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Rethinking Clinical Trials®

What are ePCTs?

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Essentials of Embedded Pragmatic Clinical Trials Seminar

Learning goals

- Identify key considerations in the design and conduct of ePCTs and how they differ from explanatory trials
- Learn about the advantages and disadvantages of ePCTs, and when a pragmatic approach can be used to answer the research question
- Provide an understanding of the PRECIS-2 tool and its ability to assist teams in the design of an ePCT

Important things to know

- ePCTs are designed to answer important, real-world clinical questions
- Broad stakeholder engagement and support are essential from beginning to end
- Tradeoffs in flexibility, adherence, and generalizability are inevitable

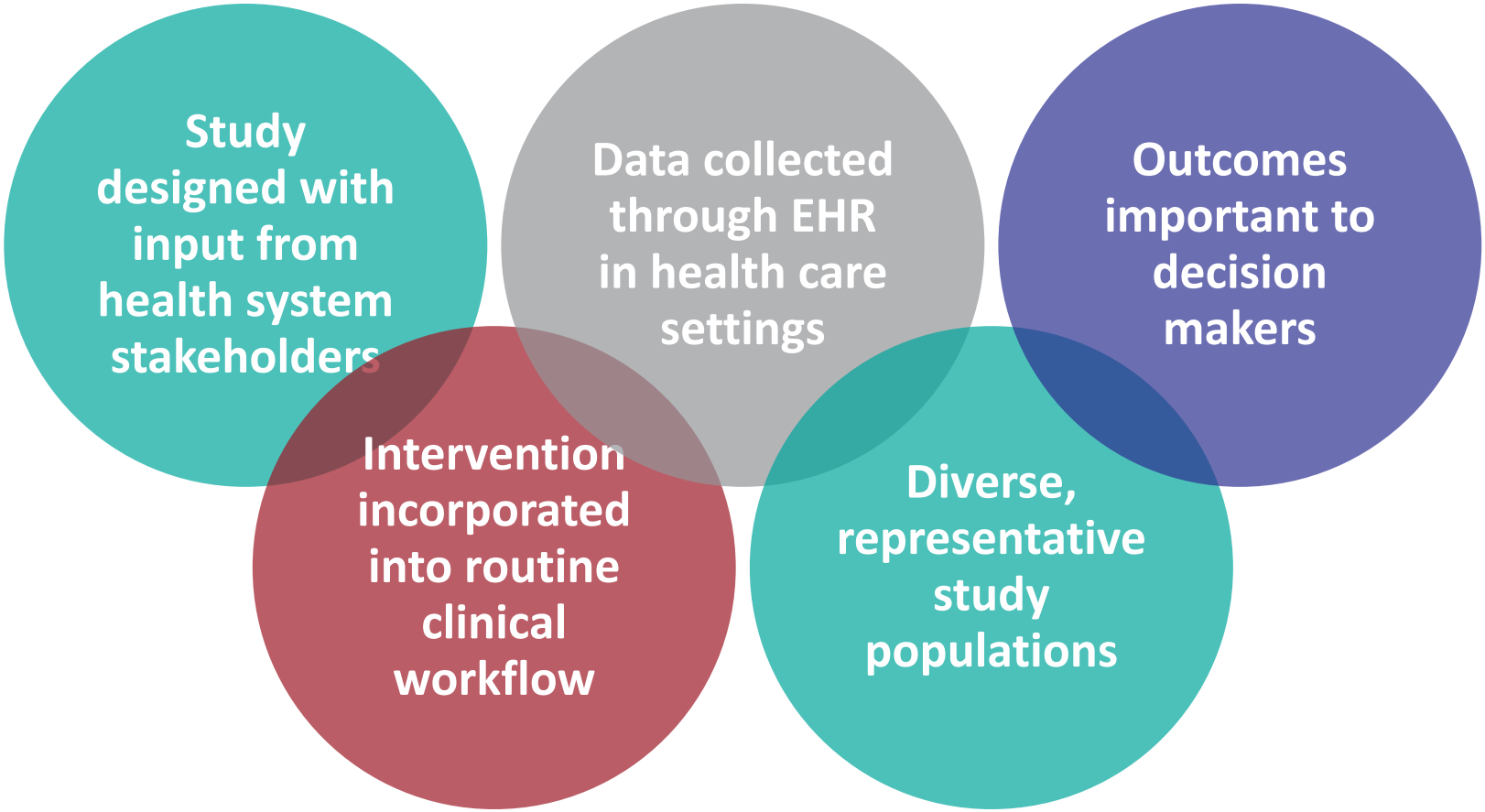
ePCT characteristics

- 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 and research



Key differences between explanatory and pragmatic trials

	EXPLANATORY	PRAGMATIC
Research question	Efficacy: Can the intervention work under the best conditions?	Effectiveness: Does the intervention work in routine practice?
Setting	Well-resourced “ideal” setting	Routine care settings including primary care, community clinics, hospitals
