

Comparative Effectiveness Research: National Institutes of Health

PCAST Session on Health Reform and CER

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CER and the NIH

- CER definition
- Rationale for NIH's interest in CER
- NIH's rich history of CER
- Current NIH activities
- Recommendations to PCAST



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.



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.

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.

(Atul Gawande)



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

ORIGINAL CONTRIBUTION

BACKGROUND
The relative effectiveness of second-generation (at

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., I. L. Weissfeld, M.D., Lance A. Yokochi, M.D., than D. Clapp, B.S., Joshua M. Rathmell, M.S., rd B. Hayes, Ph.D., Barnett S. Kramer, M.D., thony B. Miller, M.B., Paul F. Pinsky, Ph.D., . Gohagan, Ph.D., and Christine D. Berg, M.D., e PLCO Project Team*

JAMA-EXPRESS

ABSTRACT

ate-specific-antigen (PSA) testing and digital rectal

**The New England
Journal of Medicine**

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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

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

nthypertensive therapy idity and mortality, but t
To determine whether t
onverting enzyme inhib
r other cardiovascular di
: Antihypertensive and L

**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



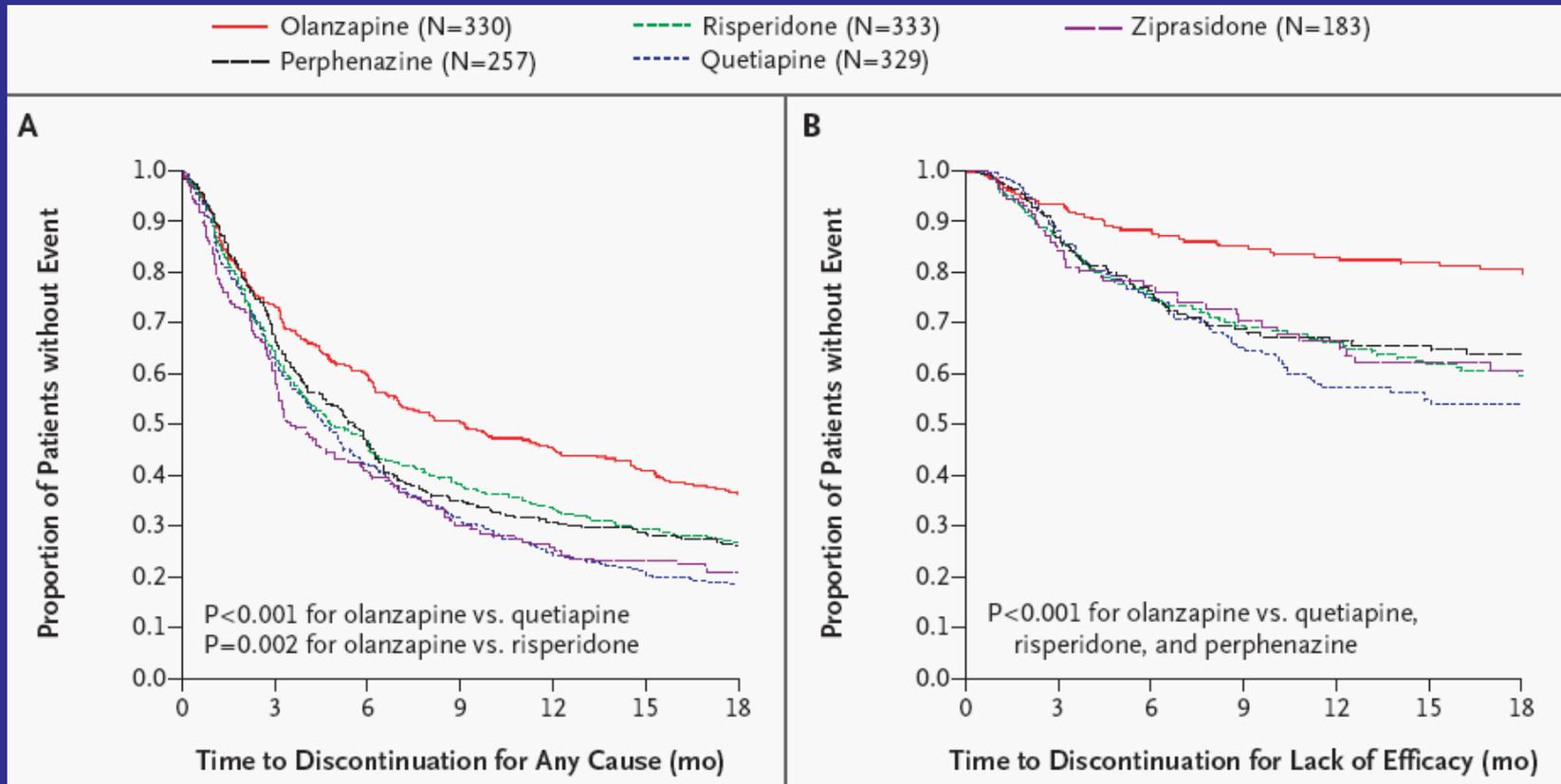
Sample NIH CER Projects

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



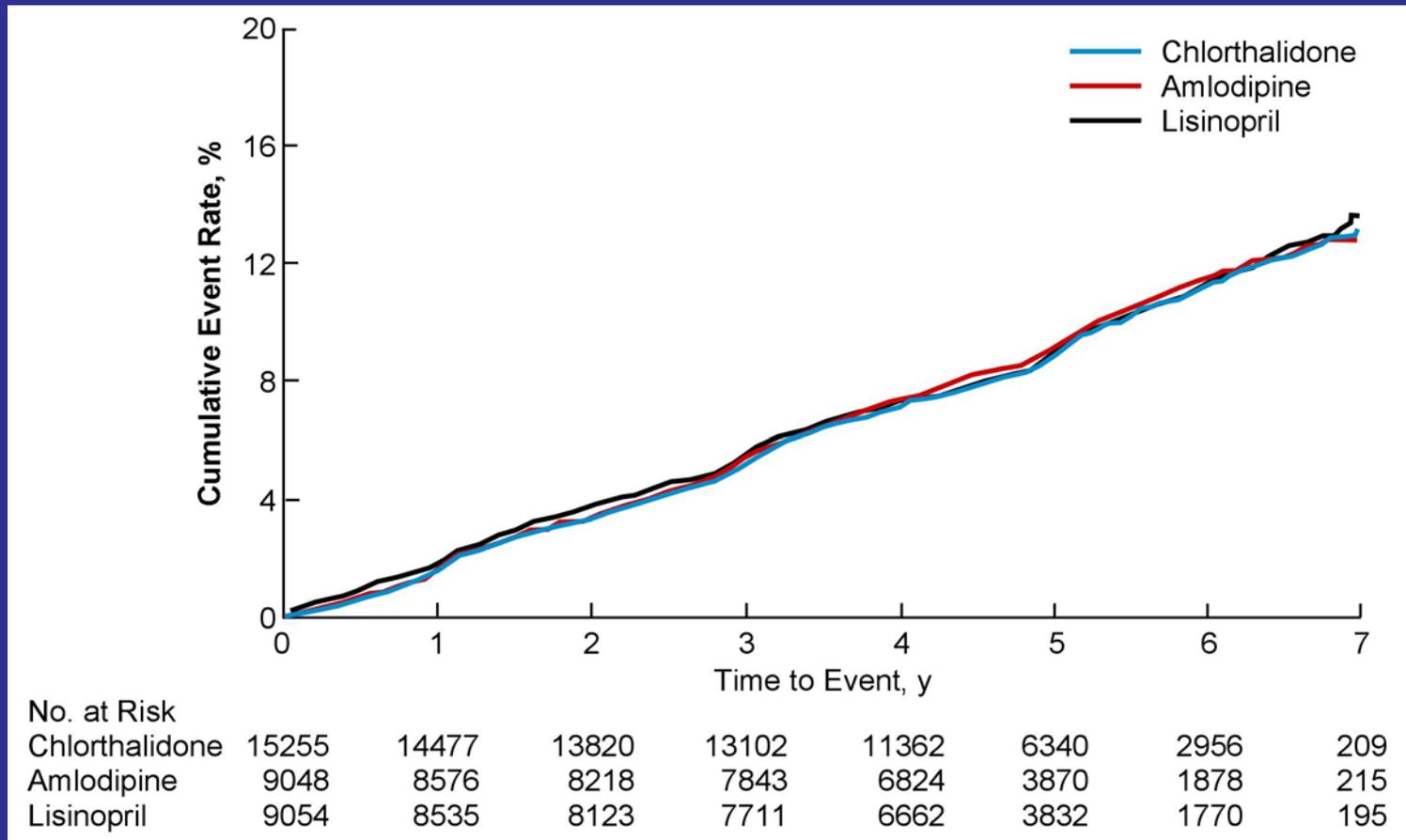
Drug versus Drug: CATIE

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.

