

Knowing What to Do: The Opportunities and Challenges of Comparative Effectiveness Research

Eugene C. Rich MD

Scholar in Residence

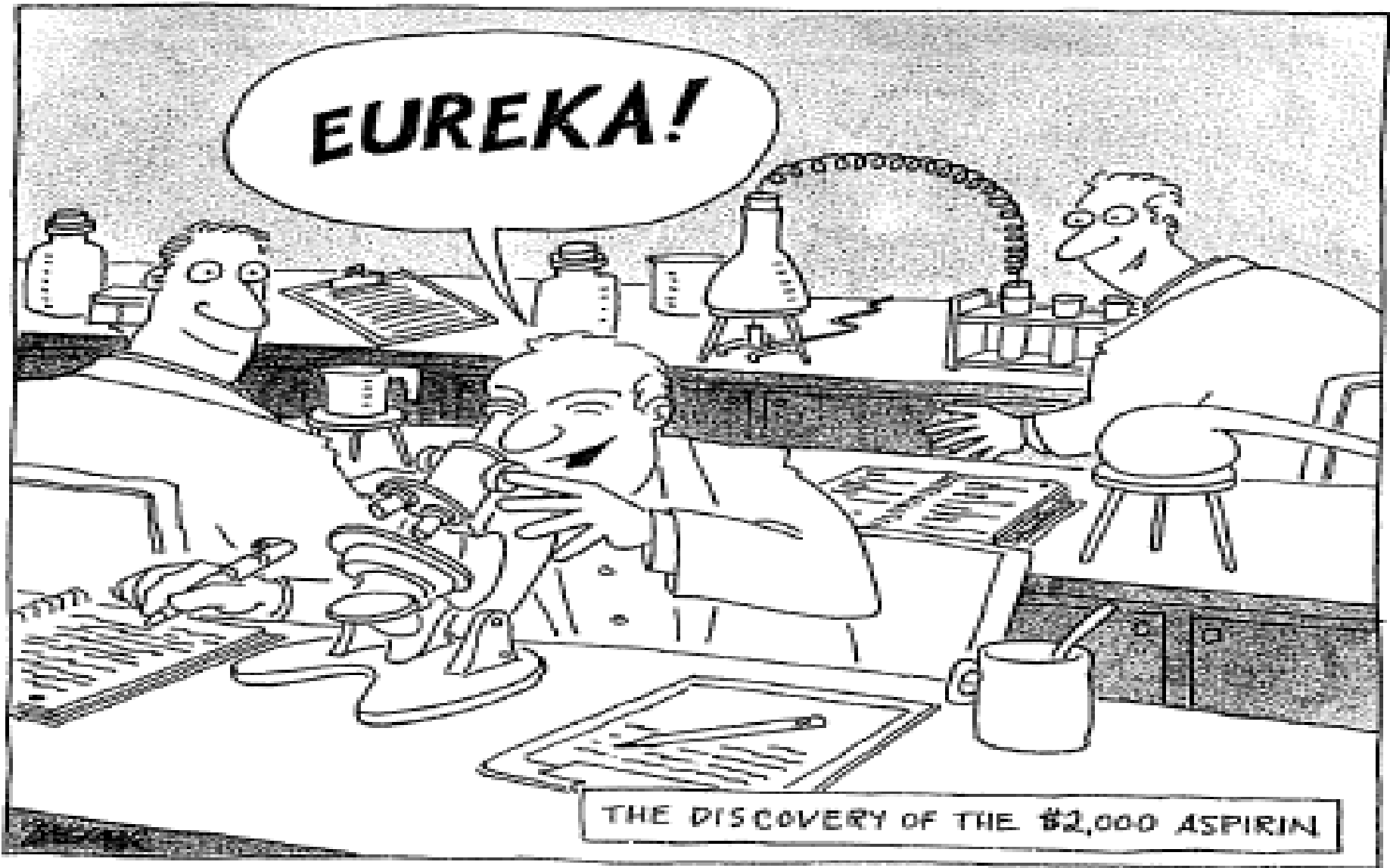
Association of American Medical Colleges

Professor of Medicine

Creighton University School of Medicine

Inside the DC Beltway

- 65 miles surrounded by reality
- Beltway view of the current role of Evidence in the US Health Care System



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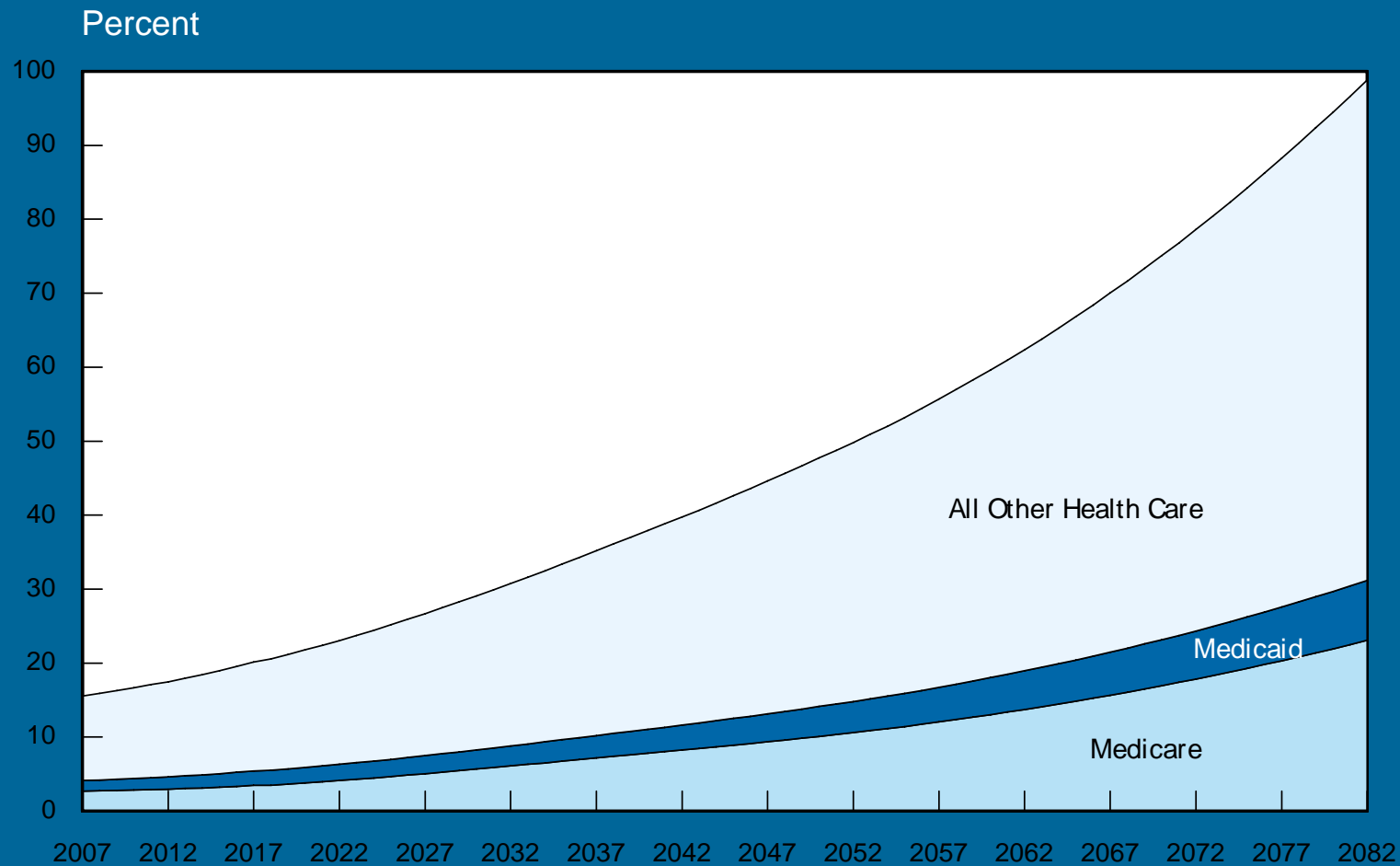
"I already wrote the paper. That's why
it's so hard to get the right data."