Participants	Highly selected	More representative with less strict eligibility criteria
Intervention design	Tests against placebo, enforcing strict protocols & adherence	Tests 2 or more real-world treatments using flexible protocols, as would be used in routine practice
Outcomes	Often short-term surrogates or process measures; data collected outside of routine care	Clinically important endpoints; at least some data collected in routine care
Relevance to practice	Indirect: Not usually designed for making decisions in real-world settings	Direct: Purposefully designed for making decisions in real-world settings

Adapted from Zwarenstein M, Treweek S, Gagnier JJ, et al. BMJ. 2008;337:a2390. doi: 10.1136/bmj.a2390. PMID: 19001484

Common-sense definition

Designed for the primary purpose of informing decision-makers regarding the comparative balance of benefits, burdens and risks of a biomedical or behavioral health intervention at the individual or population level.

Califf RM, Sugarman J. Clin Trials. 2015 Oct;12(5):436-41. doi: 10.1177/1740774515598334

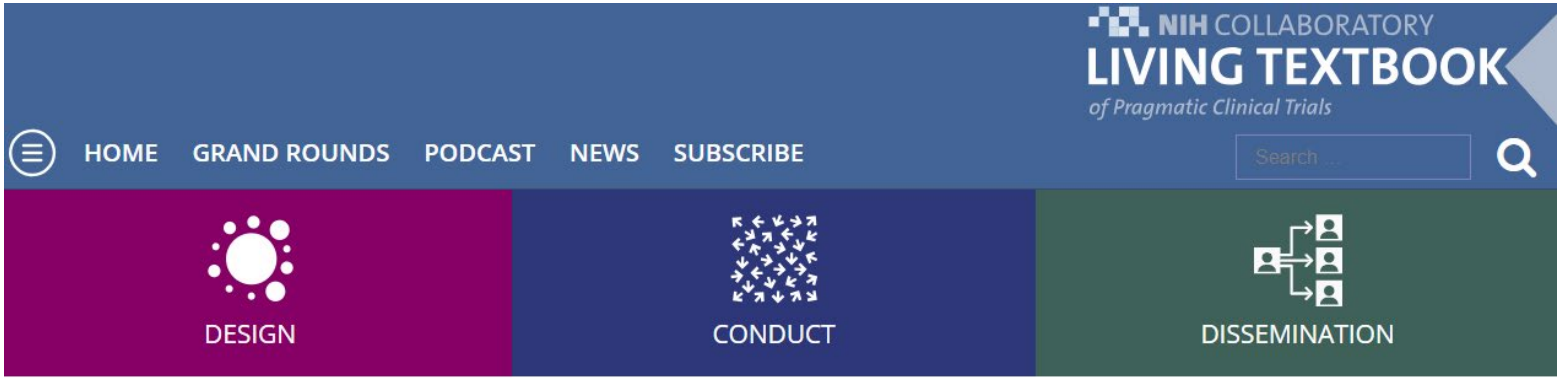
Balancing relevance and efficiency

- Achieving both relevance and efficiency is a goal of pragmatic trials, yet 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

Resource: What are ePCTs?