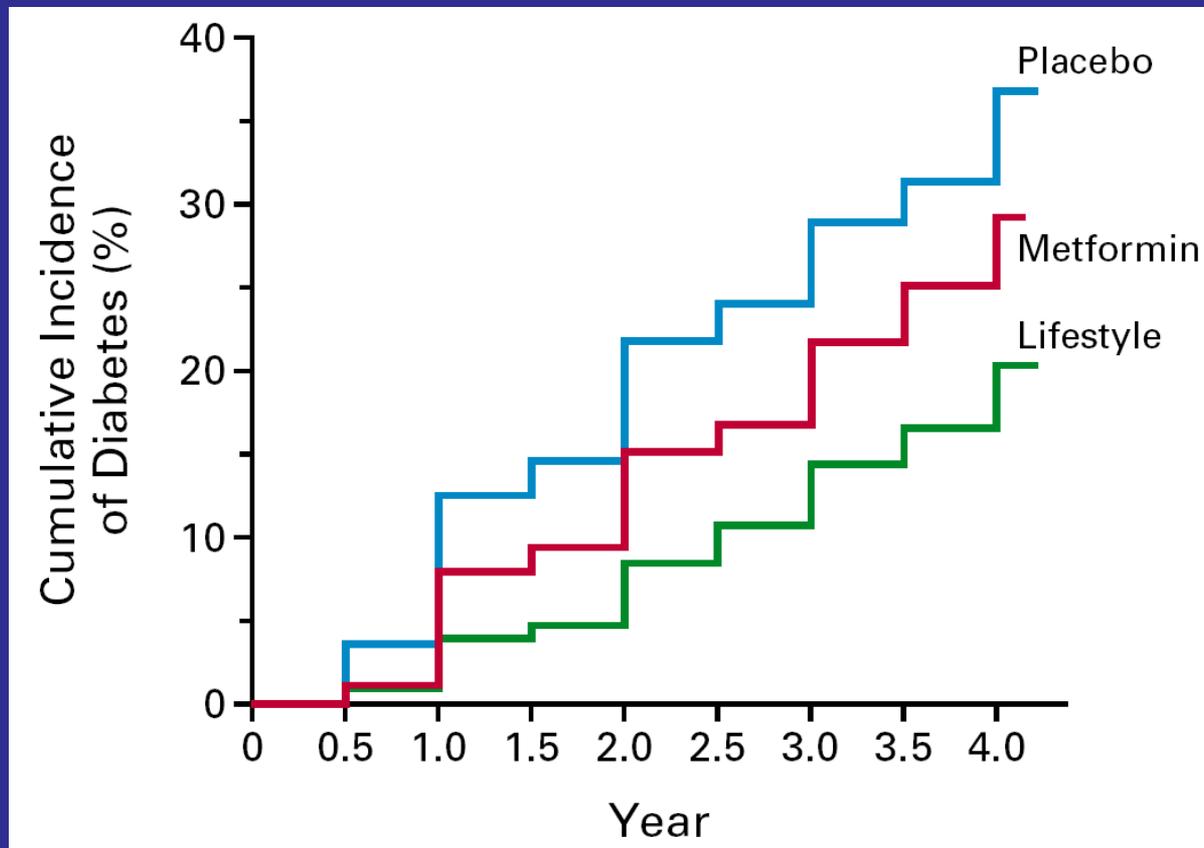


ALLHAT Officers. *JAMA* 2002;288:2981-7



