NIH Collaboratory *Rethinking Clinical Trials®*

Health Care Systems Research Collaboratory

Living Textbook Grand Rounds Series
Pragmatic Clinical Trials: How Do I Start?

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Greg Simon, MD, MPH
Senior Investigator
Kaiser Permanente Washington Health Research Institute

Lesley H. Curtis, PhD
Chair and Professor
Department of Population Health Sciences
Duke University School of Medicine
Interim Executive Director, Duke Clinical Research Institute

Agenda

- What is a PCT and why do we need them (Lesley)
- Choosing/developing a research question (Greg)
- Matching methods to questions (Lesley)
- Engaging with stakeholders (Greg)
- Building a study team (Greg and Lesley)
- Q & A

What is a PCT?

Large, efficient study conducted in the real world that provides evidence for adoption of an intervention into clinical practice

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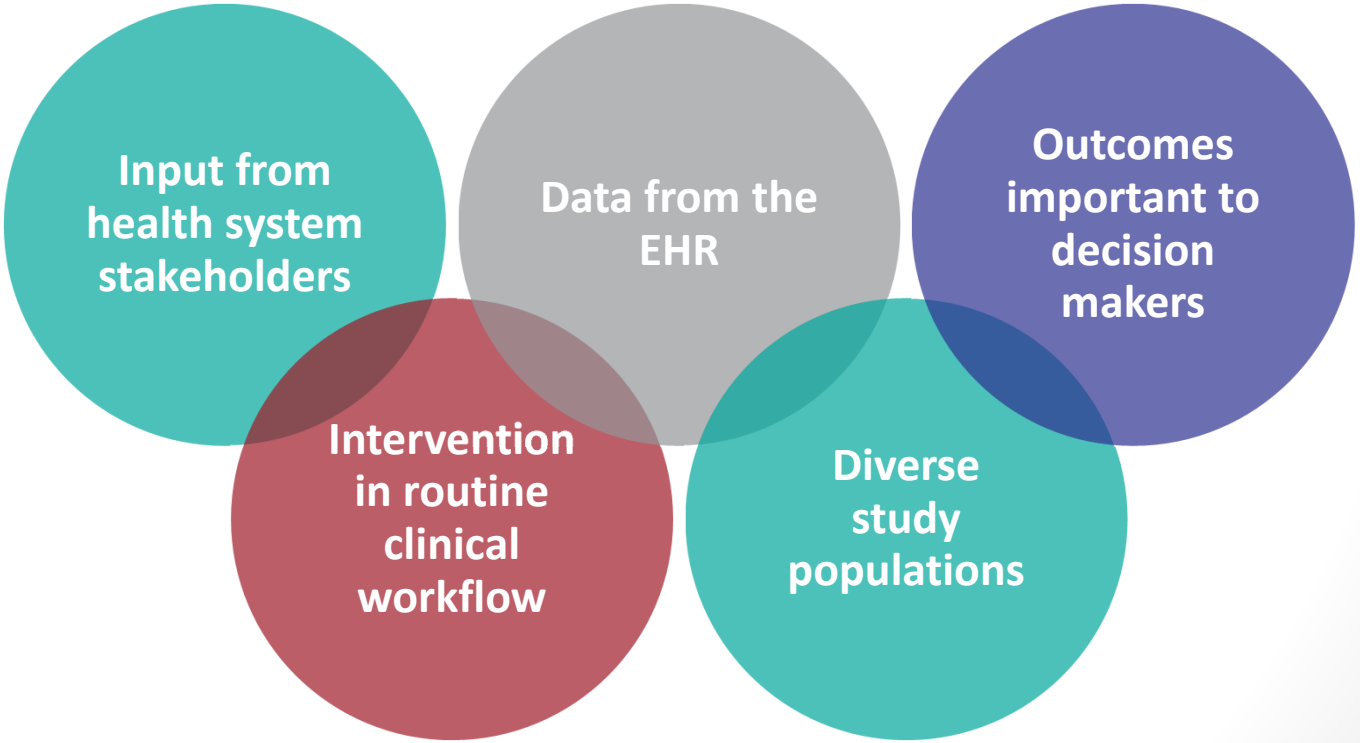


Why a PCT?

- Real-world evidence to inform real-world decisions
- Faster and cheaper evidence generation

Often these motivations are aligned, but sometimes they are not!

