Learning Objectives

01 Define pragmatic and hybrid trials and explain their use in dissemination and implementation research

02 Describe the use of the PRECIS-2 framework to design a pragmatic trial

03 Specify steps in planning pragmatic research including selection of appropriate study designs and data sources
Bio

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  • Pragmatic trials of chronic disease management interventions in primary care
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  • Conference chair, Colorado Pragmatic Research in Health Conference
Pragmatic Trial

• A trial conducted in typical “real world” settings with typical patients, using study design features readily achievable under typical practices conditions (i.e., “usual care”)

• Comparator arm(s) are real-world alternatives

• Results are intended to support decisions about intervention adoption by health care providers and patients

  • Maximize applicability across a range of common care settings
Pragmatic vs Explanatory (Efficacy) Trials

- **Explanatory**
  - Focused more on efficacy than effectiveness
  - Focused more on internal validity than external validity
  - Engagement with stakeholders often minimal as that is seen as a later step
  - Outcomes prioritize efficacy and component analysis

- **Pragmatic**
  - Focused more on effectiveness than efficacy
  - Focused more on external validity than internal validity
  - Stakeholder engagement is critical to ensure relevance to those who will later apply these approaches
  - Outcomes include both effectiveness and process measures to more fully define impact


www.PRECIS-2.org;
Characteristics of Pragmatic Research

• The research question of interest...
  • …tests if an intervention is effective in routine practice or service settings, often compared to well-defined usual care or existing programs and/or other comparator interventions.
  • …considers the setting in which the intervention will be used (and its existing personnel and infrastructure) and how the intervention will be implemented and sustained in real-world contexts
Characteristics of Pragmatic Research

• The settings studied are…
  • …typical delivery settings (e.g., typical workplaces, schools, or communities rather than highly specialized types of these settings).

• Those delivering the intervention are…
  • …those who typically exist in typical delivery settings

• The population of interest will include…
  • ….broad eligibility criteria to represent “typical real-world” recipients of this program
  • …a recruitment path identified in typical ways for clinical/community settings (e.g., registry data, best practice alerts, other)
Dissemination and Implementation Research

• The systematic study of the adoption and use of evidence-based interventions
  • Interventions with proven efficacy and effectiveness
Dissemination and Implementation Research

• **Dissemination** is an active approach of spreading evidence-based interventions to the target audience via determined channels using planned strategies
  - **Dissemination research** is the systematic study of processes and factors that lead to widespread use of an evidence-based intervention by the target population
  - **Dissemination strategies** describe mechanisms and approaches that are used to communicate and spread information about interventions to targeted users.
Dissemination and Implementation Research

- **Implementation** is the process of putting to use or integrating evidence-based interventions within a setting.
  - **Implementation research** seeks to understand the processes and factors associated with successful integration of evidence-based interventions within a particular setting (e.g., worksite, school, clinic).
  - **Implementation strategies** are the systematic processes or methods, techniques, activities, and resources that support implementation of evidence-based interventions in practice.
Planning Pragmatic Research

• **Pragmatic research features**
  • Characterizing the setting and resources required for real-world use
  • Designing the study protocol to mirror usual care workflows, systems, resources, and delivery settings
  • Ensuring outcomes to be assessed reflect outcomes that matter to those who will use the results of the research
  • Ensuring that data collection is low burden (e.g., secondary use of existing data)
  • Emphasis on external validity

• **I spy D&I...**
  • Evaluate and describe the context in which an intervention will be delivered (population, setting, resources, infrastructure, systems and workflows)
  • Engage stakeholders in the design, conduct, and/or dissemination of research including selection of outcomes, relevance of research questions, and alignment with existing systems, processes, and workflows
  • Consider strategies needed to communicate to real-world practice settings the value of participating in research and prepare practice personnel to deliver interventions according to protocol
D&I Context Assessments

- Readiness to change
- Implementation climate
- Existing infrastructure and systems and processes of care
The COPRHP Pragmatic Research Plan Workbook
Designing Research for Real World Impact

https://cophres.learningtimesevents.org/
Stakeholder Engagement

A bi-directional, longitudinal relationship between stakeholders and researchers that informs decision-making about research prioritization, conduct, and dissemination.

Involving multiple stakeholder types (e.g., patients, care partners, health care providers, advocacy groups, policy makers) in research helps to ensure the research is feasible, scientifically rigorous, and relevant.

https://dicemethods.org/WhatIsStakeholderEngagement
Welcome! The purpose of this tool is to help your team select the most appropriate engagement method or tool for your particular project.

Before using the tool, consider the following:

- **Purpose**: What do you hope to achieve through stakeholder engagement?
- **Budget**: What budget do you expect to have for your engagement activities?
- **Number of Interactions**: Over what period of time do you expect to engage your stakeholders?
- **Time per Interaction**: How much time do you expect from your stakeholders in any given interaction?
- **Staffing/expertise**: What types of staffing and expertise are available to you?
Your chosen research stage(s): Planning
Your chosen purpose(s) of engagement: Develop research questions relevant to stakeholders

Use the sliders to further refine your search. You may use the sliders to set a range or to select one point.