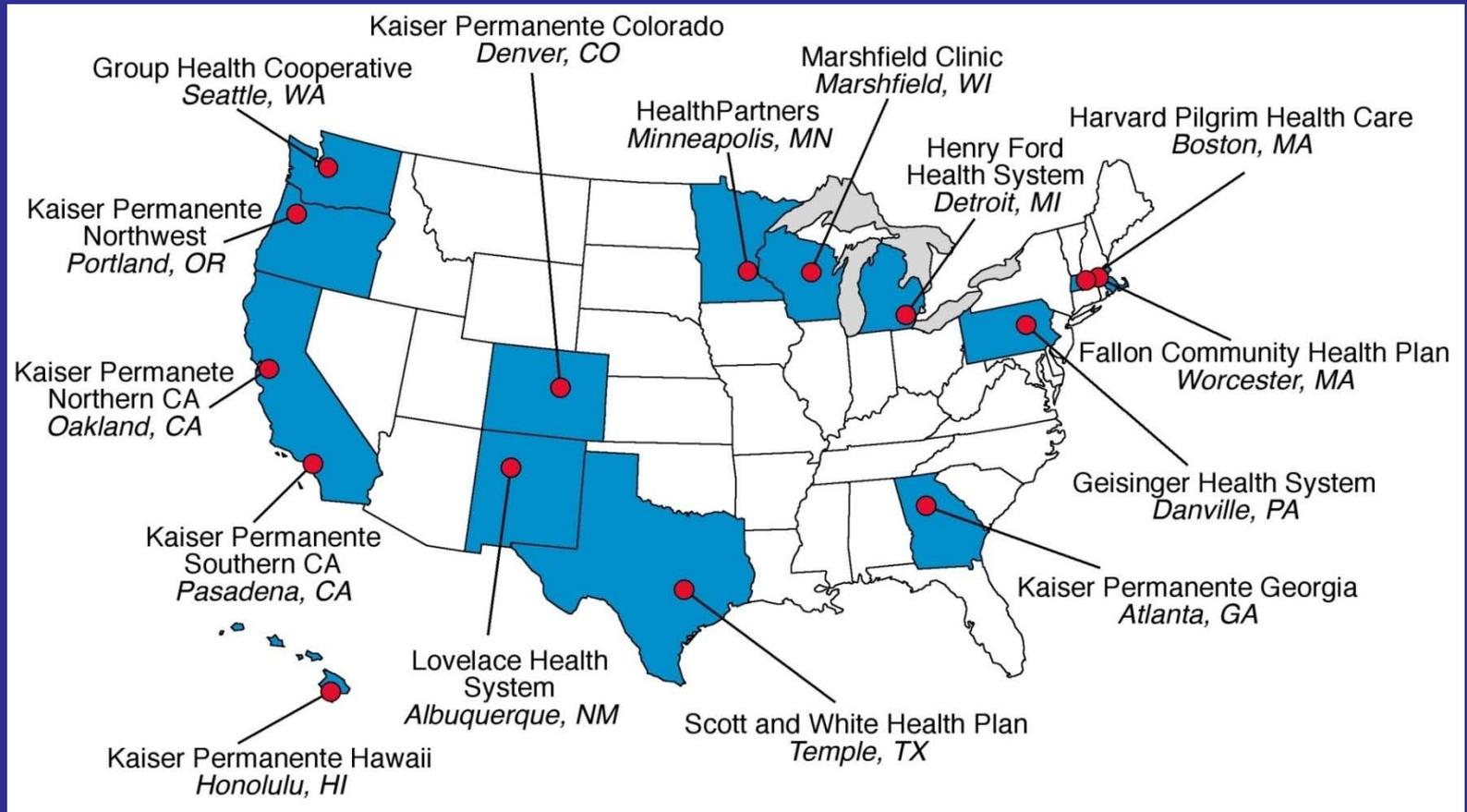
Lifestyle versus Medical: Diabetes Prevention Program

