

Role of the NIH in Comparative Effectiveness Research National CER Summit

Elizabeth G. Nabel, M.D.
Director, NHLBI

September 16, 2009



CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- Current NIH activities: ARRA CER
- Future directions



CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- Current NIH activities: ARRA CER
- Future directions



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 access 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 access comparative effectiveness and actively disseminate the results.



CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- Current NIH activities: ARRA CER
- Future directions



Why Do We Need CER?

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

Orszag

Peter



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.

ORIGINAL CONTRIBUTION

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Pierluigi Tricoci, MD, MHS, PhD

Joseph M. Allen, MA

Judith M. Kramer, MD, MS

Robert M. Califf, MD

Sidney C. Smith Jr, MD

CLINICAL PRACTICE GUIDELINES are systematically developed statements to assist practitioners with decisions about appropriate health care for spe-

Context The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

Objective To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

Data Sources and Study Selection Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.



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)



CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- Current NIH activities: ARRA CER
- Future directions



NIH has a Long and Continuing Tradition of CER

**The NEW ENGLAND
JOURNAL of MEDICINE**

ESTABLISHED IN 1812 SEPTEMBER 22, 2005 VOL. 353 NO. 12

Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia

Jeffrey A. Lieberman, M.D., T. Scott Stroup, Robert A. Rosenheck, M.D., Diana Sonia M. Davis, Dr.P.H., Clarence E. D and John K. Hsiao, M.D., for the Clinical Antipsychotic Trials in Schizophrenia (CATIE) Study Group*

ORIGINAL CONTRIBUTION

BACKGROUND
The relative effectiveness of second-generation (atypical) antipsychotic drugs compared with first-generation (typical) antipsychotic drugs in patients with chronic schizophrenia is uncertain.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mortality Results from a Randomized Prostate-Cancer Screening Trial

Gerald L. Andriole, M.D., E. David Crawford, M.D., Robert L. Grubb III, M.D., Sandra S. Buys, M.D., David Chia, Ph.D., Timothy R. Church, Ph.D., Mona N. Fouad, M.D., Edward P. Gelmann, M.D., Paul A. Kvale, M.D., Daniel L. Weissfeld, M.D., Lance A. Yokochi, M.D., Nathan D. Clapp, B.S., Joshua M. Rathmell, M.S., Richard B. Hayes, Ph.D., Barnett S. Kramer, M.D., Anthony B. Miller, M.B., Paul F. Pinsky, Ph.D., Robert J. Gray, Ph.D., and Christine D. Berg, M.D., for the Prostate Cancer Prevention Trial (PCPT) Investigators*

JAMA-EXPRESS

ABSTRACT
Background: Prostate-specific antigen (PSA) testing and digital rectal examination (DRE) are used to detect prostate cancer. The effect of PSA testing and DRE on mortality is uncertain.

**The New England
Journal of Medicine**

Copyright © 2002 by the Massachusetts Medical Society

VOLUME 346 FEBRUARY 7, 2002 NUMBER 6

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 the fasting state, obesity, and a family history of diabetes — are associated with an increased risk of developing type 2 diabetes. To determine whether lifestyle intervention or metformin could reduce the risk of developing type 2 diabetes in individuals at high risk, we conducted a randomized trial.

**The NEW ENGLAND
JOURNAL of MEDICINE**

ESTABLISHED IN 1812 JANUARY 20, 2005 VOL. 352 NO. 3

Amiodarone or an Implantable Cardioverter-Defibrillator for Congestive Heart Failure

Gust H. Bardy, M.D., Kerry L. Lee, Ph.D., Daniel B. Mark, M.D., Jeanne E. Poole, M.D., Douglas L. Packer, M.D., Robin Boineau, M.D., Michael Domanski, M.D., Charles Troutman, R.N., Jill Anderson, R.N., George Johnson, B.S.E.E., Steven E. McNulty, M.S., Nancy Clapp-Channing, R.N., M.P.H., Linda D. Davidson-Ray, M.A., Elizabeth S. Fraulo, R.N., Daniel P. Fishbein, M.D., Richard M. Luceri, M.D., and John H. Ip, M.D., for the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators*



