurse care manager;  TA – Technical assistance;  PC – Primary care
PROUD Trial: Organization

Administrative Team
- Addie Luce
- Weekly
- Contracts
- OUs, OTs
- Scheduling
- IRB
- Staff meetings/ action items
- Regulatory with CCC

Implementation Monitoring Team
- Bradley Lee
- Weekly
- Monitor training & TA support
- BMC Team debrief - Weekly
- Collect NCM reports - Weekly
- Formative evaluation
- Site PI debrief - Quarterly
- Monitor & describe Usual Care
- Monitor & describe Exemplar

Technical Assistance Team (BMC)
- LaEvelle
- Weekly
- Provide PROUD Manual
- NCM hiring guidelines
- NCM Training
- Intervention site visits (O2)
- Provide TA to each NCM

Lead Node Team (LNT)
- Bradley Addis
- Weekly
- Updates from teams
- Administrative
- Implementation
- Data & Analytics
- Investigators
- Site Updates

Operations Team
- McCormack
- Monthly
- Communications & oversight with LNT, C-CTN, DSC, CCC

Data & Analytics Team
- Bourdreaux Lampham
- Weekly
- SAP
- Data collection & cleaning
- Collaborate with sites on quality checks
- Coding
- DSM data
- Baseline analyses
- De-identifying data for DGC

Publication Team
- Saxon Bradley
- Monthly
- Review Implementation
- Barriers
- Plan Papers
- Write papers

Paper sub-groups
- Phase 1
- Phase 2

Ancillary Studies
- Economics
- Death
- Organizational

All Site Meetings
- Bradley
- Weekly
- Implementation - Lee
- Data - Bourdreaux Lampham
- Administrative - Addis
- Site updates
Small Group Activity: Communication Plan for PROUD

Communication Plan: Use the PROUD description and organizational structure (on next pages) as well as your real-world experience working in research to guide your work. What kind of communication plan would you create for PROUD? What things do you need to consider to create a plan? Develop a list of issues to consider, decide on a type of plan, and then discuss how you would approach drafting the plan.

Bonus (for fast groups): Briefly discuss your experience developing or using a communication plan for a study you’ve worked on. Or, an experience that made you wish you had one.
3. Ethical & Regulatory Issues
Traditional CTs and Health Care Delivery

Research

Health Care Delivery

Laws

Regulations

Ethics

Laws

Regulations

Ethics
PCTs and Health Care Delivery

Laws
Regulations
Ethics

Research
Health Care
PCT
Delivery

Laws
Regulations
Ethics
PCTs and Health Care Delivery

Laws
Regulations
Ethics

Laws
Regulations
Ethics
Navigating the Ethical & Regulatory Issues

- Provider responsibility to patient(s)
- Researcher responsibility to subject(s)/participant(s)
- Responsibility to funder(s)
- Responsibility to healthcare delivery system
- QI or Research?
- Human Subjects Review?
- Vulnerable populations
- HIPAA
- Privacy
- ct.gov
- DSMP/DSMB
Small Group Activity: Ethical and Regulatory Issues for PROUD?

As a group choose any ethical or regulatory issue(s) that might arise in the design and conduct of PROUD and discuss. Some possibilities:

**PRACTICAL ISSUES**
- *Should there be informed consent for the patients and/or providers in this study? Why?*
- *Who should be credited as authors on the project? Why?*

**SLIGHTLY MORE ABSTRACT ISSUES**
- *How do providers’ obligations to patient(s) differ from researchers’ obligations to subject(s) in PCTs?*
- *Does research team have any long-term obligations to the healthcare delivery system?*
References, Resources, and Thanks

RESOURCES
NIH Collaboratory: http://rethinkingclinicaltrials.org/

THANKS
Ella Thompson
PROUD team
NIH Collaboratory

REFERENCES


Weinfurt, K. What is a Pragmatic Clinical Trial. NIH Collaboratory, http://rethinkingclinicaltrials.org/
### Key Differences PCTs and Quality Improvement

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<th>Quality Improvement</th>
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<td><strong>Intent</strong></td>
<td>Inform practice and policy by testing effectiveness in situ</td>
<td>Inform clinic decision making, improve care locally</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Test two or more real-world treatments using flexible protocols and local customization</td>
<td>Implementation of an intervention into care delivery</td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Usual care settings</td>
<td>Usual care setting. Local clinic(s) or hospital(s)</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Representative of patients in usual care setting</td>
<td>Patients in clinical care setting</td>
</tr>
<tr>
<td><strong>Measures</strong></td>
<td>Brief and designed so data can be easily collected in clinical settings</td>
<td>Outcomes are directly relevant to patients!</td>
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