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 is 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



Ongoing NIH CER Projects

- FY08: 616-847 projects, \$323M-\$454M single year costs
- Projects map to the IOM 100 priority topics and the MMA 14 priority conditions
- Examples:
 - National Lung Screening Trial
 - Comparison of Age-related Macular Degeneration Treatments
 - Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA)
 - Systolic Blood Pressure Intervention Trial (SPRINT)



NIH CER Coordinating Committee

- Provide advice to NIH Director:
 - Short-term: Priorities for NIH ARRA CER funds
 - Ongoing and Long-term:
 - NIH CER portfolio analysis
 - Coordination and integration with AHRQ, other DHHS OPDIVS, and other Federal agencies
 - CER dissemination and translation
- Participation by senior NIH leadership:
 - Co-chaired by Richard Hodes and Betsy Nabel
 - Members include IC Directors, Deputy Directors, Clinical Directors, and Senior Program Leaders



NIH CER Coordinating Committee

Workgroups to facilitate coordination and integration:

- NIH-AHRQ CER Workgroup
- NIH-FDA CER Workgroup
- NIH-VA CER Workgroup



NIH-Funded CER Aligns with the IOM's Top 100 “Initial National Research Priorities for CER”

- Secretary Sebelius requested that the NIH undertake an analysis of NIH-funded CER that aligns with the IOM's top 100 priorities.
- Over 1500 projects – which either directly align, or are peripherally related to the IOM priorities – were submitted.
- Preliminary analyses indicates that 88 of the 100 IOM priorities appear to be addressed by currently funded NIH projects.



CER Evidence Gaps

Many groups contribute to identifying evidence gaps

- | | | |
|---|---|---|
| <ul style="list-style-type: none">▪ AHRQ▪ National Health Council▪ American Medical Association▪ America's Health Insurance Plans▪ Biotechnology Industry Organization▪ American Nurses Association▪ Consumers Union▪ AAFP, AAP, ASOC, ACC, AAMC▪ Pharmaceutical Research and Manufacturers of America▪ BCBS Association▪ National Minority Quality Forum | <ul style="list-style-type: none">▪ Duke University Medical Center▪ National Medical Association▪ Center for Advancement of Health▪ Advanced Medical Technology Association▪ Network for Regional Healthcare Improvement▪ United Bio Source Corporation▪ WA State Health Care Authority▪ OR Health and Science University and Portland VA Medical▪ CA Department of Public Health | <ul style="list-style-type: none">▪ International Society for Pharmacoeconomics & Outcomes Research▪ Society of Thoracic Surgeons▪ CIGNA▪ National Alliance for Hispanic Health▪ United States Pharmacopeia▪ American Psychiatric Association▪ Developing Families Center▪ American Heart Association▪ Center for Science in the Public Interest▪ Friends of Cancer Research▪ National Pharmaceutical Council |
|---|---|---|

NIH is the primary agency for evidence generation



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.



Recommendations to PCAST - I

- Strongly encourage PCAST to contribute to CER policy discussions
- Three fundamental assumptions:
 - Patient-centered health research is vital to health reform.
 - CER will be a critical component of the Health Care landscape post-Health Care Reform legislation.
 - There will be ongoing DHHS coordination and integration of CER activities.



Recommendations to PCAST - II

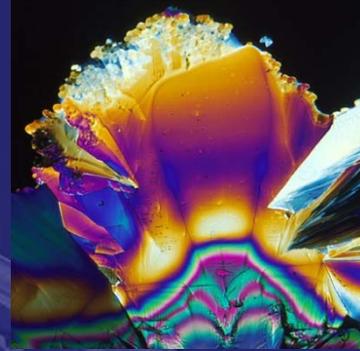
Key questions:

- How will the information and knowledge generated by CER be used?
 - To improve medical practice and patient care?
 - To impact the cost of care by “bending the curve”?
- What is the best structure for CER decision making and oversight ?
 - Public-Private Partnership?
 - Health Board?
 - Super MedPAC?
 - Should this structure be an independent agency to achieve real change?

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*

