



Comparative Effectiveness Research: Informing Health Care Decision Makers

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Current Challenges

- Concerns about health spending – about \$2.3 trillion per year in the U.S. and growing
- Large variations in clinical care
- A lot of uncertainty about best practices involving treatments and technologies
- Pervasive problems with the quality of care that people receive
- Translating scientific advances into actual clinical practice
- Translating scientific advances into usable information for clinicians and patients

HHS Organizational Focus



NIH

Biomedical research to prevent, diagnose and treat diseases



CDC

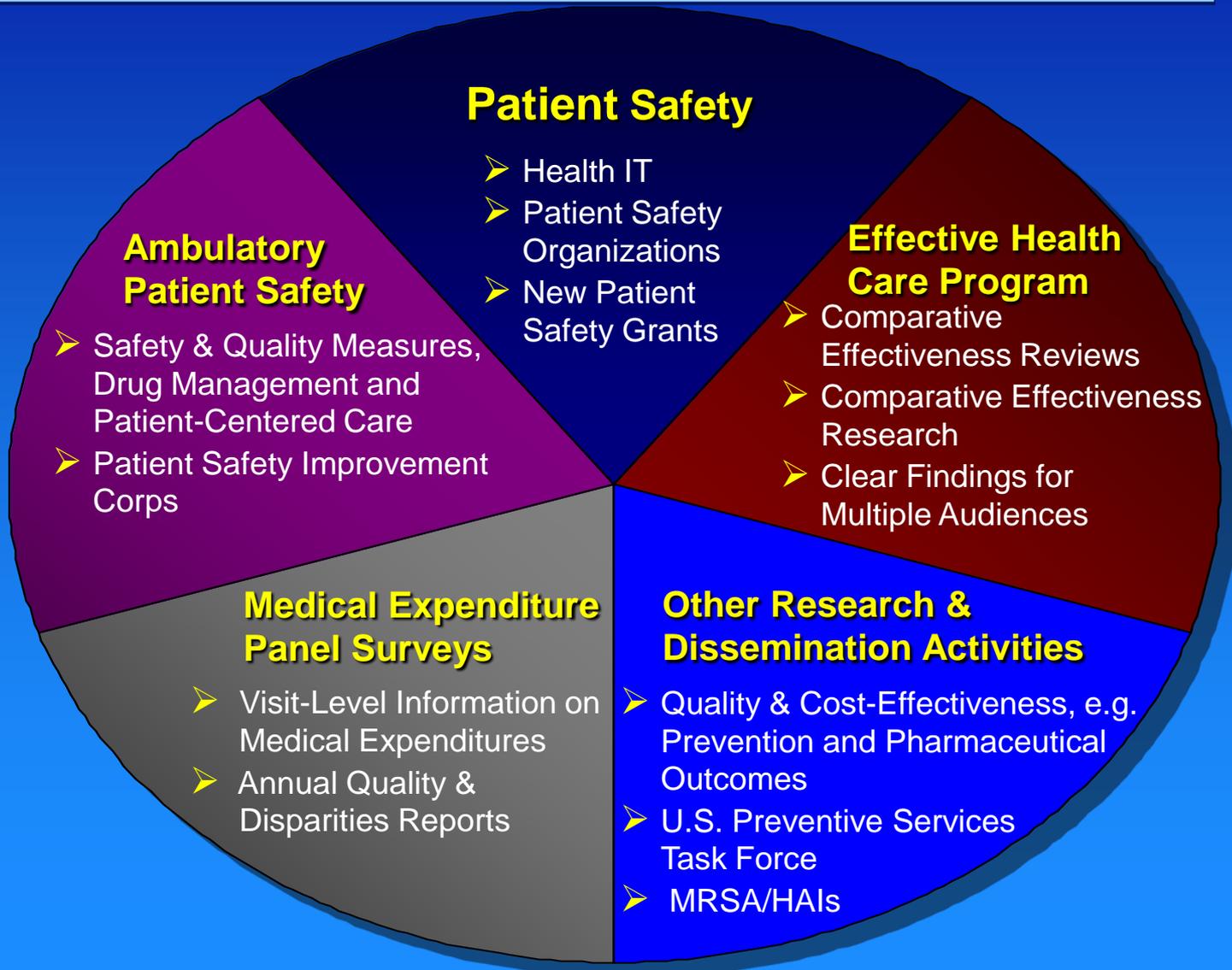
Population health and the role of community-based interventions to improve health



