NIH Has a Long History of CER

Patient Centered Research
- Prevention
- Diagnosis
- Treatment
- Behavior change
- Health systems
- Special populations

FY08: Clinical Research $9.6B
Initial analysis maps current NIH CER to 88 of 100 IOM priorities
The NEW ENGLAND JOURNAL of MEDICINE

Established in 1812

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Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia

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BACKGROUND
The relative effectiveness of second generation antipsychotic agents in the treatment of chronic schizophrenia, and the nature of the clinical settings in which these agents are used, is not well characterized.

OBJECTIVES
- To describe the clinical settings and characteristics of patients treated with antipsychotic medications in the CAIT Group
- To assess the effectiveness of second generation antipsychotic agents in the treatment of chronic schizophrenia
- To identify factors associated with treatment success

METHODS
CAIT was a randomized, controlled, multicenter study of second generation antipsychotics in the treatment of chronic schizophrenia. The study included 25 sites in the United States and Canada.

RESULTS
- The study included 648 patients with chronic schizophrenia
- The mean duration of the study was 24 weeks
- The primary outcome measure was change in the Positive and Negative Syndrome Scale (PANSS)
- Significant improvements were observed in the PANSS total scores in the second generation antipsychotic group
- The most commonly reported side effects were extrapyramidal symptoms

CONCLUSIONS
Second generation antipsychotic agents were effective in the treatment of chronic schizophrenia, with significant improvements in symptoms and treatment compliance.

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Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin

Diabetes Prevention Program Research Group

ABSTRACT
Background Type 2 diabetes affects approximately 8 percent of adults in the United States. Some risk factors — elevated plasma glucose concentrations in

Type 2 diabetes mellitus, formerly called non-insulin-dependent diabetes mellitus, is a serious, costly disease affecting approximately 8 percent of adults in the United States. Risk factors for type 2 diabetes include obesity, physical inactivity, and family history. Lifestyle interventions, such as weight loss and increased physical activity, have been shown to reduce the risk of type 2 diabetes. Metformin, a biguanide that reduces hepatic glucose production and enhances peripheral glucose uptake, has also been shown to reduce the risk of type 2 diabetes.

Methods We randomly assigned 3309 subjects to lifestyle intervention, metformin treatment, or placebo. The primary end point was incident diabetes during 5.6 years of follow-up. Secondary end points included changes in body weight, waist circumference, fasting plasma glucose, and insulin concentration.

Results The incidence of diabetes was 9.2% in the lifestyle-intervention group, 11.0% in the metformin group, and 13.6% in the placebo group (P = 0.004 for the comparison of the lifestyle-intervention group with the placebo group). The risk of diabetes was reduced by 31% in the lifestyle-intervention group and by 30% in the metformin group compared with the placebo group (both P = 0.002). The risk of diabetes was reduced by 35% in the lifestyle-intervention group compared with the metformin group (P = 0.02). The incidence of diabetes was highest among those with a history of diabetes in a first-degree relative and lowest among those who did not achieve a 7% or greater weight loss.

Conclusion Lifestyle intervention and treatment with metformin are associated with a reduced risk of type 2 diabetes, with lifestyle intervention being more effective than metformin.

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Amiodarone or an Implantable Cardioverter–Defibrillator for Congestive Heart Failure


ABSTRACT
Background The incidence of sudden cardiac death is increased in patients with advanced heart failure due to left ventricular systolic dysfunction. previous studies have shown that amiodarone reduces the risk of sudden cardiac death in patients with advanced heart failure.

Methods We randomly assigned 11,368 patients with advanced heart failure (ejection fraction, 20% to 40%, who had at least one clinical indicator of cardiovascular risk) to amiodarone, an implantable cardioverter–defibrillator (ICD), or a control group. The primary end point was the occurrence of any of 6 clinical events—sudden cardiac death, cardiovascular death, noncardiovascular death, hospitalization for worsening heart failure, heart failure death, or rehospitalization for heart failure.

Results The risk of the primary end point was reduced by 36% in the amiodarone group and 25% in the ICD group compared with the control group (P = 0.001 for each comparison). The reduction in the risk of the primary end point was greatest in patients with a previous history of sudden cardiac death or coronary artery disease and in patients with a left atrial diameter greater than 45 mm. The rate of serious adverse events was higher in the amiodarone group than in the ICD or control groups.

Conclusion Among patients with advanced heart failure, amiodarone and an ICD reduced the risk of sudden cardiac death and cardiovascular death compared with no treatment, with amiodarone being more effective than ICD treatment in reducing the risk of sudden cardiac death.

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Mortality Results from a Randomized Prostate-Cancer Screening Trial

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ABSTRACT
Background The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial was a randomized, controlled trial to determine whether screening with prostate-specific antigen (PSA) testing and digital rectal examination reduces mortality from prostate cancer.