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"Take these pills three times a day, unless you read in the paper that they've been proven ineffective."

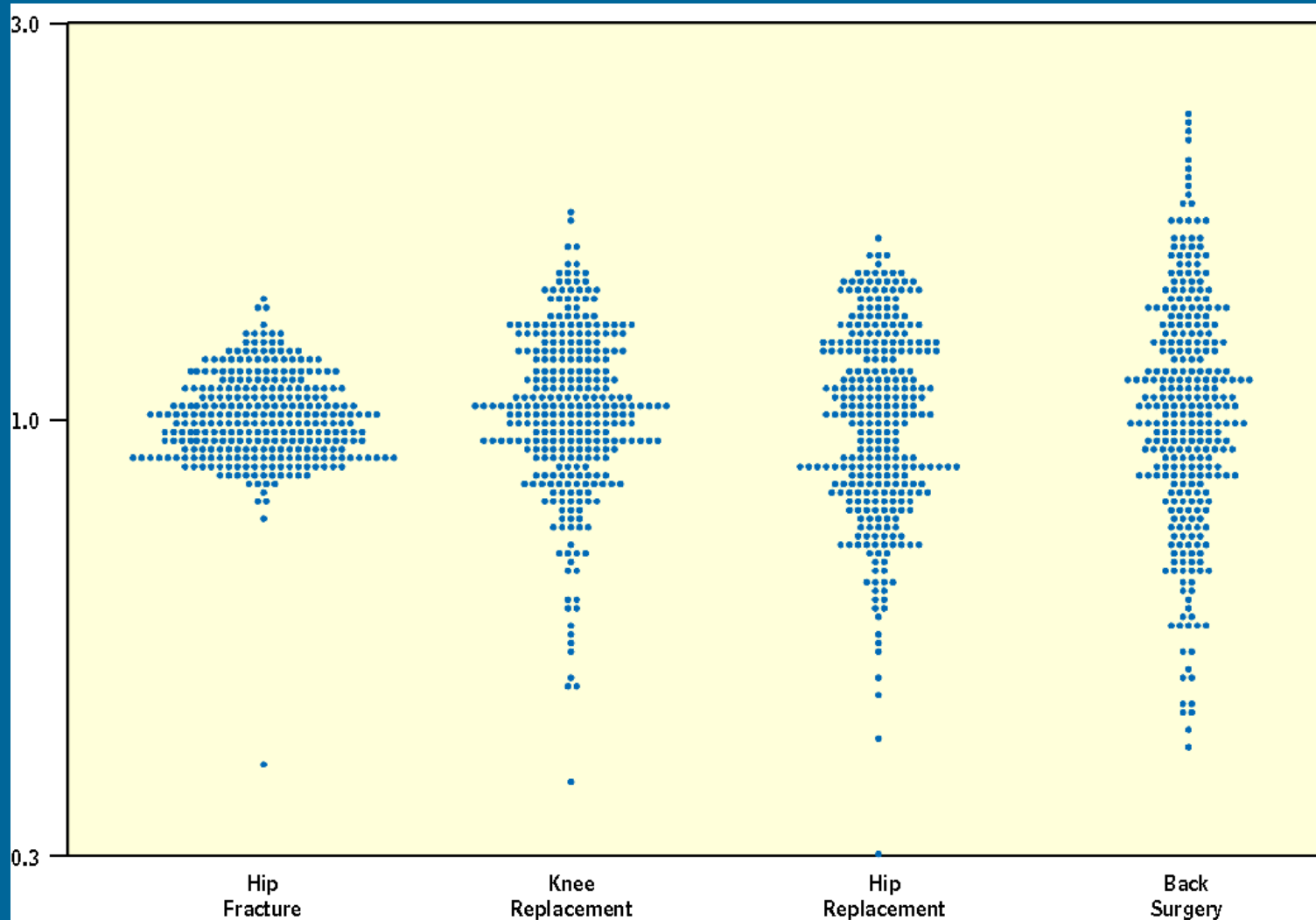
If Healthcare spending growth continues: the economy becomes healthcare in 2082



Source: CBO Long-Term Outlook for Health Care Spending, Dec 2007



Rates of Four Orthopedic Procedures among Medicare Beneficiaries



Source: Dartmouth Atlas

High Hopes for Comparative Effectiveness research

- Rising health care costs are unsustainable
- Costs are driven by technology-related changes in medical practice
- When evidence is unclear geographic variations in care are high
- Some US communities achieve lower costs and high quality
- Therefore
 - production and use of better evidence MAY lower unnecessary costs
 - without reducing quality or access!

Stakeholders agree on- need for more Comparative Effectiveness Research

- Advisors to Congress: CBO, MEDPAC, IOM
- Policy Experts: Republicans (eg Gail Wilensky, Mark McClellan) and Democrats (e.g. Jeanne Lambrew, Peter Orszag,)
- Health Plans: AHIP; BCBSA
- Employers: eg NBGH, Dow
- Drug and Device Manufacturers: PHARMA, ADVAMED, BIO
- Professional Associations: Academy Health, ACP, AAFP, AMA, AAMC

Stakeholders disagree on- a few details

- What is CER?
- Who should pay for it?
- How should it be directed?
- How should it be used?

What is CER?

- Efficacy vs effectiveness
- Systematic reviews, traditional RCT's, practical clinical trials, observational studies
- Comparative effectiveness vs health services research about delivery system
- Comparative effectiveness vs cost effectiveness

The Role of Science in Fixing the US health care crisis

- “relatively little rigorous evidence is available about which treatments work best for which patients...”
 - Need for more **clinical effectiveness research (CER)**



		RISKS	BENEFITS
HAMBURGER	\$2.35	WEIGHT GAIN	LOW FIBER CONTENT
CHEESEBURGER	\$2.95	HEALTHY FAT	PROTEIN & B12
TUNA SALAD	\$2.75	LOW FIBER	FEW OTHER NUTRIENTS
EGG SALAD	\$2.25	HEALTHY FAT	LOW FIBER CONTENT
OMELETTE	\$3.10	HEALTHY FAT	LOW FIBER CONTENT
BEEF STEW	\$3.45	HEALTHY FAT	LOW FIBER CONTENT
FISH FIL	\$2.15	HEALTHY FAT	LOW FIBER CONTENT

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The Role of Science in Fixing the US health care crisis

- “relatively little rigorous evidence is available about which treatments work best for which patients...”
 - Need for more **clinical effectiveness research (CER)**
- “...the financial incentives for both providers and patients tend to encourage the adoption of more expensive treatments...even if evidence of their relative effectiveness is limited.”
 - Need for more **research to guide delivery system changes (HSR)**
 - e.g. knowledge translation, patient engagement, quality improvement, practice transformation, health system reform



Cost effectiveness analysis

- CEA: an economic evaluation in which costs and health outcomes of different programs or interventions are evaluated on a common metric, often the ratio of net costs over net effectiveness
- E.g. \$/quality adjusted life year (quale)
- ON the OP-ED page- the distance between CEA and Rationing
- “ ”

