CHAPTER 2

Producing comparative-effectiveness information

RECOMMENDATION

The Congress should charge an independent entity to sponsor credible research on comparative effectiveness of health care services and disseminate this information to patients, providers, and public and private payers.

COMMISSIONER VOTES: YES 15 • NO 0 • NOT VOTING 0 • ABSENT 2

CHAPTER 2

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Chapter summary

For the past several decades, the United States has spent an expanding share of its resources on health care. In 1960, national health expenditures made up about 5 percent of gross domestic product. That share had grown to 16 percent by 2004, and CMS projects that it will make up 20 percent by 2015 (Borger et al. 2006). Even though substantial resources are devoted to health care in the U.S., the value of services furnished to patients is often unknown.

There is not enough credible, empirically based information for health care providers and patients to make informed decisions about alternative services for diagnosing and treating most common clinical conditions. Many new services disseminate quickly into routine medical care with little or no basis for knowing whether they outperform existing treatments, and to what extent.

Comparative-effectiveness analysis compares the relative value of drugs, devices, diagnostic and surgical procedures, diagnostic tests, and medical services. By value, we mean the clinical effectiveness

In this chapter

of a service compared with its alternatives. Comparative-effectiveness information has the potential to promote care of higher value and quality in the public and private sectors.

Comparative information would help patients and providers become better informed and make value-based decisions. Most public payers—including Medicare—and private payers do not encourage patients or providers to consider the value of a service when making health care decisions. Information about the value of alternative health strategies might improve quality and reduce variation in practice styles. Use of comparative-effectiveness research might improve health but will not necessarily reduce spending. Many effective treatments are underused, and effectiveness research might encourage their greater and more appropriate use (McGlynn et al. 2003). On the other hand, comparative-effectiveness research might reduce spending if, among a set of clinically comparable services, less costly services replace more costly services.

Although several public agencies conduct comparative-effectiveness research, it is not their main focus. For private-sector groups, conducting this type of research is costly. Because it is a public good, the benefits of comparative effectiveness—when it is publicly available—accrue to all users, not just to those who pay for it. Researchers have shown that some industry-sponsored studies are biased. In addition, some health plans have expressed reluctance to use comparative-effectiveness information for fear of litigation.

Consequently, the Commission concludes that the Congress should establish an independent entity whose sole mission is to produce and provide information about the comparative effectiveness of health care services.

Recommendation

The Congress should charge an independent entity to sponsor credible research on comparative effectiveness of health care services and disseminate this information to patients, providers, and public and private payers.

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Since the information can benefit all users and is a public good, a federal role is necessary to produce the information and make it publicly available.

Such an entity would:

- be independent and have a secure and sufficient source of funding;
- produce objective information and operate under a transparent process;
- seek input on agenda items from patients, providers, and payers;
- re-examine comparative effectiveness of interventions over time;
- disseminate information to providers, patients, and public and private payers; and
- have no role in making or recommending coverage or payment decisions for payers.

There are different ways to carry out a federal role. The Commission prefers a public–private option, to reflect that all payers and patients will gain from comparative-effectiveness information. Funding could come from some public and some private sources or from all public sources. An independent board of experts should oversee the development of a research agenda and ensure that the research is objective and methodologically rigorous.

The entity's primary mission is to sponsor studies that compare the clinical effectiveness of a service with its alternatives. While cost effectiveness is not a primary mission, the Commission does not rule it out. In the simplest case, cost may be an important factor to consider for two services that are equally effective in a given population. But even when clinical effectiveness differs, it may be important for end users to be aware of costs. We emphasize that the entity would not have a role in how public and private payers apply this information—that is, coverage or payment decisions. Instead, it would produce and disseminate comparative-effectiveness information to purchasers, providers, and patients who would then decide how to use it.

The Commission envisions that the entity would contract out most of the research to outside groups, including existing governmental agencies, with

experience conducting comparative-effectiveness studies. Thus, a federal role need not result in a large expansion of the government. To ensure that its research is credible, the entity would collaborate with other researchers to help establish high standards for the methods used to conduct comparative-effectiveness studies.

Widespread use of the information will depend on the credibility of the entity conducting the studies. Operating under a transparent process and providing a public forum for stakeholders to critique ongoing work will enhance the credibility of the research. Because comparative effectiveness is a public good, the entity's agenda should reflect priorities of public and private groups and encompass all patient groups.

Disseminating the research findings to a wide audience will be an important function of the entity; it should not be treated as a minor activity to be undertaken after studies are completed. The entity should communicate its findings to reach audiences with different levels of sophistication. ■

The United States needs more credible comparative information sponsored by an independent entity

Comparative-effectiveness information would help patients and health care providers become informed and make value-based decisions (see text box, p. 34, for more information on comparative-effectiveness analysis). It might also help CMS and other public and private payers formulate better payment policies. The United States does not have an independent entity whose sole mission is to sponsor and disseminate information about services' comparative effectiveness. Although manufacturers do sponsor research on comparative effectiveness, it does not always focus on populations with multiple comorbidities and older and disabled populations. In addition, researchers have shown that some industry-sponsored studies are biased.

More comparative information could help support better decision making by providers and beneficiaries

Changes in technology are a major driver of health care spending, but public and private payers often incur high spending for services whose effectiveness is unknown. Providers and payers frequently do not know the extent to which the increased use of new, costly services improves patients' outcomes. Providers lack enough scientific evidence to determine the likelihood of patients having improved outcomes with a certain course of treatment. In addition, scant scientific evidence is available to help identify which types of patients are most likely to benefit from a service.

Many new services disseminate quickly into routine medical care without providers knowing whether they outperform existing treatments, and to what extent. For example, a recent study showed that inexpensive diuretics may control hypertension as effectively as expensive calcium-channel blockers (ALLHAT 2002). In other cases, providers do not discover side effects of a service until it has diffused into medical practice.[1]

The regulatory process of the Food and Drug Administration (FDA) for approving new technologies does not in general generate evidence that shows a service's effectiveness relative to its alternatives.[2] Most manufacturers conduct studies (referred to as phase III studies) that show the efficacy and safety of their drug or biologic relative to a placebo (inactive) agent. The FDA requires information about a drug's or biologic's effectiveness and safety relative to its alternatives only if the manufacturer wants to claim that its product is superior. For devices, the FDA requires safety and effectiveness information only for high-risk devices, such as stents, that pose a significant risk of illness or injury to patients.[3] Finally, for new diagnostic and surgical procedures, less clinical information is available because the FDA does not review their safety and effectiveness.

Even for products approved by the FDA, little information is available about their long-term safety and effectiveness. Phase III clinical studies do not typically provide this information for drugs or devices because manufacturers usually conduct the studies over a relatively short time with a relatively small number of patients. Thus, long-term side effects may go undetected during phase III studies (Hunter 2006). In addition, the safety and efficacy of products in patients with conditions or comorbidities not included in phase III studies are unknown. Some clinical studies may be limited, excluding older patients and those with multiple illnesses. In addition, after the FDA approves a product, providers can prescribe it off-label—that is, to patients with conditions not evaluated in a clinical trial.

The FDA has limited authority to require that manufacturers conduct postmarketing surveillance studies (GAO 2006). Postmarketing studies can either be required of or agreed to by a manufacturer after the FDA has approved its product for marketing.[4] The FDA may request that a manufacturer conduct postmarketing studies to provide additional information on how a drug works in expanded patient populations or to identify safety issues that occur rarely or in special patient populations. The agency can require that manufacturers conduct postmarketing studies only for drugs that: (1) the FDA approved under the accelerated approval program because they are used to treat life-threatening illnesses, (2) providers prescribe to children, or (3) the FDA approved without information about their efficacy in humans.