NIH has an Extensive CER Research and Training Infrastructure

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



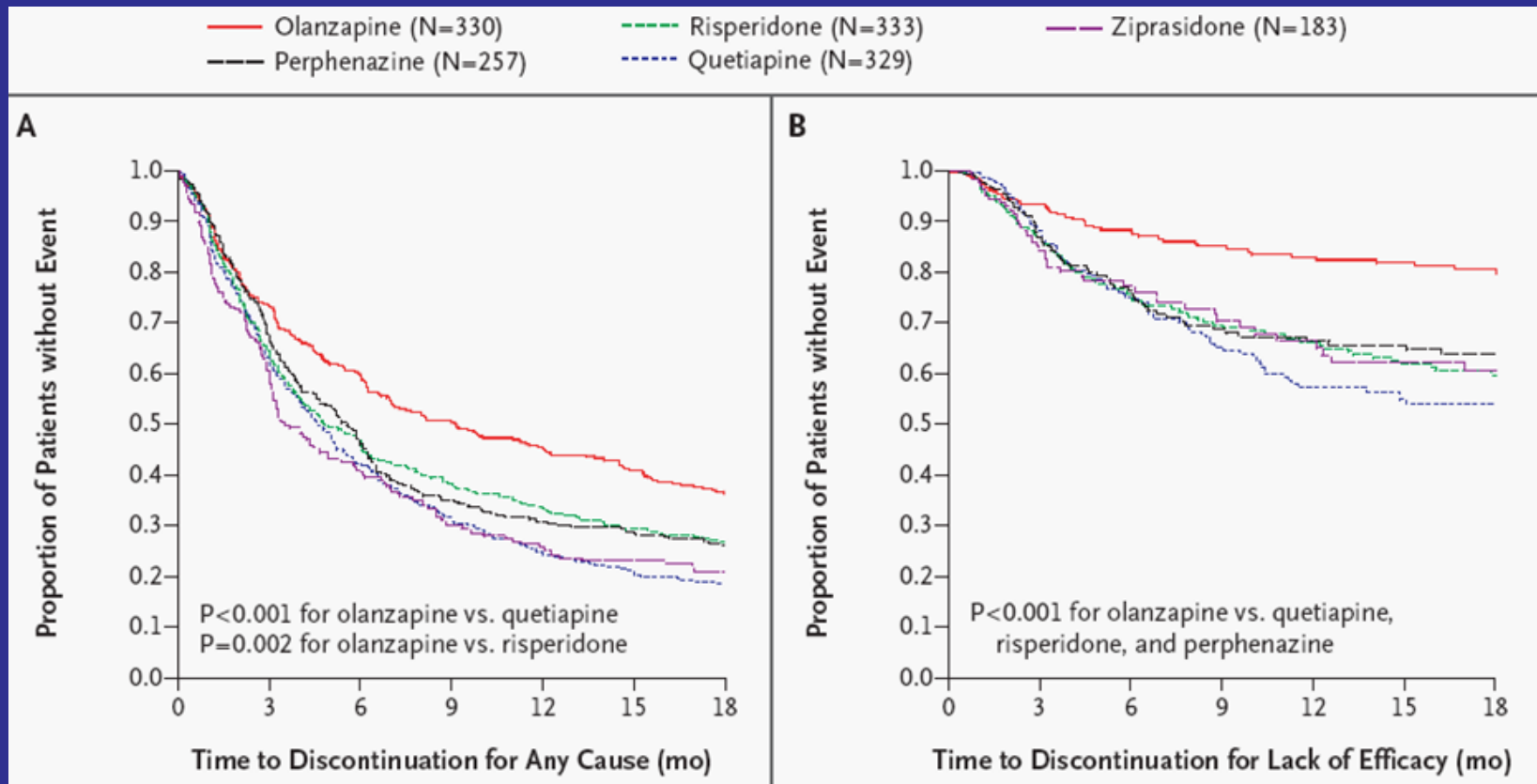
Sample NIH CER Projects

- Drug versus drug
- Surgery versus medical
- Lifestyle versus medical
- Surgery versus surgery
- Screening versus usual care
- Observational analyses based on EHR