Methods We randomly assigned 76,609 men aged 55 to 74 years from primary care practices in the United States and Canada to the intervention group (PSA testing and digital rectal examination) or the control group (usual care). The primary end point was prostate cancer–specific mortality.

Results The incidence of intermediate-risk prostate cancer was 4.3% in the intervention group and 4.9% in the control group (P = 0.02). The incidence of high-risk prostate cancer was 0.4% in the intervention group and 0.7% in the control group (P = 0.01). The incidence of fatal prostate cancer was 0.2% in the intervention group and 0.3% in the control group (P = 0.001). The incidence of prostate cancer at any level of risk was 9.1% in the intervention group and 9.7% in the control group (P = 0.002). The incidence of fatal prostate cancer was 0.1% in the intervention group and 0.2% in the control group (P = 0.002). The incidence of fatal prostate cancer was 0.2% in the intervention group and 0.3% in the control group (P = 0.002).

Conclusion PSA testing and digital rectal examination do not reduce mortality from prostate cancer.
Drug versus Drug: ALLHAT

Community based study of 33,357 hypertensive individuals found that an inexpensive generic diuretic was as effective as more expensive agents in reducing heart disease and stroke.

ALLHAT Officers. JAMA 2002;288:2981-7
Exercise and lifestyle changes yield substantially better health and economic outcomes than metformin alone or placebo in preventing the onset of diabetes (N=3234).

Diabetes Incidence Rates by Age

![Bar chart showing diabetes incidence rates by age and treatment group.]

- **25-44 (n=1000)**
  - Lifestyle: 6 cases/100 person-yr
  - Metformin: 6 cases/100 person-yr
  - Placebo: 12 cases/100 person-yr

- **45-59 (n=1586)**
  - Lifestyle: 3 cases/100 person-yr
  - Metformin: 9 cases/100 person-yr
  - Placebo: 12 cases/100 person-yr

- **≥ 60 (n=648)**
  - Lifestyle: 3 cases/100 person-yr
  - Metformin: 9 cases/100 person-yr
  - Placebo: 12 cases/100 person-yr

Source: Diabetes Prevention Program, 2001
NIH Has an Extensive CER Research and Training Infrastructure

- Trial networks, cooperative groups
- NIH Consensus Development Program
- NLM National Center on Health Services Research
- CTSAs and community collaborations
- Integration of CMS and SEER databases
- HMO Research Network
HMO Research Network

- A consortium of 16 integrated health systems covering 11 million lives
- Funding from NIH, AHRQ, FDA, CDC

http://www.hmoresearchnetwork.org/about.htm
NIH disseminates its research evidence

- Public through website, press, education programs
- Patient groups
- Professional organizations

www.NIH.gov 500,000 to 1,000,000 visitors a day

NIH coordinates with DHHS Agencies
Why Do We Need CER?

“Only a limited amount of evidence is available about which treatments work best for which patients . . .”

Peter Orszag

Congressional Budget Office 2007
Examples of Findings: The Cardiovascular Evidence Gap

Nearly half of current clinical practice recommendations from the American College of Cardiology and the American Heart Association are not evidence based.

Tricoci P, et al. JAMA 2009;301:831-41
Patient-Centered Health Research is Vital to Health Reform

In situations where the right thing to do is well established, physicians from high- and low-cost cities make the same decisions. But in cases where the science is more unclear, some physicians pursue the maximum possible amount of testing and procedures; some pursue the minimum. And what kind of doctor they are depends on where they came from. In case after uncertain case, more was not necessarily better.

(Dr. Atul Gawande)
NIH and ARRA CER

- Active leadership role in Federal Coordinating Council and CER CIT

- NIH CER Coordinating Committee coordinates NIH CER programs and develops funding recommendations for the NIH Director

- CER CC Subcommittees to coordinate and integrate Inter-Agency activities:
  - NIH-AHRQ CER Workgroup
  - NIH-VA CER Workgroup
  - NIH-FDA CER Workgroup
CER Activities Approved for ARRA Funding from NIH’s $400 Million (as of 11/2009)

<table>
<thead>
<tr>
<th>Funding Mechanism</th>
<th># Submissions</th>
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<tr>
<td>Grand Opportunity Grants (RC2)</td>
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<td>Challenge Grants (RC1)</td>
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<td><strong>TOTAL APPROVED</strong></td>
<td><strong>166</strong></td>
<td><strong>$341,910,008</strong></td>
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</tbody>
</table>
Highlights of ARRA funded CER projects

- SPRINT Senior - the NHLBI/NIDDK/NIA/NINDS study adding an enhanced older adult population to compare control of systolic BP to 140 versus 120 on multiple real-world end-points, including cardiovascular, renal cognitive function.