Why Are We Talking About Pragmatic Clinical Trials?

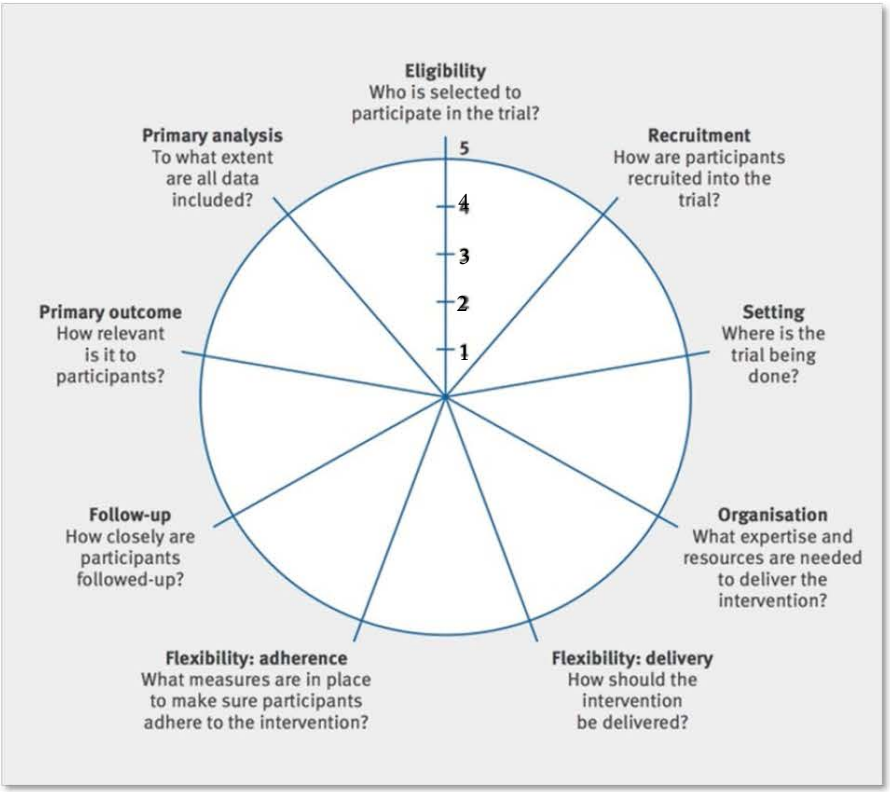
From the *Living Textbook of Pragmatic Clinical Trials*
www.rethinkingclinicaltrials.org



Introducing PRECIS-2

PRECIS-2 can be a useful tool for understanding variability in pragmatic trial characteristics

Pragmatic–Explanatory Continuum Indicator Summary (PRECIS) tool



PRECIS-2: Kirsty Loudon et al. BMJ 2015;350:bmj.h2147. Copyright 2015 by British Medical Journal Publishing Group. Used by permission.

PRECIS-2: Designing trials fit for purpose

Tool assesses trial across 9 domains

Explanatory — **Pragmatic**

1. Eligibility
2. Recruitment
3. Setting
4. Organization
5. Flexibility: delivery
6. Flexibility: adherence
7. Follow-up
8. Primary outcomes
9. Primary analysis

PRECIS-2: Eligibility

Who is selected to participate in the trial?

Explanatory ⟷ **Pragmatic**

Highly selected patients, strict inclusion criteria

Typical patients, minimal inclusion criteria

PRECIS-2: Recruitment

How are participants recruited into the trial?

Explanatory ⟷ **Pragmatic**

Uses methods and resources outside of, or in addition to, what is typical

Recruited in usual healthcare settings; participants may include patients, providers, or health systems

PRECIS-2: Setting

Where is the trial being done?

