Pragmatic Trials 101

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The Interacting Elements of Integrating Science, Policy and Practice*

Evidence from community or population

Identify and Specify Problem

Sustainable Ongoing Learning System

Policy, Program & Practice Implementation

Refinement

Evaluation

Consider Multi-level Context

Assess Relevant Knowledge/Evidence

Intervention Evidence from Efficacy Studies, and Use of Theory to Fill Gaps

Evidence from Etiologic Research

D&I Science

Partnerships

Sustainability

E-Health

Health Disparities

Framework/Logic Model

Global Health

Scale-Up

Fidelity/Adaptation

Types of Evidence

Rapid Learning Systems

External Validity

Complex Intrv.

Cost Effect.

Pragmatic Trials

Designing for Diss.

CER

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Figure adapted with permission from Ward V, House A, Hamer S. Developing a framework for transferring knowledge into action: a thematic analysis of the literature. J Health Serv Res Policy 2009 14:156—164
Overview - What are Pragmatic Trials (PTs)? Why Important?

How are PTs Different than Explanatory Trials?

Comparison/Control Conditions in PT

PRECIS Criteria

An example: Be Fit Be Well Study

Summary and Discussion
A pragmatic (or practical) trial seeks to answer the question, “Does an intervention work under usual conditions?”

An explanatory (or efficacy) trial seeks to answer the question, “Can an intervention work under ideal conditions?”
The “type” of trial matters for interpretation of the results.

A “positive” explanatory trial is not proof that its intervention will work in real world settings, or context different than those in which it was conducted, whereas a “negative” explanatory trial is assumed to suggest that its intervention would not work in the real world (although this is debated).
We are:

- Not reaching patients with complex, comorbid problems and those most in need
- Not testing in settings and with staff that are typical to most clinical situations
- Not addressing issues important to clinicians, policy makers, and patients
- Many ‘evidence-based’ Tx not feasible in most real world settings
- Bottom Line - Research not seen as RELEVANT
### Key Contextual Characteristics

- Questions from and important to stakeholders
- Multiple, heterogeneous settings
- Representative populations
- Comparison conditions are real-world alternatives
- Multiple outcomes important to decision and policy makers

Thorpe KE et al., Can Med Assoc J, 2009, 180: E47-57
Tunis SR et al. Practical clinical trials... *JAMA* 2003;290:1624-1632
Glasgow RE et al. Practical clinical trials... *Med Care* 2005;43(6):551-557
### Two Approaches to a Medication Adherence Trial: The EXPLANATORY Trial vs. PRAGAMATIC TRIAL (Glasgow & Steiner)

<table>
<thead>
<tr>
<th>Design decision</th>
<th>Explanatory</th>
<th>Pragmatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which clinics to approach?</td>
<td>Highly motivated site(s) within high performing systems having excellent EMR resources</td>
<td>Randomly selected site(s) from multiple, diverse delivery systems</td>
</tr>
<tr>
<td>Which clinicians to approach?</td>
<td>Highly motivated clinicians within those sites</td>
<td>All clinicians within those sites</td>
</tr>
<tr>
<td>Which patients to enroll?</td>
<td>Highly motivated patients with minimal comorbidity</td>
<td>All patients newly prescribed a statin, regardless of comorbid physical or psychosocial problems</td>
</tr>
<tr>
<td>What level of comfort with cell phones to select for?</td>
<td>Comfortable using wide range of cell-phone features</td>
<td>No cell phone (need to provide one and instruct), or wide range of comfort with cell-phone features</td>
</tr>
<tr>
<td>How frequently to send text messages?</td>
<td>Frequently; isolated from workflow in clinic, close highly individualized intensive monitoring</td>
<td>Less frequently, but consistent with workflow patterns in clinic</td>
</tr>
<tr>
<td>What level of training to require from supporting clinical pharmacist?</td>
<td>Single individual, highly experienced, trained in motivational interviewing</td>
<td>Multiple clinical pharmacists with standard training in patient counseling</td>
</tr>
<tr>
<td>What kind of advice protocol to provide?</td>
<td>Highly scripted, standardized</td>
<td>Unscripted or general guidelines and suggestions for adapting</td>
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<td>How to monitor implementation of advice protocol?</td>
<td>Careful assessment of fidelity to protocol, and intensified intervention if not optimal</td>
<td>Qualitative assessment of advice actually delivered by pharmacists</td>
</tr>
<tr>
<td>How to monitor adherence?</td>
<td>Active, continuous assessment with electronic medication monitors</td>
<td>Surveillance by patient self-report and/or prescription refill records</td>
</tr>
<tr>
<td>How to monitor impact on cholesterol?</td>
<td>Fasting cholesterol levels drawn at pre-specified intervals during additional visits for that purpose</td>
<td>Fasting cholesterol levels drawn in the course of routine practice visits</td>
</tr>
<tr>
<td>Which patient subgroups to monitor for differences in effectiveness?</td>
<td>Few subgroups assessed (due to exclusions in recruitment), homogeneous patients not on other medications</td>
<td>Multiple pre-specified subgroups (particularly for subgroups oft excluded in an efficacy trial, e.g. individuals with multi-morbidity, limited cell phone comfort, low health literacy/numeracy participants)</td>
</tr>
<tr>
<td>Duration of follow-up?</td>
<td>Short-term (e.g. 3-6 months), allowing identification of individuals who soon stop treatment</td>
<td>Long-term (12-24 months), allowing identification of individuals who later restart treatment</td>
</tr>
<tr>
<td>Continuation of intervention?</td>
<td>To end of grant funding</td>
<td>Long-term incorporation into clinic operations</td>
</tr>
<tr>
<td>Does this intervention have any effects, positive or negative, on clinic operations? Cost of intervention</td>
<td>Not relevant to assess Not assessed</td>
<td>Critical to assess through staff interviews, observations and qualitative assessments Assessed from perspective of adopting organization and patient, includes cost-effectiveness indices</td>
</tr>
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</table>
Must be a Realistic Alternative

