



Forum Session Meeting Announcement

Friday, September 26, 2008

8:45–9:15am — Breakfast

9:15–11:15am — Session

Exploring Comparative Effectiveness: Activities of NIH, FDA, and AHRQ to Advance Evidence-Based Health

A Discussion Featuring:

Bryan R. Luce, PhD

Senior Vice President for Science Policy
United BioSource Corporation

Michael Lauer, MD

Director
Division of Prevention and Population Science
National Heart, Lung, and Blood Institute
National Institutes of Health

Robert J. Temple, MD

Director
Office of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration

Carolyn M. Clancy, MD

Director
Agency for Healthcare Research and Quality

Location

**Reserve Officers Association
of the United States**

One Constitution Avenue, NE
Congressional Hall of Honor
Fifth Floor

*(Across from the Dirksen Senate
Office Building)*

Registration Required

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as soon as possible.

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Exploring Comparative Effectiveness: Activities of NIH, FDA, and AHRQ to Advance Evidence-Based Health

OVERVIEW

In developing an expanded federal capacity for comparative effectiveness, it will be instructive to draw on the experience and expertise of the numerous federal agencies involved in obtaining better information to guide health decisions. Many of these agencies have been engaged with the issues for decades, and many of their current activities fall under the rubric of comparative effectiveness. Much is at stake: how can the activities that are working well and are integral to the key functions of these agencies be preserved? How can greater sharing of expertise and linkages across public and private domains be stimulated? And how should new activities be positioned to maximize their effectiveness?

This session, the second in a series intended to clarify the complex set of issues surrounding comparative effectiveness, will examine the sometimes contentious evolution of the concept and discuss activities at three agencies extensively engaged in the development and assessment of health evidence: the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Agency for Healthcare Research and Quality (AHRQ). A subsequent session will provide data on current comparative effectiveness activities in both the public and private sectors, and will examine three additional federal agencies engaged in the generation and application of evidence: the Centers for Disease Control and Prevention, the Centers for Medicare and Medicaid Services, and the Veterans Health Administration.

SESSION TWO

Recently, comparative effectiveness has become all the rage. Although many people are using the term and have advanced a variety of proposals for increasing U.S. capacity, it is not clear they all have quite the same thing in mind. However, they do seem to share a common frustration at all levels—from the individual to the federal government—with the nature of the information available for making choices and decisions about personal health, health care, public health, and health policy, as well as a growing consensus that we must have better information in order to advance the health of the nation.¹

A Crowded Landscape: Evidence-Based Health Activities of Federal Agencies

In addition to a wide variety of private and other public sector entities, numerous federal agencies are involved in obtaining better information to

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guide health decisions, and much of their activity fits even the narrowest definitions of comparative effectiveness. One can find examples at a long list of federal agencies of efforts to develop and use the best information to make decisions about health. Many—but not all—of them are concentrated in the Department of Health and Human Services (HHS). Increasing efforts to develop and use best evidence to inform health decisions are viewed positively in most cases, but even advocates for further expansion bemoan the redundancies, gaps, and inefficiencies in the current system.

A particular challenge in the United States is that each of the many pieces in the growing evidence-based health enterprise functions relatively independently, and, thus far, they have not been optimally coordinated. This can be said even about the pieces within HHS and those focused primarily on health care services. Proposed expansions of federal capacity for comparative effectiveness have the potential to either further clutter this landscape or to improve its cohesiveness. The hope expressed by many involved is that future efforts will at least be consonant with this large array of existing activities, and ideally serve to improve overall comprehensiveness and coordination.

This session and a subsequent one will familiarize participants with the activities at several agencies that have been extensively engaged with comparative effectiveness and examine it from their perspectives. While by no means the complete picture, the agencies selected provide examples of agencies that develop, assess, and use health evidence; are inside and outside of HHS; focus on health care and public health; and are concerned with researching, regulating, financing, and delivering health products, programs, and services.

After an overview of the sometimes turbulent evolution of comparative effectiveness, this session will focus on three agencies within HHS: the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Agency for Healthcare Research and Quality (AHRQ). A few of the relevant activities of each agency are highlighted below.

