Clinically Relevant Complex Systematic Reviews (CRCSR's) & the Next Challenges in Comparative Effectiveness Research & Analysis

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UCLA Center for Maximizing Outcomes and Research on Effectiveness (C-MORE)
Comparative Effectiveness Research (CER) and analysis entails:

"...the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care...”.

The purpose of CER is:

“...to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels...”.

(The Institute of Medicine, 2009)
CER Funding as of 2009

Table 2: Estimated CER Grant/Study Counts FY 2006 – FY 2009\(^1\)

<table>
<thead>
<tr>
<th>Agency</th>
<th>CER Grants/Studies FY2006-FY 2009 (YTD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHRQ</td>
<td>144</td>
</tr>
<tr>
<td>DoD</td>
<td>25</td>
</tr>
<tr>
<td>VHA</td>
<td>96</td>
</tr>
<tr>
<td>NIH(^2)</td>
<td>463</td>
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</tbody>
</table>

\(^1\)As of June 2009, based on review of agency/department websites and agency/department generated lists

\(^2\)NIH is in process of cataloging CER. This primarily represents FY 2008.

NOTE: Roughly 86\% of the CER studies across agencies focus on at least one priority disease/condition, among which leading are mental health disorders, substance abuse, cardiovascular disease, and diabetes.
The Process of Generating & Synthesizing Research Evidence & how *to quantify* it and how to operationalize it

- **Research Synthesis**
  - Best available evidence
  - Systematic Review
  - Meta-Analysis

  - Search, inclusion/exclusion
  - Level of evidence
  - Quality of evidence
  - Analyses
  - Inference, consensus
From Systematic Reviews (SR’s) to Clinically Relevant Complex Systematic Reviews (CRCSR’s)

SR’s & CRCSR’s in Effectiveness vs. Efficacy Decisions

CER Agenda for the Next Decade
Systematic Reviews (SR’s) = Reports on Research Synthesis

CER & EBP

Applications to the patient Revised CPG’s

Consensus

Systematic Reviews

Critical appraisal of evidence (“best”)

Search for all the evidence (“available”)

Answerable Question

Published Research

Treatment & Policy Decisions

Complaint Signs Symptoms

Research Synthesis
The body of research is evaluated for:
the level of evidence (**what** was done)

AND

the quality of evidence (**how** it was done: based on common criteria of methodology, design, data analysis)

**Level of Evidence**

- Systematic Review & Meta-Analysis
- Randomized Controlled Trial
- Cohort studies
- Case Control studies
- Case Series/Case Reports
- Basic Research and Animal research

R-Wong 2006
R-AMSTAR 2010
Ex-GRADE 2011
Bridging the Gap between Acceptable sampling & Clinical Relevance

The best available evidence suggests this treatment for you.

Adapted from Kung et al, 2010
In brief: SR’s for Obtaining the Best Available Evidence

Fundamental Research, Observational Studies, Clinical Trials

Research Synthesis

Meta-Analyses

Systematic Reviews (acceptable sampling)

The Best Available evidence
Best available evidence

Consensus among several SR’s

CRCSR’s

Ex GRADE

Fundamental Research

Systematic Review

Research Synthesis

EBDM

EBCP

EBR

Consensus: Best available evidence Revised CPG’s

Patient’s Needs & Wants
Clinician’s Expertise
Coverage & Payment
From Systematic Reviews (SR’s) to Clinically Relevant Complex Systematic Reviews (CRCSR’s)

SR’s & CRCSR’s in Effectiveness vs. Efficacy Decisions

CER Agenda for the Next Decade
Comparative effectiveness differs from efficacy research because it (comparative effectiveness research) … [applies]… to real-world needs and decisions faced by patients, clinicians, and other decision makers [generally including assessment of risks, costs vs. benefits].

[by contrast, i]n efficacy research, …the question is typically whether the treatment is efficacious [i.e., works clinically] under ideal, rather than real-world, settings …[and]…. [t]he results … are … not necessarily generalizable to any given patient.
Research Synthesis

Systematic Review

Cost-Effective Decisions

Individualized Patient care Decisions

Adapted from Chiappelli et al, 2009
Clinical Decision Models in Effectiveness vs. Efficacy Research

Adapted from AHRQ
Strength of clinical recommendations
Quality of Evidence

Primary Sources
- Clinical Trials: 9 - 27
- Other Primary Sources: 8 - 24

Systematic Reviews
- R-Wong
- R-AMSTAR

Strength of Recommendation
- 8 - 15: Weak
- 16 - 23: Uncertainty remains
- 24 - 32: Strong

Percentile of score

<table>
<thead>
<tr>
<th>RA</th>
<th>Score</th>
<th>Percentile</th>
<th>Ranking</th>
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<tr>
<td>4</td>
<td>32.00</td>
<td>91</td>
<td>A</td>
</tr>
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Extension of the Grading of Recommendations Assessment, Development, and Evaluation

Adapted from Phi et al, 2011 (in press) & Kung et al, 2010
From Systematic Reviews (SR’s) to Clinically Relevant Complex Systematic Reviews (CRCSR’s)

SR’s & CRCSR’s in Effectiveness vs. Efficacy Decisions

CER Agenda for the Next Decade
Unprecedented Investment in Research Synthesis

Until today...

- 2005-2009 - AHRQ received $129 million from Congress for comparative effectiveness research

For the next decade...

- 2009 - The American Recovery and Reinvestment Act contained $1.1 billion for comparative effectiveness research...
Priority Recommendations: ARRA funding portfolio (M$400)

I. data infrastructure, including HIT

II. dissemination and translation of CER findings

III. comparing priority patient groups & priority types of interventions

IV. methods and training viewed as essential to the CER enterprise

“...doing so empowers doctors and patients, and helps make our practice of medicine more evidence-based...”

Federal Coordinating Council for Comparative Effectiveness Research
Report to the President and the Congress June 30, 2009
Federal Coordinating Council - Priority ONE:

Further Development of CER methodologies to generate evidence about the comparative effectiveness, comparative safety, and cost effectiveness of clinical interventions

How should CER best be undertaken?

Need for a broad Federal CER enterprise that cuts across treatment, prevention, promotion, and health-determinant interventions designed for both people and populations.

Need for information principles and tools to prioritize CER investments on those studies where there is a greater likelihood that the research will lead to changes in practice.

Need for funding instrument to support research, including multi-center research, into “the science of CER” to build a foundation for this work, and to ensure generalizability of the findings.
Comparative Effectiveness Research

Clinical Encounter

Evidence-Based Efficacy Research

Patient-Centered Decisions (logic-based model)

Benefit/Cost/Risk Decisions (Markovian tree; utility model)

CRCSR’s

Translational -- Global

A place for UCLA…?
Thank you for your attention

...and thank you for my collaborators in these endeavors:
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Linda Phi

"Knowledge is of two kinds: we know a subject ourselves, or we know where we can find information upon it."
— Samuel Johnson (1709 - 1784)
English author and critic