



# Topic 1: What Are Embedded Pragmatic Clinical Trials?

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***Collaboratory ePCT Training Workshop***

# Overview

- How ePCTs are different from traditional explanatory trials
  - Rationale
  - Setting
  - Design
  - Outcomes
- ePCTs bridge real-world clinical care & research
- Emphasizing the pragmatic in ePCTs
  - Introducing PRECIS-2 as a tool for study teams in the design phase

# Key ePCT characteristics

- ePCT intervention is embedded in healthcare system culture & workflow
- Needs broad stakeholder engagement & support (Topic 2)
- Uses data collected from EHR in routine clinic visits (Topic 6)
- Will involve tradeoffs in flexibility, adherence & generalizability
- Promotes a learning healthcare system where research informs practice & practice informs research

# Differences

	<b>EXPLANATORY</b>	<b>PRAGMATIC</b>
<b>Research question</b>	Efficacy: Can the intervention work under the best conditions	Effectiveness: Does the intervention work when used in normal practice?
<b>Setting</b>	Well-resourced “ideal” setting	Normal care settings including primary care, community clinics, hospitals
<b>Population</b>	Highly selected	More representative with less strict eligibility criteria
<b>Intervention design</b>	Tests against placebo, enforcing strict protocols & adherence	Tests 2 or more real-world treatments using flexible protocols
<b>Outcomes</b>	Often short-term surrogate or process measures; data collected outside routine care	Clinically important endpoints; data collected in routine care
<b>Clinical relevance</b>	Indirect: Not usually designed for making decisions in real-world settings	Direct: Purposely designed for making decisions in real-world settings

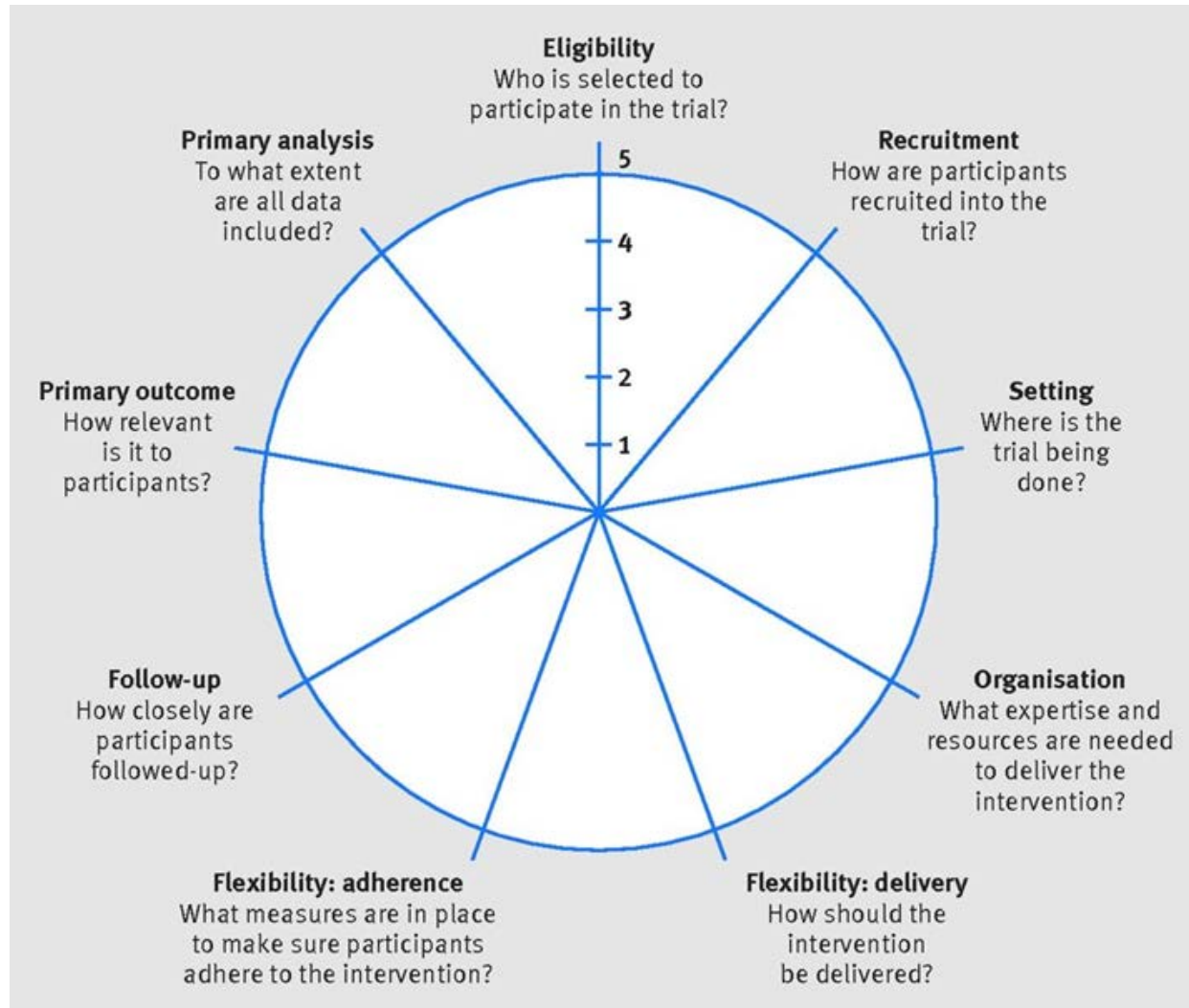
# Where does QI fit?