Once the FDA approves a drug, few manufacturers initiate further studies that examine its: (1) long-term safety, (2) effectiveness in patients not included in the approval clinical trials, or (3) effectiveness relative to its alternatives. Manufacturers spent 0.3 percent of sales on postmarketing studies in 2003 compared with 15.6 percent of sales on research and development, which includes premarketing studies (Ridley et al. 2006). Between 2002 and 2006, the proportion of postmarketing commitments—studies that manufacturers are required to conduct or have agreed to conduct—that were on

Defining comparative effectiveness

Comparative-effectiveness analysis evaluates the relative effectiveness, safety, and cost of medical services, drugs, devices, therapies, and procedures used to treat the same condition (AcademyHealth 2005). Effectiveness implies the "real-world" performance of clinically relevant alternatives provided to patients with diverse clinical characteristics in a wide variety of practice settings.

The outcomes that researchers assess in comparative-effectiveness studies may include:

- clinical outcomes, including traditional clinical endpoints, such as mortality and major morbidity;
- functional endpoints, such as quality of life, symptom severity, and patient satisfaction; and
- economic outcomes, including the cost of health care services and cost effectiveness.

Some comparative studies only contrast the clinical and functional outcomes of alternative treatments while others also compare cost and assess cost effectiveness. An example of a comparative-effectiveness study is the National Emphysema Treatment Trial in which the National Institutes of Health compared lung-volume-reduction surgery to medical therapy for patients with severe emphysema (National Emphysema Treatment Trial Research Group 2003). This study concluded that surgery increases the chance of improved exercise capacity but does not confer a survival advantage over medical therapy. It also concluded that the cost effectiveness for surgery compared with medical therapy was relatively unfavorable because of the high costs of the surgical procedure and the hospital stays during the first few months after surgery.

Researchers use two basic approaches to conduct comparative-effectiveness studies. In trial-based studies, they conduct a clinical trial and collect information on a wide variety of patient outcomes. Researchers often call these studies "practical clinical trials." Alternatively, in review-based studies, researchers combine evidence from existing trials, studies published in the scientific literature, and other secondary data sources such as administrative claims data to answer the research questions. Practical clinical trials are more costly to conduct than review-based studies.

Researchers can use multiple approaches to assess the comparative effectiveness of a given service. For example, they might first analyze existing published clinical evidence and conduct studies using secondary data sources. Conducting head-to-head trials will be necessary for services that lack sufficient evidence in the literature and with outcomes that secondary data sources do not collect, such as tumor growth in cancer patients. To evaluate the effectiveness of services in different patient populations and to assess changes in the effectiveness of services over time, researchers may need to conduct more than one head-to-head trial.

Cost-effectiveness analysis provides information about a service's value relative to its alternatives. It synthesizes functional, clinical, and economic data to allow users to trace all the consequences of a particular decision. Researchers assess cost effectiveness by quantifying the incremental net health benefits (e.g., reduced mortality) and economic costs of alternative services. They calculate a cost-effectiveness ratio by dividing the incremental costs by the incremental benefits. Researchers refer to services with a smaller cost-effectiveness ratio as being more cost effective than those with a larger ratio. ■

schedule ranged from 15 percent to 21 percent of all commitments for drugs and 24 percent to 46 percent of all commitments for biologics (FDA 2007c, 2006, 2005, 2004, 2003). During this same time period, the proportion of postmarketing commitments that manufacturers had not yet started (pending) ranged from 61 percent to 71 percent of all commitments for drugs and 24 percent to 37 percent of all commitments for biologics (FDA 2007c, 2006, 2005, 2004, 2003).[5] The Government Accountability Office found that the FDA lacked clear and effective processes

for making decisions about, and providing management oversight of, postmarket drug safety issues (GAO 2006).

Patients have some information about differences among health care providers and the prices they charge but often they have little or no information about how well different treatments work. CMS and some private payers post information about the quality of care certain providers furnish but do not disseminate information to consumers on the effectiveness of alternative medical services. Often patients cannot make informed decisions rationally because the information on which to base the decision does not exist or is not understandable. Often, they rely on their health provider to decide for them (Slutsky 2007).

As copayments and deductibles rise, patients may become more value conscious and their demand for comparative information may increase. For example, enrollees in consumer-directed health plans are more likely to identify and consider treatment alternatives and ask providers about cost than traditionally insured patients (McKinsey & Company 2005). Fronstin and Collins reported that patients in either high-deductible or consumer-driven health plans are more likely to use information about quality and cost than patients in comprehensive health plans (Fronstin and Collins 2005). Nonetheless, little information is available to patients about the effectiveness of treatment alternatives. Even when it is available, the lack of standardization in measurement and reporting across treatments and providers poses a challenge to patients trying to use the information (Buntin et al. 2006).

Comparative information could help CMS make better policies

In making national coverage determinations, CMS considers the clinical effectiveness of a service, but the clinical evidence is often for a younger population rather than for the elderly and disabled. As mentioned earlier, phase III clinical trials that manufacturers conduct to obtain FDA approval do not always demonstrate long-term safety and effectiveness in all patient populations who will eventually receive the service. In addition, evidence about the effectiveness of the service compared with its alternatives is infrequently available. CMS rarely uses clinical information to set payments.

Some researchers contend that CMS needs to base its payment decisions on more complete clinical evidence when dealing with costly new services (Redberg 2007). Investment in building a process for conducting comparative-effectiveness studies could lead to future use of this information in Medicare's payment policies. Researchers have suggested several ways for CMS to use comparative-effectiveness information in the payment process including:

- Creating a tiered payment structure that pays providers more for services that show more value to the program;
- Creating a tiered cost-sharing structure that costs patients less for services that show more value to the program;
- Using the cost-effectiveness ratio to inform the payment level;
- Not paying the additional cost of a more expensive service if evidence shows that it is clinically comparable to its alternatives; and
- Requiring manufacturers to enter into a risk-sharing agreement, which links actual beneficiary outcomes to the payment of a service based on its comparative effectiveness. Manufacturers might rebate the Medicare program for services that do not meet expectations for their effectiveness (Chernew et al. 2007, MedPAC 2006).

Medicare might use comparative-effectiveness information to prioritize pay-for-performance measures, target screening programs, or prioritize disease management initiatives. A pay-for-performance program could link providers' bonuses to the provision of services that are clinically effective and of high value. Medicare could consider comparative effectiveness when choosing measures for pay-for-performance programs; there are usually more potential measures than are practical to use.

Finally, Medicare's national coverage process does consider a service's clinical effectiveness but not its cost effectiveness or value. The coverage process may not be the area to begin to use cost-effectiveness information. Stakeholders raised many concerns when CMS tried to use cost-effectiveness information in the national coverage process (MedPAC 2005). Rigid use of cost-effectiveness information in the coverage process may not be consistent with Americans' fear of limits set by public and private organizations and interest in access to new medical technology (Neumann 2004).

Comparative research sponsored by public and private entities

Private entities assessing comparative effectiveness include health plans, pharmacy benefit managers, and manufacturers, but none systematically produces and publicly reports the information. Conducting this type of research is costly and, when it is publicly available, its benefits accrue to all, not just to those who pay for it. In addition, some health plans do not use the information because of concerns about litigation. Some researchers have shown that clinical and review studies sponsored by manufacturers may contain biases that affect the design of the study, methods, transparency, and results. These critics postulate that funding a study influences the outcomes reported in the study (Peppercorn et al. 2007, Heres et al. 2006). These findings color public confidence in the conclusions.

