NIH Collaboratory

Health Care Systems Research Collaboratory

Rethinking Clinical Trials®

Essentials of ePCTs

Important things to think about and do when designing, conducting, and disseminating embedded PCTs

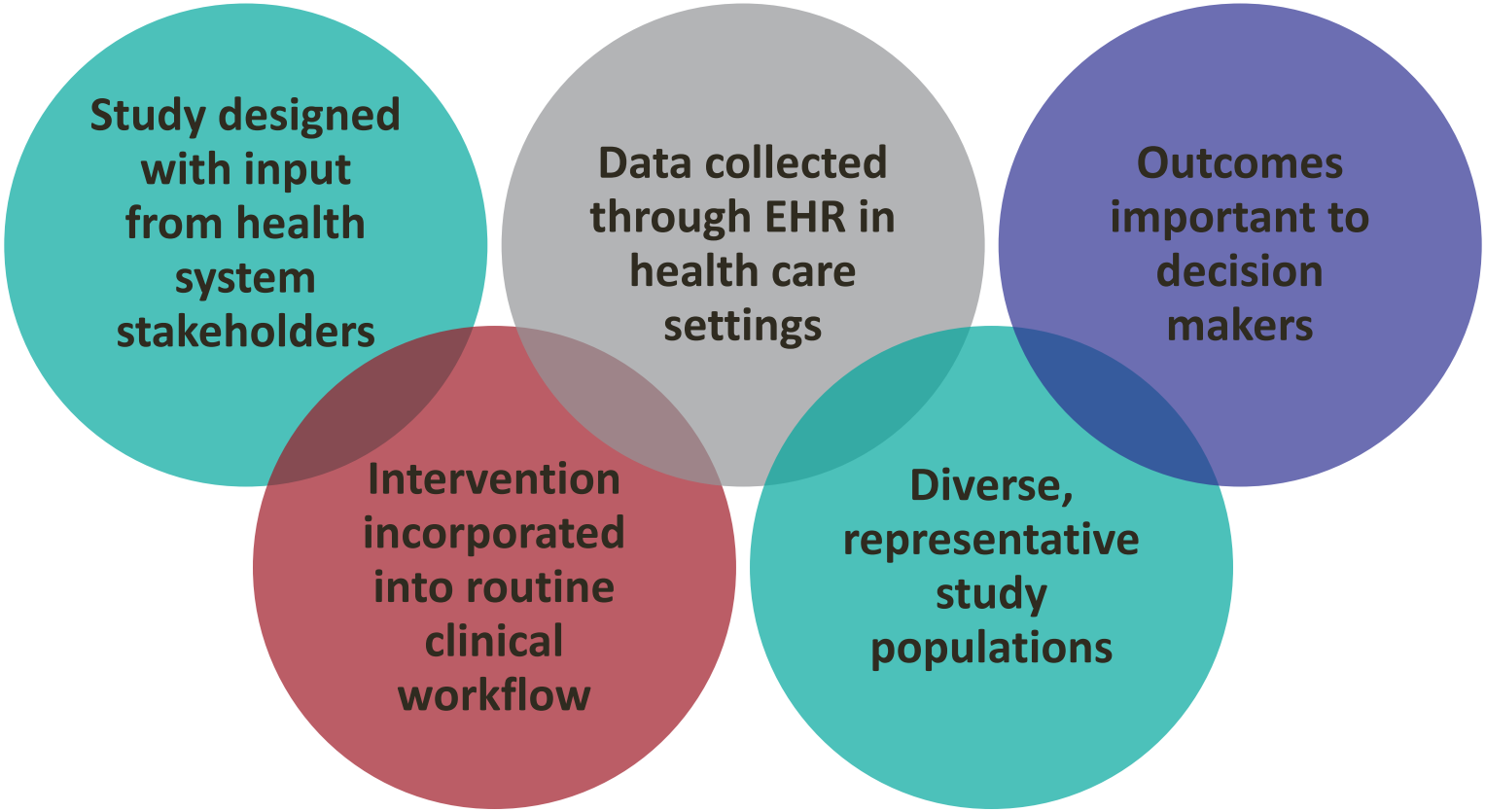
What are embedded pragmatic clinical trials?

- 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



"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."