The **NIH** is the primary federal agency for conducting and supporting medical research, including research on the causes, diagnosis, prevention, treatment, and cure of human diseases; the processes of human growth and development; the biological effects of environmental contaminants; and the understanding of mental, addictive, and physical disorders. It includes the National Library of Medicine and also directs programs for the collection, dissemination, and exchange of information in medicine and health. NIH conducts and funds many types of medical research, including comparative effectiveness research, from the kind done in laboratories in test tubes to that done with databases of various kinds to the kind done with people in clinical settings. NIH characterizes roughly one-third of its funding as supporting clinical research and roughly one-third of that as supporting clinical trials, many of which are the randomized controlled trials considered the gold standard for determining whether a treatment

works. Some of these trials directly compare treatments and provide good examples of both the potential for and limitations of such comparative effectiveness studies to affect health care.

A prominent example of a major comparative clinical trial supported by NIH is the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). This trial involved over 40,000 people and lasted for eight years. It had two parts: one compared several different drugs for lowering blood pressure, and the other compared two approaches to lowering cholesterol (diet alone or diet plus drug). The first results were published in 2002. However, six years later, analysis, discussion, debate, development of recommendations and guidelines, and implementation in practice continue, illustrating the complexity of putting the results to use.

Through the National Library of Medicine and in collaboration with the FDA, NIH also supports ClinicalTrials.gov, a publicly available database of federally and privately supported clinical trials for a wide range of diseases and conditions. It was developed as a result of the FDA Modernization Act (1997) to aid patients with life-threatening diseases and conditions in finding clinical trials for which they might be eligible. Its scope has steadily expanded, most recently as a result of the FDA Amendments Act (2007), to include all diseases and conditions and to provide better linkages to more information available at FDA and NIH about the trials.

The **FDA** is a regulatory agency that has been concerned with comparing treatments since a 1962 amendment to The Food, Drug, and Cosmetic Act required that manufacturers demonstrate prior to marketing that their products are not only safe, but also that they are effective. Typically, the effectiveness studies that manufacturers are required to submit to FDA compare the new drug to a placebo (that is, something that appears identical to the real thing but contains none of the active ingredient). Such placebo-controlled studies are deemed necessary in order to determine whether a drug works, because many conditions will improve or resolve over time without treatment and because the “placebo effect” is often powerful.

But placebo-controlled studies are not the only kind that FDA evaluates. With increasing frequency, manufacturers also submit to FDA many studies that compare the new treatment to existing treatments. Reasons for such studies include:

- The need for comparisons with existing treatments instead of or in addition to a placebo. For example, in some cases it may be unethical to use a placebo, or it may be important to understand how the new treatment compares to an existing standard.
- The global market for medical products. Many other countries require comparative information, so manufacturers may try to minimize the number of studies they have to conduct by designing ones that will satisfy the requirements of several markets simultaneously.

- Requirements for making comparative claims about a product. Like all claims, such claims have to be based on the approved labeling, and thus the manufacturer needs to submit comparative studies to support the labeling.

Consequently, FDA has been increasingly concerned with developing the standards and methods for comparative studies as well as with assessing them to support the regulation of medical products. Especially in the past two decades, FDA's role in assessing comparative effectiveness, use of its vast clinical database, and its relationship to other agencies such as AHRQ, NIH, and the Centers for Medicare & Medicaid Services have been the focus of legislation and other initiatives.

AHRQ is involved in—and in some cases is leading—many of the federal efforts currently being discussed under the rubric of comparative effectiveness. For example, the Effective Health Care Program is dedicated to providing current, unbiased evidence on health care interventions for patients, health care providers, and policymakers to inform their decision making. This program originates from the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, which authorizes AHRQ to conduct and support research with a focus on outcomes, comparative clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services. The Program includes:

