As the current Administration and responsible agencies work to develop regulations to implement the HITECH Act's (and GINA's) new privacy and security provisions, it will be incumbent on them to consider the impact the regulations will have on comparative effectiveness and other health services research, with the ultimate goal of reasonably balancing individual privacy rights against scientific discovery, biomedical innovation, and quality improvement. The stakes are far too high to continue pursuing the goals of scientific and medical advancement, on one hand, and protection of individual privacy rights, on the other, in separate silos. It is my hope that, pursued together, these initiatives will result in reasonable compromise, for example by enhancing education and transparency about research uses of secondary data (and excess biospecimens) while reducing unnecessary regulatory barriers to *bona fide* research uses of these invaluable resources.

N.B. The views expressed above are my own and are not necessarily those of my current or former employers or clients.

Submitted by
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Thank you for the opportunity to participate in this Listening Session. My name is Patricia Adkins and I am the Chief Operating Officer and the Director of Public Policy for the Home Safety Council, a national nonprofit in Washington, DC.

The mission of the Home Safety Council is to help prevent and reduce the deaths and injuries that happen in and around the home such as falls, poisoning, fires and burns, choking and suffocation, and drowning. The Home Safety Council is one of the leading public health and safety nonprofit organizations working in the injury and violence prevention and response community. Our primary goal is to improve the opportunity for all individuals to lead healthy, active, and fulfilling lives.

I believe it is imperative that the Federal Coordinating Council include public health as a priority, with a specific focus on injury and violence prevention and response, when it makes its recommendations to the President, the Congress and the Federal agencies.

Purpose and Goals of the Federal Coordinating Council

Under the American Recovery and Reinvestment Act of 2009, the purpose of the Council is to assist the Federal departments and agencies in reducing duplication and encouraging coordination of comparative effectiveness and related health services research, as well as advising the President and Congress on its progress through its initial report which is due on June 30, 2009.

By definition, comparative effectiveness research compares treatments and strategies to improve health. And by knowing what works best, clinicians and patients can decide on the best treatment. Ultimately, this research enables our nation to improve the health of communities and the performance of the health system.

The White House Forum on Health Reform

The White House Forum on Health Reform was held on March 5, 2009. The President invited a diverse group of people to participate in this event to begin the process of addressing what he called "one of the greatest threats not just to the well-being of our families and the prosperity of our businesses, but to the very foundation of our economy – and that is the exploding cost of health care in America today."

During Breakout Session One at the Forum, the Executive Summary of the discussions highlighted the following: "Nearly every participant stressed the importance of investing in public health prevention…The group agreed this that would both improve health and reduce costs."

In response to the question, "how can we contain rising health care costs," one Congressional Member observed, "the model of our system is sick care, not health care…" Other comments centered around "wellness programs that focus on managing and preventing illness…" and another "noted the importance of public health and prevention."

Why injury and violence prevention and response are important to the work of the Council?

In 1998, the National Academy of Science stated - "Injury is probably the most under-recognized public health threat facing the nation today."

Each year, injuries resulting from a wide variety of physical and emotional causes – motor vehicle crashes, sports trauma, violence, poisoning, fires and falls – keep millions of children and adults from achieving their goals and making the most of their talents and abilities.

This is some of what we know:

- Nationally and in every state in the United States, injuries are the leading cause of death in the first 44 years of a person's life.
- In a single year, more than 50 million injuries required medical attention, with an estimated total lifetime cost of $406 billion.
- This total lifetime cost includes $80 billion in medical care costs and $326 billion in productivity losses, including lost wages and benefits and the inability to perform normal household functions.

These three statistics clearly show the consequences of injuries and the major burden on the health care system.

Fortunately, because of scientific discoveries and injury research, there are steps that can be taken to stop injuries before they happen and increase the likelihood for full recovery when they do. By incorporating these strategies into the community and everyday activities, we can improve the opportunity for all individuals to lead active, useful, and fulfilling lives.

An Injury Example – Protecting Older Adults

We all want a society where people, including our older citizens, can live to their full potential. And we can help many older adults avoid injuries. There are a variety of actions we can take to prevent injuries and premature death to our parents, grandparents, and friends. Some of the most important include preventing older adults from falling or from being injured in fires or motor vehicle crashes.

Let's focus on one of the injuries that affect the quality of life for older adults – falls. Falls are the leading cause of fatal and nonfatal injuries for those 65 and older. Each year, 1.8 million older adults are treated in emergency departments. Every 35 minutes, an older adult dies from a fall-related injury and every day 5,000 adults 65 and older are hospitalized due to fall-related injuries.

The cost for treatment is enormous - over $19 billion annually; and most of these expenses are paid for by CMS through Medicare.

While falls are a threat to the health and independence of older adults and can significantly limit their ability to remain self-sufficient, the opportunity to reduce falls among older adults has never been better. Today there are proven interventions and strategies that can reduce falls and help older adults live better and longer. They include medication review and adjustment, vision correction, and physical exercise. These evidence-based interventions can help save health care costs and greatly improve the lives of older adults. The costs are small compared to the potential for savings. For every $1 invested in a comprehensive falls prevention program, it returns a $9 benefit to society.

How the Council Can Help

The Council can be a catalyst for changing people's perceptions of the value of preventing and responding to injury and violence by helping to create the social and political will to more fully support this public health issue.

Whether it's the lack of knowledge that solutions exist to reduce the impact of injury and violence; or not understanding that injury and violence are public health issues; or believing that unintentional injury is unpredictable and not preventable, the Council can address these challenges and provide a common foundation for collaboration.

The American Recovery and Reinvestment Act provides for $400 million to be allocated at the discretion of the Secretary of Health and Human Services. Incorporating the public health prevention strategies and interventions into the comparative effectiveness research is critical to developing a comprehensive plan for health reform. I urge the Council to reinforce the adoption of these public health strategies within the injury and violence prevention and response field to ensure that Americans remain healthy and live their lives to the fullest potential.

Submitted by
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I appreciate the opportunity to provide comments on behalf of Virtual Radiologic Corporation, a provider of teleradiology services, headquartered in Minneapolis. vRad was founded by radiologists and is a leader in teleradiology, with more than 140 contracted U.S.-based radiologists, of which 70% are fellowship trained, serving 1,025 medical facilities nationwide and providing more than 2.2 million interpretations in 2008.

vRad and teleradiology provide a number of well-established healthcare system features including:

- Infrastructure for electronic and digital transmission, reading, interpretation, reporting and record-keeping for diagnostic imaging services
- Efficient and cost-effective 24/7 deployment of highly-skilled diagnostic resources
- Access by rural and small community-based facilities to specialized, subspecialty-trained radiologists
- A resource for supporting clinical registries, clinical data networks, and other forms of electronic health data that could be used to generate or obtain outcomes data.

We recognize the magnitude of the Council's task in recommending priorities for the Comparative Effectiveness funding provided by Congress. You have the opportunity to look broadly across many divergent and competing segments of the U.S. healthcare system and we urge you to select topics that will have broad cross-cutting impacts.

We urge the Council to consider the following issues and priorities for comparative effectiveness research:

- Existing teleradiology and telemedicine resources should be developed and utilized as part of the infrastructure to establish registries, networks and other e-health data to

analyze comparative effectiveness on diagnostic and treatment pathways for targeted health conditions.