Stakeholders positions on what is CER

- CBO, MEDPAC: CER narrowly defined; +/- CEA
- Policy Experts:
 - Republicans: Various; NOT CEA
 - Democrats: CER (Orszag- AND CEA)
- Health Plans: CER AND CEA
- Employers: CER, ?CEA
- Drug and Device Manufacturers: CER, HSR, NOT CEA
- Professional Associations: Various

What is CER? Legislative Answers

- 2007 HR 3162: CHAMP Act (Section 904)
- 2008 S 3408: Comparative Effectiveness Research Act of 2008
- 2009 HR 1 (ARRA)

What is CER? ARRA

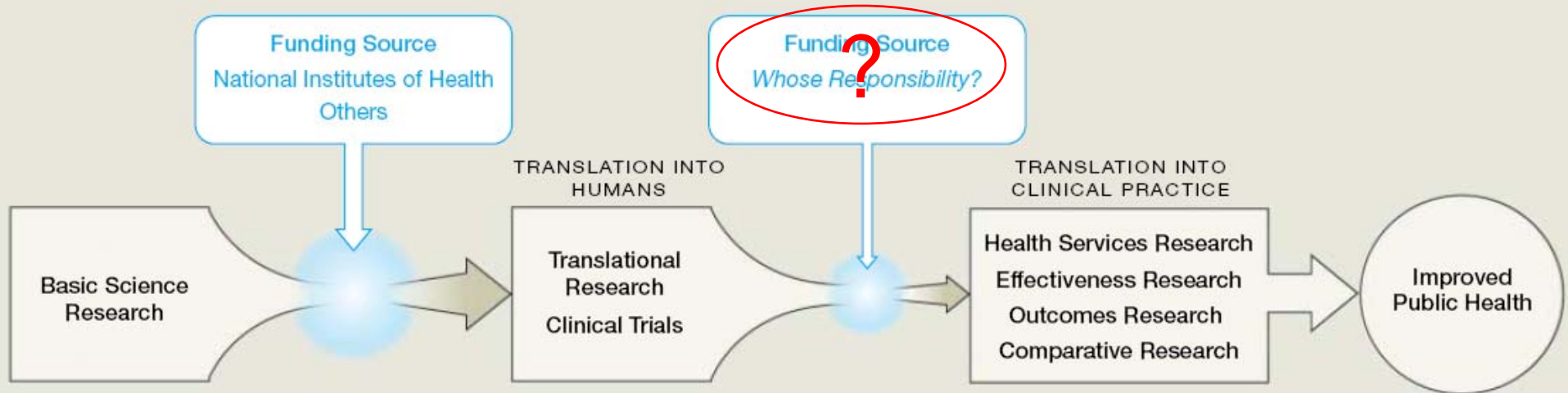
Legislation

- disseminate research findings from such {CER} grants and contracts to clinicians, patients, and the general public

Conference Report Language

- “...research to evaluate and compare the clinical outcomes, effectiveness, risk and benefits of two or more medical treatments and services that address a particular medical condition”
- “... the conferees recognize that a "one-size-fits-all" approach to patient treatment is not the most medically appropriate solution to treating various conditions... and include language to ensure that subpopulations are considered...”

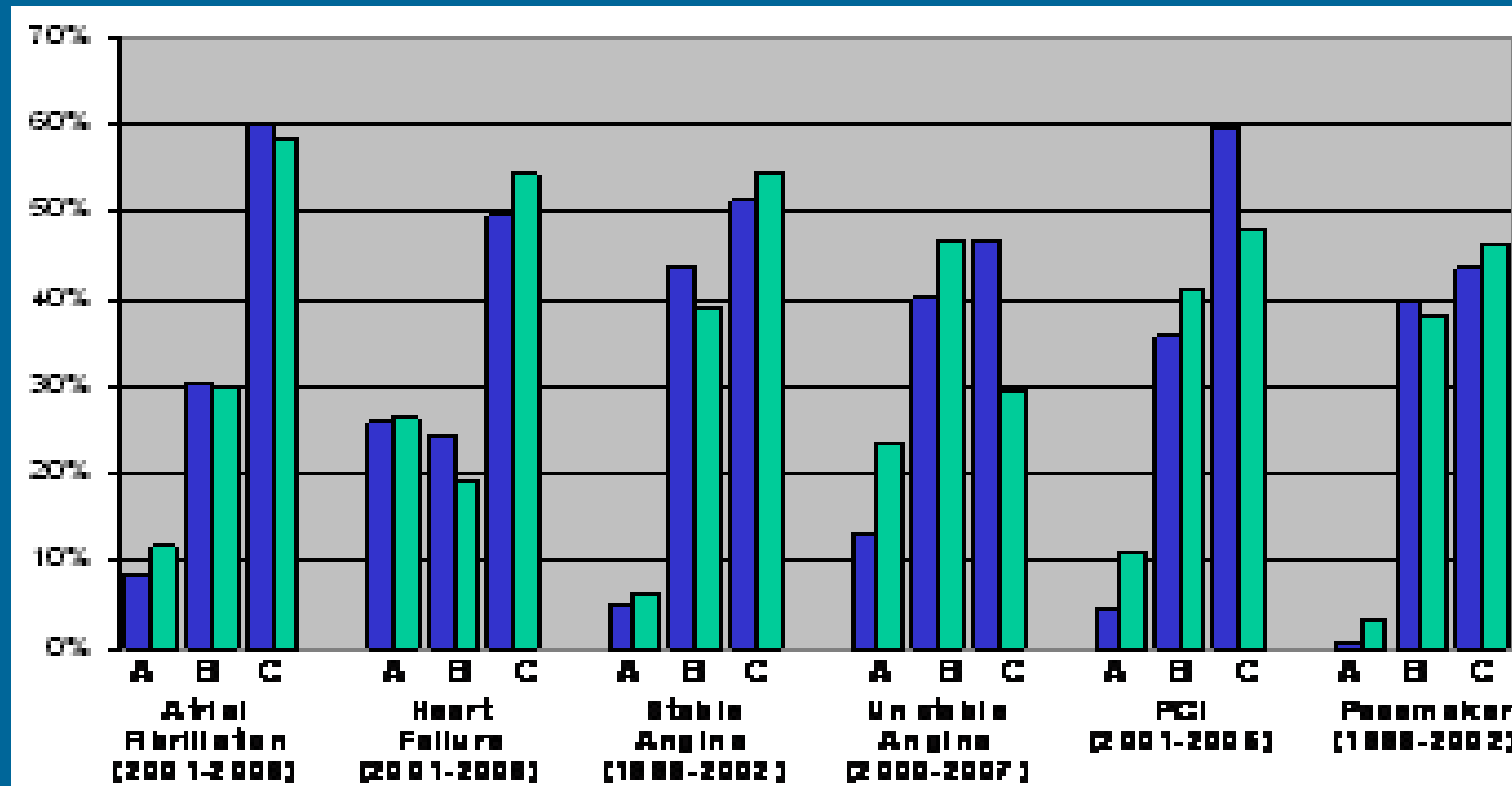
Who should pay for CER?



Crowley WF, et al. JAMA 2004;291:1120-1126

Enough Evidence?