- QI is designed to change local processes to achieve accepted standards of care
- ePCTs are designed to determine standards of care

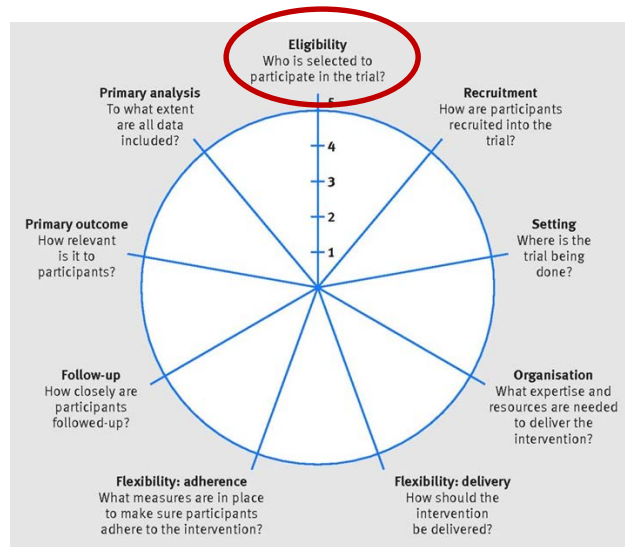
# PRECIS-2: Trials fit for purpose

- Pragmatic–Explanatory Continuum Indicator Summary (2<sup>nd</sup> version) evaluates 9 domains of the trial
  - Eligibility
  - Recruitment
  - Setting
  - Organization
  - Flexibility: delivery
  - Flexibility: adherence
  - Follow-up
  - Primary outcomes
  - Primary analysis

# PRECIS-2 wheel



# PRECIS-2: Eligibility

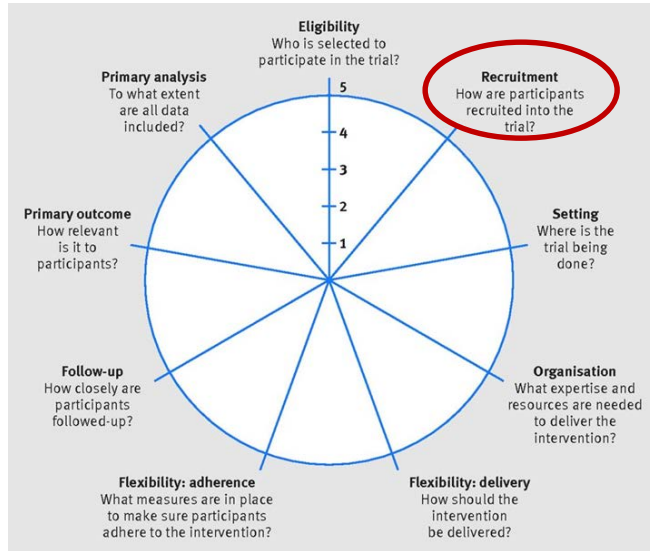


The more similar the participants are to people in usual care, the higher the PRECIS-2 score

Average enrollment in an explanatory trial in low single digits as % of patient population; highly pragmatic trials include a substantial proportion of the patient population

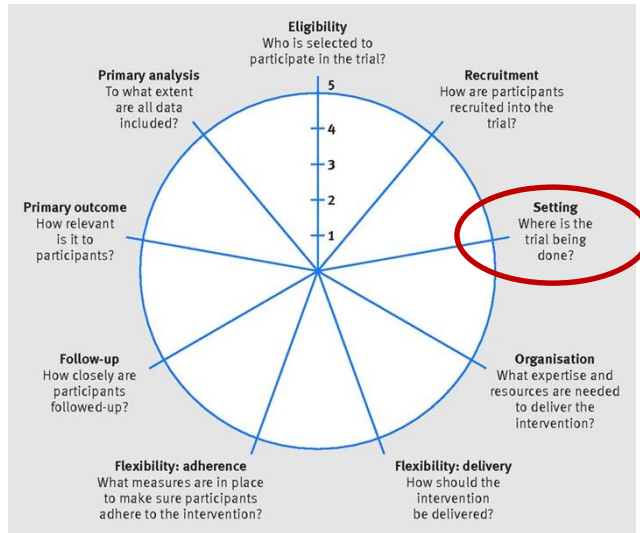


# PRECIS-2: Recruitment



Mass recruitment via email with no provider contact and recruitment via usual appointments yield higher PRECIS-2 scores