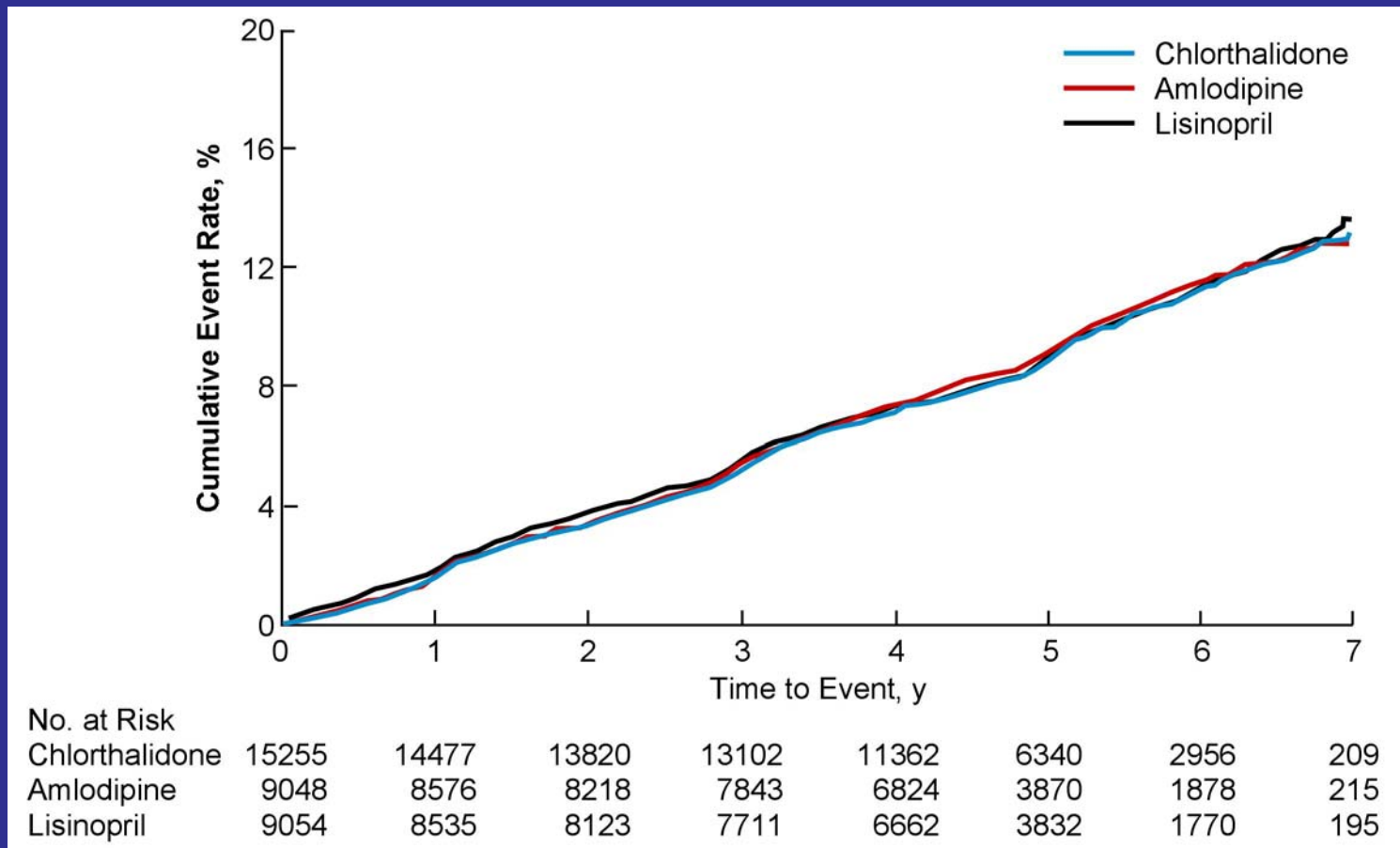
Drug versus Drug: CATIE

Newer generation antipsychotics for schizophrenia are no more effective than conventional agents, which are less expensive.
(N=1493)