There is no comprehensive federal effort to conduct comparative-effectiveness studies designed to meet the needs of patients, providers, and payers. Conducting comparative-effectiveness studies is not the primary focus of any agency within the Department of Health and Human Services, although the following agencies generate this information:

- CMS reviews and collects information about a service's clinical effectiveness to help guide its national coverage decisions. On occasion, CMS requests help from the Agency for Healthcare Research and Quality (AHRQ) and the National Institutes of Health (NIH) to assess a service's clinical and cost effectiveness.
- AHRQ conducts systematic reviews of the literature to compare the clinical effectiveness of alternative services (see text box). While these reviews do not include cost-effectiveness analysis, the prices of the comparative services are included in some reviews.[6] For other projects, AHRQ has sponsored and conducted research examining patients' outcomes, health care costs, and cost effectiveness.
- NIH is the largest sponsor of clinical trials that compare alternative treatments.

The FDA does not look at the clinical or cost effectiveness of a service relative to its alternatives. As mentioned earlier, the FDA typically reviews a service's efficacy and safety compared with a placebo that manufacturers obtain from planned clinical trials. Table 2-1 (p. 38) summarizes the efforts and uses of clinical- and cost-effectiveness information by selected U.S. and international groups.

CMS's efforts

CMS assesses the clinical effectiveness of services when making national coverage decisions. In the past, the agency based these assessments primarily on reviewing available literature about the service. CMS is beginning to gather information about services' clinical effectiveness through registries and clinical trials for services the agency might not have covered in the past because of insufficient data about the service's clinical value. CMS refers to this approach as coverage with evidence development. In some cases, CMS supplements its research by sponsoring outside groups, such as NIH, to conduct head-to-head trials and AHRQ and the Medicare Evidence Development & Coverage Advisory Committee (MedCAC) to conduct and review technology assessments. A technology assessment studies the medical and economic implications of the development, diffusion, and use of services. MedCAC advises CMS on whether a service is reasonable and necessary under Medicare by reviewing and evaluating medical literature, reviewing technology assessments, and examining data and information on the effectiveness of the service under consideration.[7] CMS then uses these recommendations to determine Medicare's coverage policies for the service.

CMS does not consider clinical information in its payment process, with few exceptions. CMS uses patients' anemia status when paying for erythropoietin for patients with end-stage renal disease on dialysis. In addition, the agency uses clinical information to determine when new technologies qualify for add-on payments under the inpatient hospital prospective payment system and pass-through payments under the outpatient hospital prospective payment system.

CMS does not routinely assess a service's cost effectiveness in its coverage or payment process. The agency twice considered using information on cost effectiveness or value for national coverage decisions. Stakeholders raised a number of concerns about its use including that: (1) it would impair beneficiaries' access to care and lead to rationing, (2) the methods researchers use to conduct the analyses are not sufficiently robust, and (3) it might slow innovation of new health care services. The Commission's June 2005 and June 2006 reports discuss these issues (MedPAC 2006, 2005).

Agency for Healthcare Research and Quality sponsors comparative clinical effectiveness research

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) authorized the Agency for Healthcare Research and Quality (AHRQ) to synthesize, sponsor, and disseminate comparative clinical-effectiveness research. Specifically, Section 1013 of the MMA charges AHRQ with conducting research on the: (1) appropriateness, comparative clinical effectiveness, and outcomes of services; and (2) organization, management, and delivery of care.

To fulfill this mandate, AHRQ established the Effective Health Care Program, a coordinated and transparent program that funds:

- thirteen evidence-based practice centers to perform systematic evidence reviews of the comparative effectiveness of alternative interventions;
- the DEcIDE (Developing Evidence to Inform Decisions about Effectiveness) Network to develop new evidence on effectiveness and comparative effectiveness of health care services using existing data sources, such as registries and electronic health records;
- eleven centers to perform research on the safe and effective use of drugs, biologics, and medical devices; and
- John M. Eisenberg Clinical Decisions and Communications Science Center to communicate comparative-effectiveness findings to diverse audiences, hold symposia on translational issues, and provide models for translational work.

Beginning in 2005, the Congress has appropriated $15 million per year for the agency to fulfill its MMA mandate (the MMA authorized up to $50 million for this research effort). Since initiating this effort, AHRQ has completed studies on:

- the comparative effectiveness of epoetin and darbepoetin for managing anemia in patients undergoing cancer treatment,
- the effectiveness of noninvasive diagnostic tests for breast abnormalities,
- gastroesophageal reflux disease,
- renal artery stenosis,
- the comparative effectiveness of second-generation antidepressants in the pharmacologic treatment of adult depression,
- the efficacy and comparative effectiveness of off-label use of atypical antipsychotics,
- choices for pain medicine for osteoarthritis, and
- Medicare Part D plans' medication therapy management programs.

In addition, 39 studies are ongoing under AHRQ's Effective Health Care Program. The Eisenberg Center has held its first symposium on communicating risk to consumers, and a series of papers on this topic are awaiting publication in a peer-reviewed journal. ■

AHRQ'S efforts

AHRQ compares the clinical effectiveness of alternative treatments under a provision in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) that mandated the agency to conduct and support research with a focus on outcomes, comparative clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services. The text box describes AHRQ's comparative-effectiveness research activities. To fulfill the MMA mandate, AHRQ has: (1) put processes in place to select topics for analysis, review and synthesize the scientific literature, and obtain input from the public and private sectors; (2) developed the infrastructure to conduct comparative-effectiveness research and disseminate the information to providers and patients; (3) completed 8 effectiveness studies, with more than 30 studies in progress; and (4) disseminated the research findings to end users.

Outside of the MMA mandate, AHRQ has conducted studies examining both the clinical effectiveness and cost

TABLE 2–1

Roles of selected organizations in conducting and using information about clinical and cost effectiveness

Organization	Type of analysis	Description of analysis
CMS	Requires and collects clinical-effectiveness information for some services Sponsors and uses comparative-effectiveness studies and technology assessments*	Uses clinical information when making national coverage decisions. Limited use in payment decisions (e.g., erythropoietin for dialysis patients). Beginning to gather information about some services' clinical effectiveness in the national coverage process—coverage with evidence development—through registries and practical clinical trials.
AHRQ	Conducts and sponsors comparative-effectiveness reviews, technology assessments, and CEAs	Has developed infrastructure to conduct comparative-effectiveness reviews of health care services from the literature. Contracts with 13 evidence-based centers to conduct reviews and technology assessments. Has conducted CEAs for CMS for selected services (e.g., fecal occult blood tests). Has sponsored CEAs conducted together with clinical trials.
NIH	Conducts comparative-effectiveness studies	Largest federal sponsor of clinical head-to-head trials.
FDA	Requires information about a service's efficacy and safety	Reviews information about the efficacy and safety of drugs, biologics, and devices for marketing in the U.S.; most manufacturers conduct trials comparing a service with a placebo (an inactive treatment). Does not require cost-effectiveness information. May request manufacturers to collect clinical data after a service's approval (i.e., postmarketing surveillance studies).
VA	Conducts and uses clinical and comparative-effectiveness studies and CEAs	Requires CEAs from manufacturers of drugs that have small differences in quality but large differences in cost compared with their alternatives. Uses information in the formulary decision-making process. Cooperative studies program conducts clinical research including comparative-effectiveness trials. Program on health services research and development examines the organization, delivery, and financing of health care. Research on a wide variety of services ranging from assessing the cost effectiveness of ICDs to improving safety culture and outcomes in VA hospitals.
Oregon University's Drug Effectiveness Review Project	Sponsors comparative-effectiveness studies of drugs	Conducts comparative-effectiveness reviews to obtain effectiveness comparisons between drugs. Collaborative effort of 14 organizations. Does not review information about cost effectiveness.
Washington state	Sponsors technology assessments	Recently signed into law a health technology assessment program to consider evidence about the safety, efficacy, and cost effectiveness of services.