- Reimbursement policies and claims processing systems aimed at controlling costs are impeding rather than facilitating the development of teleradiology and other innovative systems that provide cost-effective health IT-based services. Conflicting quality, credentialing and state policies under Medicare and Medicaid also impede access to quality teleradiology. Comparative effectiveness studies involving diagnostic services must be cognizant of the impact of these forces and provide solutions to improve access.
- Coordinating, leveraging, and providing synergies with Recovery Act and ongoing projects in developing and implementing the infrastructure for health IT, digital image transmission, e-health records, telemedicine, and teleradiology.

vRad is extremely well-positioned and very interested in serving as a partner in these important efforts to improve the nation's healthcare system.

Submitted by
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The National Association of Children's Hospitals and Related Institutions (NACHRI) is a not-for-profit membership organization of more than 215 children's hospitals. NACHRI promotes the health and well-being of all children and their families through support of children's hospitals and health systems that are committed to excellence in providing health care to children. Children's hospitals work to ensure the health of all children through clinical care, research, training and advocacy.

NACHRI supports increased investment in comparative effectiveness research (CER) to improve the quality of patient care and to support patients, families, physicians and providers in making decisions about the "right care at the right time." We welcome and appreciate the opportunity to provide this statement at the first listening session of the Federal Coordinating Council for Comparative Effectiveness.

Widespread variability in care, such as that demonstrated by the Dartmouth Institute for Health Policy and Clinical Practice in the Medicare population, exists in care for children as well. A chart book on quality of health care for children and adolescents developed for The Commonwealth Fund suggested that "one-quarter to three quarters of children do not receive the health care that is scientifically proven and/or that experts recommend to prevent disease, reduce disease complications, and achieve optimal health and development" and that "up to one in five pediatric patients receives inappropriate care" (Leatherman and McCarthy, 2004).
NACHRI offers the following considerations as the Federal Coordinating Council develops its recommendations.

- Children and adolescents should be specifically included in priorities identified for comparative effectiveness research with careful consideration for separate studies

evaluating only pediatric populations. Because many diseases afflicting adults originate in childhood and, because many of these diseases can be prevented, investing in children's health care effectiveness research is both a moral imperative and cost effective as the "impact of investments in quality will be longer lasting" (AHRQ, accessed April 9, 2009). According to the Agency for Healthcare Research and Quality, improvement in just four quality and patient safety topics could save between 3,700 and 7,400 children's lives in a single year.

- Priorities identified by the National Priorities Partnership (*Aligning our Efforts to Transform America's Healthcare: National Priorities and Goals,* 2008) and the Institute of Medicine (*Priority Areas for National Action: Transforming Health Care Quality,* 2003) should help to guide CER priorities.

- Comparative effectiveness research should address systems issues such as care models that integrate primary and tertiary care, longitudinal management of chronic conditions and transitions from pediatric to adult health care and should not focus only on specific drugs, devices and conditions. The largest immediate impact on quality and cost may not come from trials of specific drugs and devices but from identification of effective models of care delivery and avoidance of medical errors. This is especially true for children. Except for a very few conditions, the numbers of children with a single condition are small, and children and youth with special health care needs (CYSHCN) often have multiple chronic conditions. These children represent approximately 15 percent of children but consume 40 to 60 percent of health care resources devoted to children.

  Similarly, patient safety and prevention of avoidable medical errors, including safety of children's health care, should be an important focus for comparative effectiveness. For example, healthcare-associated infections (HAIs) result in significant disease burden and cost, are of great public interest and are an IOM and National Priorities Partnership priority area. HAIs are among the top 10 causes of death in the U.S. (GAO, 2009). Interventions to prevent HAIs often require adaptation for pediatrics. For example, unlike in adults in whom central line insertion bundles can eliminate Catheter Associated Blood Stream Infections (CABSIs), the insertion bundle alone does not eliminate pediatric CABSIs. A multi-center collaborative on reducing CABSI in Pediatric ICU's found that, in contrast to adult-based efforts, reliable use of nursing-oriented standardized daily line maintenance practices is the most significant factor in reducing CABSI in children. To-date the collaborative effort has reduced CABSI over 50 percent with an estimated 80 lives saved and over $23 million in health care cost savings.
- Sufficient research to establish effective and proven treatments in pediatrics is needed. It cannot be assumed that treatments shown to be effective in adults will translate into effective treatments for children. Accordingly, consideration for how to facilitate inclusion of children in randomized control trials with specific subgroup analyses and other comparative effectiveness research is required.

- Data, as well as demonstration efforts, should not focus only on the Medicare population, but should include Medicaid and CHIP as well. Investment in information to enable identification of variability, similar to that available for the Medicare population, in children's health care is critical.

- Representatives from the pediatric community should be included in any body or committees overseeing and guiding comparative effectiveness research.

Submitted by
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Thank you on behalf of CIGNA and the 12 million individuals and the companies that we serve for the opportunity to speak before the Institute of Medicine on establishing national priorities for comparative effectiveness research. It is our belief that in developing national priorities for comparative effectiveness research, there should be three guiding principles.

First, focus research on high impact areas. Research priorities should first focus on high prevalent conditions, which account for significant healthcare spending, and which have competing diagnostic or treatment pathways. Cardiovascular diseases, cancer, obesity, and arthritic conditions all have competing diagnostic and treatment pathways, and they collectively have a major impact on healthcare costs in the US in the adult population.

Second, costs should not be considered as the initial goal of comparative effectiveness research. Costs should only be considered in limited circumstances after the comparative effectiveness research shows that two alternatives are clinically equivalent: For these high impact conditions, there are often competing diagnostic modalities and treatment pathways, the comparative effectiveness has not as yet been established with the available evidence for the typical patient, or selected subpopulations. We should first establish through comparative effectiveness research, if one diagnostic modality or treatment pathway is superior to another, in terms of its safety and clinical effectiveness. This will have the effect of focusing treatment and coverage decisions on the most effective treatments available ***without*** consideration of the cost. However, if comparative effectiveness research shows that the two treatments are essentially equivalent to each other in terms of safety and clinical effectiveness, ***then and only then***, is it appropriate to consider the total medical costs associated for each treatment because patient outcomes would be the same and it would be appropriate to ask which alternative is the better value for our healthcare dollar.

Finally, we should first fund "shovel ready" projects. It is important that national priorities for comparative effectiveness research should focus initially on those studies which can be quickly approved by the NIH, AHRQ or CMS, and which can be up and running in a relatively short period of time.

Thank you for the opportunity to speak before this committee on this important topic.

Submitted by
Tony Curry
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To the Federal Coordinating Council for Comparative Effectiveness,

Thank you for your work in guiding the direction of Comparative Effectiveness research as part of the American Recovery and Reinvestment Act. Thank you also for the opportunity to share our comments today.

We believe that comparative effectiveness studies should focus on medical delivery systems and operations, resulting in information that can be leveraged to foster better clinical and cost outcomes.

With a one hundred year history of treating patients, Gundersen Lutheran Health System in La Crosse, Wisconsin is not new to medicine, but studies suggest that if the nation's healthcare organizations and health insurers replicate the way that Gundersen delivers healthcare, we could see a greater than 30% decline in national healthcare costs and improve healthcare value in the United States (2008 Dartmouth Atlas Health Study).

The annual Dartmouth Atlas Study identified La Crosse, Wisconsin as the lowest cost-of-care city in the nation for Medicare patients during the last two years of life. Health care at Gundersen Lutheran in La Crosse costs 72% less than the leading medical center in New York, 71% less than in Florida, 68% less than in California, and even 42% less than the leading medical center in Minnesota.

Why is the cost of care at Gundersen so much lower while the quality of care remains as good or better? Gundersen's cost and quality success is driven by their integrated delivery system. Every Gundersen program, from advance care planning and care coordination to heart care and breast cancer care stems from their integrated delivery approach. And each program that achieves top-in-the-nation status also has a correlating reduction – significant reduction – in healthcare costs.

