Pragmatic Trials and Comparative Effectiveness Research (CER)

Sharon Straus
Russ Glasgow
Key Take Home Points

• Many similarities between pragmatic research and CER-T

• Stakeholder (and patient) perspective is central

• Real world settings are needed- how to engage and keep stakeholders engaged? James Lind Alliance

• Questions and Outcomes are relevant to stakeholders

• YOU will have a role in defining what the field is- and is not 😊
Basic Idea

- ‘The importance of an idea or action lies in whether it makes a difference in everyday life. Ideas or actions that correspond to attractive explanations (e.g., metaphysical theories), but make no difference to outcomes, are problematic.’
  
  – Charles Peirce, Popular Science Monthly, 1878.
Main Difference

• A pragmatic trial is a real-world test in a real-world population, whereas an explanatory trial is a specialized experiment in a specialized population
  – Maclure M. CMAJ 2009;180:1

• Pragmatic does not mean being less rigorous
Formulating a Question: PICOT

• P: population or characteristics of the implicated subjects
• I: intervention or exposure that the person or population experiences
• C: control to which the exposure is compared
• O: outcome measures of interest
• T: target of the trial (is the intervention better or as good); can also refer to time!
Among families in a Canadian town, can receiving primary care from a nurse-practitioners (compared to a family physician) produce high levels of physical, social, and emotional function (as good as those achieved by a family physician)?
PICOT question

• P: among families in a Canadian town
• I: can receiving primary care from a nurse practitioner (NP)
• C: compared to a family physician
• O: produce high levels of physical, social and emotional function
• T: as good as those achieved by a family physician – non-inferiority
Can nurse practitioners produce good health outcomes under IDEAL circumstances

- Super-special training of the trial nurses, with frequent refresher courses and close monitoring
- Who are caring for highly compliant patients
- Who see their patients very frequently, offer long visits and out of hours care etc.
Conclusions from an explanatory trial

• A ‘no’ answer is informative BUT,

• A ‘yes’ answer doesn’t settle the pragmatic issue:
  – Would NPs be effective under the usual circumstances (less intensive training and monitoring, caring for typical patients, and seeing them only during illnesses or for routine preventive care)?
A pragmatic question

• Will NPs produce good health outcomes under usual circumstances?
  – Routine training of the trial nurses with no refresher courses or monitoring
  – Who are caring for typical patients
  – Who are seen only when ill or for routine preventive care
Conclusions from a pragmatic trial

• A ‘yes’ answer is informative BUT,

• A ‘no’ answer does not settle the question:
  – Are NPs not capable or was their training defective, their patients noncompliant, or their patients subjected to an unusually high burden of illness?
<table>
<thead>
<tr>
<th></th>
<th>Conclusion from this Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benefit clearly greater than harm</td>
</tr>
<tr>
<td></td>
<td>Benefit clearly no greater than harm (minimally important improvement ruled out)</td>
</tr>
<tr>
<td>Explanatory trial</td>
<td>Ambiguous: it works but will patients and clinicians jump through the hoops necessary for its success?</td>
</tr>
<tr>
<td></td>
<td>Clearly sensible to abandon this treatment for this condition</td>
</tr>
<tr>
<td>Pragmatic trial</td>
<td>Clearly worthwhile to adopt this treatment</td>
</tr>
<tr>
<td></td>
<td>Ambiguous: did it fail because it was worthless or because too few clinicians and patients followed recommendations</td>
</tr>
<tr>
<td>Attribute</td>
<td>Explanatory Trial</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>---------------------------------------------------------</td>
</tr>
<tr>
<td>Nature of the question posed</td>
<td><em>Can the RX work under ideal circumstances?</em></td>
</tr>
<tr>
<td>Participant Eligibility Criteria</td>
<td>Very strict, limited to high-risk, highly responsive, highly compliant participant</td>
</tr>
<tr>
<td>Exptl Intervention flexibility</td>
<td>No/limited co-interventions</td>
</tr>
</tbody>
</table>
Figure 2: A: PRECIS summary of a randomized controlled trial of self-supervised and directly observed treatment of tuberculosis (DOT). 8B: PRECIS summary of the North American Symptomatic Carotid Endarterectomy Trial (NASCET)

Thorpe K E et al. CMAJ 2009;180:E47-E57
• Can provide a summary score
  – Pros/cons

• At least 5 different methods have been used for this
  – From Likert scale 1 to 5 to scale 1 to 20

Pragmatic Study Methods: Key Characteristics

- Questions from and important to stakeholders
- Multiple, heterogeneous settings
- Diverse 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
Explanatory vs pragmatic trials

• Dichotomy or spectrum?

Explanatory

Pragmatic

KT trials
Exercise

• Consider the ACCESSATION Trial

• For the PRECIS domains including Intervention and Expertise, and Follow up and Outcomes how would you rate each from 1 to 20
  – 1 = entirely explanatory, and
  – 20 = entirely pragmatic
• How would you change the trial to make it explanatory?
Comparative Effectiveness Research (CER)

- “The conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnosis, treat and monitor health conditions in ‘real world’ settings. (IOM)

- Patient Oriented Outcomes Research Institute (PCORI) states that “Patient-Centered Outcomes Research helps people and their caregivers communicate and make informed health care decisions, allowing their voices to be heard in assessing the value of health care options.

Key Points about CER

• CER uses many of same approaches, philosophy and designs as pragmatic approaches

• ALWAYS compares real world alternatives-
  – Some (Russ) argue that comparison could be Minimal Interventions Needed to Change (MINC)- aka aspirin
  – Some argue- and others disagree- that costs, resources, and value are important aspects of CER

Glasgow et al . The minimal intervention needed for change. Translational Behavioral Medicine, in press
Other CER Issues

• Are many appropriate designs- RCTs, CRCTs; natural experiments; observational data, time series, stepped wedge, adaptive designs, simulation models, mixed methods.....

• BUT- Each institute and funder, many professionals –and some study sections- believe that one design is superior to others (others of us do not)
Key CER Issues

• Stakeholder perspective- are multiple stakeholders- with different perspectives

• Key stakeholders are 1) ‘patients’ and families; and 2) those staff who have to implement or deliver programs and policies

• CER may just end up being about ‘drugs and devices’….OR may end also studying systems changes, behavioral interventions, multi-level interventions and policies
• “The study of complex patients with complex problems and complex health care (or public health) teams embedded in complex systems whose goal is to evaluate complex and multifaceted outcomes (intended and unintended) of complex interventions”

*Glasgow and Steiner- chapter in your text;  
**Medical Research Council, 2008l:
http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004871
CER-T Opportunities

• Ways to use EHRs and health record systems to prioritize and communicate

• “Rapid learning systems and networks - that collaborate, share data, make rapid data-based decisions

• Public health genomics (Khoury et al)

• Ways to reduce health inequities, health literacy and numeracy interventions

• Comparative study of environmental change and policy interventions
Key Take Home Points

• Many similarities between pragmatic research and CER-T

• Stakeholder (and patient) perspective is central

• Real world settings are needed- how to engage and keep stakeholders engaged? James Lind Alliance

• Questions and Outcomes are relevant to stakeholders

• YOU will have a role in defining what the field is- and is not 😊
Final Pragmatic/CER Exercise

• Instructions: Given the description provided in your handout, make design decisions to make this project a strong CER (T) study

• Q and A