Note: AHRQ (Agency for Healthcare Research and Quality), CEA (cost-effectiveness analysis), NIH (National Institutes of Health), FDA (Food and Drug Administration), VA (Department of Veterans Affairs), ICD (implantable cardioverter defibrillator), NICE (National Institute for Health and Clinical Excellence). For more description of the activities of these organizations, see Chapter 10 in the Commission's June 2006 report (MedPAC 2006).
*Technology assessments can include a review of the clinical and economic evidence about one or more services.

TABLE 2–1

Roles of selected organizations in conducting and using information about clinical and cost effectiveness (cont.)

Organization	Type of analysis	Description of analysis
Manufacturers (of drugs and devices)	Sponsor comparative-effectiveness studies and CEA	Sponsor an increasing proportion of CEAs over the years. Use information to show value of service to purchasers, determine pricing strategies, and inform marketing decisions. Also sponsor premarketing studies, comparative-effectiveness studies, and postmarketing surveillance studies.
Commercial payers/plans	Use clinical effectiveness and CEA for drugs	Plans' pharmacy and therapeutics committees use clinical effectiveness and CEA for development of drug formularies, treatment guidelines, prior authorization and step therapy requirements, and tiered copayments.
	Use information about clinical effectiveness and cost for services other than drugs	Less reliance of CEA for services other than drugs. Primarily rely on evidence about clinical effectiveness. Some consider cost by, for example, requiring use of less costly alternatives.
Blue Cross Blue Shield Evaluation Center	Conducts reviews of the clinical effectiveness of services	Examines clinical effectiveness and appropriateness of services to subscribing commercial health plans and provider groups. Does not usually assess costs or cost effectiveness.
NICE in the United Kingdom	Sponsors and uses technology assessments including CEA	An independent group that provides guidance to the National Health Service on health care services. Commissions independent academic groups to conduct technology assessments, which includes CEAs. Uses information to develop coverage policies. Uses a National Horizon Scanning Centre to identify significant new and emerging health technologies.
Canadian Agency for Drugs and Technologies in Health	Sponsors technology assessments including CEA	An independent nonprofit body funded by the federal, provincial, and territorial governments. Provides evidence-based information on services including drugs, devices, procedures, and best practices. Uses a program that alerts decision makers to upcoming services that are likely to have a significant impact on the delivery of health care in Canada. Technology Assessment Program examines clinical and cost effectiveness of drugs, medical technologies, and health systems. For drugs, reviews clinical- and cost-effectiveness information submitted by manufacturers. Recommends reimbursement options (unrestricted use, limited use, prior authorization) to provinces. Periodically conducts CEAs of a whole class of drugs and reconsiders past reimbursement decisions.
Pharmaceutical Benefits Advisory Committee in Australia	Uses CEA for drugs	An independent statutory body that makes recommendations and gives advice to the Department of Health and Ageing about which drugs should be made available as pharmaceutical benefits. Reviews information about clinical and cost effectiveness submitted by manufacturers.

Note: AHRQ (Agency for Healthcare Research and Quality), CEA (cost-effectiveness analysis), NIH (National Institutes of Health), FDA (Food and Drug Administration), VA (Department of Veterans Affairs), ICD (implantable cardioverter defibrillator), NICE (National Institute for Health and Clinical Excellence). For more description of the activities of these organizations, see Chapter 10 in the Commission's June 2006 report (MedPAC 2006).
*Technology assessments can include a review of the clinical and economic evidence about one or more services.

effectiveness of services for CMS and NIH. For example, CMS requested that AHRQ assess the cost effectiveness of drugs used to treat rheumatoid arthritis and multiple sclerosis under a MMA-mandated demonstration (CMS 2007). CMS also requests that AHRQ conduct technology assessments, such as an assessment of the use of neuroimaging techniques in evaluating breast cancer, Alzheimer's disease, and dementia. In other instances, AHRQ completed an assessment for CMS of the cost effectiveness of fecal occult blood tests. AHRQ also collaborates with NIH. On a recurring basis, AHRQ provides systematic reviews using its evidence-based practice centers for numerous groups within NIH, including the Office of Medical Application Research, the Office of Dietary Supplements, the Office of Women's Health Research, the National Cancer Institute, and the National Center for Complementary and Alternative Medicine.

Conducting comparative-effectiveness research is not AHRQ's main mission, although the agency's efforts in this area are significant. Its primary mission is to conduct and sponsor health services research—the multidisciplinary field of scientific investigation that studies how social factors, financing systems, organizational structures and processes, health technologies, and personal behaviors affect access to health care, the quality and cost of health care, and the health and well-being of the U.S. population (AcademyHealth 2005).

NIH's efforts

NIH is the largest sponsor of head-to-head trials. Researchers can structure head-to-head clinical trials comparing alternative services to include a diverse patient population, recruit patients from heterogeneous practice settings, and collect data on a broad range of health outcomes (Tunis et al. 2003). For example, NIH and CMS cosponsored the ongoing head-to-head trial comparing more frequent hemodialysis with thrice weekly (conventional) hemodialysis for patients with end-stage renal disease.

Examples of other public agencies' efforts

The Department of Veterans Affairs (VA) also sponsors head-to-head clinical trials and cost-effectiveness analyses specific to its patient population. Since 1994, the VA has required a formal cost-effectiveness analysis from manufacturers of drugs that have small differences in quality but large differences in cost compared with their alternatives (Aspinall et al. 2005). The VA routinely requests manufacturers to submit clinical and economic data using the Academy of Managed Care Pharmacy format and incorporates this information into the drug reviews used in the formulary decision-making process.

The Drug Effectiveness Review Project (DERP) at Oregon Health & Science University compares the clinical effectiveness of drugs within a given therapeutic class using information from the scientific literature. Now in its fourth year, the DERP is a self-governing collaboration of 14 states that aggregated their resources to review the clinical evidence of about 26 drug classes. The project does not look at the cost effectiveness of alternative drugs because health care costs vary from state to state. However, each state can conduct its own cost-effectiveness analysis by applying its own costs.

The private sector does not systematically produce and disseminate objective comparative-effectiveness information

Manufacturers conduct studies assessing the clinical and cost effectiveness of their products, but some researchers have critiqued these studies and raised concerns that these efforts may not always be objective and available to the public. Researchers have shown that industry-sponsored studies were significantly more likely to reach conclusions favorable to the sponsor than were non-industry-sponsored studies. Jorgensen and colleagues (2006) concluded that industry-supported reviews were less transparent, noted few reservations about methodologic limitations of the included trials, and had more favorable conclusions than reviews conducted by an independent nonprofit group (Cochrane Collaboration). Bias in drug trials is common and often favors the sponsor's product (Peppercorn et al. 2007, Heres et al. 2006, Als-Nielsen et al. 2003). Possible sources of bias in industry-sponsored trials include: (1) the dose of the drug studied, (2) the exclusion of patients from the study population, (3) the statistics and methods used, and (4) the reporting and wording of results.

Bekelman and colleagues have shown that financial relationships among manufacturers, scientific investigators, and academic institutions are widespread (Bekelman et al. 2003). Relationships between members of institutional review boards and manufacturers are common and members sometimes participate in decisions about protocols sponsored by companies with which they have a financial relationship (Campbell et al. 2006). Researchers have also raised concerns that manufacturers

influence the adoption of clinical guidelines that serve their own financial goals (Eichacker et al. 2006).