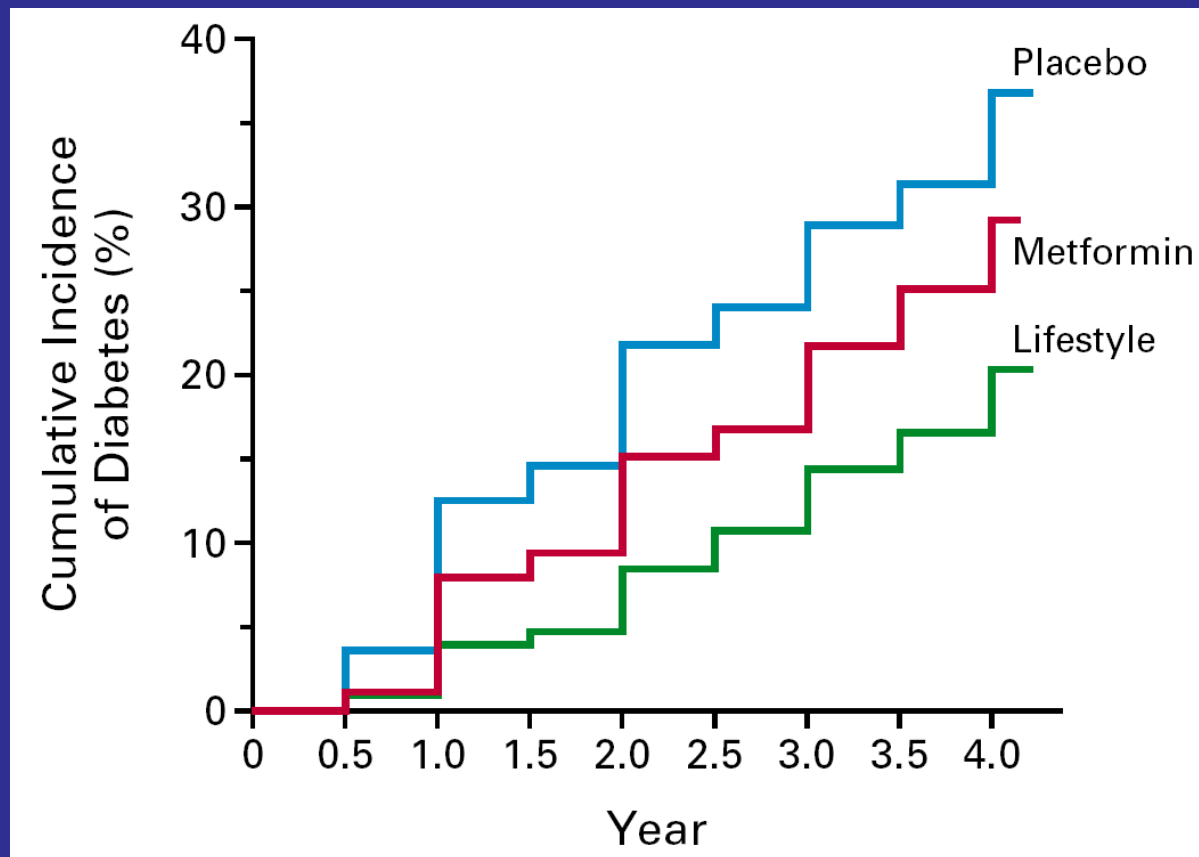
Drug versus Drug: ALLHAT

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.