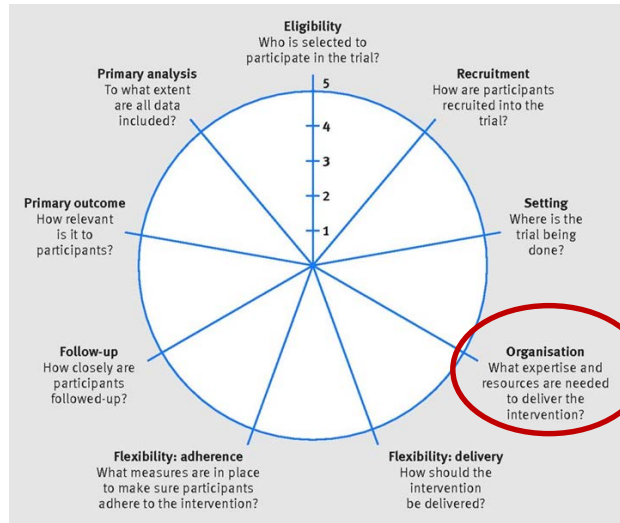
# PRECIS-2: Setting



The more similar the setting of the trial to the setting in which the results will be applied, the higher the PRECIS-2 score

**Community-based practices vs academic medical centers**

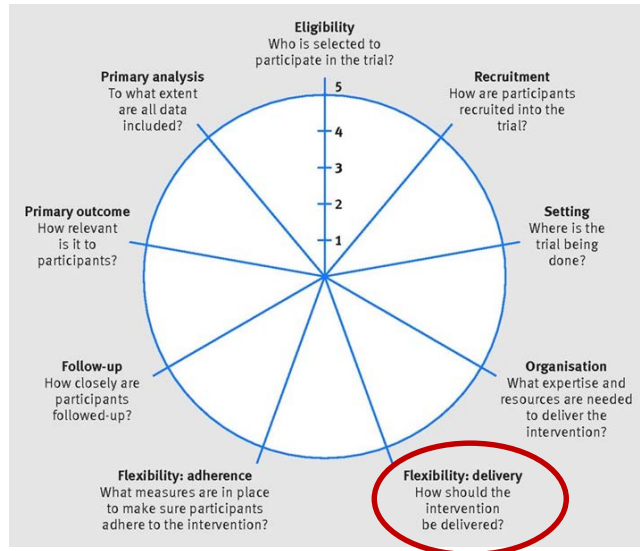
# PRECIS-2: Organization



The easier to implement in usual care, the higher the PRECIS-2 score

Oral tablet with simple instructions vs an infused medication

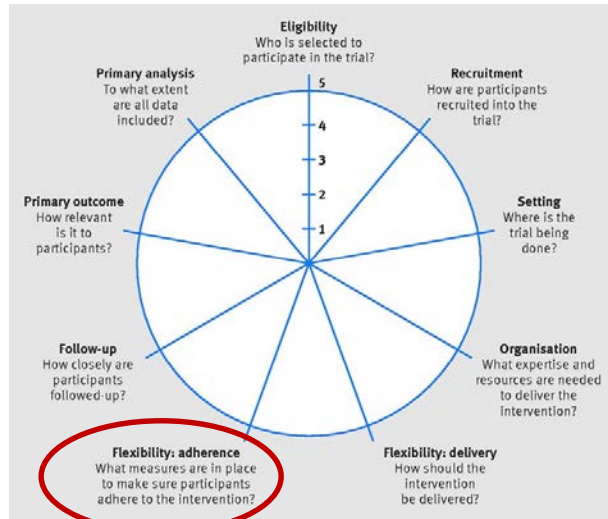
# PRECIS-2: Flexibility: delivery



The more the trial intervention looks like the way the intervention will be used in practice, the higher the PRECIS-2 score

Strict protocol,  
monitoring to improve  
compliance vs flexibility  
that's consistent with  
usual care