Pharmacy benefit managers, health plans, and other large providers (e.g., hospitals) consider a service's clinical effectiveness, cost, and cost effectiveness, particularly for their drug formularies, but do not necessarily make their evaluations public. These groups often focus on proprietary internal studies related to their health care practices (Kupersmith et al. 2005). Private-sector efforts do not typically focus on patients who are 65 years or older, disabled populations, or patients with end-stage renal disease—the populations of interest to Medicare. Few private-sector groups systematically produce clinical- and cost-effectiveness information and make it available to the public. One exception is the Technology Evaluation Center (TEC) established by Blue Cross Blue Shield Association, which posts reports on the Internet. The TEC relies on reviewing the existing literature to compare the clinical effectiveness of alternative services.

Concerns about liability might affect some private plans' use of cost-effectiveness information in their decision-making process (Jacobson and Kanna 2001). In one survey of health plan officials, most respondents said they approved equally effective but costlier treatments for fear of litigation (Singer et al. 1999). Some health plans reluctantly agreed to cover high-dose chemotherapy with autologous bone marrow transplant for breast cancer partly in response to the threat of litigation, despite its high cost and the lack of evidence that it was effective (Mello and Brennan 2001).

A public role is necessary in comparative-effectiveness research

Some researchers have noted that comparative effectiveness is a public good (Wilensky 2006, Kupersmith et al. 2005, Reinhardt 2004, Perry and Thamer 1999). An item is a public good if it demonstrates:

- *"Nonexcludability"*: Once comparative-effectiveness information is publicly available, it is difficult to stop other groups from using the research free of charge.
- *"Nonrivalness"*: One group's use of the information does not detract from its use by other groups.

Economic theory argues that the private sector will underproduce goods or services (or in this case information) that meet this definition and that a government role is necessary to ensure that a sufficient supply is available. Conducting this type of research is costly and, when it is publicly available, its benefits accrue to all, not just to those who pay for it (Bloche 2006, Kupersmith et al. 2005, Neumann et al. 2005). Although health plans have some of the clinical data to conduct more of this research, they lack incentives to support it at the needed levels.

Increasing the capacity to produce comparative-effectiveness information

Little objective, credible, and high-quality information is publicly available that compares the effectiveness and costs of health care services furnished to patients. There is no independent entity in the U.S. whose sole mission is to compare the benefits, risks, and costs of alternative services and make this information publicly available. Comparative-effectiveness research is costly to generate and sponsors have difficulty recouping the costs of producing the research because other users will not pay to use the research once it is publicly available. Consequently, the Commission concludes that a federal role is necessary to help increase the capacity to generate comparative-effectiveness information.

RECOMMENDATION

The Congress should charge an independent entity to sponsor credible research on comparative effectiveness of health care services and disseminate this information to patients, providers, and public and private payers.

RATIONALE

More information on the comparative effectiveness of health care services could increase the value of health care spending. Public and private payers could use the information to help inform their payment policies and coverage decisions. Current public and private organizations do not produce enough objective and credible information about which services work best and for which populations. This information has the potential to improve quality of care and reduce variations in health care utilization.

IMPLICATIONS

Spending

- Increasing the capacity to examine the comparative effectiveness of health care services would likely increase federal administrative spending relative to current law.

Beneficiary and provider

- Information on the comparative effectiveness of health care services could improve decision making by patients, providers, and payers.

To improve the evidence base on the effectiveness of health care services, the United States needs an impartial entity whose mission is to independently develop evidence about the comparative effectiveness of alternative treatments, including drugs, medical devices, surgical and diagnostic procedures, and medical services. The entity's functions would include systematically reviewing existing evidence, sponsoring or conducting new studies, and reporting the information to patients, providers, and public and private payers in a user-friendly format. Such an entity would:

- be independent and have a secure and sufficient source of funding;
- produce objective and credible information;
- operate under a transparent process and establish standardized and credible methods;
- seek input on agenda items from patients, providers, and payers;
- re-examine comparative effectiveness of interventions over time;
- disseminate information to providers, patients, decision support vendors, associations, and federal and private health plans; and
- have no role in making or recommending either coverage or payment decisions for public or private payers.

The entity's primary mission is to sponsor studies that compare the clinical effectiveness of a service with its alternatives. While cost effectiveness is not a primary mission, the Commission does not rule it out entirely. In the simplest case, cost may be an important factor to consider for two services that are equally effective in a given population. But even when clinical effectiveness differs, it may be important for end users to be aware of costs. We emphasize that the entity would not have a role in how public and private payers apply this information—that is, coverage or payment decisions. Instead, it would produce and disseminate comparative-effectiveness information to purchasers, providers, and patients who would then decide how to use it.

To carry out its activities effectively, the entity needs to develop a clear rationale for selecting the services to study, use rigorous methods and the best scientific evidence to conduct its research, and provide for an opportunity for comment and participation from different constituent groups, including patients, providers, specialty groups, and manufacturers. Setting up a transparent process that is understandable, clear, and documented to produce objective research will be important; people might not use the research if they consider the process subjective and the results biased. The entity should help develop the "gold standard" of research methods used to conduct comparative-effectiveness studies by collaborating with other researchers with expertise in this field.

Along with considering the functions of the entity, policymakers will also need to consider its characteristics. The remainder of this chapter describes options for configuring and financing an entity that produces comparative-effectiveness information and their advantages and disadvantages. The Commission has not yet reached a conclusion about the best approach; we intend to continue looking at the pros and cons of different options. Policy analysts have proposed different options, including placing such an entity in an existing or new federal agency, a public–private entity, or a private entity. Some policy analysts have also proposed including a board—a panel of experts—as a way to promote the entity's transparency. The entity could receive funding from voluntary or mandatory federal sources, private sources, or some combination of the two.

The independence and stability of the entity will largely depend on its governance and funding. For example, an entity that relies on federal appropriations might be more susceptible to political pressures than an entity with mandatory funding (e.g., from the Medicare trust fund). Each year, the Congress considers the spending for services financed from appropriations; by contrast, the statute guarantees spending for services financed from mandatory sources. Even so, entities with a mandatory funding source face some political pressure because the Congress always has the option to alter their funding. Private groups who voluntarily fund the entity might attempt to control the entity's research agenda. In addition, the entity's governance and funding will affect some constituents' perception of the research it produces. Some

stakeholders want an entity that is close to or within the government while others are concerned about too much government involvement. Finally, the functions of the organization should help steer its structure. The entity's staff will need to be proficient in designing comparative-effectiveness research but can take advantage of experienced public agencies and independent private groups by contracting studies to them.

Functions and activities of a comparative-effectiveness entity

Policymakers should consider numerous process issues when developing the capacity to sponsor and disseminate information about the comparative effectiveness of alternative health care services. The rest of this section, based on reports submitted by Moon and by Neumann and Cohen, discusses some of the process issues to consider (Moon 2007, Neumann and Cohen 2007).

Identifying research priorities

The Commission envisions that the entity's research agenda is broader than Medicare; the agenda would include services important to all patient groups. For the entity's research to be relevant, its users—patients, providers, and public and private payers—should help inform the agenda. To help develop its process for setting research priorities, the entity could review the criteria used by existing organizations that conduct comparative-effectiveness research, including AHRQ and the National Institute for Health and Clinical Excellence in the United Kingdom (NICE).

For its comparative clinical-effectiveness program (Effective Health Care Program), AHRQ's selection criteria include:

- the severity, incidence, and prevalence of the condition;
- the uncertainty about the service and the availability of data to support a systematic review and analysis of the topic;
- the potential impact of the research for reducing clinically significant variations in the prevention, diagnosis, treatment, and management of a condition or in the use of a service; and
- the topic's policy relevance to Medicare, Medicaid, and other federal health care programs.

In addition, AHRQ's website provides an opportunity for stakeholders—patients, providers, policymakers, health care scientists, clinical practice organizations, quality improvement organizations, and health care plans—to suggest topics for future research (AHRQ 2007a).