Develop the research question

- As with any type of research study, PCTs begin with a scientific question
- A clearly articulated research question defines
  - Phenomena of interest
  - Purpose for using EHR data
  - Possible sources of data to detect that phenomena
  - Data requirements, definitions, quality, and data collection plan
- Is a pragmatic trial the right design to answer your question?

Explanatory vs. pragmatic questions

- Explanatory trials answer questions like:

  What should we believe about _____?

- Pragmatic trials answer questions like:

  What should we do about _____?

A pragmatic trial has a customer

- Patients or caregivers
- Clinicians
- Medical group or health plan leaders
- Regulators or other policy-makers

A pragmatic trial has a customer

- Who is your customer?
- What decision do they need to make?
- When and where will they decide?
- What information will they have at the time?
- What are the most important positive and negative consequences of that decision?

PRECIS-2: Designing trials fit for purpose

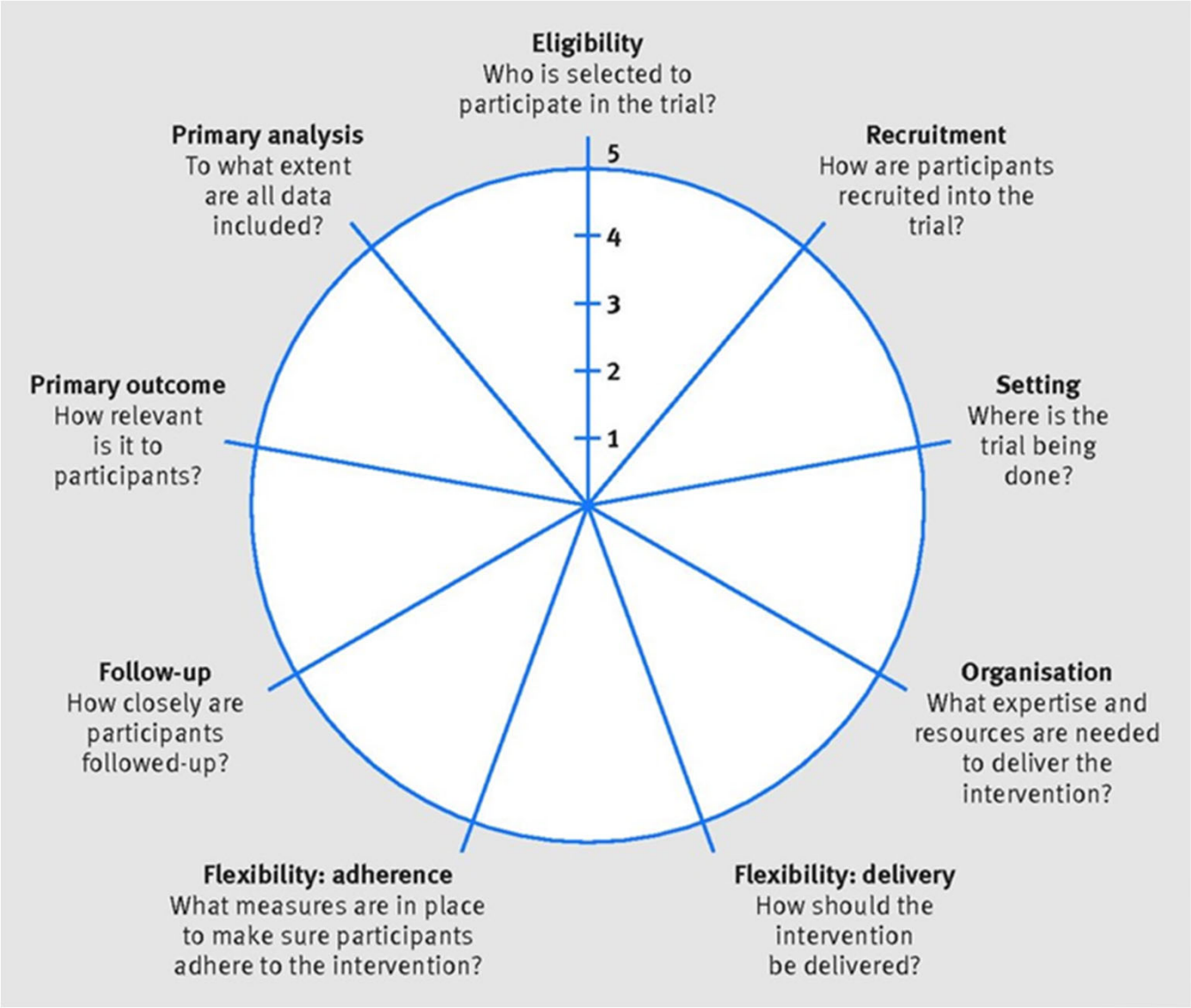
Tool assesses trial across 9 domains

Explanatory **Pragmatic**

- Eligibility
- Recruitment
- Setting
- Organization
- Flexibility: delivery
- Flexibility: adherence
- Follow-up
- Primary outcomes
- Primary analysis