Johnson KE et al. *A guide to research partnerships for pragmatic clinical trials*. BMJ. 2014

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

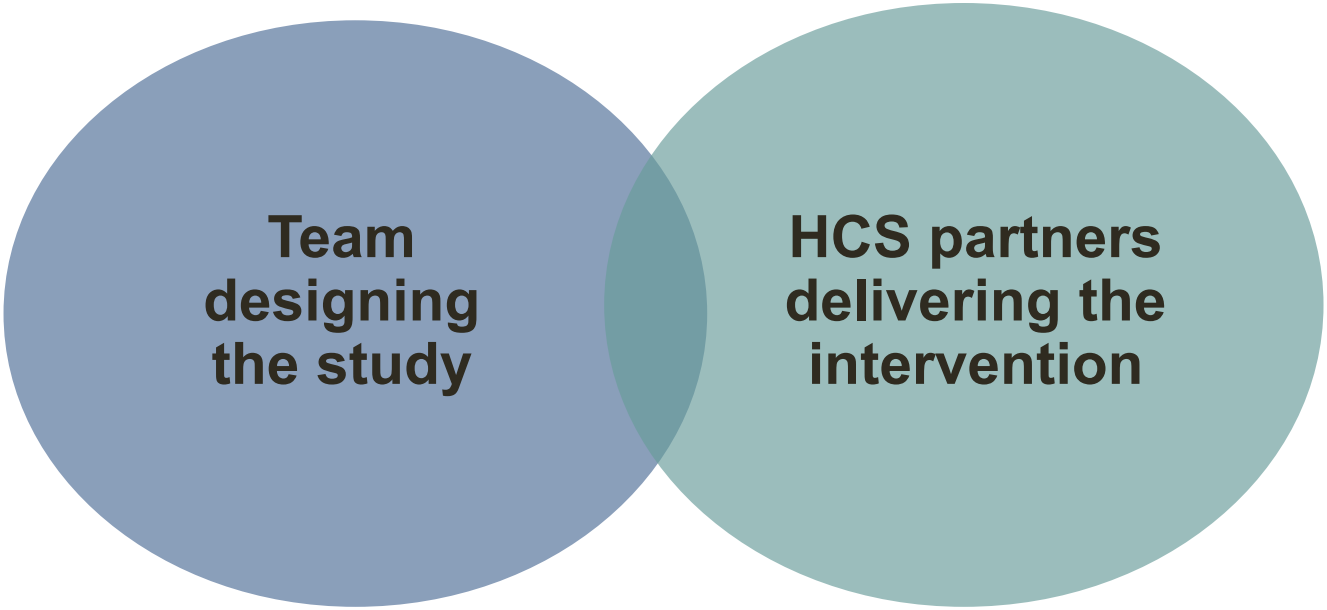
Partner with health systems

- 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



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

Three Phases

DESIGN

- 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

Endpoints & outcomes in ePCTs

Endpoints and outcomes need to be meaningful and available

- Acute MI
- Broken bone
- Hospitalization