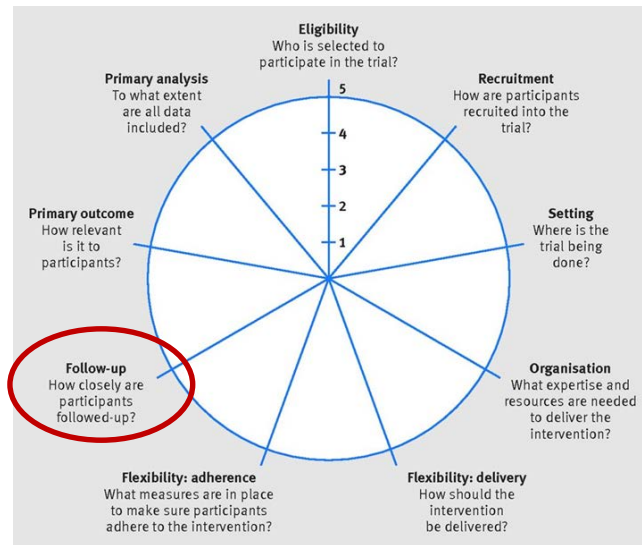
# PRECIS-2: Flexibility: adherence



The less enforcement of compliance with intervention, the higher the PRECIS-2 score

Usual encouragement to adhere to the intervention vs exclusion based on adherence

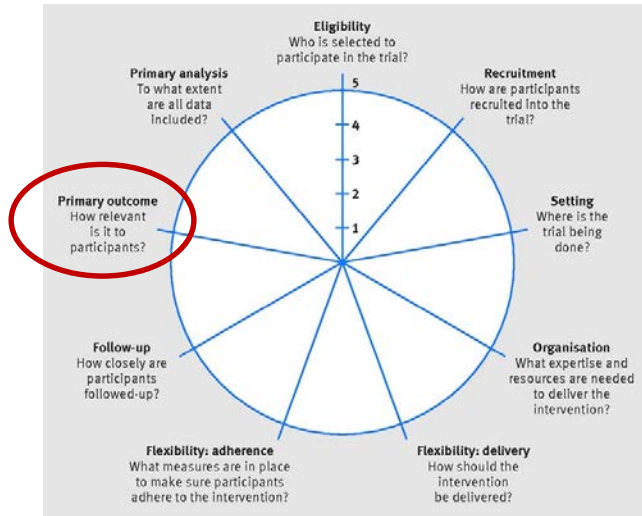
# PRECIS-2: Follow-up



The less intense the study follow-up, the higher the PRECIS-2 score

Obtaining endpoints from EHR and routine visits vs scheduled study visits

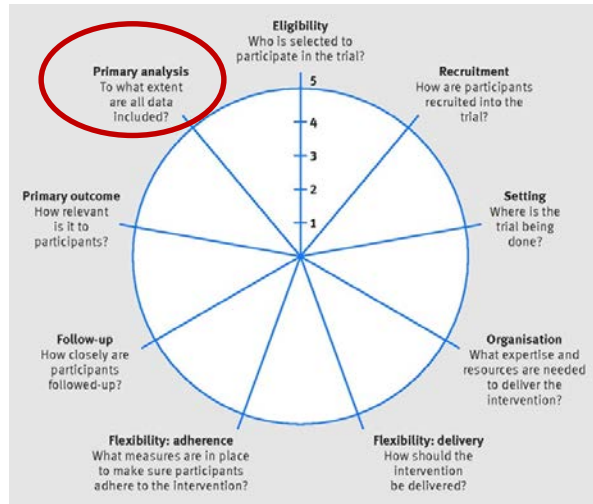
# PRECIS-2: Primary outcome



The more patient-centric the endpoint, the higher the PRECIS-2 score

Symptoms, quality of life vs biomarkers

# PRECIS-2: Primary analysis



Intention-to-treat analyses yield highest PRECIS-2 score

Excluding dropouts or noncompliant patients from the primary analysis “per protocol” analyses scores low





# Important things to know

- ePCTs bridge real-world clinical care & research
- Broad stakeholder engagement & support are essential
- Tradeoffs between flexibility, adherence & generalizability are inevitable
- Trials range across the spectrum from explanatory to pragmatic



## Important things to do

- Consider carefully the pragmatism of ALL domains of the trial



# Topic 1: What Are Embedded Pragmatic Clinical Trials?

Part 2: ePCT Case Studies: STOP CRC and TSOS

Gloria Coronado, PhD, Kaiser Permanente Center for Health Research

Doug Zatzick, MD, University of Washington School of Medicine

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# Case studies

1. STOP CRC: Gloria Coronado, PI
2. TSOS: Doug Zatzick, PI



# STOP CRC PRECIS-2 wheel



# TSOS PRECIS-2 wheel





# Important things to know

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

*What would a PRECIS wheel diagram look like for the trial you are developing?*

**5 min**



**10 min**