- The Oregon lottery study - NIA supported analysis of the Oregon randomized lottery experiment, where multiple health behavior consequences of health insurance policy will be analyzed.

- Follow-on to the NIDDK/NIA - supported diabetes prevention study to determine effects on relevant health end-points associated with diabetes complications.

- Schizophrenia clinical trial of treatment post acute episodes, NIMH-funded.

- Multiple registries which will allow tracking of populations for variables including outcomes and relationship to treatment.

- CER Centers such as the Center for CER in Cancer Genomics (NCI), the Comparative Effectiveness and Outcomes Improvement Center (NHLBI) and CTSAs (NCRR).
More ARRA funded CER projects

- Center for Comparative Effectiveness Research in Cancer Genomics
- Comparative effectiveness of breast imaging strategies in community practice
- Contemporary Treatment and Outcomes for Atrial Fibrillation in Clinical Practice
- Comparative Effectiveness of Interventions for Chronic Pain Management
- Comparative effectiveness of FIT vs. colonoscopy for colon cancer screening
- Minimally Invasive Surgical Pulmonary Vein Isolation vs. Medical Management in Patients with AF and Stroke
- Data Infrastructure for Post-Marketing for Comparative Effectiveness Studies
- Conservative Versus Dialytic Management in Stage V Chronic Kidney Disease
- Developing a Community-Based Autism Spectrum Disorders Research Registry
Key NIH CER Activities

- **Research** to generate evidence that enables physicians and patients to make optimal health care decisions
- **Research Training** to develop the CER workforce of tomorrow
- **Personalized Medicine** highlights uniqueness of individuals and special populations
- **CER Centers** to support research, training and dissemination of evidentiary knowledge
- **Behavioral Economics** to increase “uptake” of CER findings by providers and payers
AHRQ CER Spend Plan

- AHRQ plans to use their $300 million in ARRA funds to broaden pre-existing CER activities initiated in response to Section 1013 of the MMA (2003).

- AHRQ views CER as a process that includes the following steps, and for which they will fund various projects/initiatives:
  - Horizon Scanning: identification of current or emerging medical interventions ($9.5 M in contracts)
  - Evidence Synthesis: review and synthesis of current medical research ($25 M in contracts)
  - Identification of Evidence Needs and Gaps ($25 M)
AHRQ CER Spend Plan Initiatives (cont.)

- Evidence Generation ($173 M)
  - CHOICE Studies
  - Requests for Registries
  - DEcIDE Consortium Support
  - Unfunded Meritorious Applications

- Dissemination and Translation ($34.5 M)
  - CE Dissemination and Translation Innovation Grants
  - Eisenberg Center Modification

- Research Training and Career Development ($20 M)
  - Institutional Training Awards and CE Fellowship

- In addition, AHRQ plans to convene a Citizen Forum on Effective Health Care in order to formally engage stakeholders in the CER enterprise ($10 M)
Office of the Secretary  
CER Spend Plan

- As of November 19, 2009, approximately 95% of the Secretary’s $400 Million has been allocated to specific projects across the following categories:
  - Data Infrastructure
  - Dissemination & Translation
  - Research
  - Inventory and Evaluation

- NIH will take the lead on the following projects being funded by the Office of the Secretary
  - Centers of Excellence for Racial and Ethnic Minority-focused CER (NIH/OMH)
  - Behavioral Economics and Change (NIH/AHRQ)
CER and Personalized Medicine

- CER should be guided by the emerging science of genomic and personalized medicine.

- CER will generate research hypotheses relevant to personalized medicine by exploring why certain groups may or may not respond to an intervention.

- Participant genomic and environmental exposure data could be included in CER studies, in order to understand why some individuals benefit from a treatment while others do not. NIH is uniquely positioned to evaluate the effect of these factors.
Summary

- The NIH is committed to CER as a research priority
- CER can be an effective tool to:
  - Generate evidence that demonstrate “what works”
  - Inform medical decision-making
  - Support decisions based upon quality and value
  - Possibly “bend the curve” on health care costs
- A key challenge is getting the results of NIH supported CER studies implemented by providers, payers, and the public
NIH
Transforming medicine and health through Comparative Effectiveness Research
DHHS Definition of CER

Comparative effectiveness research is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor 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, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.

- To provide this information, CER must assess a comprehensive array of health-related outcomes for diverse patient populations and sub-groups.
- Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
- This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and actively disseminate the results.
NIH and AHRQ have Complementary Roles

NIH
Evidence Generation

AHRQ
- Research Analysis
- Systematic Reviews
- Evidence Synthesis

Informs

Payers and Providers