- Suicide attempts
- Gout flares
- Silent MI
- Early miscarriage

Endpoints & outcomes

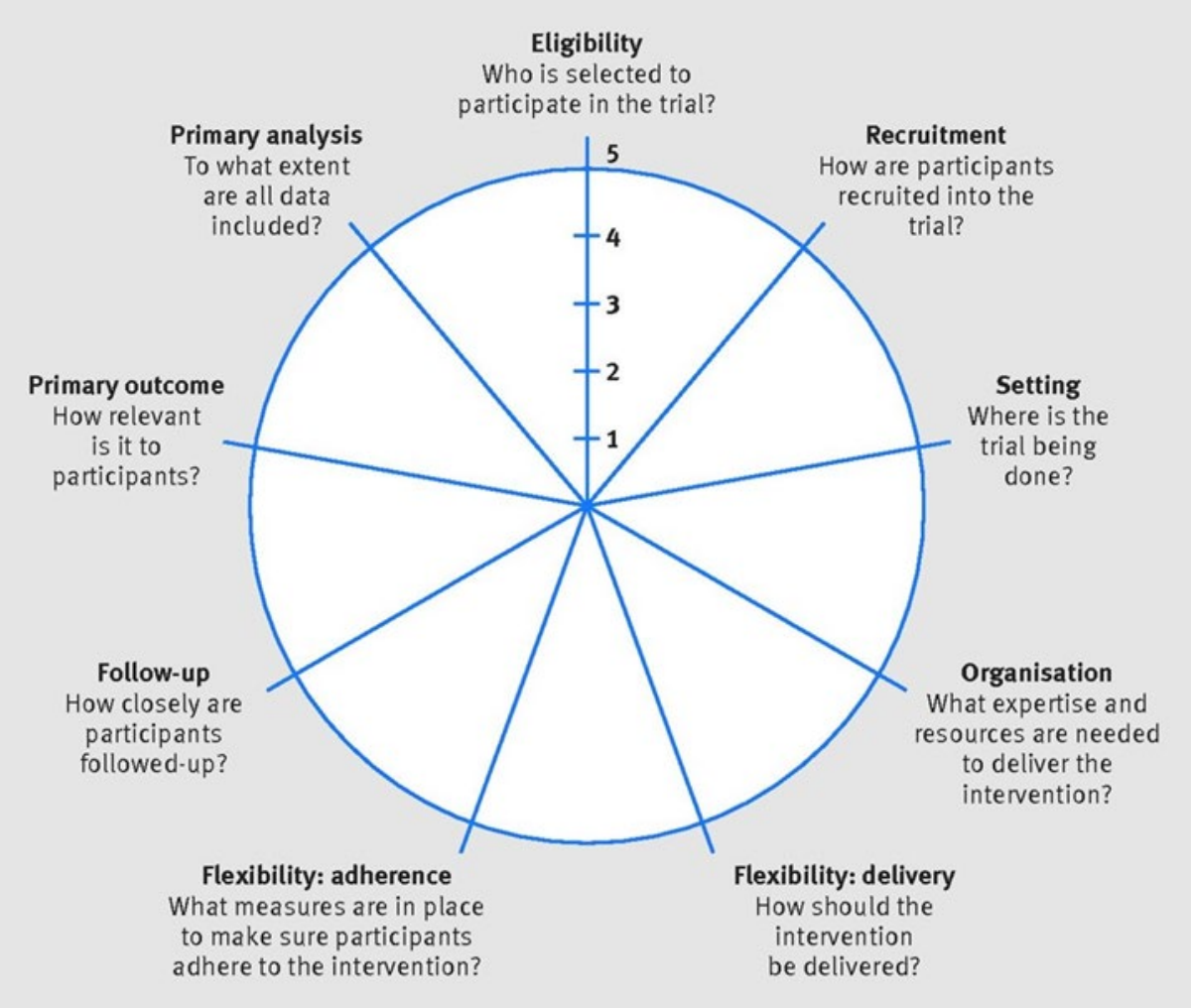
- What is your primary endpoint?
- Is that endpoint meaningful to stakeholders?
- What challenges do you anticipate in trying to ascertain that endpoint, and how might you address those challenges?

Resources: Endpoints and outcomes

Choosing and Specifying Endpoints and Outcomes

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

Pragmatic elements



PRECIS-2 source: Kirsty Loudon et al. BMJ 2015;350:bmj.h2147.