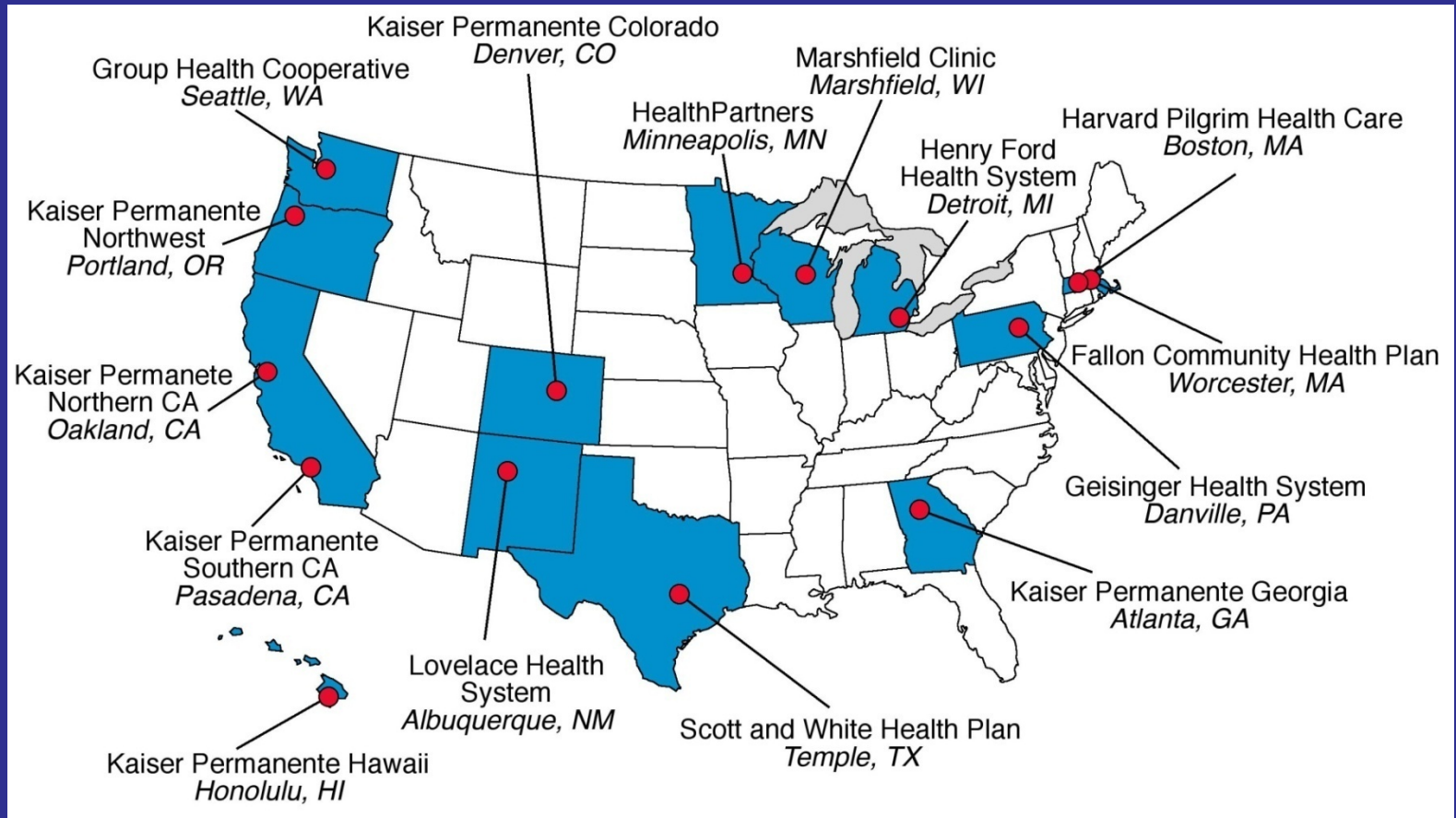
Lifestyle versus Medical: Diabetes Prevention Program

Exercise and lifestyle changes yield substantially better health and economic outcomes that metformin alone or placebo in preventing the onset of diabetes (N=3234).