As one example, Gundersen Lutheran's breast cancer program has become the first and only in the nation to achieve the highest level of distinction from the National Quality Measures for Breast Centers™ (NQMBC) Program. Gundersen Lutheran is also one of only two organizations in the country with every available accreditation for the full scope of breast care, diagnosis and treatment from the American College of Radiology. Gundersen's interdisciplinary model of caring for breast cancer patients has the potential to save an estimated $4.15 billion dollars in healthcare costs if it is implemented on a national scale.

As a lean and medium-sized medical center, however, putting resources into researching their programs' results for wider dissemination or use as a national best practice are resources Gundersen Lutheran just hasn't had in the past. This comparative effectiveness funding represents a mechanism by which organizations like Gundersen Lutheran can share their results and best practices.

So, in addition to investing comparative effectiveness dollars into treatment approaches for specific conditions, comparative effectiveness funds should invest in comparing the most

effective health system delivery approaches in the United States. Only then, can comprehensive, sustainable healthcare delivery and payor system reform take root.

Gundersen Lutheran is a living lab for applied comparative effectiveness research. Understanding how and why Gundersen's approaches work will help lower U.S. healthcare costs, improve quality and create a more sustainable payment system that incentives the outcomes it seeks to achieve. Gundersen Lutheran is willing to share further information and our program data to help move this work forward.

Thank you again for the opportunity to share our recommendations for comparative effectiveness research as part of the American Recovery and Reinvestment Act. We hope for the opportunity to contribute to this movement toward healthcare reform.

Headquartered in La Crosse, Wisconsin, Gundersen Lutheran Health System is a not-for-profit organization that provides quality health services to patients at its hospital and clinics throughout western Wisconsin, southeastern Minnesota and northeastern Iowa. Gundersen Lutheran is comprised of nearly 700 medical, dental and associate staff, and supported by a staff of more than 6,300. Gundersen has been consistently ranked in the top 5% of hospitals in the country.

For additional information, contact Gundersen Lutheran's Joan Curran, Chief of Government Relations and External Affairs, at (608) 775-1400, located at 1900 South Avenue, La Crosse, WI 54601. You may also contact our Washington-based associate Ladd Wiley, Akin Gump, at (202) 887-4083.

Submitted by
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My name is Meridith Mitchell and I am presenting on behalf of M2S, Inc. I thank you for the opportunity to comment today and appreciate the willingness of this committee to seek public input with regard to Comparative Effectiveness Research (CER.) The focus of this statement is on the utilization of a Clinical Technology Organization (CTO) to effectively facilitate CER.

M2S has significant and specific expertise in the development of patient registries, endovascular 3-D modeling, and medical imaging core lab service. M2S is a CTO with experience, flexibility and efficiency, delivering the highest quality benchmarked reporting at the lowest total delivery cost.

As funds are allocated for CER and Health Services Research (HSR) it will be critical to utilize a CTO. A CTO is a clinical research company that focuses on clinical informatics and optimizes

the use of technology to increase efficiency, reduce cost and maintain or enhance clinical quality. Equally important is to rely on a CTO that is knowledgeable in CER initiatives and capable of delivery today. A CTO is powerful when actively used in the clinical pathway as well as for research initiatives such as CER.

M2S recognized the need for CER as it relates to endovascular aneurysm repair beginning in 2001. M2S' Patient Evaluation and Management System (PEMS®) is the largest radiological/clinical footprint in the world relied upon by highly respected physician investigators. It is a database of 150,000 patient entries providing CER of FDA approved Aortic Stent Grafts. The service has been broadly adopted by health care advocates in both practice and industry having recognized the impact that this vast and valuable repository of data has on quality improvement.

In the past Comparative Effectiveness studies have evaluated a particular therapy only against itself. M2S evaluates the full scope of information including the patient health record, radiologic information with patient input. This model is unique, highly effective and patient centric and has direct impact on the quality of patient care.

M2S believes that simplifying the work flow facilitates summarization of comparative data and enhances a clinician's ability to make informed treatment decisions. An effective CTO collects data simultaneously as fields are populated by the institution or Electronic Medical Record (EMR) system. The flow of data provided for comparative analysis is aggregated, risk-adjusted, evaluated and reported on by an independent panel of physician thought leaders.

We all agree that the goal of CER is to enhance patient care; a web-based integrated clinical technology platform is a key component in the success of these projects. Health care organizations are striving to make better use of clinical informatics as an adjunct to Comparative Effectiveness. Involving a CTO early in the planning phase will streamline the process, reduce costs, and facilitate better data aggregation with one accessible portal for all relevant information.

Submitted by
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As an organization focused on information and education for physicians and other healthcare professionals, Medscape, LLC endorses the increased funding for comparative effectiveness research ("CER").

Results of the CER are highly relevant to all stakeholders, consumers, patients, physicians, nurses and healthcare professionals. Furthermore, it is extremely important that the latest results on effectiveness, safety and quality measures be incorporated into clinical practice as rapidly as possible. A multidisciplinary, multi-modal approach is essential to accomplish this result.

Therefore, it is important that communications and education for both healthcare professionals and consumers/patients be incorporated into the overall strategy for CER.

In measuring significance of comparative effectiveness research on clinical practice, one must not overlook the importance of disseminating the results to as wide-spread a professional audience as possible.
It is particularly critical to include educational components and educational outcomes studies in order to determine the effect of this research on changes in clinician behavior and patient health.

An AHRQ Evidence Report on Continuing Medical Education (CME) published in 2007 concluded that, despite limited evidence, CME appears to be effective at the acquisition and retention of knowledge, attitudes, skills, behaviors and clinical outcomes. In addition, the study suggested the following:[1]

- Live media was more effective than print. In fact, print interventions were either not beneficial or very weak in their ability to improve attitudes.
- Multimedia was more effective than single media interventions.
- Multiple exposures were more effective than a single exposure.

Furthermore, evidence is increasingly demonstrating that on-line CME may have particularly large positive effects on outcomes.[2] According to a 2008 meta-analysis published in JAMA, 16 of the 17 studies analyzed revealed improved knowledge, behavioral outcomes, or both for participants using Web-based interventions.[3] In a recent randomized controlled trial of 113 primary care physicians, those who viewed an on-line diabetes seminar were 63% more likely to order an eye exam for diabetes patients than physicians in the control group (27%).[4]

MedscapeCME is currently a major provider of online CME/CE, reaching over 1.5 million physicians and nurses each month. In an analysis of outcomes studies on 97 Medscape on-line CME activities taken by 13,520 physicians, participants were 52% more likely than non-participants to make diagnostic and therapeutic choices based on clinical evidence. [5]

Specifically, over the past two years, Medscape has published CME activities based on several AHRQ Effectiveness Report Executive Summaries:

- Comparative Effectiveness of Treatments To Prevent Fractures in Men and Women With Low Bone Density or Osteoporosis: http://www.medscape.com/viewprogram/17304
- Comparative Effectiveness of Therapies for Clinically Localized Prostate Cancer: http://www.medscape.com/viewprogram/17364
- Comparative Effectiveness of Angiotensin-Converting Enzyme Inhibitors (ACEIs) and Angiotensin II Receptor Antagonists (ARBs) for Treating Essential Hypertension http://www.medscape.com/viewprogram/8669
- Comparative Effectiveness of Off-Label Use of Atypical Antipsychotics http://www.medscape.com/viewprogram/7361
- Comparative Effectiveness of Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression: http://www.medscape.com/viewprogram/7793

These activities have been viewed by 5,000 to 18,000 nurses, physicians, and medical students and the CME participation rates for each AHRQ activities have ranged from 3,300 to over

8,500. In 2007, Medscape commissioned an educational outcomes study with a third party research group based on the CME activity for *Comparative Effectiveness of Second-Generation Antidepressants in the Pharmacologic Treatment of Adult Depression.* Over 3,000 physicians participated in this on-line activity and the outcomes study results suggested that these participants are 68% more likely than non-participants to make evidence-based choices in the diagnosis and treatment of adult depression. It should be noted that these 3000 physicians are estimated to see at least 72,000 patients each week who have adult depression, suggesting the significant positive impact of online CME based on these Effectiveness Reports.