AHRQ

Long-term and system-wide improvement of health care quality and effectiveness

AHRQ Priorities





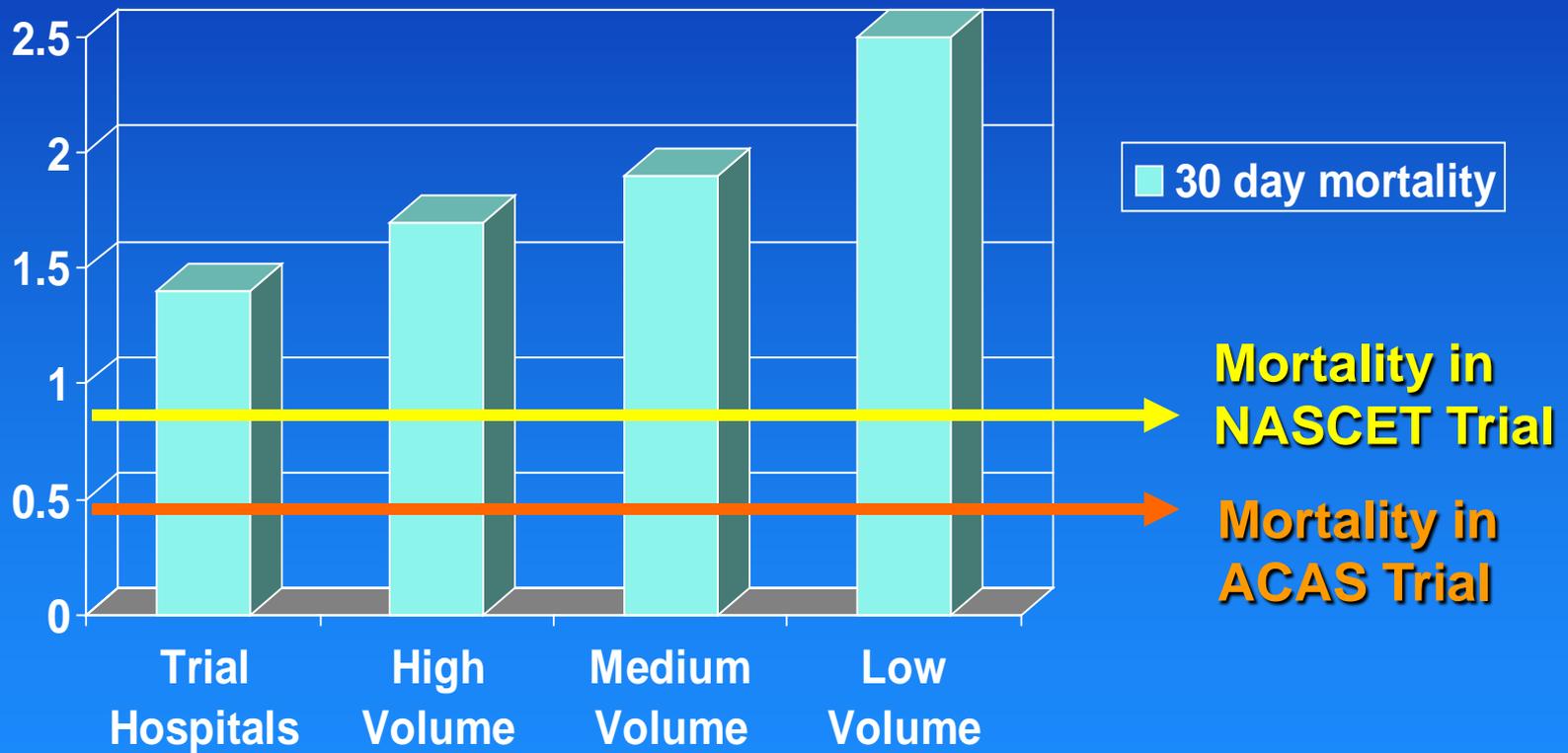
What Healthcare Decision Makers Need To Know

- *Can it work?*
- *Will it work?*
 - For this patient?
 - In this setting?
- *Is it worth it?*
 - Do benefits outweigh harms?
 - Do benefits justify costs?
 - Does it offer important advantages over existing alternatives?

