Essentials of ePCTs

Important things to think about and do when designing, conducting, and disseminating embedded PCTs
What are embedded pragmatic clinical trials?

- Conducted within healthcare systems
- Use streamlined procedures and existing infrastructure
- Answer important medical questions
Why conduct ePCTs?

ePCTs have the potential to inform policy and practice with high-quality evidence at reduced cost and increased efficiency compared with traditional clinical trials.
ePCTs bridge clinical care into research

- Study designed with input from health system stakeholders
- Intervention incorporated into routine clinical workflow
- Data collected through EHR in health care settings
- Diverse, representative study populations
- Outcomes important to decision makers
“A successful PCT starts with a strong partnership between researcher and healthcare system, goes through a rigorous objective evaluation of the ability of the partner healthcare system to participate, and ends with evidence about sustainable ways to improve care, as well as long-term scientific relationships.”

Broad stakeholder engagement & support

- Get to know your stakeholders, their values, priorities, and expectations
- Assess the capacity and capabilities of your health system partners
- Engage across all trial phases: design, conduct, and dissemination
Partner with health systems

- Will the intervention add long-term value to the system?
- Can data be collected at all clinical sites?
- Are sufficient patient numbers and data available for analysis?
- How do the sites vary in services and capabilities?
Consider implementation early

• Design the intervention with implementation and sustainability in mind
• Consider how your intervention fits with the target patient population & setting
• Can it be designed to be delivered in a wide variety of healthcare settings?
Collaborate

- Team designing the study
- HCS partners delivering the intervention

- Put in place a study team with the right skillset
- Identify local champions for all your sites
Study team composition

- What clinical specialties will be needed to deliver the intervention?
- What roles will support clinic operations?
- What aspects of the trial will require IT staff expertise?
Resources: ePCTs

Why Are We Talking About Pragmatic Clinical Trials?

From the *Living Textbook of Pragmatic Clinical Trials*
[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)
Three Phases
• Statistical design and analysis
• Endpoints and outcomes
• Pragmatic elements
• Regulatory and ethics
• Pilot and feasibility testing
Develop the research question

• The research question drives the design
• Collaborate with a biostatistician while developing the research question
Statistical design & analysis

• What unit of randomization makes the most sense for your study and why?
• For statistical reasons, individual is preferred, but cluster or group randomization is often needed
Resources: Design and analysis

Experimental Designs and Randomization Schemes

Analysis Plan

From the *Living Textbook of Pragmatic Clinical Trials*

[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)
Endpoints & outcomes in ePCTs

Endpoints and outcomes need to be meaningful and available

**Easy**
- Acute MI
- Broken bone
- Hospitalization

**Hard**
- Suicide attempts
- Gout flares
- Silent MI
- Early miscarriage
Endpoints & outcomes

- What is your primary endpoint?
- Is that endpoint meaningful to stakeholders?
- What challenges do you anticipate in trying to ascertain that endpoint, and how might you address those challenges?
Resources: Endpoints and outcomes

Choosing and Specifying Endpoints and Outcomes

From the Living Textbook of Pragmatic Clinical Trials
www.rethinkingclinicaltrials.org
Pragmatic elements

Eligibility
Who is selected to participate in the trial?

Recruitment
How are participants recruited into the trial?

Setting
Where is the trial being done?

Organisation
What expertise and resources are needed to deliver the intervention?

Follow-up
How closely are participants followed-up?

Flexibility: adherence
What measures are in place to make sure participants adhere to the intervention?

Flexibility: delivery
How should the intervention be delivered?

Primary outcome
How relevant is it to participants?

Primary analysis
To what extent are all data included?