In conclusion, funding for a massive educational program is imperative for changing clinician behavior and effecting improved patient health and cost effective care. Both the evidence and Medscape's experience emphasize the benefits of a comprehensive online educational program. It is imperative not to neglect this component of the CER funding available in the Recovery Act. Finally, it should be strongly noted that educating the patient on the results of this research is critical to the effectiveness of these programs in improving health and reducing medical costs.

[1] Marinopoulos SS, Dorman T, Ratanawongsa N, Wilson LM, Ashar BH, Magaziner JL, Miller RG, Thomas PA, Prokopowicz GP, Qayyum R, Bass EB. Effectiveness of Continuing Medical Education. Evidence Report/Technology Assessment No. 149 (Prepared by the Johns Hopkins Evidence-based Practice Center, under Contract No. 290-02-0018.) AHRQ Publication No. 07-E006. Rockville, MD:Agency for Healthcare Research and Quality January 2007.

[2] Casebeer L, Engler S, Bennett N, Irvine M, Sulkes D, DesLauriers M, Zhang S.A controlled trial of the effectiveness of internet continuing medical education. BMC Med. 2008 Dec 4;6:37.

[3] Cook DA, Levinson AJ, Garside S, Dupras DM, Erwin PJ, Montori VM. Internet-based learning in the health professions: a meta-analysis. JAMA. 2008 Sep 10;300(10):1181-96. Links

[4] Weston CM, Sciamanna CN, Nash DB. Evaluating online continuing medical education seminars: evidence for improving clinical practices. Am J Med Qual. 2008 Nov-Dec;23(6):475-83.

[5] Poster Presentation at CME Congress 2008 in Vancouver, BC; C. Grimes, M. Irvine, DJ Sllkes, L Casebeer, M Abdolrasulnia, M DesLauriers, Medscape LLC, New York, NY, USA, Outcomes, Inc. Birmingham, AL, USA

Submitted by
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National Patient Advocate Foundation (NPAF) is a non-profit organization dedicated to improving access to healthcare services through policy reform. Our mission of creating avenues of patient access through improved access to, and reimbursement for,

evolving therapies, therapeutic agents, and devices is influenced by the experience of patients who receive case management services from our companion organization, Patient Advocate Foundation (PAF). Last year, PAF received more than 9.5 million inquiries from patients throughout the United States seeking information and assistance for access to care issues resulting from diagnoses of a chronic, debilitating or life-threatening disease. Of those, 48,369 became full patient cases involving communications made by PAF staff on behalf of a patient in order to reach positive resolution.

The *"American Recovery and Reinvestment Act of 2009"* includes $1.1 billion in new funding for comparative effectiveness research. NPAF supports comparative effectiveness research and believes it should be used as a tool between providers and their patients to determine the best course of action in treatment. However, NPAF is concerned that the Federal Coordinating Council established in the stimulus bill does not include roles for patient representatives.

NPAF strongly believes that the Federal Coordinating Council should consist of all relevant stakeholders, including patient and consumer groups, government, providers, insurers and manufacturers of drugs and medical devices. These stakeholders should be involved in every step of the process, from setting the research agenda, and developing study methodology, to the translation and dissemination of findings.

While we appreciate the invitation to participate in today's public listening session, other health agencies, such as FDA and CMS routinely appoint patient representatives to their scientific research panels, and we encourage the council to seek to correct this situation.

In addition, NPAF is concerned that comparative effectiveness research may ultimately be used to make cost-effectiveness decisions. NPAF would like to emphasize our support for comparative effectiveness research for the purpose of improving the quality, safety and delivery of care; however, NPAF does not support using this research to limit access, deny treatment or reimbursement.

Many European countries have already developed a system for comparative effectiveness research but many of these countries impose cost-effectiveness analysis in ways which ultimately deny patients access to more expensive drugs. In the United Kingdom, the National Institute for Health and Clinical Excellence (NICE) conducts research and develops guidelines for the country's National Health System (NHS). In the last several years, NICE has instituted certain coverage decisions based on cost-effectiveness that severely impact patient access to appropriate care. As recent as January 2009, Ministers in the Welsh Assembly overturned a NICE decision that prohibited kidney cancer patients from accessing drugs such as Sutent, Avastin, Nexavar and Torisel, all of which have been proven to treat kidney cancer effectively. In the United States, it is common practice for these drugs to be prescribed to a kidney cancer patient. Advancing comparative effectiveness research in the U.S. can be a

positive tool for patients and providers, only when it focuses on clinical comparative effectiveness.

NPAF also believes that a national comparative effectiveness program should prioritize the linking of data from federal and private entities to build upon existing data collection efforts and research capabilities. Insufficient funding for any public or private entity responsible for aligning and maintaining a robust data network has resulted in isolated clinical outcomes research efforts. Expansion of CER activities should include public-private coordination of data collection and interoperability of both clinical research networks and healthcare databases in order to increase the available data.

CER should support for the development of "personalized" or stratified medicine by further examining individual factors that contribute to disease susceptibilities and differences in clinical outcomes.

NPAF urges you to consider these issues as the Council makes its recommendations to the Secretary on comparative effectiveness research priorities so that comparative effectiveness research will have beneficial long-term consequences for patient care and access.

Submitted by
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The Society of Thoracic Surgeons (STS) appreciates the efforts of the Federal Coordinating Council for Comparative Effectiveness Research in soliciting input for consideration of priorities for comparative effectiveness research studies as called for in the American Recovery and Reinvestment Act of 2009 (ARRA). We welcome the opportunity to submit the following testimony as you consider recommendations on research priorities.

STS is a not-for-profit organization representing cardiothoracic surgeons, researchers, and allied health professionals worldwide who are dedicated to ensuring the best possible surgical care for patients with diseases of the heart, lung, esophagus, and other organs in the chest. Founded in 1964, the mission of STS is to enhance the ability of cardiothoracic surgeons to provide the highest quality patient care through education, research and advocacy. STS supports data-driven

approaches to quality measurement, quality improvement, and quality reporting because we recognize that the collection of clinical data and the feedback of those data to physicians improve patient outcomes.

The STS National Database is the premier voluntary clinical data registry for cardiothoracic surgery; it includes three component parts: the Adult Cardiac Surgery Database, the General Thoracic Surgery Database, and the Congenital Heart Surgery Database. Surgeons add new patient data to the database semiannually or quarterly each year, thereby providing a highly dynamic, up-to-date picture of cardiothoracic surgical practice.

Our comments focus on the Adult Cardiac Surgery Database that contains detailed clinical information relevant to the processes and outcomes of care in adult cardiothoracic surgical procedures (STS ACD). This information, collected over a 20-year period, has been used to improve the quality of care for patients undergoing cardiothoracic surgical procedures. The STS ACD captures data on all adult patients undergoing cardiac surgical procedures performed by participants throughout the United States and, with more than 960 participants representing more than 2,800 individual surgeons, STS estimates that it captures approximately 90 percent of all adult cardiac surgery performed nationwide. Currently, the STS ACD contains more than 3.6 million surgical records and is the largest clinical cardiac surgery database in the world.