*adapted from Brian Haynes
ACP Journal Club*

30 Day Mortality in Older Patients Undergoing Endarterectomy

vs. trials and by annual volume





Endarterectomy for Asymptomatic Carotid Stenosis

- Major trial of surgery for asymptomatic carotid stenosis (ACAS) in 1995
- Short term risks of surgery offset by long-term prevention of stroke and death
- 5% absolute reduction in major stroke or death over 5 years (i.e., 20 operations prevent one major stroke over 5 years)
- Surgeons and centers in trial were carefully selected for low operative complication rate

Defining/Refining Health Care Delivery

- Fostering more precise application of biomedical discoveries
 - Substantial variations in care
 - ‘cost without benefit’?
 - Pervasive disparities
 - Care delivery: platform for discovery and rapid translation
 - An “Abundance of Riches”



Comparative Effectiveness and the Recovery Act

- The American Recovery and Reinvestment Act of 2009 includes \$1.1 billion for comparative effectiveness research:
 - AHRQ: \$300 million
 - NIH: \$400 million (appropriated to AHRQ and transferred to NIH)
 - Office of the Secretary: \$400 million (allocated at the Secretary's discretion)



www.hhs.gov/recovery



Definition: IOM

- Comparative effectiveness research (CER) is 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.

*National Priorities for Comparative Effectiveness Research
Institute of Medicine Report Brief*