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

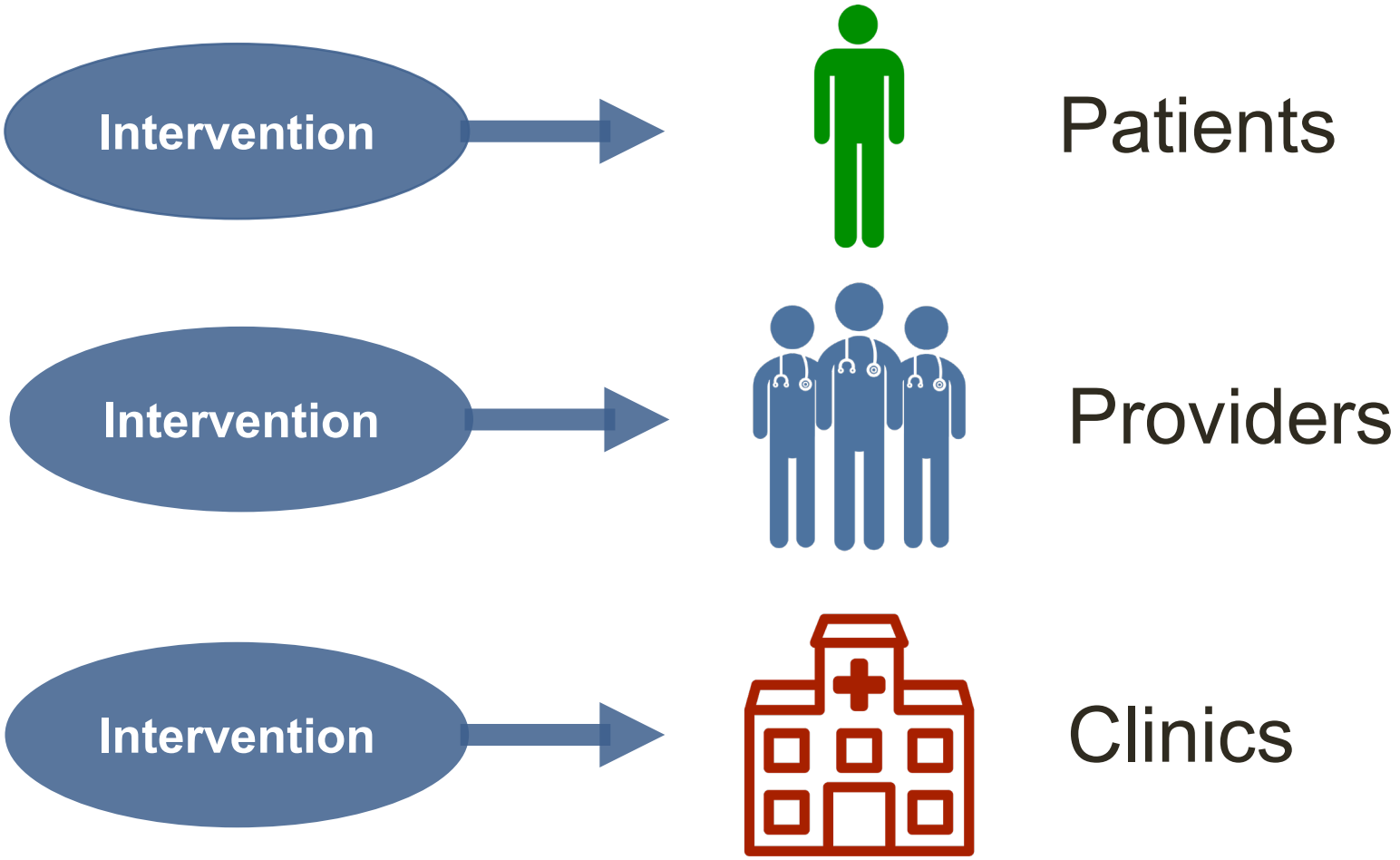
From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