NICE uses similar criteria in identifying topics for study. Specifically, NICE considers: (1) the burden of the disease (e.g., its prevalence and mortality), (2) cost impact, (3) policy importance, and (4) whether the service's use varies across the country. Like AHRQ, NICE's website allows the public to suggest a topic for future study; NICE also meets with health professionals, patients, and policymakers. Finally, the National Horizon Scanning Centre (NHSC) provides information on new and emerging technologies, including different uses of existing technologies, that might require NICE's evaluation (NHSC 2007). The scope of its activity includes pharmaceuticals, devices, diagnostic tests and procedures, surgical and other interventions, rehabilitation and therapy, public health, and health promotion activities. NHSC produces briefings that outline what the technology is, its likely patient group, the current treatment alternatives, the level and amount of research evidence available, and a prediction of its relevance both clinically and to the U.K.'s National Health Service.

Other researchers have developed methods to set priorities for evaluative research by quantifying the gains from research. Phelps and Parente, for example, developed an index of expected gains from research, which incorporates spending levels for a particular condition and the degree of variation in intervention strategies to establish a first-cut priority list (Phelps and Parente 1990). The researchers use variation to suggest the degree of uncertainty associated with a particular technology and thus the opportunity for research to affect practice patterns. Areas with high spending and large variation receive higher priority.

Designing safeguards to ensure that private funding sources do not affect study results

If private groups with a vested interest in the outcome of the research help fund the research entity, it is important to ensure that they cannot influence the study results. Otherwise, some stakeholders may not consider information the entity produces to be objective. As mentioned earlier, researchers have shown that some private groups that fund clinical- and cost-effectiveness research affect the objectivity of the research and the likelihood of publishing the findings.

No single private group should dominate the process or bias the research. Policymakers might consider limiting the amount any private group can contribute to funding the entity. Requiring all private groups to fund the entity might ensure that no single private group can influence the entity's research. For example, assessing a small fee on all private health-related groups—including manufacturers, payers, and providers—would provide for broad-based funding rather than funding limited to one group (Reinhardt 2004). Another option is for a nonprofit foundation to distribute private contributions to the entity conducting comparative-effectiveness research. We discuss some pros and cons of different funding approaches later in the chapter.

Producing unbiased information

Some clinical- and cost-effectiveness studies show biases of investigators and their sponsors. As mentioned earlier, industry-sponsored analyses tend to report more favorable results than non-industry-sponsored studies (Peppercorn et al. 2007). Ensuring that analysts work independently and objectively will be a critical issue. Ethics rules might help ensure that analysts working on behalf of the entity avoid involvement in any real or apparent conflict of interest. Ethics rules would address issues such as whether analysts can accept compensation from outside sources and requirements for regularly reporting financial interests.

Scope of activities

Whether the entity is new or an existing group, it will need to conduct and sponsor comparative-effectiveness research. This section describes the scope of activities that we envision an entity would carry out.

Comparative-effectiveness research involves synthesizing existing data and research from the scientific literature. Another option is to design studies that use administrative claims data from public and private payers. There may be opportunities to use databases developed by providers and other private-sector groups. In the future, electronic medical records might become a source of important data for comparative-effectiveness research if providers widely adopt information technology. When existing data sources do not provide sufficient information on comparative effectiveness, the entity will need to sponsor head-to-head clinical trials to generate the data needed to assess comparative effectiveness. Researchers could collect information on patients' functional and clinical outcomes as well as measures of value and resource use.

The entity will need in-house staff with experience in designing and conducting comparative-effectiveness research. To avoid duplicating expertise, the entity could contract out research to federal and state agencies and research groups with experience conducting comparative-effectiveness research and communicating the information. AHRQ, for example, supports 13 evidence-based practice centers that review relevant scientific literature to produce evidence reports and technology assessments (Clancy et al. 2004).[8]

The research the entity sponsors will need to examine comparative effectiveness in relevant patient populations and in different patient care settings. Because the health care delivery system might affect the usefulness of some services, it will also be important to consider the effectiveness of services provided under different delivery systems.

The entity will need to establish guidelines for studies that it conducts and that it contracts out to public and private research groups. Work conducted by other U.S. and international organizations can help inform this process. It will not be necessary to reinvent mechanisms that are now working well. Consensus on the entity's methods from the research community is essential to establish the entity's credibility.

As the key U.S. entity focused on comparative-effectiveness research, the entity could have other responsibilities apart from conducting or sponsoring comparative-effectiveness research. For example, the organization could also sponsor conferences or scientific symposia on a host of issues surrounding the use of comparative-effectiveness analysis, including methodologic questions.

The organization should be aware of the comparative-effectiveness research done by other organizations. As mentioned earlier, the research of other groups, such as AHRQ, CMS, NIH, and the VA, may overlap with the entity's comparative-effectiveness research agenda. Coordination with public and private groups would ensure that agencies do not duplicate research.

Transparency and stakeholder input

It will be important for the organization to have a transparent process and to obtain input from stakeholders, including manufacturers. For example:

- AHRQ posts draft reports online and accepts public comments for about four weeks. AHRQ then considers public comments for incorporation into the final report.

- NICE publishes its studies on its website at several stages, including the scope of study, the literature review, and draft guidance. Moreover, NICE meets with all stakeholder groups, including relevant patient organizations, doctors, pharmaceutical companies, and a citizens' council.

Re-examining a service's effectiveness over time

For some services, the entity will need to re-examine their clinical and cost effectiveness as new information becomes available. Reasons for a service's re-evaluation include its use in populations not examined by the original study, new information about the service's clinical effectiveness, and a change in practice patterns that affects the use or cost of the service. Moreover, it will be important to validate models as new clinical evidence emerges. Some researchers have found that predictions from models were more optimistic than results in subsequent clinical trials demonstrated.

Disseminating information to all users

It will also be important to disseminate the findings from the comparative-effectiveness research to multiple audiences of different levels of sophistication, in culturally appropriate and consumer-friendly ways. Disseminating the findings is not a minor activity and should not be isolated from the review process. Rather, the entity needs to view dissemination as a crucial component of developing the capacity to produce comparative-effectiveness research. Otherwise, efforts to circulate the findings may be disorganized and haphazard and the findings may not reach all potential users. Matchar and colleagues concluded that failing to integrate research and dissemination goals could derail efforts to translate research into meaningful action, while actively integrating research and dissemination goals can promote more effective dissemination (Matchar et al. 2005). Thus, the entity should consider the tasks involved in disseminating the results when it initiates a study.

It will be important to tailor the reporting of the study and its results to its audience. Getting the input of consumers and providers early in the process might be valuable in designing materials that will reach all potential users. Information will be useful to patients only if the entity provides the results in a format that is concise and easy to understand. AHRQ has experience in developing information that targets multiple users. For example, the agency developed separate guides for consumers and clinicians that summarize in plain language the effectiveness, risks, and prices of the different drug treatments for osteoarthritis (AHRQ 2007b). AHRQ based both guides on the findings of its comparative-effectiveness review of analgesics for osteoarthritis that it carried out under the MMA mandate to conduct comparative-effectiveness research.

Researchers will need to translate the technical results from comparative clinical- and cost-effectiveness analysis to plain language that patients and providers can understand. Pearson developed a framework for displaying information about a service's comparative clinical effectiveness and value in a user-friendly fashion. For each service, a grid ranks the service's clinical effectiveness as superior, incremental, comparable, promising, or uncertain and ranks its comparative value as superior, reasonable, or poor (Health Industry Forum 2006).

Training potential users—including patients, providers, professional associations, and schools of medicine—is an important function to ensure that the information is used. The entity could help to set up the process by developing standards for training and technical assistance, which can take many forms, including face-to-face, by video and teleconference, or via the Internet. The goal of training and technical assistance is to foster widespread adoption of evidence-based practices. Training and technical assistance may not be a direct responsibility of the entity, but the entity could contribute to this important activity.

