Topic 1: What Are Embedded Pragmatic Clinical Trials?

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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

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<thead>
<tr>
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<th>EXPLANATORY</th>
<th>PRAGMATIC</th>
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<tbody>
<tr>
<td><strong>Research question</strong></td>
<td>Efficacy: Can the intervention work under the best conditions</td>
<td>Effectiveness: Does the intervention work when used in normal practice?</td>
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<tr>
<td><strong>Setting</strong></td>
<td>Well-resourced “ideal” setting</td>
<td>Normal care settings including primary care, community clinics, hospitals</td>
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<td><strong>Population</strong></td>
<td>Highly selected</td>
<td>More representative with less strict eligibility criteria</td>
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<td><strong>Intervention design</strong></td>
<td>Tests against placebo, enforcing strict protocols &amp; adherence</td>
<td>Tests 2 or more real-world treatments using flexible protocols</td>
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<td><strong>Outcomes</strong></td>
<td>Often short-term surrogate or process measures; data collected outside routine care</td>
<td>Clinically important endpoints; data collected in routine care</td>
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<td><strong>Clinical relevance</strong></td>
<td>Indirect: Not usually designed for making decisions in real-world settings</td>
<td>Direct: Purposely designed for making decisions in real-world settings</td>
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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 (2nd version) evaluates 9 domains of the trial
  - Eligibility
  - Recruitment
  - Setting
  - Organization
  - Flexibility: delivery
  - Flexibility: adherence
  - Follow-up
  - Primary outcomes
  - Primary analysis
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.
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
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.
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
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
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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
Case studies

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

- Eligibility
- Recruitment
- Setting
- Organization
- Flexibility Delivery
- Flexibility Adherence
- Follow-Up
- Primary Outcome
- Primary Analysis
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