- **Evidence-based Practice Centers**, which synthesize existing scientific literature about important health care topics and promote evidence-based practice and decision making. Their activities include Comparative Effectiveness Reviews on medications, devices, and other relevant interventions. These reviews systematically and critically appraise existing research to synthesize knowledge on a particular topic, identify gaps in knowledge, and recommend approaches to fill those gaps.
- The **DEcIDE (Developing Evidence to Inform Decisions about Effectiveness) Network** of research centers, which generates new knowledge. It conducts accelerated practical studies about the outcomes, comparative clinical effectiveness, safety, and appropriateness of health care items and services. The network is comprised of research-based health organizations with access to electronic health information databases and the capacity to conduct rapid turnaround research. Initial research focuses on the outcomes of prescription drug use and other interventions for which randomized controlled trials would not be feasible or timely, or would raise ethical concerns that are difficult to address.
- The **Centers for Education and Research on Therapeutics**, a national demonstration program whose mission is to conduct research and provide education that advances the optimal use of drugs, biologicals, and medical devices. It is organized as a network of research centers, each of which focuses on an area where limited comparative information exists on the risks, benefits, and interactions of new and older therapeutic agents.

- The **Eisenberg Center**, which is devoted to developing tools to help people make decisions about health care. It translates the complex scientific information from other AHRQ programs into appropriate materials for three groups: consumers, clinicians, and policymakers. It also develops and tests decision aids derived from the comparative effectiveness reviews to improve patient participation in decision making about their health care.

Speakers for this Forum session include an analyst, who will describe the evolution of comparative effectiveness, and officials from each of these three agencies, who will review the relevant activities of their respective agencies and provide perspectives on how their agency would ideally relate to the new activities under discussion.

KEY QUESTIONS

- How has the concept of comparative effectiveness evolved? What federal agencies have been involved in this evolution? What scope of activities is under discussion, and how much agreement and/or disagreement is there?
- What are the responsibilities of NIH, FDA, and AHRQ for advancing evidence-based health? How does each define comparative effectiveness, and what related activities does each engage in? How do they relate to each other and to nonfederal entities?
- What challenges does each agency face, and what are the opportunities to enhance their individual and collective capacity?
- What role could these agencies play in expanding capacity for evidence-based health, with or without a new comparative effectiveness entity?

SPEAKERS

Bryan R. Luce, PhD, senior vice president for science policy at United Bio-Source Corporation, is an analyst with extensive experience in both the public and private sectors in technology assessment, outcomes research, health policy, and health economics. He will begin the session with an overview of the evolution of and current context for comparative effectiveness. **Michael Lauer, MD**, is a board-certified cardiologist who has practiced, taught, and conducted research in cardiovascular medicine and epidemiology. Since 2007, he has served as the director of the Division of Prevention and Population Science at the National Heart, Lung, and Blood Institute of the National Institutes of Health. **Robert J. Temple, MD**, has served at the Food and Drug Administration since the 1970s, first as a reviewer and currently as the director of the Office of Medical Policy in the Center for Drug Evaluation and Research. Prior to joining the FDA, he completed his medical training in endocrinology and served as a researcher

at the National Institutes of Health. **Carolyn M. Clancy, MD**, is a general internist who has served as a clinician, teacher, and researcher in a variety of settings. She joined the Agency for Healthcare Research and Quality in 1990, directed its Center for Outcomes and Effectiveness Research, and has served as the agency's director since 2003.

ENDNOTES

1. For a more detailed introduction to this series, see the information on the first session, and other related resources: www.nhpf.org/index.cfm?fuseaction=Details&key=704.

Exploring Comparative Effectiveness: Information About the Series

This series of Forum sessions is intended to support understanding and evaluation of existing and anticipated proposals re-

lated to comparative effectiveness and to clarify the complex set of issues bundled under that heading. The series began with a review of the fundamentals of evidence-based health and an introduction to the Cochrane Collaboration, one of the premier global resources for evidence-based health. It will conclude with a comparison of specific proposals under discussion. The series is designed to address the following general questions:

- What is evidence-based health? What is the big picture, and what are the basic concepts? How does comparative effectiveness fit into the picture?
- To what extent do we have evidence-based health in the United States? What is our current capacity for obtaining good information and putting it to use? How could it be enhanced? Which aspects can be affected by federal policy?
- What are the relative strengths and weaknesses of the various proposals under discussion? What actions by the federal government do they call for, and how can they best be addressed?



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