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

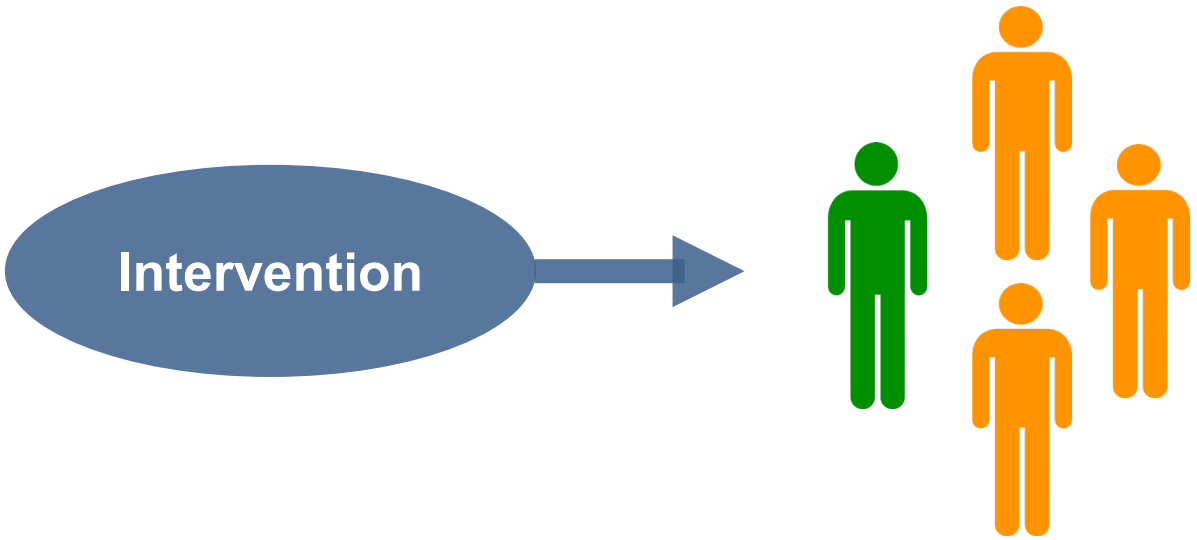
Direct participants

Immediate or mediated targets of the intervention

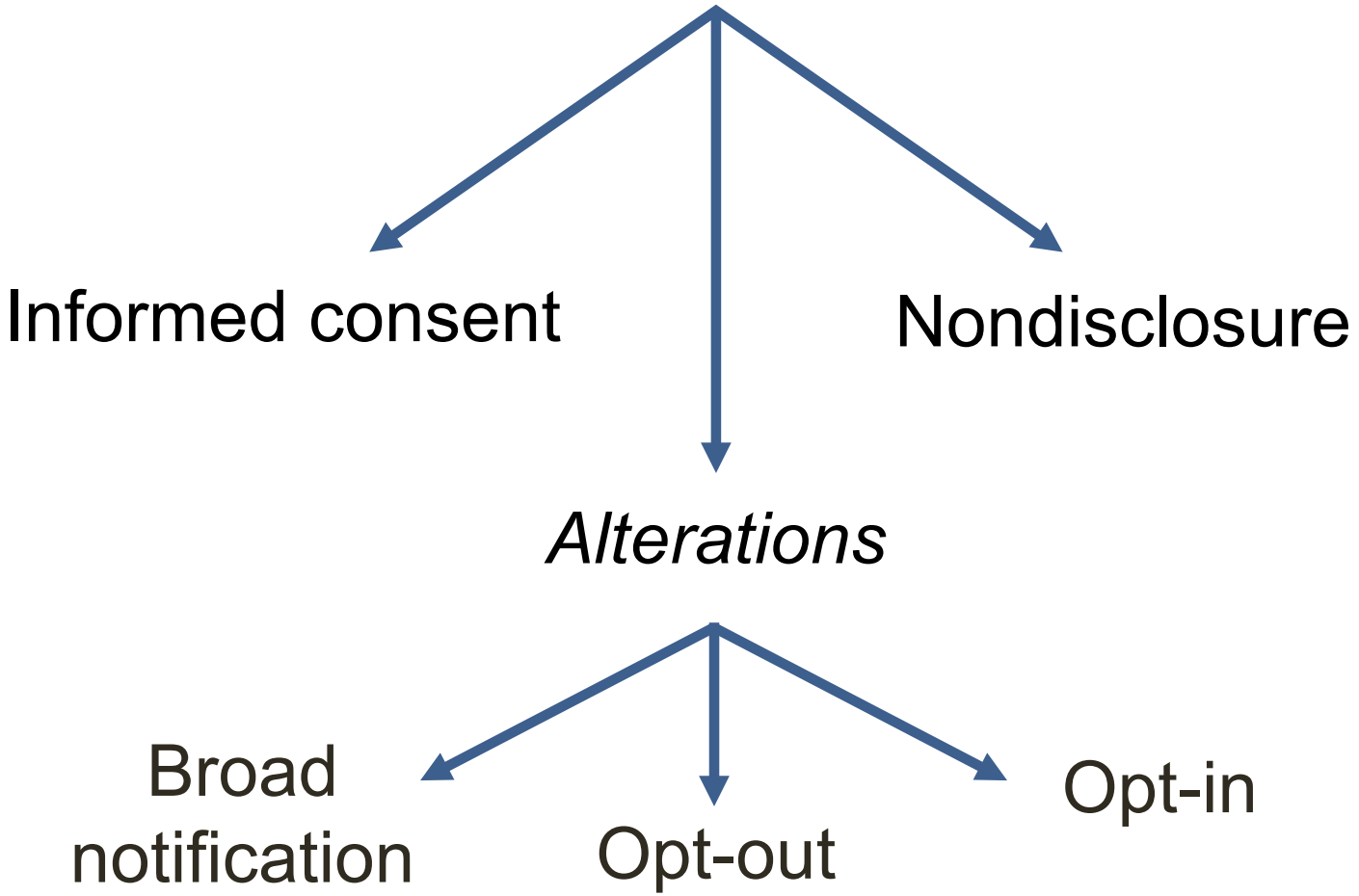


Indirect participants

Those affected by routine exposure to the environment (eg, family/caregivers)



Approaches to notification & authorization



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

Resources: Consent

Consent, Disclosure, and Nondisclosure

From the *Living Textbook of Pragmatic Clinical Trials*
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

CONDUCT

- 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?