Clinical registries developed by STS and the American College of Cardiology (ACC) have been at the forefront of quality improvement activities in cardiovascular medicine for a number of years. Combined, STS and ACC databases cover virtually the entire spectrum of cardiovascular care. The STS ACD and the ACC's National Cardiovascular Data Registry (ACC NCDR) have provided clinicians with important feedback on their practice patterns and performance, and are invaluable tools for use in real world medical practice and health services research. The ACC NCDR is the ACC's group of clinical databases that measure and quantify outcomes in the delivery of quality cardiovascular patient care. It is designed to improve the quality of cardiovascular patient care and to identify gaps in care by providing information, knowledge and tools, implementing quality initiatives, and supporting research that improves patient care and outcomes.

The information in these registries supports performance assessment, and comparative effectiveness studies, as well as the integration of new treatments into routine clinical practice. These registries contain detailed information, including demographics, cardiovascular history, patient risk factors and co-morbid illnesses present on admission, interventions, care processes, and risk-adjusted outcomes surrounding specific clinical events. The STS ACD and ACC NCDR represent the "gold standard" of clinical databases in the country and can serve as the prototypes for registries across medicine.

Specific provisions in the ARRA call for funding to accelerate the development of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data. STS believes that by linking clinical data from the STS ACD and the ACC NCDR with Centers for Medicare and Medicaid Services (CMS) administrative data, a powerful, longitudinal data set

could be produced. Such a data set would contain process, outcomes, utilization, pharmacy, and cost data spanning at least a three to five year period. This linking project has the potential to cover virtually the entire spectrum of care for cardiovascular disease. Ultimately, the information obtained from this collaborative effort will produce new insight into the comparative effectiveness of coronary revascularization treatment strategies, such as coronary bypass grafting and stenting procedures. Because the STS and ACC databases are mature, there exists the real potential to achieve extraordinarily meaningful results in a timely manner, certainly within the time frame set forth to fund comparative effectiveness research projects under the ARRA.

A similar collaboration between STS and ACC is also under way in congenital heart surgery. ACC is collaborating with STS in the development of its pediatric database, harmonizing data definitions with STS's Congenital Heart Surgery Database. Down the road, this collaboration will facilitate following patients through episodes of care as well as longitudinal follow-up and comparison of outcomes.

The approach used in this project can be adopted by other specialties and their professional societies for comparative effectiveness studies and quality improvement. The techniques of analysis will have broad application to the entire field of medicine.

The results of these comparative effectiveness studies will almost certainly improve the care of cardiovascular patients while shedding new light on ways to provide care more efficiently. The above mentioned linked data set would also be a valuable source of data to examine appropriate use criteria, efficiency of care, cost of care, and value-based health care. Accordingly, we urge the Council to strongly support the development of this collaborative STS-ACC project that would reflect and effectuate the intent of the ARRA to utilize clinical registries in the analysis of comparative effectiveness research studies.

Additionally, we ask the Council to strongly consider the following comparative effectiveness research studies in cardiothoracic surgery:

1. STS-CMS longitudinal follow-up to assess the long-term impact of compliance with NQF-endorsed performance measures;
2. STS-CMS assessment of comparative effectiveness of valve replacement and repair procedures;
3. STS-CMS longitudinal follow-up of patients undergoing surgery for various forms of lung cancer treatment; and
4. Using IT links between the STS National Database, the ACC NCDR, and the CMS MEDPAR dataset, examine the comparative effectiveness of percutaneous *versus* surgical treatment of atrial fibrillation.
5. Assessment of the comparative effectiveness of new technologies and treatments as they are introduced;
6. IT Projects Facilitating Healthcare Data for Research;

We applaud the Council for convening this meeting to obtain input from various stakeholders and inform its development of priorities for comparative effectiveness research. Thank you again for this opportunity to provide testimony.

Submitted by
David Wray
Standard Biologics, Inc
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Standard Biologics, Inc., is a U.S. Registered and Resident Corporation. Mr. Joseph A Cerceo, is the President and Founder of Standard Biologics, Inc. ('S.B.Inc.').

Mr. Cerceo has many very successful years of experience in the field of **Scientific Applications Research** including work on behalf of the **US Government**.

After studies that involved Chemistry for the Health Sciences; The Vitamins; Advanced Nutrition, Macronutrients and Micronutrients; Nutrition and Exercise Immunology; Nutrition and Gene Expression; Nutrition applied to Sports Medicine and Injury Rehabilitation; Athletic Injuries and Rehabilitation; Cell Biology of Trauma; Endocrine Physiology; Bone, Fracture Repair and Regeneration and the Bioavailability of Nutrients Mr. Cerceo discovered the extensive natural medicinal abilities of a **very high quality Proteolytic enzyme** (i.e. a Protease, termed by S.B.Inc. also as its 'Protocol').

Several years of research were completed culminating in the successful Application of a US Patent that covers inter alia the invention of the techniques of successful assessments for treatment of patients and methods of the Administration of the Protease to mammals (and, by extension, to a broad diversity of other animals) with the initial very successful treatments being of **inflammation** and **trauma** in their *many manifestations*.
The Proteolytic enzyme is attracted to and acts rapidly at sites of inflammation in the host.

So effective are such capabilities of the Protease that lives that could well have been lost due to uncontrollable inflammation occurring post surgery and otherwise, were saved by the administration of the Protease following Mr. Cerceo's invented Administration techniques. S.B.Inc. has documents related to this point in formats applicable to technical explanation as well as several 'Proof of Concept' statements.

Further research and development and a substantial number of 'Proof of Concept' trials firmly established further extremely important capabilities of the Protease that can be described in relation to the dictum, "**Inflammation is everything** !!"

Additional important aptitudes relating to the Protease's beneficial powers are in respect of:

The treatment of **Cancer tumours** including those in inoperable or life-threatening bodily positions thereby helping to reduce dangerous invasive surgery.
The Protease suppresses angiogenesis (the development of the vasculature of the tumours), that 'feeds' the tumour, thereby starving the tumour. A precautionary course of anti-biotics can be applied to treat potential secondary infection from the resulting necrotic tumour tissue.
A consequent further advantage is that there will be a range of cancer cases **where treatment of the patient by radiotherapy and chemotherapy will be unnecessary** with all the benefits to both the patient and to the finite treatment resources available that that advantage will bestow – the avoidance of those treatments will not be the case for all cancer patients.
The neutralization of VEGF, vital to the progress / metastasis of such as bone cancer. **VEGF** is promoted by inflammatory proteins which are hydrolyzed by the Protease.

Cell-signalling, i.e. the utilisation by the Proteolytic enzyme of this phenomenon to enhance its ability to identify and attack non-self proteins - including the hydrolyzation of a **variety of viruses and pathogens** (not just individual viruses or pathogens) such as various strains of Influenza, Common Cold, HCV / HIV (these are currently under long-term trial), and such other serious viruses as Avian Influenza, Ebola hemorrhagic fever, Rift Valley and Yellow Fevers and so on (a capability enabled by a characteristic of the Protease of having a **broad spectrum peptide specificity**).
Other non-self protein-bearing pathogens may be hydrolyzed such as Malarial protozoan parasites and Babesiosis and other zoonotic parasites similarly with non-self proteins (as detailed by Professor Brian Greenwood of the London School of Hygiene and Tropical Medicine).

Pain Medication is brought about in varying meaningful degrees by the beneficial impact of both S.B.Inc. products on the body's pain response mechanisms.