June 2009

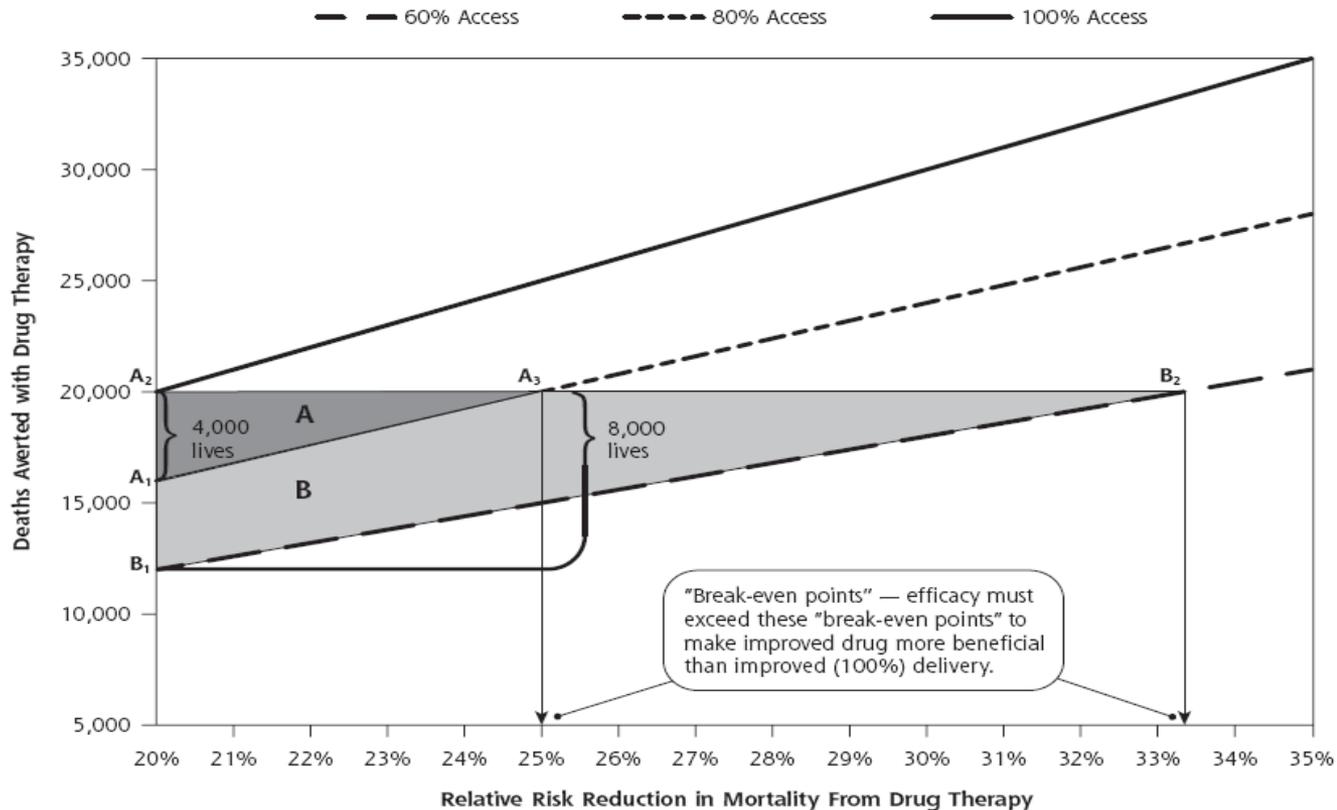


Definition: Federal Coordinating Council

- CER is the conduct and synthesis of research comparing the benefits and harms of various interventions and strategies for preventing, diagnosing, treating, and monitoring health conditions in real-world settings. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision makers about which interventions are most effective for which patients under specific circumstances.

Potential lives saved through quality improvement

Figure 1. "The Break-even Point" (for a drug that reduces mortality by 20%).



Triangle A. If 100,000 patients are destined to die from a disease, a drug that reduces death rates by 20% (relative risk reduction [RRR] = 0.20) will save 16,000 Lives (A1) if delivered to 80% of eligible patients. Increasing delivery to 100% would save 4,000 more Lives (A2). To save as many lives with without improving upon the delivery rate of 80% (A3), the RRR of the drug must be increased to at least 25% ("break-even point").

Triangle B. Delivering the drug to only 60% of patients would save only 12,000 Lives (B1), and improving delivery to 100% would save 8,000 additional Lives. To save