Resources: Recruitment

Participant Recruitment

From the *Living Textbook of Pragmatic Clinical Trials*
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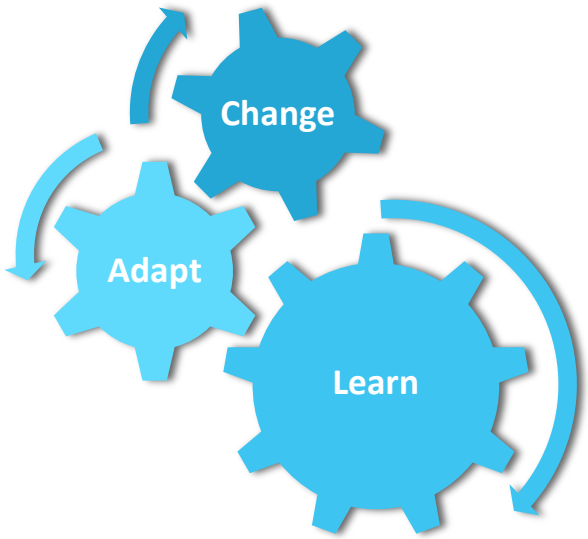
Change will happen



- 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

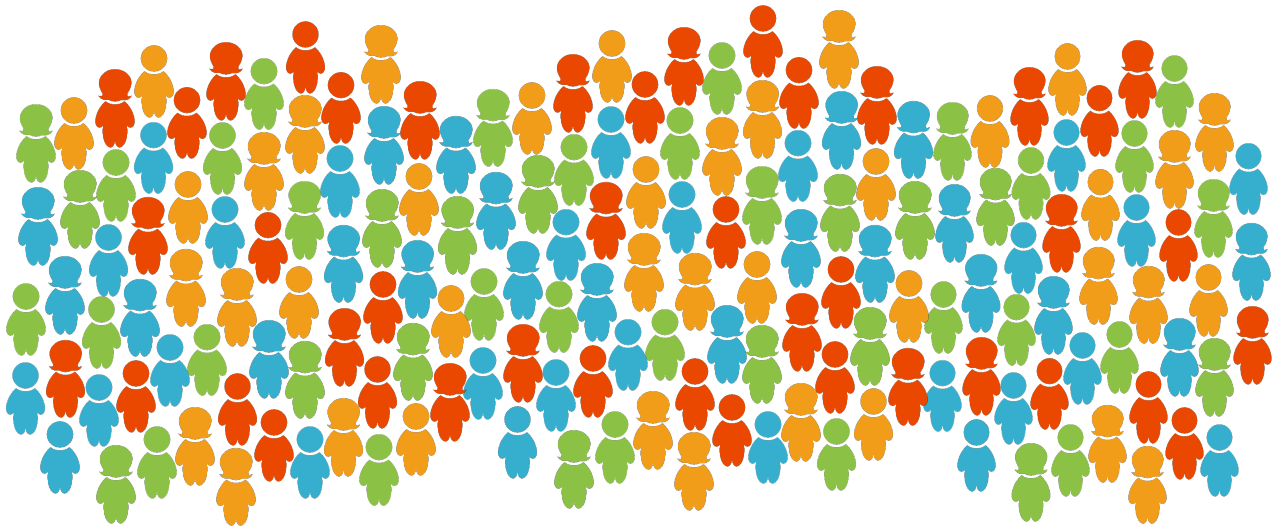
From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org

DISSEMINATION

- Results reporting
- Sustainability
- Learning health system
- Data sharing

Reporting your findings

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

https://www.ncbi.nlm.nih.gov/pubmed/28923013

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

https://www.ncbi.nlm.nih.gov/pubmed/?term=26772801

Loudon et al., 2015. PRECIS-2 tool: designing trials that are fit for purpose

https://www.ncbi.nlm.nih.gov/pubmed/?term=25956159

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

https://www.nihcollaboratory.org/Pages/Grand-Rounds-01-22-16.aspx