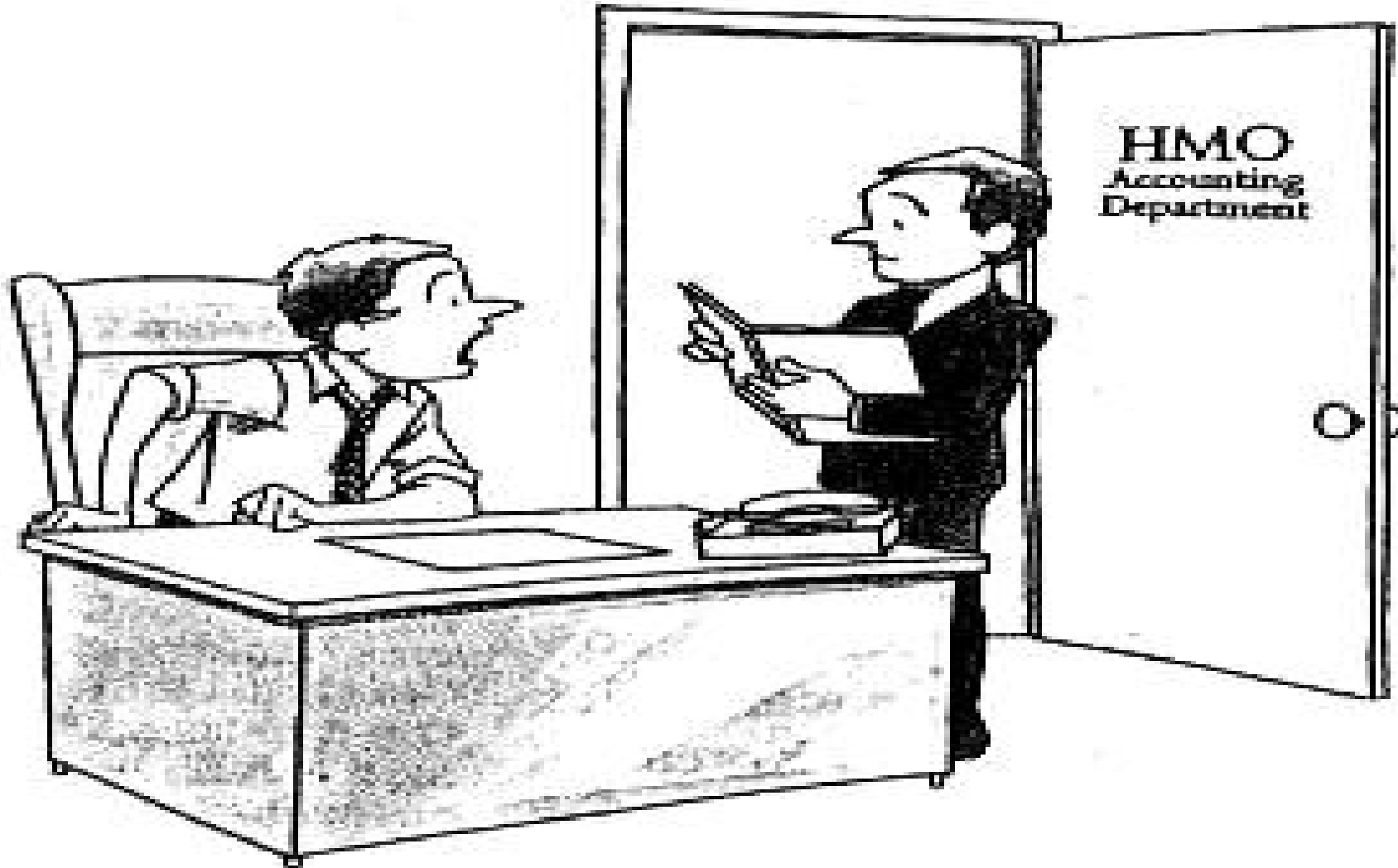
23,000+ clinical trials/yr



Robert Califf, IOM Meeting, 12 December 2008. Less than 20% of AHA/ACC heart disease management recommendations are based on a high level of evidence and over 40% are based on the lowest level of evidence: Level A evidence (multiple populations and risk strata) to Level C (very limited population risk strata). The proportion of recommendations with high evidence levels has not increased over time.

Why there isn't enough privately funded CER

- Health Economists (eg CBO)
 - “...the private sector generally will not produce as much research on comparative effectiveness as society would value..”
- Drug/device Manufacturer CEO:
 - “Why did we do a comparative clinical trial that just handed the market to our competition?”
- Health plan CFO:
 - “This study you medical directors want costs \$50 million; takes 5 years, and all our competitors can benefit from the information?”
- Consumer handbook publisher:
 - “I need to invest 100s of millions in research before I have a product to sell? And then do I sue patients using this “copyrighted” information without a subscription?”



**"Of course we want to make a profit.
Do you think we're in this for our health?"**

Why isn't there more CER at Federal Research Agencies?

- NIH Mission: science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.
- CER questions and priorities rarely involve issues of fundamental knowledge.
- Agencies and Academe place a high value on investigator initiated research
- Federal Research Agencies rely on Appropriator enthusiasm, but CER creates losers who really HATE losing (ask AHCPR!)

AHCPR and CER

- Established in 1989
- statutory responsibilities regarding outcomes research and practice guideline development
- Increased funding over former NCHSR : \$53 million 1989; \$97 million 1990; peak \$162 million 1995
- Patient Outcomes Research Teams (PORTs)
 - multidisciplinary centers focused on particular medical problems; review and synthesize available research, analyze practice variations and patient outcomes, disseminate the results, and evaluate the effects of dissemination.
- Back surgeon and device manufacturer hostility to PORT back pain research, and related guidelines
- Funding decline; loss of PORTs and Guidelines functions, name change 1999 (to AHRQ)

Who Should Pay for CER?

Legislative Answers

- 2009 ARRA:
 - \$1.1 B appropriated over 2 years (FY 2009 and FY2010)
 - AHRQ receives \$700 M for CER; AHRQ transfers \$400 M to NIH to conduct or support CER.
 - HHS Secretary receives \$400 M to “accelerate the development and dissemination of CER”

NIH initial use of ARRA Funds

- “Solicitation of NIH CER proposals can be found in the Challenge Grants (RC1), Administrative Supplements, and Competitive Revision Application announcements”
- Some “Grand Opportunities” RFAs as well
- Further use of HHS CER \$ to be guided by FCC-CER (see below)

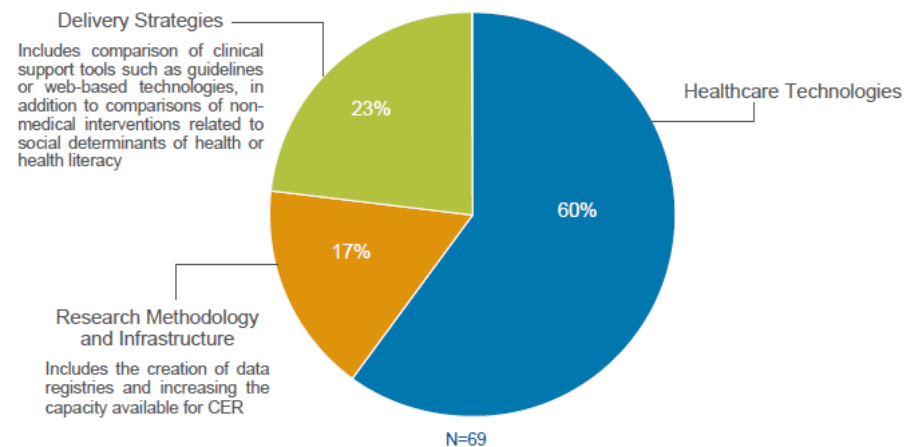
NIH Challenge Grants: 69 CER Topics

- focus on:
 - Developing research trial protocols that may be initiated later
 - Completing analyses using existing data
 - Building data registries and other tools to allow for future analyses
- Funding capped at \$1M for two years; \$500K per year
- Apr 27 deadline