FCC Framework and IOM

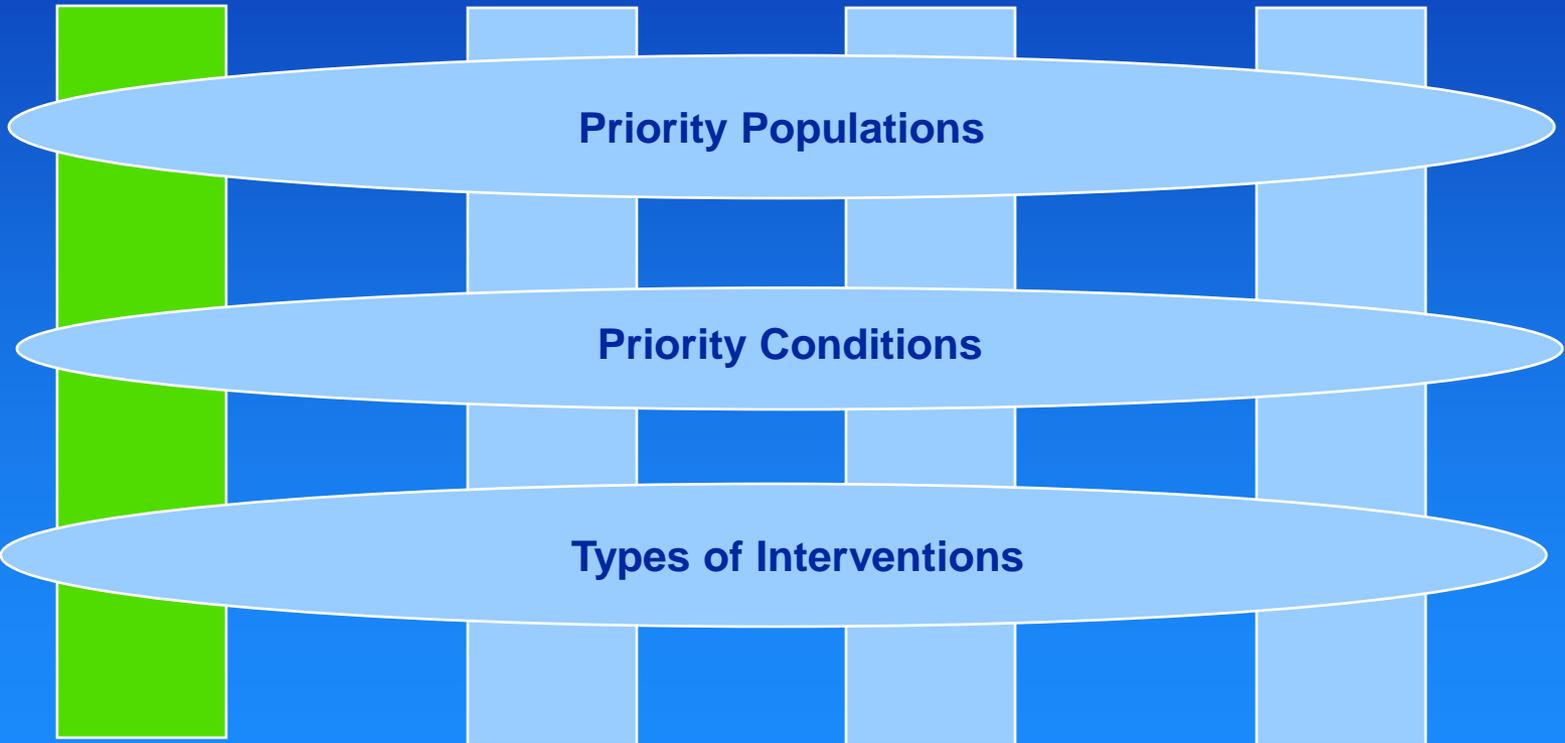
Research

Human & Scientific Capital

Data Infrastructure

Dissemination and Translation

Crosscutting Priority Themes



Legend



Specific CER funding priorities outlined



General Considerations only

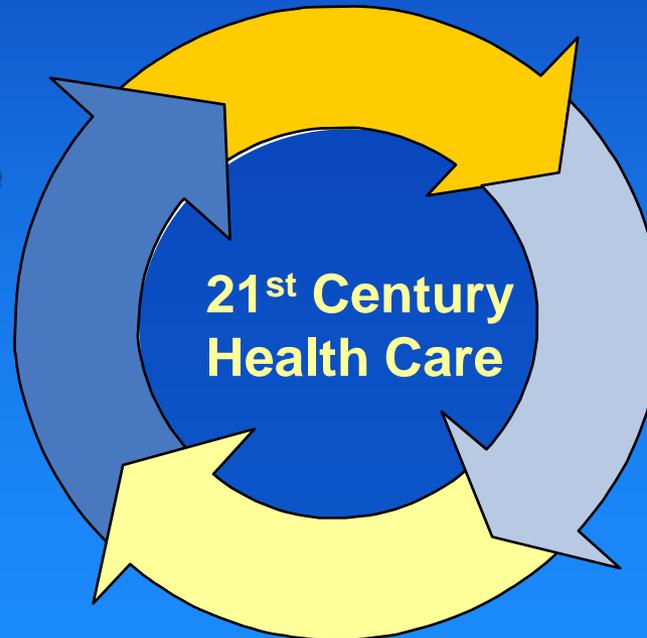


AHRQ's Role in Comparative Effectiveness

Using Information to Drive Improvement: Scientific Infrastructure to Support Reform