- **Budget**
  - $
  - $$$
  - $$$$$

- **Time per interaction**
  - An hour or less
  - Half a day
  - A full day

- **Number of interactions**
  - 1-2 times
  - Appx. 5 times
  - 10+

After adjusting sliders, click on highlighted strategies below to discover more.
7Ps stakeholder framework

- Patients and the public
- Providers
- Policymakers
- Purchasers
- Payers
- Product makers
- Principal investigators

• The research question of interest...
  • …tests if an intervention is effective in routine practice or service settings, often compared to well-defined usual care or existing programs and/or other comparator interventions.
  • …considers the setting in which the intervention will be used (and its existing personnel and infrastructure) and how the intervention will be implemented and sustained in real-world contexts.
Hybrid Implementation-Effectiveness Trials

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Hybrid Type 1</th>
<th>Hybrid Type 2</th>
<th>Hybrid Type 3</th>
</tr>
</thead>
</table>
| Research Aims | *Primary Aim*: Determine effectiveness of an intervention  
*Secondary Aim*: Better understand context for implementation | *Primary Aim*: Determine effectiveness of an intervention  
*Co-Primary* Aim*: Determine feasibility and/or (potential) impact of an implementation strategy  
*or Secondary Aim* | *Primary Aim*: Determine impact of an implementation strategy  
*Secondary Aim*: Assess clinical outcomes associated with implementation |

Types of D&I
Aims

• Engage stakeholders in the design, conduct, and/or dissemination of research
• Evaluate and describe the context in which an intervention will be delivered (population, setting, resources, infrastructure, systems and workflows)
• Evaluate dissemination and implementation of an intervention, such as adoption, feasibility, fidelity and adaptations
• Design and test implementation strategies
• Design and test dissemination strategies
**PRECIS-2**

**Pragmatic-Explanatory Continuum**

Intent or attitude
Series of dimensions

**PRECIS-2**

9-domain framework for evaluating how pragmatic an intervention is relative to usual care
Useful for planning and reporting

Source: Loudon et al., *BMJ*, 2015
How Pragmatic is your Study? The PRECIS-2 Tool

**Eligibility**: the extent to which participants in the trial are similar to those who would potentially receive the intervention in usual care settings

- Highly pragmatic (rating of 5): selection criteria are highly inclusive
- In-between (rating of 3): selection criteria limit study population to some extent, but most “typical” patients are included.
- Highly explanatory (rating of 1): step-wise selection criteria, restricted to participants highly responsive to experimental intervention
**Settings**: how different are settings of the trial from usual care?

- **Highly pragmatic (rating of 5)**: setting is nearly identical to location where results are intended to be applied (usual care)
- **In-between (rating of 3)**: setting is partially representative of usual care sites; at least 2 sites are involved
- **Highly explanatory (rating of 1)**: study is not at all representative of usual care – highly specialized center or tertiary-care center, only one center involved

**PRECIS-2 domains**

**Organizational infrastructure:** the difference between the resources, provider expertise, and the organization of care delivery employed in the intervention arm of the trial as compared to those available in usual care

- **Highly pragmatic (rating of 5):**
  - No extra non-reimbursable time for staff required or additional staff resources required beyond what would be expected in usual care – but may consider emerging models of usual care such as patient-centered medical homes
  - Staff require no or minimal additional training beyond what is expected in usual care

- **In-between (rating of 3):**
  - Intervention requires some extra staff time, infrastructure, and training – any reimbursements for the extra staff time could raise this rating to be more pragmatic than if that was not present

- **Highly explanatory (rating of 1):**
  - Intervention requires many extra hours of staff time and additional infrastructure
  - Requires highly specialized staff and/or significant extra training

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**Panel A:** Explanatory trial of cognitive behavioral therapy to prevent chronic pain: limited attention to external validity
- High score for Eligibility but low scores for Recruitment and Settings: the results are likely to be relevant to patients in the TYPES OF SETTINGS studied, but these patients will not necessarily represent patients in the general population
- Low score for Organization means that the resources used for this trial are not common in real-world settings

**Panel B:** Pragmatic trial of computer-supported tailored asthma education mailers: major attention to external validity
- High scores for Eligibility, Recruitment methods, and Setting suggests excellent generalizability to other patients and settings
- High score for Organization means most settings could deliver this program
- High scores for Flexibility means that real-world implementation is likely to find the same results as in the study
- Middle score for primary outcome (hospital admissions for asthma) suggests this may not be the most meaningful outcome to patients


Steps to applying PRECIS-2 to trial design

• **Step 1.** Consider your intent for the trial you are designing – more explanatory or more pragmatic? *Be deliberate in selection of the design, based on the research question.*

• **Step 2.** Assess your trial design choices for each of the 9 domains. *Bear in mind your intent.*

• **Step 3.** Score choices and mark on the wheel from 1 (very explanatory) to 5 (very pragmatic)

• **Step 4.** Review scores with collaborators and stakeholders and revise design choices as necessary. *Check that design choices are consistent with your intent (Step 1).*