Explanatory ⟷ **Pragmatic**

Specialist practice or academic medial center

Settings where the trial's results will be applied

PRECIS-2: Organization

What expertise and resources are needed to deliver the intervention?

Explanatory ⟷ **Pragmatic**

Changes the workflow, adds equipment or staff training, or affects how care is typically delivered

Changes to clinical delivery and resources are minimal, easy to implement in usual care after the trial

PRECIS-2: Flexibility-delivery

How should the intervention be delivered?

Explanatory — **Pragmatic**

Highly specified, protocol-driven with timing of intervention tightly defined

Details of intervention delivery left to the care provider

PRECIS-2: Flexibility-adherence

What measures are in place to ensure participants adhere to the intervention?

Explanatory ⟷ **Pragmatic**

Measures to monitor patient adherence and excludes patients judged not to be adherent

No special measures to enforce intervention engagement or compliance

PRECIS-2: Follow-up

How closely are participants followed up?

Explanatory — **Pragmatic**

Frequent follow-up visits scheduled outside of clinical encounters, extensive data collection

Few follow-up visits, outcome data obtained through EHR, questionnaires, or other data sources

PRECIS-2: Primary outcome

How relevant is it to participants?

Explanatory — **Pragmatic**

Surrogate outcomes or measures distinct from the research question

Outcomes of importance to patients, measured as they would be in usual care

PRECIS-2: Primary analysis

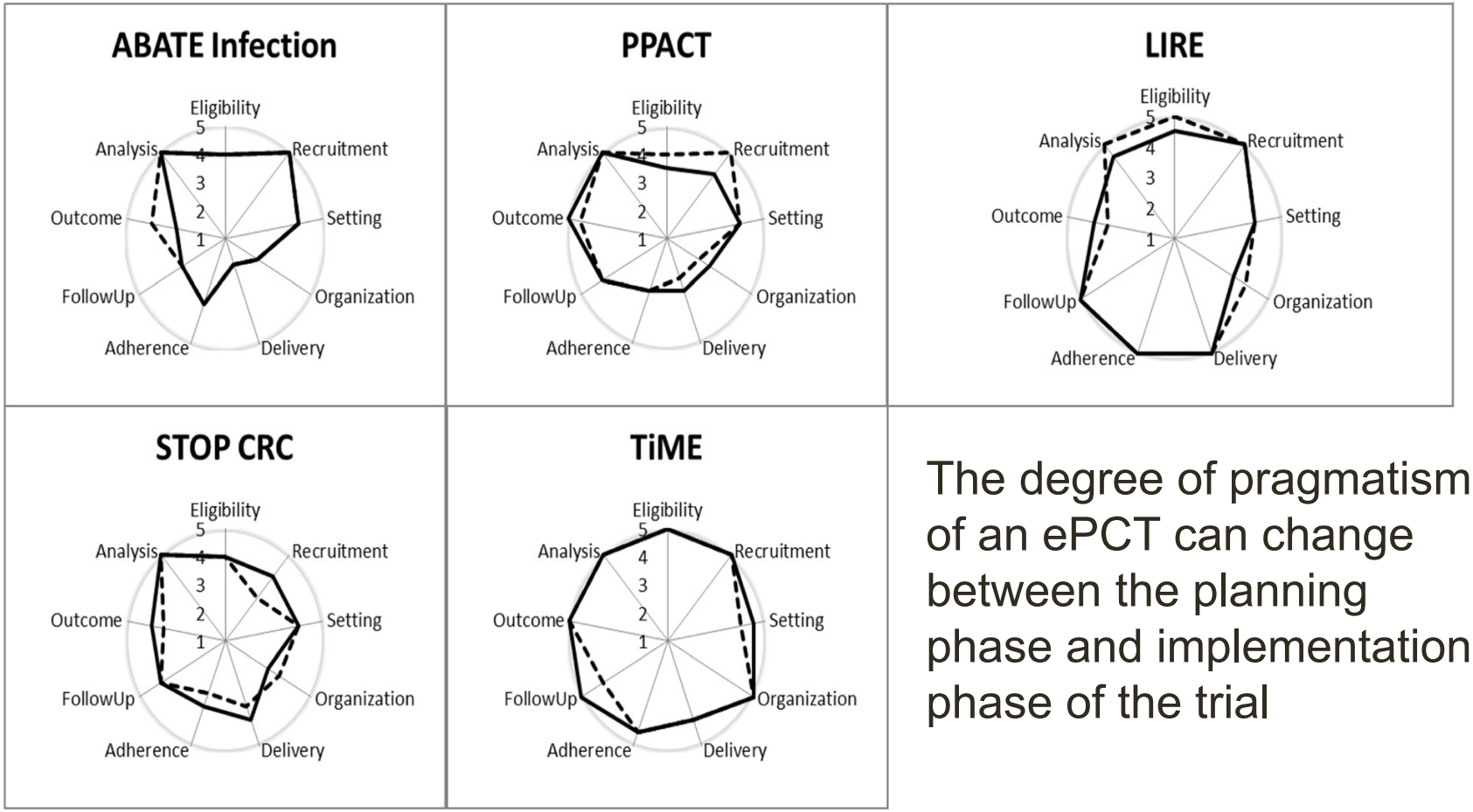
To what extent are all data included?