Top Six Conditions Targeted

Ranked By Percentage	
1.	Substance Abuse (13%)
2.	Cancer (12%)
3.	Cardiovascular (7%)
4.	Diabetes (4%)
4.	Mental Health (4%)
4.	Neuroscience/Neurology (4%)

NIH CER Challenge Grants By Research Focus



NIH CER Grand Opportunities

- NHLBI
 - Comparative Effectiveness
- NCI
 - Comparative Effectiveness Research in Genomic and Personalized Medicine
 - Comparative Effectiveness Research in Cancer Prevention, Screening and Treatment
- NINDS
 - Grand Opportunities in Comparative Effectiveness Research
- NIA
 - Comparative Effectiveness Trials of Treatment Modalities of Sleep Disorders
- NIDCR
 - Treatment of Tobacco and Drug Dependence in Multiple Dental Clinics
- NCCAM
 - Comparative Effectiveness Studies of Non-Pharmacological Treatments for Chronic Low Back Pain
 - Comparative Effectiveness Studies of Complementary and Alternative Medicine

NIH CER Grand Opportunities

- NHLBI Comparative Effectiveness: This funding opportunity will support two-year efforts that will substantially accelerate CER, advance methods development and priority setting, and forge robust infrastructure to support the conduct of comparative effectiveness research... Responsive projects include those that...
 - Plan initiatives (including feasibility and vanguard studies) to prepare for the launch of large-scale pragmatic comparative effectiveness trials of interventions for medical conditions of substantial public health or public policy importance.
 - Develop and/or advance analytic techniques and quantitative methods for analyzing comparative effectiveness clinical trials.
 - Design and evaluate complex simulations and statistical models designed to enable researchers, funding agencies, practitioners, and policymakers to make informed systematic decisions regarding priorities for studies of comparative effectiveness.
 - Establish or enhance user-friendly registries that can be queried and used to identify subjects, enroll them rapidly, and then follow them over time for large-scale trials or other CER studies.

After the ARRA?: Paying for CER LONG-TERM

- 2007 HR 3162 (CHAMP Act): Section 904
- 2008: S 3408: Comparative Effectiveness Research Act
 - Comparative Effectiveness Research Trust Fund
 - fees charged to ...Medicare and all forms of private health insurance
 - \$300-400 M per year
 - Gail Wilensky, others have called for \$1-3 B per year

How should CER be directed?

- IOM Roundtable on EBM: discussion of CER entity functions...
 - Priority setting
 - Budget allocation
 - Study selection
 - Research design/methods improvement
 - Study management
 - Study conduct (field)
 - Study certification
 - Study conclusions

2007 Hill Topics for CER were High Stakes!

1. Erythrocyte stimulating agents in cancer care
 - key profit/revenue for AMGEN, Oncology Centers
 - advocates- AMGEN, ASCO,ASH, patient groups
2. Inpatient rehabilitation of hip fracture surgery
 - Key revenue/profit for IRF's, rehab professionals
 - Advocates- AHA, IRFs, rehab professionals, patient groups
3. Bidil vs generic alternative in CHF
 - Key revenue/profit for Bidil manufacturer (NitroMed)
 - Advocates: NitroMed, patient groups, physicians

Hot Topics for CER- Still High Stakes!

CT Coronary Angiograms for chest pain

- Key revenue/profit for
 - manufacturers,
 - hospitals,
 - radiologists,
 - physician owners of Angio-capable hi slice CT (NY Times reports fees from imaging account for half of cardiologists income)
- Advocates: manufacturers, hospitals, specialty groups, patient groups

Conflicting Evidence: Informing or Permitting?

- Medline search for articles published in the last year
- Humans, Clinical Trial, English, adult, “coronary arteriogram computed tomography”
 - 30+ competing views
 - Multidetector CT angiography accurately identifies the presence and severity of obstructive coronary artery disease and subsequent revascularization in symptomatic patients.
 - The negative and positive predictive values indicate that multidetector CT angiography cannot replace conventional coronary angiography at present.
 - NEJM Nov 2008

CMS: Coverage Without Evidence

- Payers/researchers
 - want RCT with death/AMI outcome
 - 20k patients, 2+ years of follow-up
 - Non-experimental options rejected
- Vendors / clinicians
 - existing evidence sufficient
- Medicare final decision (March 2008)
 - “We believe large, well-designed prospective trials needed”
 - But broad coverage by local contractors retained

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“According to an article in the upcoming issue of ‘The New England Journal of Medicine,’ all your fears are well founded.”

How Should CER be directed?

HR 3162

CER Center at AHRQ

- Conducts support, and synthesizes research and systematic reviews of clinical research
- Establishes standards for CER methods
- Encourages development and use of clinical registries, clinical effectiveness research data networks from EHRs, etc
- Advisory Commission oversight
 - Set CER priorities, confirm credible methods
 - Clinical perspective advisory panels

Federal CER Infrastructure

- AHRQ,
- NIH,
- VA,
- CDC,
- DOD,
- etc



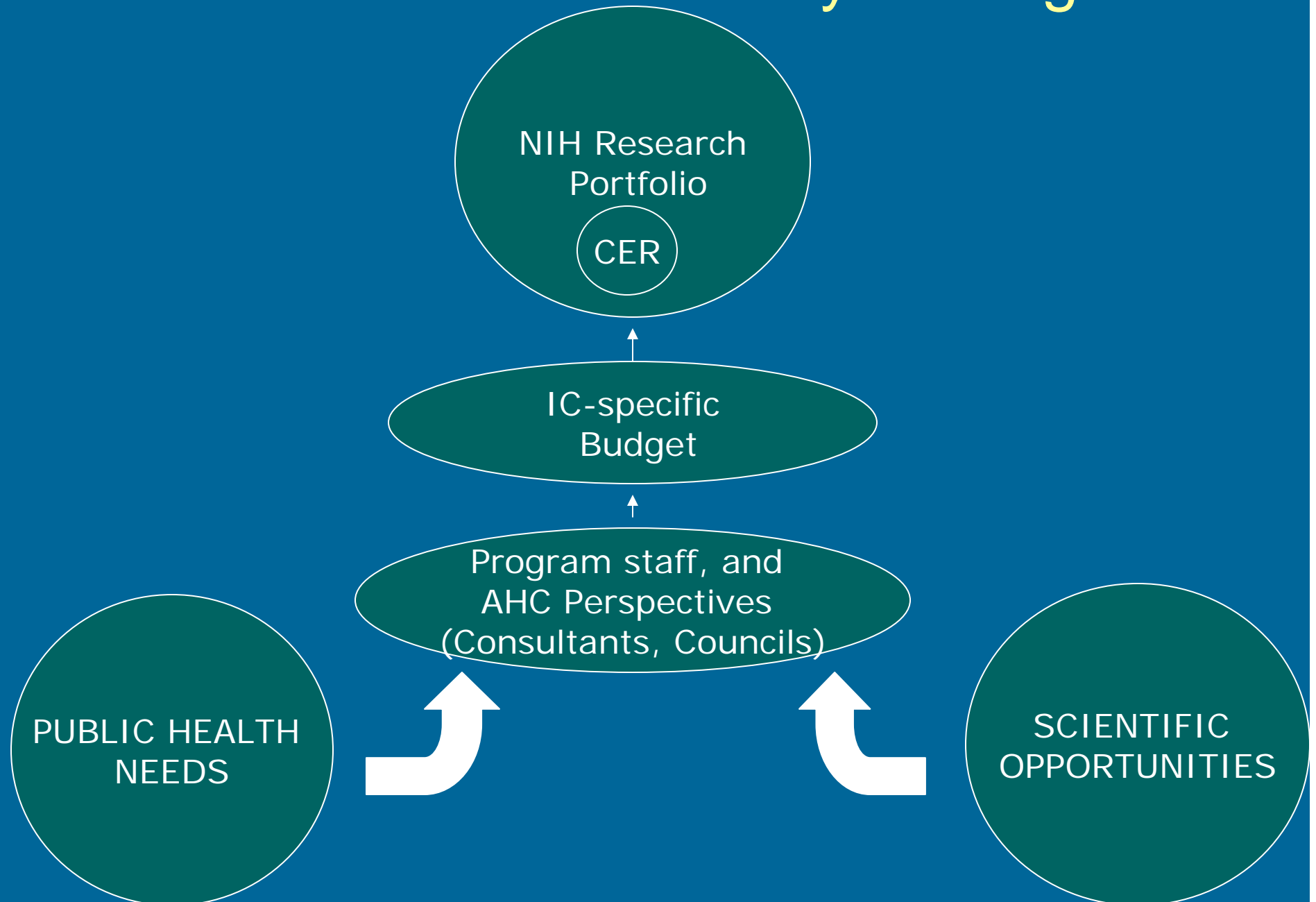
Just the standard? Or do you want a high-ranking government official to expunge it personally?