Importantly, this 'Protocol' has the Approval of **EPA** and **FDA** and also it is approved by FDA as a Food Grade Additive (it is considered as safe as any other food ingredient monitored by the US Government).

NB: An important attribute of this Company's products is that when they are administered to a patient in accordance with our straightforward and not unpleasant procedure(s) ***NO adverse side-effects are experienced in virtually ALL patients***.
An American adage with particular relevance to our Adjuvant *Anti-Inflammatory Protocol*, our enzyme, is that it is analogous to 'Chicken Soup', i.e. the enzyme can't hurt; it will only do good. The human body produces, normally, a very small amount of such an enzyme and the corollary is that **the mammalian system actually welcomes the administration of our Protease**.

Product costs: Standard Biologics, Inc. confidently expects that both its medical treatment developments – the Proteolytic enzyme and the complementary Therapeutic Nutritional Supplements will prove to be substantially less costly than pharmaceuticals measured as at both point of use and also when costed taking into consideration that they do not cause adverse side-effects that can be expensive and resource-consuming to treat.

Standard Biologics, Inc., ('S.B.Inc.') has either sent or will send shortly Corporate and Product Information to:

BARDA (Biomedical Advanced Research and Development Authority) @ H&HS;

The DTRA at the DOD;

CDC - The Influenza Division;

CDC - The NCHHSTP Division;

The NIH – the Office of Dr. Anthony Fauci, M.D., Director of NIAID;

U.S. Homeland Security Department;

The Department of State – the Office of the Global Aids Coordinator;

United States Army Institute of Surgical Research, Fort Sam Houston, Texas 78234-6315;

USDA - ADOL in East Lansing, Michigan;

USDA – SEPRL in Athens, Georgia;

And other U.S. Government areas.

Submitted by
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I am Sam Lin, a Family Physician, representing the *American Medical Group Association* based in Alexandria, Virginia. *AMGA* is a professional medical association representing some of this nation's largest, best known, and prestigious integrated health care delivery systems. More than 95,000 physicians practice in *AMGA* member organizations and provide health care services for approximately 95 million patients.

Today, in the context of the Comparative Effectiveness Research to be funded by the Recovery Act, you are hearing comments with a focus on disease conditions and treatments. And while those viewpoints are critical to the discussion, it is imperative that we also examine the context in which healthcare is given. Unless the delivery system is considered, we otherwise would continue to promote fragmented care, leaving our patients to wander on their own. *AMGA* supports the fundamental concepts of comparative effectiveness information use in health care delivery, but we also believe that delivery systems matter. There is an emerging body of evidence that supports this idea, and this premise is also being tested in several CMS demonstration projects. We, therefore, strongly recommend that the Coordinating Council consider comparative effectiveness in its broadest terms and not be limited only to research on treatments and devices alone.

CER should be undertaken for quality, efficiency, effectiveness, and other appropriate dimensions for health care delivery systems along the entire spectrum of systems integration. This spectrum should include integrated delivery systems, multi-specialty group practices, single-specialty groups, "virtual" groups such as IPAs, PHOs, and small medical practices (solo, duo, small groups), and perhaps others.

Use of comparative effectiveness information on delivery systems would facilitate and strengthen provision of patient care, disease states, and related financial determinations. By knowing what works best in treating patients, this nation's healthcare delivery system could make substantial strides toward improving clinical outcomes and closing gaps in geographic and population variations, while reducing health care expenditures. While we favor CER, we temper that view with a caution that such information must be objective, developed by disinterested parties, and should be equally applied.

Submitted by
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University Hospitals (UH) is a world-renowned academic health care facility located in Cleveland, Ohio with research specialties that span 21 academic and clinical departments. UH is also the primary affiliate of Case Western Reserve University School of Medicine (CWRU). Together, UH and the CWRU form the largest biomedical research center in the state of Ohio. In order for UHC to continue to provide effective, quality health care for its patients, the need for comparative effectiveness research (CER) must be met. The mission of UH is To Heal. To Teach To Discover. This drives the ability to responsibly grow research and scientific innovation to improve patient care. In order to achieve the organization's overall mission, the research arm must provide sufficient infrastructure to drive the To Heal part of the mission. CER is a necessary component of that research infrastructure and without out CER the link back to patient care would not be as direct. CER at UH is primarily driven in two ways: 1) interdisciplinary outcome databases to record patient treatment information from admission to discharge are created and maintained throughout the organization; and 2) the large clinical populations in the areas of Surgery, Oncology, Pediatrics, Cardiovascular Medicine and Neurology drive the innate ability to conduct large scale CER.

1) Department of Surgery: Serving as the tertiary referral hub for UH, the Department of Surgery is comprised of the Divisions of General Surgery, Vascular Surgery, Cardiac and Thoracic Surgery, Plastic Surgery and Pediatric Surgery. Surgeons have faculty appointments at Case Western Reserve University School of Medicine and are either Board Certified or Board eligible in their respective surgical disciplines. Across the United States, most hospitals use several databases to record patient treatment information from admission to discharge. To date, such databases are typically unable to communicate with each other, thereby making it time consuming (if not impossible) to efficiently and accurately track patient treatment and outcomes information. Therefore, physicians (and hospitals) are unable to routinely monitor and compare the effectiveness and true costs of different treatments/procedures as well as physician performance. An example of this needed database is currently being developed on a small-scale pilot basis "in-house" by UH physicians in the Department of Surgery to readily view patient outcomes by surgical sub-specialty. This is helping to overcome the difficulties in having so many disparate clinical information systems and makes the data more valuable than before. This program interfaces with each hospital database to extract the information necessary to recreate a patient's hospital stay from admission to discharge, as well as the occurrence of any readmissions and outpatient visits and procedures. It provides physicians and hospitals with treatment and outcome information that was previously unavailable such as: true patient treatment history, including physician's costs and data, combined with hospital costs and data; comparison of recovery time and costs for competitive treatments (e.g., laparoscopic versus open);

physician performance (operating room time, recovery time, length of stay, etc.); readmissions based on type of surgery, physician, etc.; and research or educational purposes (for example, outcomes relating to a particular surgery with patients having particular complications or diagnoses). However, this type of database is needed not just for one clinical and academic department, but for all UH and CWRU departments; and not just for information within UH, but also for information between UH and other institutions. Currently, the cost of creating and sustaining such a system is prohibitive. For the above mentioned "in-house" database for the Department of Surgery is estimated that it will take ten full time employees and $1.1 million to create, run, and sustain this integrated database system. Federal support is necessary if this type of technology is to be fully developed and maintained.

2) Cancer Care: The Ireland Cancer Center at UH is one of only 39 Comprehensive Cancer Centers in the country designated by the National Cancer Institute. (NCI), allowing Ireland to offer cutting-edge treatments earlier than most other cancer centers. Our affiliation with CWRU provides ongoing studies aimed at cancer treatment and prevention. Cancer therapies change on a case by case basis and most institutions are turning to a multidisciplinary approach, employing experts in surgery, medical oncology, radiation therapy, pathology, nursing, social work and psychology working together to create a personalized treatment plan that meets the physical, emotional and spiritual needs of patients. Moreover, new treatments and investigational procedures are tested every day in cancer patients. At UH alone there are more than 300 cancer clinical trials, many of them featuring new drugs developed by our own clinician-scientists. With such a large group of medical care providers and variety of cancer treatments, Federal funding for CER is needed not just to continue expanding available cancer treatments, but also to standardize and prioritize these cancer therapies based on patient outcomes to ensure proper allocation of resources.