Loudon K et al *BMJ* 2015;350:h2147

PRECIS-2 wheel



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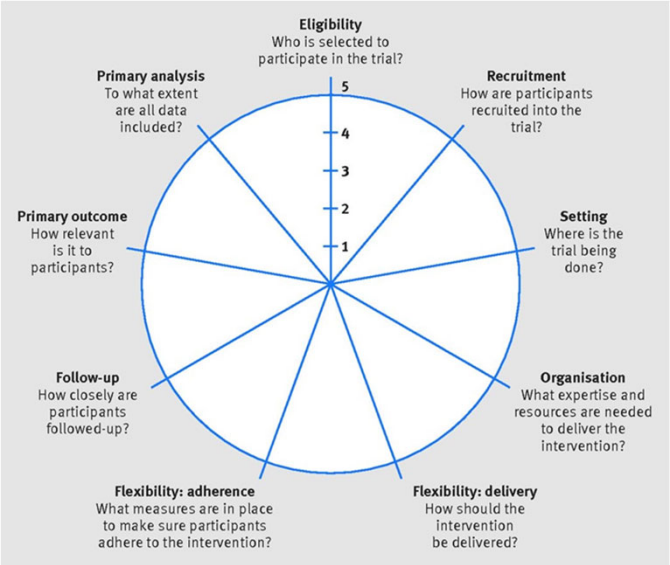


Determine the approach that is most appropriate for answering your research question

Loudon K et al *BMJ* 2015;350:h2147

It's a balancing act

- High relevance to real-world decision-making may come at the expense of trial efficiency

  For example, a trial measuring outcomes that matter most to patients and health systems may not be able to rely exclusively on information from the EHR, and instead need to assess patient-reported outcomes, which is more expensive and less efficient

Important things to know

- Embedded PCTs (ePCTs) are designed to answer important, real-world clinical questions
- Tradeoffs in flexibility, adherence, and generalizability are inevitable
- ePCTs may have some elements that are more pragmatic and some that are more explanatory

Who are ePCT stakeholders?

Potential stakeholders have varied priorities, values, work cultures, and expectations:

- Healthcare delivery organization leaders
- Clinicians
- Operational personnel
- Patients, caregivers, patient advocacy groups
- Payers, purchasers
- Policymakers, regulators
- Research funders
- Researchers
- Product manufacturers

What's the value of engagement?

- Defines relevant questions and selects high-priority outcomes
- Improves efficiency and diversity of participant enrollment
- Continuously helps improve methods and overcome challenges
- Reduces missing data and loss to follow-up
- Increases the uptake and impact of research