How Should CER be directed?

S3408

- Establishes the Health Care Comparative Effectiveness Research Institute, a private, nonprofit corporation
- Institute duties
 - establish a national agenda of research priorities
 - contract with federal agencies, such as AHRQ and appropriate private entities to conduct CER,
 - Research findings publicly disseminated in ways patients and healthcare providers can easily understand.
 - establish procedures to ensure transparency, credibility, etc:
- 21 member Board of Governors

NIH Research Priority Setting



Doing CER- Not your Mentor's R0-1

- Setting CER Research priorities
 - Broad representation of stakeholders in identifying priority research topics and specifying research questions.
 - Research questions- “what physicians and patients need to know to make bedside decisions”
 - NOT an agenda directed by investigators, study sections, IC Councils or program staff
- Conducting CER projects
 - CER studies be funded as contracts, with research questions and methods specified in the RFP
 - NOT grants in response to PI-initiated proposals

DOGBERT CONSULTS

EVERY CREDIBLE
SCIENTIST ON EARTH
SAYS YOUR PRODUCTS
HARM THE ENVIRONMENT—

Patients

I RECOMMEND PAYING
WEASELS TO WRITE
ARTICLES CASTING
DOUBT ON THE DATA.

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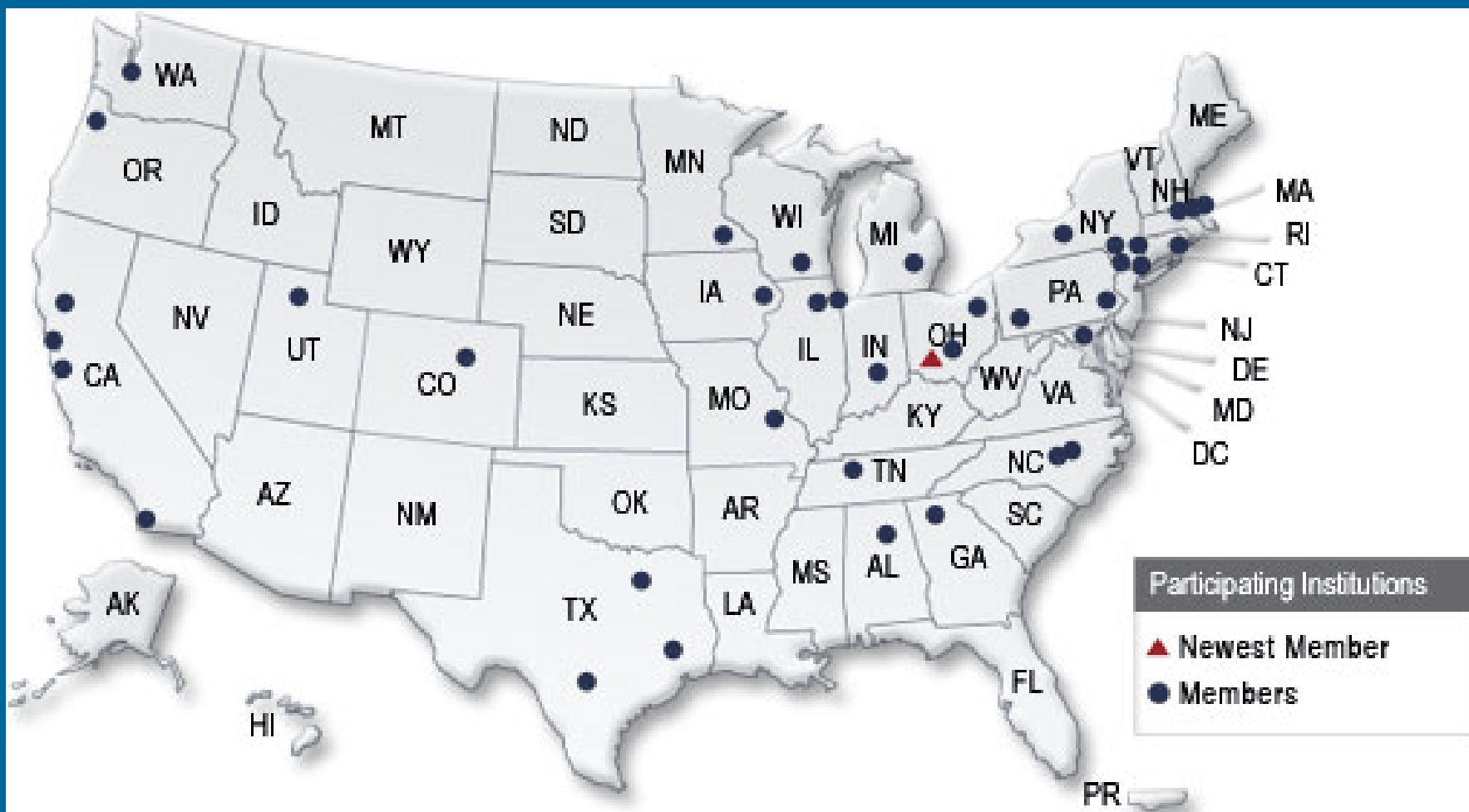
Tradeoffs in options for governing CER

	HHS (AHRQ) Center	NFP CER “Institute”
Public Accountability	↑	↓
Consistency	↑	↑
Use of existing capacity	↑	↓
Political Feasibility	?	↑
Objectivity	?	?
Responsiveness	?	↑
Scientific rigor	?	?
Transparency	↑	↓

Coordinating Federal CER Research Infrastructure

- AHRQ
 - 41 CER research centers nationwide
 - Evidence-Based Practice Centers;
 - Centers for Education and Research on Therapeutics (CERTs);
 - DEcIDE Centers (Developing Evidence to Inform Decisions About Effectiveness) -HIT Databases
 - Access to >120 different databases
- VA Cooperative Studies program
 - 30+ active studies 2008
- NIH
 - \$9.6 Billion in “clinical research” funding 2008
 - \$3.6 Billion for “clinical trials”

NIH Clinical & Translational Science Awards



CTSAs and CER

- Opportunities
 - CE Research infrastructure
 - CER Faculty development
 - CER Methods development
- CTSA Consortium Strategic Goals Sub-Committee:
 - “develop capacity and methods for the translation of research results into practice across the healthcare system, including but not limited to health services and health policy research, **comparative effectiveness research**, and **research into the generation and implementation of evidence-based medicine**,”
- Threats
 - NIH Mission Creep
 - Competing priorities –
 - CER ethos may conflict with goal of “**Speeding** the translation of biomedical science discoveries into clinical practice”
 - Patient advocates- eg. Specter’s “Cures Acceleration Network”
 - Traditional research constituencies (eg FASEB)
 - How to distribute CER \$/studies to CTSAs?
 - Other NIH Institutes

NIH IC-funded Clinical Research Networks

- AIDS malignancies
- Asthma
- Leukemia
- Drug-induced liver injury
- Bariatric surgery
- Maternal-fetal medicine
- Alzheimer's disease
- Drug abuse
-many, many more (over 80)

Engaging Federal Resources for CER: Senate Finance Vision

CER TRUST FUND

\$

Contracts for evidence reports,
registries,
observational studies
clinical trials
Contracts with WHOM?