Providing information that can be used on the frontlines of treatment

Helping to make decisions more consistent, transparent and rational



Promoting an open and collaborative approach to comparative effectiveness

Ensuring the effectiveness data is more widely used



Priority Conditions for the Effective Health Care Program

- Arthritis and non-traumatic joint disorders
- Cancer
- Cardiovascular disease, including stroke and hypertension
- Dementia, including Alzheimer Disease
- Depression and other mental health disorders
- Developmental delays, attention-deficit hyperactivity disorder and autism
- Diabetes Mellitus
- Functional limitations and disability
- Infectious diseases including HIV/AIDS
- Obesity
- Peptic ulcer disease and dyspepsia
- Pregnancy including pre-term birth
- Pulmonary disease/Asthma
- Substance abuse



AHRQ Operating Plan for Recovery Act's CER Funding

- **Stakeholder Input and Involvement:** To occur throughout the program
 - **Horizon Scanning:** Identifying promising interventions
 - **Evidence Synthesis:** Review of current research
 - **Evidence Generation:** New research with a focus on under-represented populations
 - **Research Training and Career Development:** Support for training, research and careers
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Translating the Science into Real-World Applications

- Examples of Recovery Act-funded Evidence Generation projects:
 - Clinical and Health Outcomes Initiative in Comparative Effectiveness (CHOICE): First coordinated national effort to establish a series of pragmatic clinical comparative effectiveness studies (\$100M)
 - Request for Registries: Up to five awards for the creation or enhancement of national patient registries, with a primary focus on the 14 priority conditions (\$48M)
 - DEcIDE Consortium Support: Expansion of multi-center research system and funding for distributed data network models that use clinically rich data from electronic health records (\$24M)

Additional Proposed Investments

- Supporting AHRQ's long-term commitment to bridging the gap between research and practice:
 - Dissemination and Translation
 - Between 20 and 25 two-three-year grants (\$29.5M)
 - Eisenberg Center modifications (3 years, \$5M)
 - Citizen Forum on Effective Health Care
 - Formally engages stakeholders in the entire Effective Health Care enterprise
 - A Workgroup on Comparative Effectiveness will be convened to provide formal advice and guidance (\$10M)





PCTs vs. ECTs

Practical Clinical Trials	Explanatory Clinical Trials
<p>Hypothesis and study design are formulated based on information needed to make a decision</p>	<p>Designed to better understand how and why an intervention works</p>
<p>Addresses risks, benefits, and costs of an intervention as they would occur in routine clinical practice</p>	<p>Maximize the chance that biological effect of a new treatment will be revealed by the study</p>



Roles of Nonrandomized Studies to Complement RCTs

- Adherence and persistence of therapy
- Relationship between short- and long-term outcomes
- Similarity/differences between trial population and typical target population
- Similarity/differences between trial intervention and typical interventions
- Harms/safety in less selected patient population, subgroups



Can Observational Studies Reduce Need for RCTs?

- RCTs may be impractical or unethical
 - Subjective standard
 - Don't want to reduce incentive to do rigorous study
- Glasziou et al – BMJ 2007
 - Stable or predictable background course
 - LARGE, consistent, temporal effect
 - Rate ratios > 10
 - Dose response, specific effect, biologically plausible, coherent with other knowledge (Bradford Hill criteria)
- When potential for bias is low
 - How likely is confounding by indication or selection bias?



Advantages of Observational Studies

- RCT's rarely powered for ADE's.
- RCT's have poor external validity.
 - May not generalize to the patient population for whom the intervention may be applied.
 - Women, children, minorities, very elderly are under-represented.
 - Multiple drug choices and alternatives.
 - Co-morbid conditions.
 - RCT setting, health care providers is “artificial”.
- Longer term follow-up is usually achievable.
- Facilitates risk management and risk minimization.
- Enables better translation.
 - Interventions that are efficacious under a highly specific set of circumstances often fail to replicate across a wide variety of settings, conditions, patients.

CER and Innovation

- CER will enhance the best and most innovative strategies
- Can open up new populations for which something can be useful in
- Can bring early attention to potential issues