• **Repeat.** *Iterate until the design matches the intent*

Loudon et al BMJ 2015
PRECIS-2-PS (Provider Strategies)

## Study Designs

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Design Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomization is possible...</td>
<td>Participant-level RCT (intent-to-treat)</td>
</tr>
<tr>
<td>...but there is likelihood of contamination within clusters</td>
<td>Cluster randomized trial (ITT)</td>
</tr>
<tr>
<td>...and sites are unlikely to accept randomization to control or implementation resources are limited</td>
<td>Stepped wedge design (ITT)</td>
</tr>
<tr>
<td>The intervention has multiple components that need to be optimized in terms of combination, dose, sequence, timing...</td>
<td>Randomized factorial design (ITT)</td>
</tr>
<tr>
<td>...and there may be participant- or setting-level criteria (such as non-response to first-line treatment) that dictate which sequence or combination is optimal</td>
<td>Sequential multiple assignment randomized trial (ITT)</td>
</tr>
<tr>
<td>Randomization is not ethical or feasible...</td>
<td>Adaptive trial (ITT)</td>
</tr>
<tr>
<td></td>
<td>Observational, quasi-experimental, or natural experiment design</td>
</tr>
</tbody>
</table>
Pragmatic Research Outcomes

Stakeholder-centered outcomes
- Information needed to inform decisions about what health services to adopt, use, or pay for
- Long-term and short-term

Framework-aligned constructs and outcomes
- Key domains from a conceptual model or theoretical framework

https://re-aim.org/resources-and-tools/measures-and-checklists/
Data Sources for Pragmatic Research

Use of secondary data sources
- Electronic health records
- Publicly available registries and data sets

Pragmatic measures characteristics
- Brevity
- Criterion validity (does it predict what it is supposed to)
- Reliability (especially test-retest)
- Sensitivity to change (e.g., ability to detect intervention effects)
- Actionable and understood by users
- Quickly and easily scored
- Broad availability (e.g., validated in multiple languages and applicable across populations)
- Availability of norms

Case Example

• Cluster randomized pragmatic trial (Hybrid type 2)
• Comparative effectiveness of patient-driven vs standardized diabetes shared medical appointments (SMAs)
  • SMA models use the same curriculum
  • Both are 6 sessions, about 2 hours each session
  • Models differ in terms of who delivers the curriculum (health educator vs multidisciplinary care team including behavioral health and a peer mentor) and tailoring module order and emphasis on topics to cohort needs and preferences
• Funded by PCORI Improving Healthcare Systems Award
• Patient and practice stakeholders engaged in research prioritization, design, conduct, and dissemination

Implementation and Adaptation

How pragmatic is it?

Protocol Refinement


Table 3: Invested in Diabetes protocol refinements by PRECIS-2 domain, invested in Diabetes study team, 2018–2021

<table>
<thead>
<tr>
<th>PRECIS-2 domain</th>
<th>Original protocol</th>
<th>Protocol refinement</th>
<th>Reason for refinement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligibility</td>
<td>Patients are adults with type 2 diabetes who are existing patients of the practice; excludes pregnancy or plans to become pregnant within 6 months, life expectancy less than 6 months, cognitive inability to participate, plans to leave area within next year.</td>
<td>Practices encouraged to recruit any adult with type 2 diabetes they believed would be able to participate in and benefit from SMAs (i.e., no explicit assessment of eligibility criteria; provided review lists of patients to assess suitability).</td>
<td>Not typical for practices to ask patients if planning to become pregnant or leave the area prior to offering care; Assessment of cognitive ability, life expectancy, and other 'suitability' factors based on provider judgment.</td>
</tr>
<tr>
<td>Recruitment</td>
<td>Practices would recruit patients using existing personnel and processes of care.</td>
<td>Practices shared strategies used to meet recruitment goals during practice stakeholder calls. Engaged patient stakeholders helped develop marketing materials. Research team provided recruitment fliers and coaching sessions to support recruitment strategies.</td>
<td>Recruitment was listed as a top barrier from every practice and they needed extra support and guidance to achieve recruitment goals.</td>
</tr>
<tr>
<td>Setting</td>
<td>Diverse clinic settings: FQHCs, private practices, and community mental health centers with integrated behavioral health and primary care, including small/large and urban/suburban/rural sites in Colorado. Practices had ≥100 adult patients with type 2 diabetes (able to commit to 72 patients over 2 years, including 60 with complete PRO data).</td>
<td>No community mental health centers recruited. Allowed &quot;half-sites&quot; to provide 36 patients instead of 72. Allowed participating organizations to combine smaller practices into one &quot;site&quot; for randomization purposes.</td>
<td>Policy-level changes to billing/payment structures for community mental health centers came into effect during practice recruitment. Smaller practices allowed to participate to reach practice recruitment goals and to ensure results were relevant to a greater range of practice sizes.</td>
</tr>
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Resources

- https://www.precis-2.org/
- https://coprhcon.learningtimesevents.org/ (2020 and 2021 Archives)
- https://dicemethods.org

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Thank you!

Questions? Comments?

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