CER Contracts

CER Results

NFP CER "Institute"

Sets priorities, standards
develops research questions,
contracts for studies
(internal and external)

Reports/
No Reccds

THE PUBLIC

Engaging Federal Resources for CER: Senate Finance Vision

Contract for CER Study ...
on CT Coronary Angio
With AHRQ EPC?
With NIH?
•NHLBI?
•CTSA?
•CV Research Network?
With VA Coop Studies?
With Private foundations?
With Contract Research
Organizations?

CER Contracts

CER Results

CER TRUST FUND

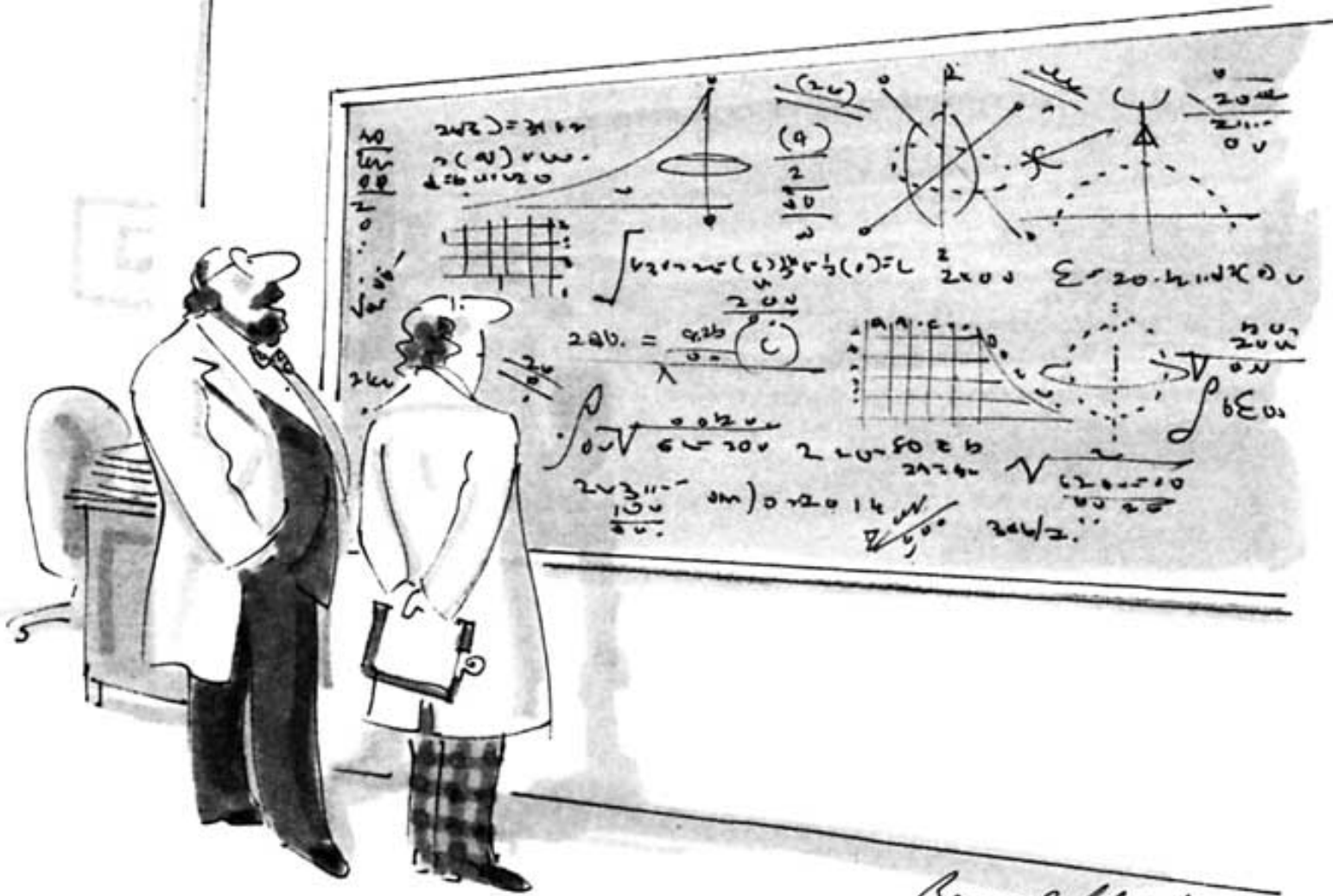
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NFP CER "Institute"

Sets priorities, standards
develops research questions,
contracts for studies
(internal and external)

Reports/
No Reccds

THE PUBLIC



Bernard Scholbaum.

"Oh, if only it were so simple."

Coordination of Other Federal CER efforts

- CER research workforce development
- CER Methods development (Standards)
- Sample CER methods controversies/competencies
 - Systematic reviews and meta-analysis
 - Clinical trials
 - Outcomes measurement
 - Cost measurement
 - Role of observational studies
 - Cost-effectiveness analysis