Developing human capital

An adequate supply of qualified researchers will be needed to conduct comparative-effectiveness research. The entity could develop programs that train investigators and institutions to do the research. For example, AHRQ provides predoctoral and postdoctoral educational and career development grants in health services research. AHRQ also provides institutional-level grants to support the planning and development of health services research in certain types of institutions. NIH also offers a wide variety of research training opportunities, including programs for postbaccalaureate, postdoctoral, medical, and dental students.

Structuring an entity to examine and report on comparative effectiveness

In this section, the Commission begins to explore the pros and cons of different ways to configure and finance the entity that produces comparative-effectiveness information. At this point, the Commission reaches no

conclusions and plans to evaluate these options in the future.

In evaluating the different governance and funding options, policymakers might consider whether: (1) users will judge the research as being objective, credible, and produced with minimal or no conflict of interest and bias; (2) the entity is independent of various stakeholders and political pressures; and (3) the entity is stable (Wilensky 2006).

Governance options

One option is to establish the entity within an existing federal agency or a new federal agency. An entity within an existing federal agency could build on the existing capacity of the agency, such as AHRQ, NIH, or CMS. Another option is to create a new agency not under an executive branch agency. Establishing an external board composed of independent experts to advise the entity about research priorities and to provide oversight for conducting research might promote transparency and the credibility of the findings.

Some constituents are concerned about creating a new bureaucracy. Others have raised concerns about placing the entity within an existing federal agency. Providers and patients may be more distrustful of the motives of an entity if an existing federal agency that will ultimately use the entity's research findings (e.g., CMS) houses the center. As mentioned earlier, stakeholders in the past had many concerns when CMS considered including cost effectiveness or value in the national coverage process, including that it would lead to rationing of care. Another disadvantage of expanding the scope of an existing federal agency is that stakeholders who do not support conducting comparative-effectiveness research could place funding for all its functions at risk. Placing an entity within the federal government could limit opportunities for private-sector funding, although the FDA does accept private funding in the form of user fees the manufacturers pay.

A public–private entity with an external board is another option to consider. For example, the Federal Reserve System (the central bank of the United States) has a unique public–private structure that enables it to operate independently within government but not independent of government. Although the Federal Reserve is required to report to the Congress on its activities, neither the president nor the Congress approves its decisions. The Federal Reserve consists of a federal agency (the Board of Governors) and private entities (12 federally chartered corporations known as Federal Reserve Banks). The Board of Governors, appointed by the president and confirmed by the Senate, represents the public sector.[9] The Reserve Banks and the local citizens on their boards of directors represent the private sector. This structure provides accountability while avoiding centralized, governmental control of banking and monetary policy (GAO 1996). Unlike most other federal commissions, the Federal Reserve is a self-financing entity; it does not receive congressional appropriations.

Other examples of public–private entities discussed by researchers for situating a comparative-effectiveness entity include federally funded research and development centers (FFRDCs) and congressionally chartered nonprofit organizations. The 37 existing FFRDCs are organizations that an executive branch agency sponsors but an academic or private organization operates and that can perform work for organizations other than the sponsoring agency (AcademyHealth 2005, CRS 2005) (Table 2-2, pp. 48–49). By contrast, congressionally chartered nonprofit organizations do not have a "parent" agency and can receive more funding from the private sector. The text box provides more information about FFRDCs, congressionally chartered organizations, and other types of public–private entities.

A public–private entity might address some stakeholders' concerns about too much federal government involvement but still provide for strong public-sector involvement and oversight. In addition, a public–private entity might provide a better balance of different perspectives than an entity that is either all public or all private. However, voluntary funding of a public–private entity would make it as susceptible to stakeholder pressures as an entity within a federal agency.

Another option is to establish a comparative-effectiveness entity within a private-sector entity—for example, a new or existing independent nonprofit group could take the lead generating comparative-effectiveness information. A private-sector entity would minimize concerns about the government's influence on the research agenda and the entity's findings. On the other hand, it would be difficult for the federal government to fund such an entity without being involved in its governance. Some stakeholders who are already uneasy about the influence of manufacturers on clinical trials and reviews might be concerned about the potential for bias if a private-sector group took the lead to generate comparative-effectiveness information.

Examples of public–private entities

Public–private (quasi-government) entities are organizations that have some legal relation or association with the federal government. The term includes many different types of organizations that share one common characteristic: They are not agencies of the federal government (CRS 2005). Researchers have considered three types of quasi-government entities for housing a comparative-effectiveness center: federally funded research and development center (FFRDC), agency-related nonprofit organization, and congressionally chartered nonprofit organization. We also describe government corporations, another public–private entity, in this text box.

FFRDCs are nonprofit private organizations that federal agencies can sponsor to achieve a long-term research need that cannot be met as effectively by using in-house or contractor resources. The first FFRDC was RAND, created by the Air Force in 1947; currently 37 FFRDCs exist (Table 2-2, pp. 48–49) (NSF 2007). Academic, nonprofit, or corporate organizations operate the centers on behalf of the sponsoring agency. FFRDCs may perform work for organizations other than the sponsoring agency; 30 percent of their funding may come from the private sector (AcademyHealth 2005).

An agency-sponsored nonprofit organization also has a legal relationship with a department or agency of the federal government, but this relationship may differ from one situation and organization to the next. Agency-sponsored nonprofit organizations have boards and can receive funding through private sources. This organization type often performs functions that the agency finds difficult to integrate into its regular policy and financial tasks. For example, the Congress established:

- The Foundation for the National Institutes of Health (NIH) to match the interests of donors—private individuals and organizations—to the needs of NIH, and
- The National Park Foundation to accept and administer gifts given to the National Park Service.

There are some 90 congressionally chartered organizations (also commonly referred to as "Title 36" corporations). The federal chartering process is honorific; these organizations do not receive direct appropriations (CRS 2005). The National Academy of Sciences, which includes the Institute of Medicine (IOM), is one example of such an organization. These organizations can accept private funds; for example, the private sector funded about one-quarter of IOM's grants and contracts in 2005.

Finally, another public–private entity is a government corporation. The Congress established government corporations to carry out business-type programs that need more autonomy and flexibility than what a conventional government agency structure provides. These organizations: (1) are predominantly of a business nature, (2) produce revenue and are potentially self-sustaining, and (3) involve a large number of business-type transactions with the public (GAO 1995). Examples of a government corporation include the Tennessee Valley Authority, the Federal Deposit Insurance Corporation, and the Pension Benefit Guaranty Corporation. ■

Funding options

Whether public or public–private, mandatory federal funding might result in the entity being more stable than if it had voluntary federal funding. One option for funding is for the Congress to appropriate funds, which would require policymakers to annually consider the priority of such research compared with other health programs. However, variations in the level of federal appropriations may reflect factors other than the priority of the research. In addition, voluntary funding could result in an unpopular report affecting the entity's budget.