Not Placebo or Wait List or No Treatment

Can be Component or Less Expensive Tx

Consider “Minimal Intervention Needed for Change (MINC)"

What is ‘Usual Care’?
Key PT Features: Implementation Science Perspective

- Reach
- Generalizability- across settings, staff, and subgroups
- Context-dependent
- ‘Real-world’ emphasis- including cost and feasibility
- Replication
Questions and/or Comments?
Labels such as pragmatic or explanatory are an over-simplification and imply a dichotomy.

In reality, there is a continuum between the extreme cases of either type, and very few actual studies are completely explanatory or totally pragmatic.
Describes ten domains that affect the degree to which a trial is pragmatic or explanatory.

1. Participant eligibility criteria
2. Experimental intervention flexibility
3. Practitioner expertise (experimental)
4. Comparison intervention
5. Practitioner expertise (comparison) outcome
6. Follow-up intensity
7. Primary trial outcome
8. Participant compliance
9. Practitioner adherence
10. Analysis of primary

The pragmatic approach leaves the details of how to implement the experimental intervention up to the practitioners and would not dictate which co-interventions were permitted or how to deliver them.

What factors would be associated with a more Explanatory approach?
Discussion

- PRECIS CAN BE applied by:
  - a design team during the planning stages
  - by an implementation team
  - post-hoc by reviews from study report

- The graphical representations are helpful for readily identifying domains that are not as pragmatic or explanatory as the trial designers desired.
A weight reduction and maintenance effectiveness trial in routine clinical practice in Boston Community Health Centers
Participating Community Health Center Clinics

Whittier Street Health Center
50% Black; 4% White
Demonstration site in HSRAs
Cancer collaborative project
EMR

Bowdoin Street CHC
43% Black, 7% White
EMR

Dimock CHC
75% Black; 2% White
Paper charts; automated billing system

Overview  The Difference  Comparison/Controls  PRECIS  An Example  Summary
The focus of the study:

- Help obese, low-income adults lose weight, become more active, and keep their blood pressure under better control.
- Aim was to set realistic and meaningful goals that lead to small, sustainable behavior change that will continue past the end of the study.
Eligibility Criteria

- BMI ≥ 30 and
- Diagnosed hypertension
  - Prescribed medication
- Not participating in inflexible food support program
- No family members in study
- 1 or more CHC visit in past year
- Other trial-wide eligibility criteria
Comparison Condition participants receive:

- General health information about blood pressure, diet and activity
- Clinic visit every 6 months where Weight/BP measurements are taken
- Grocery cards: $50 x 4 and $75 at completion of study (total $275 over 2 years)
- Encouragement to continue with their doctor’s instructions for care.
- NHLBI Weight Loss Pamphlet
Intervention Components

- Goal-Setting & Attainment, Using Various Tools and Types of Support
  - Electronic Support
    - Web or IVR Phone System
  - Socio-environmental support
    - Community Health Worker
    - Individual Coaching
    - Group Activity Sessions
Diet Goals:
- Avoid Sugar-Sweetened Beverages; Avoid Fast Food; Eat 5-7 Fruits and Veggies Every Day; Eat Low-Fat Dairy 3 Times a Day; Avoid White Flour; Avoid High-Fat Meats; Avoid High-Calorie Snacks

Exercise Goals:
- Walk 10,000 steps each day; Get Brisk Exercise (20 minutes/most days of week); Do Strength Training (2 days/week)

Everyday Habits:
- Take Blood Pressure Medicine the right way every day; Weigh Yourself Every Day; Watch 2 Hours or Less of TV a day; Stop Eating 2 Hours Before Bedtime
Healthy Habits

Avoid High-calorie Snacks

Be Fit, Be Well recommends that you stay away from high-calorie snacks.

Sweets like cookies and candy have lots of calories, but not much nutrition. Salty foods like chips have way too much fat and salt. Eat healthy snacks instead.

Get Brisk Exercise

Be Fit, Be Well recommends that you do 20 minutes of brisk exercise every day.

You should do this all at once, without stopping. Start slow and aim for this goal. Work toward exercising hard enough to make you sweat.
Strengths of PRECIS

- Enhances transparency
- Will greatly improve information reported for reviews
- Gets around “either/or” debates
- CONSORT endorsement will enhance wide adoption
Pragmatic Trials: Take Home Points

- Real world focus - relevant to stakeholders
- Multi-level representativeness and diversity
- Endorsed by CONSORT; PRECIS criteria
- Congruent with Comparative Effectiveness, VA, HMO, PBRN research

Bottom Line: TRANSPARENCY
References


- **Thorpe KE et al., Can Med Assoc J, 2009, 180: E47-57

- Tunis SR et al. Practical clinical trials…JAMA 2003;290:1624-1632

QUESTIONS ANSWERED HERE EVEN THE SILLY ONES