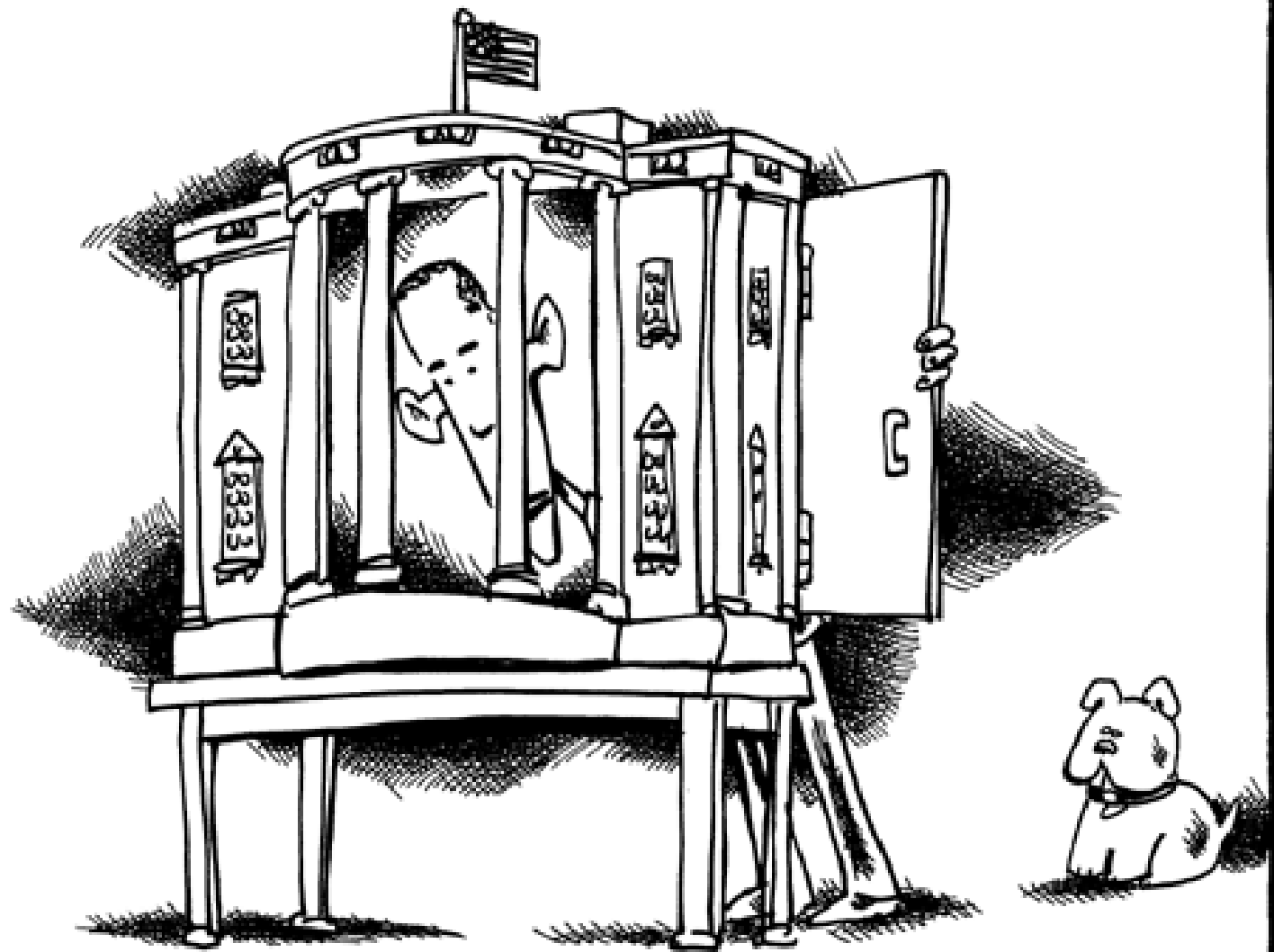
How Should CER be directed?

ARRA

- Federal Coordinating Council for Comparative Effectiveness Research
 - 15 representatives of federal agencies—at least half would have to be physicians or other experts with clinical expertise
 - Recommendations re coordination of CER and related HSR to HHS Sect by June 30
- IOM CER Priorities Study
 - recommend national priorities for CER by June 30
 - to include input from stakeholders.
- HHS Secretary Report to Congress
 - Report on plans for use of \$400 M to “accelerate the development and dissemination of CER”
 - Report on plans by AHRQ and NIH for their \$700 M
 - Due July 31

How should CER be used?

- CBO “Score” for CER in HR 3162
 - \$2.9 Billion spending on CER 2008-2017
 - Federal Health Care savings \$1.3 Billion-
 - Federal investments in CER would equal savings after 7 years
 - Assumes no changes in Medicare coverage rules
 - Anticipates evidence leads to changes in physician practice and patient choice
 - Private Health Care Savings \$5 Billion
 - Anticipates private insurers would use CER



But When He Got There, the Cupboard Was Bare.

TOLLS

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AND THE DOLLAR SIGNS
HAVE BEEN PRIED OFF
ALL THE KEYBOARDS. —



How Policymakers would use CER to “Bend the Curve”

Negotiating with Manufacturers

- E.g....“Coverage with evidence development” - speeding collection of additional comparative effectiveness info thru mandated studies or registries tied to coverage

Engaging Consumers

- E.g....Value-based insurance design- e.g. no “co-pays” for highly effective therapies

Rewarding Providers

- E.g.... Value –based provider payments – e.g. pay providers more for highly effective therapies

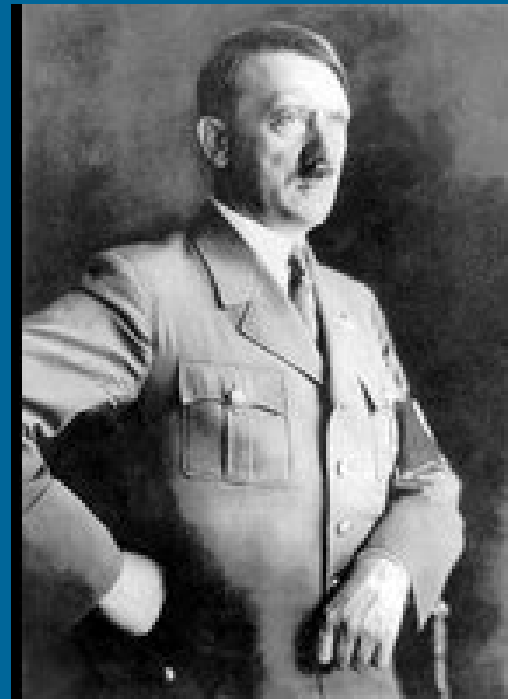
Commonwealth Report: savings from Federal investment in CER

- Center for Medical Effectiveness and Health Care Decision-Making.
 - Invest in the knowledge needed to improve decision-making
 - incorporate information about the relative clinical and **cost-effectiveness** of alternative treatment options into **insurance benefit design**.
 - **payment and cost-sharing incentives for providers and consumers** to use CER
 - Potential health system savings of **\$368 billion over 10 years**, shared by all payers.

The Washington Times

EDITORIAL: Health 'efficiency' can be deadly

Wednesday, February 11, 2009



How should CER be used?

Legislative Answers

- 2007 HR 3162 (CHAMP Act): Section 904
 - Commission is to “provide guidance or recommendations to health care providers and consumers...”
- 2008 S 3408
 - None of the reports submitted under this section or research findings disseminated by the Institute shall be construed as mandates, guidelines, or recommendations for payment, coverage, or treatment.”
- 2009 ARRA:
 - **Conference Report language** “The conferees do not intend {CER funding}... be used to mandate coverage, reimbursement, or other policies for any public or private payer. The funding ... shall be used to conduct or support research....”
 - **Legislative Language:** Rules of Construction re above

The Key Controversies re CER

- What is it?
- Who should pay for it?
- How should it be directed?
- How should it be used?

AAMC Support for CER

- “Comparative effectiveness research (CER), and related research on knowledge translation, patient engagement, and health system transformation are key to converting biomedical discoveries into effective new approaches to the diagnosis, treatment, and prevention of human illnesses.”

AAMC Position

- The AAMC strongly supports...
 - investments to further develop research methods to support the national comparative effectiveness research enterprise
 - investment in research training in the disciplines relevant to comparative effectiveness research
 - investments to develop and sustain the national research infrastructure for CER
 - research to inform clinical care delivery and the development of delivery system reforms.
 - developing and using CER through means that are synergistic with continued discovery of clinical innovations through biomedical science.

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"Let's change 'brink of chaos' to 'Everything is wonderful.'"

Readings

- CBO
 - Technological Change and the Growth of Health Care Spending
January 2008
 - Research on the Comparative Effectiveness of Medical Treatments:
Issues and Options for an Expanded Federal Role
December 2007
- IOM
 - Knowing What Works in Health Care: A Roadmap for the Nation; Jan
2008
 - Comparative Effectiveness in Health Care; Sept 2007
- MedPAC
 - Chapter 5: Producing Comparative effectiveness information; in
Reforming the Delivery System; June 2008
- ACP
 - American College of Physicians*,. Information on Cost-Effectiveness:
An Essential Product of a National Comparative Effectiveness Program.
Ann Intern Med. 2008