Voluntary contributions from private groups—such as private plans and payers and manufacturers of drugs, biologics, and medical devices—could also be vulnerable

TABLE 2–2 **Current FFRDCs**

Sponsoring agency	FFRDC	Administrator
Office of the Secretary of Defense	Institute for Defense Analyses Studies and Analyses Federally Funded Research and Development Center	Institute for Defense Analyses
	National Defense Research Institute	RAND Corporation
	C3I Federally Funded Research & Development Center	MITRE Corporation
National Security Agency	Institute for Defense Analyses Communications and Computing Federally Funded Research and Development Center	Institute for Defense Analyses
Department of the Navy	Center for Naval Analyses	The CNA Corporation
Department of the Air Force	Lincoln Laboratory	Massachusetts Institute of Technology
	Aerospace Federally Funded Research and Development Center	The Aerospace Corporation
	Project Air Force	RAND Corporation
Department of the Army	Software Engineering Institute	Carnegie Mellon University
	Arroyo Center	RAND Corporation
Department of Energy	Idaho National Laboratory	Battelle Energy Alliance
	Los Alamos National Laboratory	Los Alamos National Security
	Sandia National Laboratories	Sandia Corporation
	Savannah River Technology Center	Westinghouse Savannah River Co.
	Ames Laboratory	Iowa State University of Science and Technology
	Argonne National Laboratory	University of Chicago
	Ernest Orlando Lawrence Berkeley National Laboratory	University of California
	Fermi National Accelerator Laboratory	Universities Research Association, Inc.
	Lawrence Livermore National Laboratory	University of California Livermore
	Princeton Plasma Physics Laboratory	Princeton University
	Stanford Linear Accelerator Center	Leland Stanford, Jr., University
	Thomas Jefferson National Accelerator Facility	Southeastern Universities Research Association, Inc.
	Brookhaven National Laboratory	Brookhaven Science Associates, Inc.
	National Renewable Energy Laboratory	Midwest Research Institute; Battelle Memorial Institute; Bechtel National, Inc.
	Oak Ridge National Laboratory	UT–Battelle, LLC
	Pacific Northwest National Laboratory	Battelle Memorial Institute

Note: FFRDC (federally funded research and development center), C3I (Command, Control, Communications & Intelligence).

Source: National Science Foundation 2007.

TABLE 2–2 **Current FFRDCs (cont.)**

Sponsoring agency	FFRDC	Administrator
National Institutes of Health	National Cancer Institute at Frederick	Science Applications International Corp.; Charles River Laboratories, Inc.; Data Management Services, Inc.; Wilson Information Services, Inc.
Department of Homeland Security	Homeland Security Institute	Analytic Services, Inc.
National Aeronautics and Space Administration	Jet Propulsion Laboratory	California Institute of Technology
National Science Foundation	National Astronomy and Ionosphere Center	Cornell University
	National Center for Atmospheric Research	University Corporation for Atmospheric Research
	National Optical Astronomy Observatories	Association of Universities for Research in Astronomy, Inc.
	National Radio Astronomy Observatory	Associated Universities, Inc.
	Science and Technology Policy Institute	Institute for Defense Analyses
Nuclear Regulatory Commission	Center for Nuclear Waste Regulatory Analyses	Southwest Research Institute
Department of Transportation	Center for Advanced Aviation System Development	MITRE Corporation
Department of the Treasury	Internal Revenue Service Federally Funded Research and Development Center	Center for Enterprise Modernization, MITRE Corporation

Note: FFRDC (federally funded research and development center), C3I (Command, Control, Communications & Intelligence).

Source: National Science Foundation 2007.

to budget uncertainties. Private sponsors might decide to withhold or withdraw funding for any number of reasons, such as disagreeing with the selection of a service for consideration. The influence of private groups that directly fund the research on a study's design and findings could be a concern.

Not linking the funding to either annual federal appropriations or voluntary funding from private groups is another option. Policy analysts have suggested alternatives including:

- imposing a dedicated tax on products that threaten human health, such as tobacco, products with trans fats, and alcohol; or
- obtaining financial support from users of the evidence, including health plans, payers, and purchasers.

Review of options other researchers have recently discussed

AcademyHealth is the professional society for health services researchers and health policy professionals. This group issued a report that addressed AHRQ's role as the lead agency for health services research and the importance of producing comparative-effectiveness research (AcademyHealth 2005). AcademyHealth recommended that an agency of the Department of Health and Human Services (HHS), currently AHRQ, be the lead agency for health services research and that a comparative-effectiveness research entity be established either within or

outside of AHRQ.[10] AcademyHealth discussed, but did not endorse, the following options:

- AHRQ sponsors and conducts research, with guidance from an external board and panel of experts;
- AHRQ establishes a FFRDC and receives guidance from an external board;
- The Congress creates a quasi-government entity, with AHRQ remaining as currently structured; or
- The Congress reconstructs AHRQ as a quasi-government agency, which would keep most of its existing functions and add comparative-effectiveness research to its research portfolio.

Compared with other quasi-government entities, AcademyHealth preferred the FFRDC model because it would: (1) be more focused on comparative-effectiveness research, (2) provide for a strong public-sector involvement and oversight, and (3) provide for a close link between AHRQ and the entity conducting comparative-effectiveness research. Table 2-2 (pp. 48–49) lists the 37 FFRDCs.

Reinhardt (2004) endorsed the creation of nonprofit, independent institutions to analyze the cost effectiveness of drugs. He proposed that the proceeds from a small surcharge (0.5 percentage point or less) on the annual outlays on prescription drugs could establish permanent endowments for the independent nonprofit organizations. Reinhardt considered housing the infrastructure in a federal agency to which the Congress would appropriate funds but concluded that it would be too vulnerable to political pressures. Reinhardt also noted that the private sector does not produce cost-effectiveness information in "socially efficient quantities" because "the private costs of producing the information can easily exceed the private benefit to its producer, even if the potential social benefits of the information far exceed the cost of its production."

Kupersmith and colleagues (2005) recommended a public–private consortium to include federal agencies, payers, insurers, drug companies, device companies, patient advocacy and interest groups, professional societies, hospitals, academics, and health foundations. Under this proposal, new federal appropriations would fund the consortium, with the expectation that the private sector would also contribute.

Wilensky (2006) considered four options: (1) placing the entity within AHRQ, (2) placing the entity within HHS as a new or existing entity, (3) placing the entity within a quasi-government organization, and (4) placing the entity within the private sector. Wilensky concluded that placing the center within a quasi-government entity is the most attractive alternative and that an FFRDC associated with either AHRQ or a newly established board within HHS are options worth exploring. ■

Endnotes

1 Examples of approved drugs and devices in which important side effects were not well documented until after the technology diffused into medical practice include: drug-coated stents, erythropoietin, telithromycin, and rofecoxib (FDA 2007a, 2007b).

2 For certain conditions, such as cancer and AIDS, clinical trials often compare the most accepted treatment with a new treatment.

3 The FDA approves most devices for marketing in the United States based on their similarity to previously approved devices.

4 The FDA has the authority to require that manufacturers report adverse events to the agency with different reporting schedules based on the seriousness of the event and whether the event has been previously identified and is included in the prescribing label (GAO 2006).

5 According to the FDA, a study that is pending is one that the manufacturer has not yet initiated but is not delayed. The FDA defines a delayed study as one that is behind the original schedule.

6 For example, the summary guide on choosing pain medicine for osteoarthritis includes the prices of the different drugs included in the analysis.

7 MedCAC meets about six times each year. MedCAC functions on a committee basis by reviewing and evaluating medical literature, reviewing technology assessments, and examining data and information on the effectiveness and appropriateness of medical items and services that are covered or are eligible for coverage under Medicare. Each committee includes 13 to 15 members.

8 The evidence-based practice centers include: Blue Cross and Blue Shield Association, Technology Evaluation Center; Duke University; ECRI; Johns Hopkins University; McMaster University; Oregon Health & Science University; RTI International–University of North Carolina; Southern California Evidence-Based Practice Center–RAND; Stanford University–University of California, San Francisco; Tufts University–New England Medical Center; University of Alberta, Edmonton, Alberta, Canada; University of Minnesota, Minneapolis; University of Ottawa, Canada.

9 The top officials of the Board are seven members, who are appointed by the President and confirmed by the Senate.

10 Because of renewed interest in comparative-effectiveness research, the AcademyHealth Board of Directors established a special Committee on the Placement, Coordination, and Funding of Health Services Research within the Federal Government.

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