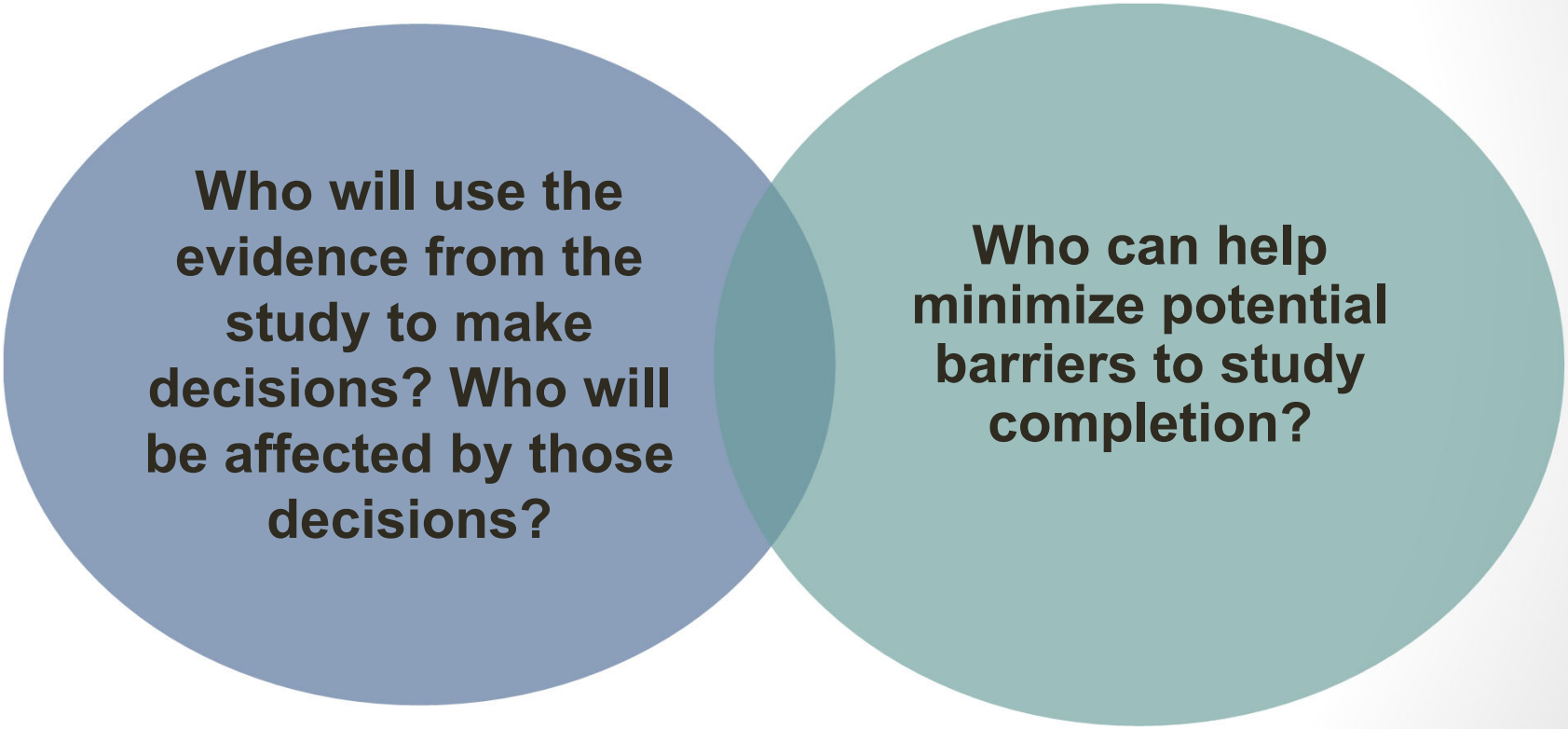
Types of stakeholders

- The wider community of stakeholders is needed to define the question and design the intervention:
  - *"We really want to know what you need"*
- Local stakeholders are essential to implementing the ePCT at sites:
  - *"We really need your help to get this done"*

Establish partnerships with health systems

- Consider whether your intervention will add long-term value to the health system and its patients
- Get to know your stakeholders, their values, priorities, and expectations at all levels: from C-suite to care providers

Determine which stakeholders are important for your ePCT



Lessons from the Collaboratory

LISTEN TO THE FRONTLINE

"The purpose of the healthcare system is not to do research, but to provide good healthcare. Researchers often have a tail-wagging-the-dog problem. We assume if we think something is a good idea, the healthcare system will too … We need to remember that we're the tail and the healthcare system is the dog."

– Greg Simon, MD, MPH (SPOT)

Lessons from the Collaboratory

USE EXISTING WORKFLOWS

"The more complicated the intervention is to the existing workflow, the more difficult it is to get compliance—you can't just add on a new thing, you have to change what happens on the floor."

– Vincent Mor, PhD (PROVEN)

Important things to know

- Be patient: relationships take time to build and nurture
- Assess the capacity and capabilities of your health system partners in the pilot phase
- Engage across all trial phases: design, conduct, and dissemination
- Expect turnover and disruption