Observational Analyses: HMO Research Network

15 integrated health systems (N=11 million)



National Library of Medicine and CER

www.clinicaltrials.gov

Drug Effectiveness Review Project

NCBI **PubMed** A service of the U.S. National Library of Medicine and the National Institutes of Health [My NCBI](#) [\[Sign In\]](#) [\[Register\]](#)

All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals

Search PubMed for **lovastatin** [Go](#) [Clear](#) [Advanced Search \(beta\)](#) [Save Search](#)

[Limits](#) [Preview/Index](#) [History](#) [Clipboard](#) [Details](#)

Display Summary Show 20 Sort By Send to

All: 6874 Review: 649

Items 1 - 20 of 6874 Page 1 of 344 Next

1: [Maier O. De Jonge J. Nomden A. Hoekstra D. Baron W.](#)
Lovastatin induces the formation of abnormal myelin-like membrane sheets in primary oligodendrocytes.
Glia. 2008 Sep 23. [Epub ahead of print]
PMID: 18814266 [PubMed - as supplied by publisher]

2: [Sandhya VG. Rajamohan T.](#) [Related Articles](#)
Comparative evaluation of the hypolipidemic effects of coconut water and lovastatin in rats fed fat-cholesterol enriched diet.
Food Chem Toxicol. 2008 Sep 3. [Epub ahead of print]
PMID: 18809454 [PubMed - as supplied by publisher]

Lovastatin

- ▶ How do statins compare in reducing "bad cholesterol" (LDL-c)?
- ▶ In patients with diabetes or hyperlipidemia, how do combination drugs compare in improving long-term health?

Source: PubMed Clinical Q&A.



The NIH has been Fully Committed to CER

Our goals:

- Articulate our commitment to the best science, in this case, science that is relevant to clinical practice and public policy
- Continue a NIH leadership role in research, training, infrastructure platforms, and dissemination and translation to enhance CER return to the public
- Work closely with our DHHS colleagues
- Involve our scientific community, practitioners, consumers, industry, policymakers, IOM and other stakeholders
- Demonstrate our value to the public



CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- **Current NIH activities: ARRA CER**
- Future directions



Current NIH CER Activities

- \$1.1B in ARRA funds have been allocated to CER (\$400M to the Secretary, DHHS; \$ 400M to NIH; \$300M to AHRQ.)
- The Federal Coordinating Council for CER (FCC) was established by the Secretary to guide federal CER investments, publish a report with recommendations for expenditure of the Secretary's \$400M, forge a definition for CER and contract with IOM to list the nation's highest CER research priorities.
- The FCC Report on CER was finalized on June 30th.
- The IOM Report on the Top 100 Initial National Research Priorities for CER was published on June 30th.
- The DHHS Secretary asked NIH to undertake an immediate, formal analysis to identify in-house CER projects that align with the IOM's recently released Top 100 Initial National Research Priorities for CER.



Current NIH CER Activities: ARRA CER

- NIH established a CER Coordinating Committee (CER CC) to ensure optimal use of ARRA CER funds, develop funding recommendations for the NIH Director, and define NIH's future role in CER.
- CER CC Subcommittees were established to coordinate and integrate Inter-Agency activities:
 - NIH-AHRQ CER Workgroup
 - NIH-FDA CER Workgroup
 - NIH-VA CER Workgroup
- CER CC is developing a plan to “fingerprint” all current NIH CER activities.



Current NIH CER Activities: ARRA CER

- NIH CER CC has considered grant applications, as outlined in the NIH CER Spend Plan. The NIH Spend Plan includes \$400M of CER ARRA funds to support 2-year investigator-initiated projects using:
 - Payline Expansions
 - Challenge Grants - the RFA listed 69 CER-specific topics
 - Grand Opportunity Grants
 - other activities including Supplements and Contracts



Current NIH CER Activities: ARRA CER

- CER Evaluation Criteria:
 - DHHS/FCC definition
 - IOM 100 top priorities
 - Medicare Modernization Act 14 diseases and conditions
 - AHRQ evidence gaps