3) Children's Health Care: Rainbow Babies and Children's (RBC) Hospital at UH is one of the top Children's Hospitals in the world. RBC is a world leader in the treatment of children with heart disease , cystic fibrosis, sickle cell disease and endocrine and metabolic disorders . As part of the Ireland Cancer Center, RBC's comprehensive pediatric cancer center offers the most promising treatments to children. RBC is ranked #2 in neonatal care/NICU and among the top 10 best hospitals in the country for neurology / neurosurgery and respiratory disorders[7]. Children receiving medical care are at risk because the devices and treatments given to them are often not adapted or tested for pediatric care, but rather for adult care. This results in a focus on pediatric disease treatment instead of pediatric disease prevention even though research is beginning to show that early intervention is not only clinically effective, but also cost effective. While some Federal support has already been given to stimulate pediatric medical device development, there is currently no consensus on the priorities for products needed by pediatric healthcare providers based on verifiable reference data, and there is no roadmap for companies, investors, and grantors seeking to focus on developing the most needed and most feasible products. Federal support is needed to (1) create priorities and focus

[7] US News and World Report 2008

CER in pediatrics, (2) develop treatments and devices specific to children and specific to preventative care, and (3) generate quality system processes to deliver pediatric care.

4) UH has assembled an integrated team of some of the country's foremost experts in cardiology, interventional cardiology, heart failure and transplant, electrophysiology, cardiac and vascular surgery. This highly specialized team of experts forms the foundation of University Hospitals Harrington-McLaughlin Heart & Vascular Institute, a premier center for comprehensive care of patients with diseases affecting the heart and vascular system. Our goal is to create a national center of excellence in cardiovascular research and physician education, as well as patient care. A terrific example of CER under way in the Heart & Vascular Institute has been a large program for calcium screening through computed tomography with the aim of early detection and treatment of cardiovascular disease. In the past year alone over 3,000 people have been screened with this method and today there are significant efforts at putting these data into research databases for CER research. The CER protocols have been developed and approved by the IRB. Federal funding in this area could greatly help expand the significant screening that is already underway and could help to establish a valuable CER database for future development of clinical care screenings.

5) Neurologic Care: The Neurological Institute of UH is the first designated institute in Northeast Ohio dedicated to improving outcomes in patients with diseases affecting the nervous system. The institute includes 14 Centers of Expertise that provide patients access to services at locations across Northeast Ohio. UH offers the latest in innovative technology for the diagnosis and treatment of all neurological conditions and is committed to expanding and integrating translational research into clinical practice. The collaboration with CWRU allows basic science research and clinical trials to be quickly translated to offer patients direct and rapid access to leading-edge treatment alternatives. This is all accomplished through the use of CER methodologies that are in need of additional infrastructure in order to be expanded and maintained on a large scale over time.

UH has been, and needs to continue to be, pre-eminently positioned to design, conduct and report on CER for the benefit of the patients served not only in Northeast Ohio, but regionally, nationally and internationally. The significant resources and efforts described herein provide a snapshot of the already significant programs in this area and outline the basic needs necessary to continue to pursue these lines of scientific and clinical inquiry. Academic Medical Centers like UH and CWRU together have the obligation of providing CER data to physicians and other health care professionals in order to arm the next generation of providers with the information necessary to prevent, treat and cure diseases in the future.

Submitted by
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Good afternoon. My name is Cynthia Reilly and I am the Director of the Practice Development Division at the American Society of Health-System Pharmacists. ASHP represents 35,000 pharmacists, pharmacy students, and pharmacy technicians who practice in hospitals and health systems. Pharmacists' expertise in medication use ensures that drug therapies are used safely, effectively, and in a cost-conscious manner. I appreciate the opportunity to present the Society's perspective on comparative effectiveness research, or CER, to the distinguished members of the Federal Coordinating Council for Comparative Effectiveness.

ASHP is a member of the Alliance for Better Health Care, which advocated for inclusion of comparative effectiveness research funding within the American Recovery and Reinvestment Act of 2009. The Society is also publisher of *AHFS DI*, a comprehensive, independent reference on the clinical use of medications, which is recognized through federal legislation under Medicare Part B, Medicaid, and Medicare Part D as an official compendium. For over 50 years, *AHFS DI* has followed sound and high-quality editorial processes to synthesize complex evidence for dissemination and use by a broad range of stakeholders, including prescribers, pharmacists, individuals who make health-policy and coverage decision, patients, and others. ASHP believes there is significant need to compare the effectiveness and safety of specific drug therapies within pharmacologic classes, drug therapies within different classes, and drug therapies with other treatment modalities. *AHFS DI* can serve as a foundation for medication information to support CER and ASHP looks forward to participating in this research.

Today, ASHP requests that the Council consider three CER recommendations related to health care delivery systems that represent critical information needs to improve patient outcomes:

- Optimal practice models for delivery of patient care,
- Strategies for using IT-enabled decision support for delivery of CER, and
- Best practices for disseminating and implementing CER.

As described by the Dartmouth Atlas, the quality and cost of care is inconsistent across geographic regions, with much of this inconsistency attributed to variation in the care setting and the health care professional that provides the service. Under Medicare Part D, pharmacists provide medication therapy management services that include formulating medication treatment plans; monitoring and evaluating patients' response to therapy; performing medication reviews to identify, resolve, and prevent medication-related problems; and coordinating and integrating MTM services within the broader health care services provided to patients. Pharmacists also participate in chronic disease management and prevention activities under collaborative practice agreements with physicians. MTM programs and published research have demonstrated that

pharmacist management of disease and drug therapy significantly improves patient outcomes, while reducing overall health care costs. However, there is limited research that directly compares this practice model to models in which care is provided by other health care professionals or interdisciplinary teams. ASHP believes such research would demonstrate best practices and strongly recommends models of care as a research priority for CER.

A critical element of CER is ensuring that research findings reach the point of care where clinicians, together with patients, can use the information to make informed treatment decisions. Electronic health records and other technologies are expected to provide point-of-care information; however use of these technologies is currently limited, as described in a recent *New England Journal of Medicine* study that found less than 2% of hospitals have fully implemented an electronic health record with clinical documentation, test and imaging results, CPOE, and decision support. Decision support technology has great potential to deliver CER findings, but strategies for creating and integrating these programs within other technologies, as well as barriers to implementation, are not well-studied. ASHP encourages the Council to support research that compares approaches for using clinical decision support and other technologies in the translation and implementation of CER.

In addition to technology, other effective dissemination and translation techniques are needed to ensure that CER findings are used to make informed decisions that improve patient outcomes. However, there are significant challenges in these activities. It has been estimated that there is a 17-year lag time between evidence generation and its widespread implementation. Many strategies have been used to enhance the rate and extent of adoption of evidence-based best practices, including clinical guidelines, continuing education for health care professionals, patient education tools, and most recently, academic detailing. However, these approaches are not well studied and results are variable. ASHP would encourage the Council to support research that compares the benefits and limitations of each approach in order to determine the strategy, or combination of strategies, that facilitates use of CER by each audience, including clinicians, patients, and payers.

Finally, based on ASHP experience as a drug information publisher, we encourage the Council to consider that, similar to drug information, CER research and dissemination efforts are not single events, but rather an ongoing process that requires sustainable and ongoing effort to ensure the currency and usefulness of the information as evidence evolves.

ASHP appreciates this opportunity to provide recommendations for CER. Along with our members, we look forward to collaborating with the Council and others to ensure that CER is not only useful, but also disseminated to clinicians, payers, and patients and subsequently translated into practice.