Explanatory ⟷ **Pragmatic**

Excludes noncompliant participants, dropouts, or practice variability

Intent-to-treat analysis

Sample PRECIS-2 wheels



The degree of pragmatism of an ePCT can change between the planning phase and implementation phase of the trial

Resource: Using PRECIS-2

Pragmatic Elements: An Introduction to PRECIS-2

From the *Living Textbook of Pragmatic Clinical Trials*
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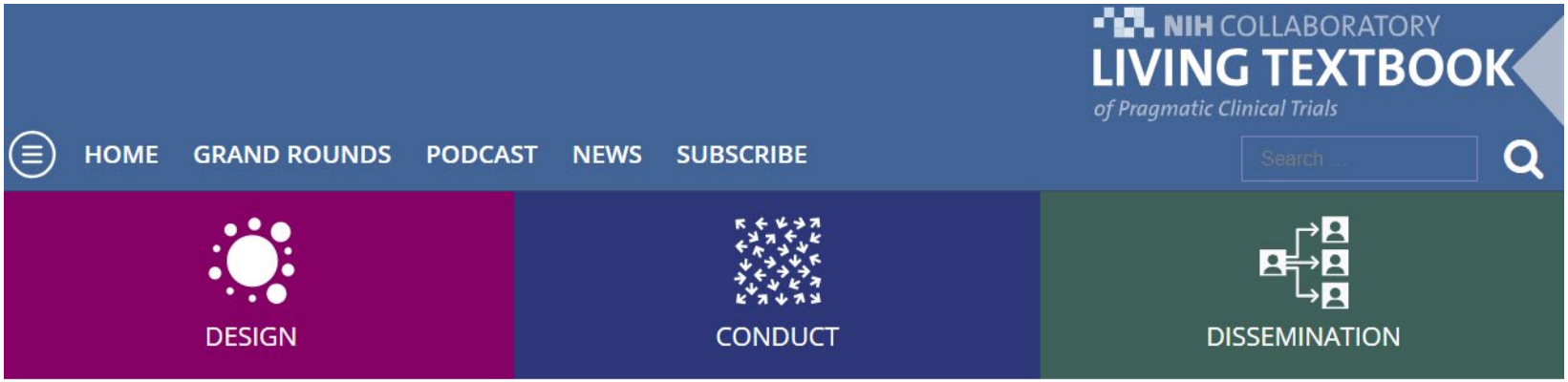

Important things to do

- For each domain of PRECIS-2, determine the approach along the pragmatic-explanatory continuum that is most appropriate for answering your research question
- Remember that trials may have some elements that are more pragmatic and some that are more explanatory