Sample IOM Priorities (in the first Quartile of the Top 100)

- Compare the effectiveness of treatment strategies for atrial fibrillation including surgery, catheter ablation, and pharmacologic treatment.
- Compare the effectiveness of the different treatments (e.g., assistive listening devices, cochlear implants, electric-acoustic devices, habilitation and rehabilitation methods [auditory/oral, sign language, and total communication]) for hearing loss in children and adults, especially individuals with diverse cultural, language, medical, and developmental backgrounds.
- Compare the effectiveness of primary prevention methods, such as exercise and balance training, versus clinical treatments in preventing falls in older adults at varying degrees of risk.
- Compare the effectiveness of upper endoscopy utilization and frequency for patients with gastroesophageal reflux disease on morbidity, quality of life, and diagnosis of esophageal adenocarcinoma.



Medicare Modernization Act (MMA)

14 Diseases and Conditions

1. Arthritis and non-traumatic joint disorders (Muscle, bone, and joint conditions)
2. Cancer
3. Cardiovascular disease, including stroke and hypertension (Heart and blood vessel conditions)
4. Dementia, including Alzheimer's Disease (Brain and nerve conditions)
5. Depression and other mental health disorders (Mental health)
6. Developmental delays, attention-deficit hyperactivity disorder, and autism (Developmental delays, ADHD, autism)
7. Diabetes
8. Functional limitations and physical disabilities
9. Infectious diseases including HIV/AIDS
10. Obesity
11. Peptic ulcer disease and dyspepsia (Digestive system conditions)
12. Pregnancy including preterm birth
13. Pulmonary disease/asthma
14. Alcohol and drug abuse



Sample AHRQ Evidence Gaps

Comparative Effectiveness of Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression - Final Research Review published January 24, 2007.

- Future research has to establish reliably the general efficacy of second-generation antidepressants for the treatment of dysthymia and subsyndromal depression. Ideally, multiple-arm, head-to-head trials, including placebo groups, should evaluate the general and comparative efficacy of second-generation antidepressants in patients with these conditions...
- Future research should also focus on differences in efficacy and effectiveness in subgroups such as the very elderly or patients with various common comorbidities.
- More evidence is needed regarding the most appropriate duration of antidepressant treatment for maintaining remission. Such studies should also evaluate whether different formulations (i.e., controlled release vs. immediate release) lead to differences in adherence and subsequently to differences in relapse or recurrence....



CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- Current NIH activities: ARRA CER
- Future directions



NIH CER Coordinating Committee

- Provide ongoing and long-term advice to NIH Director:
 - CER Centers for research and training
 - NIH CER portfolio analysis
 - Coordination and integration with AHRQ, other DHHS OPDIVS, and other Federal agencies
 - CER IT and other infrastructure needs
 - CER dissemination and translation



CER and Personalized Medicine

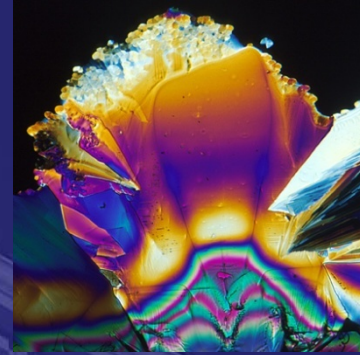
- CER should be guided by the emerging science of genomic and personalized medicine.
- CER will generate research hypotheses relevant to personalized medicine by exploring why certain groups may or may not respond to an intervention.
- Participant genomic and environmental exposure data could be included CER studies, in order to understand why some individuals benefit from a treatment while others do not.
- NIH is uniquely positioned to evaluate the comparative outcomes related to various phenotypes.



Summary

- The NIH is proud to be in the CER business for many years to come.
- CER can be an effective tool to:
 - Generate evidence which demonstrate “what works”
 - Inform medical decision-making
 - Support decisions based upon quality and value, rather than volume
 - “Bend the curve” on health care costs?





NIH *Transforming medicine and health through Comparative Effectiveness Research*