Important things to do

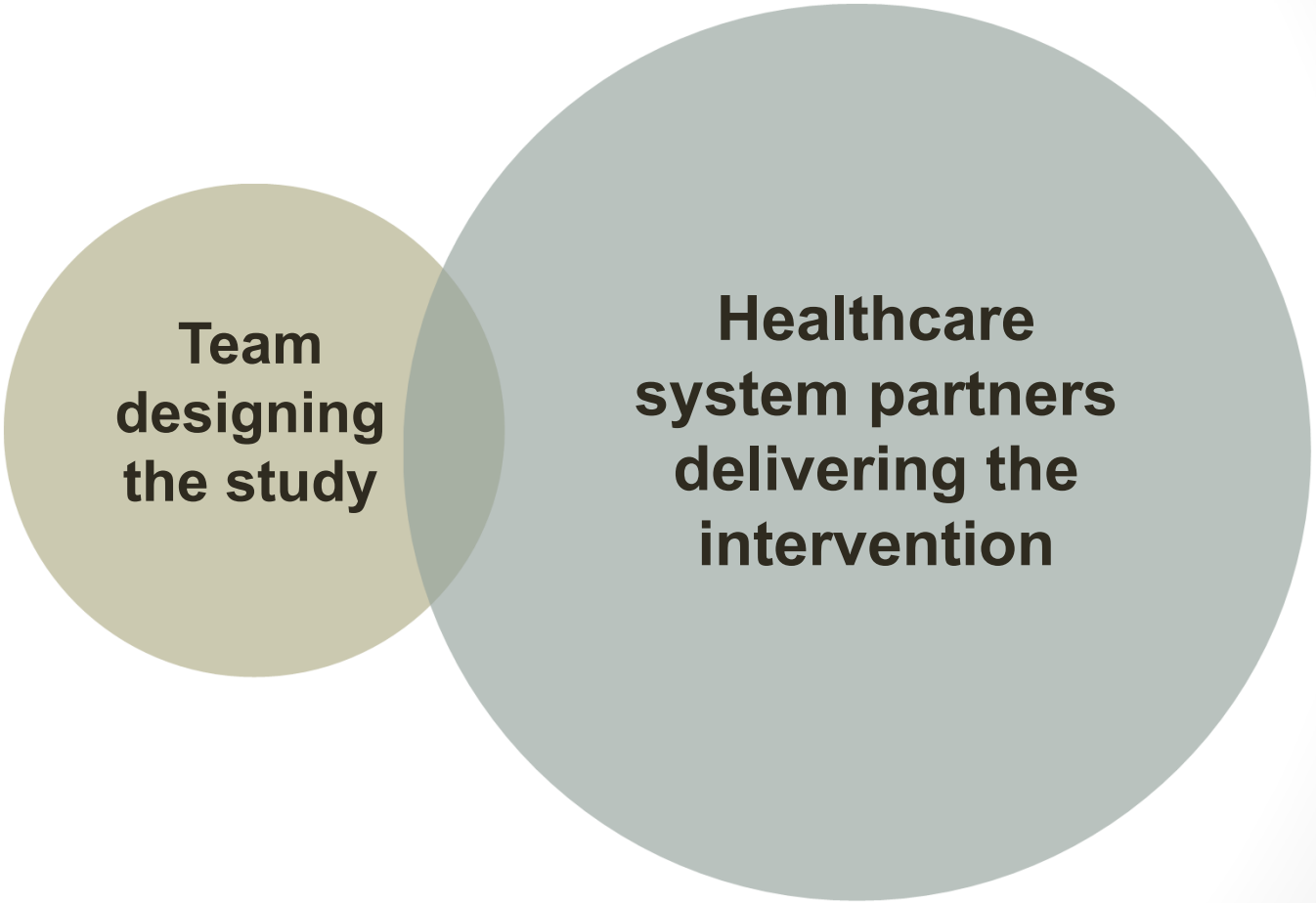
Prepare a brief, clear abstract that includes

- **Reasons to invest in intervention**
- **Alignment with organizational priorities**
- **Impact on workflows**
- **Downstream implications**
- **Potential harms or liability issues**
- **Alignment with policy makers**
- **Sustainability plans**

Compose your ePCT study team

- ePCTs are a team sport
- Necessary expertise depends on the study aims and how the intervention will be implemented
- Recruit team members during the planning phase and engage them for the duration of the trial

Who is involved?



Potential team members

- PI, Co-PI
- Clinical staff
- HCS leader or executive
- Lead clinician
- Biostatistician
- Professional society leader
- Information technology specialist
- Site champion
- Research assistant
- Practice facilitator
- Communications specialist
- Patient or patient advocate
- Project coordinator

Consider

- What clinical specialties will be needed to carry out the intervention?
- What roles will support clinic operations?
- Who will be the liaison between health system departments for interventions that are multidisciplinary?
- What aspects of the trial will require IT staff expertise?
- Will the trial need training videos, online materials, or toolkits?

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Visit the Living Textbook of Pragmatic Clinical Trials at

www.rethinkingclinicaltrials.org