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PRECIS-2 exercise

• Review the 9 domains and work with your study team to prospectively consider how your study fits along the pragmatic-explanatory continuum

• What would a PRECIS-2 wheel diagram look like for your trial?
Resource: PRECIS-2

Pragmatic Elements:
An Introduction to PRECIS-2

From the *Living Textbook of Pragmatic Clinical Trials*
[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)
Regulatory & ethical challenges of ePCTs

- Whose rights and welfare need to be protected?
- Direct participants: protections reviewed by IRB/ethics board
- Indirect participants: protections reviewed by health system gatekeepers
Direct participants
Immediate or mediated targets of the intervention

- Intervention
- Patients
- Intervention
- Providers
- Intervention
- Clinics
Indirect participants

Those affected by routine exposure to the environment (eg, family/caregivers)
Approaches to notification & authorization

- Informed consent
- Nondisclosure

Alterations

- Broad notification
- Opt-out
- Opt-in
Regulatory & ethical challenges

- Consider potential benefits and risks to participants
- Designate someone to track local and federal regulatory developments and serve as liaison with regulatory/oversight bodies
- Look for opportunities to contribute to empirical data on different approaches to consent
Consent, Disclosure, and Nondisclosure

From the *Living Textbook of Pragmatic Clinical Trials*

[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)
Pilot & feasibility testing

- Develop a working partnership with health system leaders and staff
- Engage a biostatistician in the pilot and feasibility stage
- Pilot your ePCT methods to increase the likelihood of completing the trial and preventing mistakes
Pilot & feasibility testing

- Use the pilot to maximize acceptability, maintain affordability, and consider the scalability of your intervention
- Develop a plan to address potential changes in the health system that may occur during the trial
Resources: Feasibility

Assessing Feasibility

From the *Living Textbook of Pragmatic Clinical Trials*

[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)
• Recruiting participants
• Expect changes and disruptions
• Plan for adjustments and accommodations
Recruit participants

• What recruitment methods, materials and procedures will be needed?
• How will eligible participants be contacted and enrolled?
• How will the partner health system’s EHR be used for recruitment, enrollment, intervention delivery, or outcome assessment?
• What barriers to recruitment are anticipated, and how will these challenges be addressed?
Participant Recruitment

From the *Living Textbook of Pragmatic Clinical Trials*
[www.rethinkingclinicaltrials.org](http://www.rethinkingclinicaltrials.org)
Change will happen

- Changes may happen in:
  - EHR platform
  - Leadership and staff turnover
  - Clinical workflow
  - Intervention crossover
  - Study populations

Stay in touch to handle disruptions
Resources: Accommodating changes

Scenarios from the Collaboratory’s Demonstration Projects

From the Living Textbook of Pragmatic Clinical Trials
www.rethinkingclinicaltrials.org
• Results reporting
• Sustainability
• Learning health system
• Data sharing
Who will use the research findings to make decisions?
Resources: Dissemination

Dissemination Approaches for Different Stakeholders

PCT Reporting Template

From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org
Sustainability

- Research influences practice and practice influences research
- Health systems vary in how they implement practice change from trial evidence
Learning health system

- ePCTs aim to maximize efficiency in trial design and rollout
- How does your partner health system learn?
Data sharing

• Data sharing can be an essential element of dissemination
• How do your dissemination plans meld with NIH data sharing guidelines?
Resources: Data sharing

Data Sharing and Embedded Research

From the Living Textbook of Pragmatic Clinical Trials
www.rethinkingclinicaltrials.org
Get started

• Download the ePCT Essentials Worksheet
• Use the Living Textbook and the following resources as you complete the worksheet
Resources: Key journal articles

Weinfurt et al., 2017. Pragmatic clinical trials embedded in healthcare systems: generalizable lessons from the NIH Collaboratory

Johnson et al., 2016. Use of PRECIS ratings in the National Institutes of Health (NIH) Health Care Systems Research Collaboratory

Loudon et al., 2015. PRECIS-2 tool: designing trials that are fit for purpose
Resources: PCT Grand Rounds webinars

Introduction to Pragmatic Clinical Trials
https://www.nihcollaboratory.org/Products/Introduction to Pragmatic Clinical Trials.pdf

Use of PRECIS-2 Ratings in the NIH Health Care Systems Research Collaboratory