Submitted by
Jennifer Covich Bordenick
Chief Operating Officer and
Interim Chief Executive Officer
eHealth Initiative

The eHealth Initiative thanks the Federal Coordinating Council for Comparative Effectiveness Research for this opportunity to comment on the use of real world electronic health care information for comparative effectiveness research. The eHealth Initiative (eHI) is an independent, non-profit multi-stakeholder organization whose mission is to improve the quality, safety and efficiency of health care through information and information technology. eHI engages multiple stakeholders across every sector of health care to reach agreement on and drive the adoption of common principles, policies and best practices for mobilizing information electronically to improve health and health care in a way that is responsible, sustainable, responsive to each stakeholder's needs—particularly patients, and which builds and maintains the public's trust. The eHealth Initiative is involved in work related to comparative effectiveness in several ways: through pilot projects, educational efforts, and a multi-stakeholder working group.

Electronic data sources that capture the experience of millions of patients have developed over the past few decades and will expand further. Where such records are searchable, it is possible to efficiently assess such information using statistical queries and methods. Such methods may be able to sort through this large volume of data to provide important information on the relationship of medical interventions, types of patients, and types of medical conditions. Ultimately, this type of assessment may provide more refined information on the effects of medical interventions on different populations and in the context of different mixes of therapy.

The eHealth Initiative Foundation's Connecting for Drug Safety Collaboration

The eHealth Initiative Foundation's Connecting for Drug Safety Collaboration is a public-private sector effort designed to test and evaluate the feasibility and value of using electronic health information to support post-market surveillance and medical product safety. The findings from the Collaboration are intended to help inform the Food and Drug Administration's Sentinel Initiative. This work is strongly related to comparative effectiveness issues, since many of the same issues regarding uses of different data environments and basic scientific approaches would also apply to comparative effectiveness work.

Guided by eHI's multi-stakeholder Leadership Council and the Connecting for Drug Safety Advisory Board, this collaborative effort initially launched with a focus on two community-based healthcare organizations with advanced stage clinical information systems — Partners HealthCare System in Boston, MA and the Regenstrief Institute in Indianapolis, IN. During the course of the Collaboration's work, the Department of Defense was added as a third research community; findings are expected to be available in the near future. The Food and Drug Administration plays a critical advisory role in the Collaboration. The Agency for Healthcare Research and Quality and the Brookings Institution's Engelberg Center also serve in an advisory capacity.

The eHealth Initiative Drug Safety Collaboration sought to answer two basic questions:

1) What value do the different types of health care data sources bring to post-market drug safety questions?
2) What happens when the same drug safety research question is asked of different groups of researchers with expertise in their own data environments?

The eHealth Initiative Working Group on Using Health It for Comparative Effectiveness and Outcomes Research

The eHealth Initiative has also started a Working Group on Using Health IT for Comparative Effectiveness and Outcomes Research. The new working group brings together leaders from more than 25 organizations representing every sector of health care to learn, discuss, and work on this important theme in health care. Building on eHI's extensive efforts working with diverse groups of stakeholders to share best practices, test methods in real-world settings, and find common ground on policies, principles and strategies for improving health and health care through health IT and health information exchange

Objectives for Use of Real World Electronic Health Care Data

There is much that we do not know about the value or approaches of such work. It should not be surprising that trying to understand the basic building blocks of this research is itself a difficult matter. One could start by trying to articulate the goals of such exercises. Below are few objectives that may be connected.

1. Providing the most accurate and scientifically supportable assessment of medical conditions and interventions;
2. Gaining new scientific insights;
3. Assuring transparency, objectivity, and comparability in process and methods; and
4. Providing useful information for patients, providers, policymakers and other key stakeholders.

However, there are many stakeholders interested in this area. It will be important to get a clear understanding among stakeholders regarding such objectives.

Many stakeholders have different understandings of the possibilities of this research, reliability of this work, and definitions related to comparative effectiveness. The medical community, appropriately, does not want to oversimplify the importance and complexity of this process. It is important as we proceed that we develop trust and understanding. This means providing a clear framework for such research and finding a means to evaluate and communicate its reliability to a broad range of stakeholders.

Challenges for the Use of Real World Electronic Health Care Data

We need to acknowledge the many challenges of using real world data for comparative effectiveness research. By using real world data, researchers are outside the controlled setting of a clinical trial, and therefore are studying data on patients who may be taking multiple medications or dealing with multiple medical problems. In actual clinical practice, physicians may choose to prescribe one therapy over another on the basis of severity of disease, patient characteristics, and other factors that may not be apparent in health care data bases.
Unlike clinical trials, studies based on "real world" data are more likely to rely on incomplete information, since the data was collected for clinical care, not specifically for research. First, most patients do not have a comprehensive medical history located in one data source. Second, some patient records are not in electronic form and, thus, not practical for large data base studies. Third, claims data is set out for billing purposes and can be misleading with respect to actual diagnoses. Fourth, medical information terminology can vary from data source to data source. Finally, the type and amount of information available on given patients can vary. In such situations the data may be incomplete or inaccurate. This can also make combining results of analyses from different data sources a challenge.
Studies based on real world data are more susceptible to bias than randomized clinical trials. If one does not design a project to identify and eliminate sources of bias, it will make the conclusions less valid. The process for determining definitions or criteria for "real-world" study populations is important, requires judgment, and is itself a potential source of bias.

Priorities for Research

Among the priorities for research, we want to emphasize the need for research that involves collaborations in different data environments and research that explores the use of different types of electronic health care data. This is important, basic, and practical work that can be very informative in the development of a comparative effectiveness research infrastructure. Using available information, researchers and regulators use scientific procedures and judgment to try to determine the relationship between medical interventions and outcomes among different populations. The use of clinical data, in addition to claims data, as a source of information for adverse event detection is an emerging area. Therefore, researchers are still learning about the application of different methods for using clinical data, and best practices have yet to be defined. Building a base of trust, best practices and appropriate expectations from such comparative

effectiveness research will take time. The eHealth Initiative would like to work with you to help develop such a framework.

Another area that needs attention is research on how health information technology and electronic health information exchange can be used to create more robust data sources and to help evaluate comparative effectiveness issues across a broader range of settings.

Finally, it is important to focus on projects that address how research might facilitate or assist in medical decisions. Knowledge that is generated from this comparative effectiveness research could be extremely valuable to the medical decision-making process.

The eHealth Initiative looks forward to working with the Council as it proceeds to develop its recommendations, and thanks the Council for this opportunity for comment. If you have any questions, please feel free to contact me at Jennifer.Covich@ehealthinitiative.org.

Submitted by
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Thank you for this opportunity to provide comments on behalf of the American Psychological Association (APA) regarding national priorities for comparative effectiveness research. I am Dr. James Bray, APA President and Associate Professor of Family and Community Medicine and Psychiatry at the Baylor College of Medicine.

APA is the largest scientific and professional organization representing psychology with 150,000 members and affiliates. APA is also the largest publisher of behavioral science research, with 52 premier scholarly journals.

Comparative effectiveness research is a critically important tool for advancing an evidence-based approach to health care decision-making. However, the full public health benefits of such research will only be realized if behavioral, psychosocial, and medical interventions for the prevention and treatment of mental and physical health conditions are evaluated individually and in combination. Even when strictly medical treatments are compared, it is important to expand the range of outcome measures to include behavioral and psychological outcomes, such as quality of life and adherence to treatment protocols. It is also essential to evaluate promising new models of care, such as the use of integrated, interdisciplinary behavioral and medical teams in primary care settings. And finally, the effectiveness of health interventions across the lifespan and for different minority and gender groups must be considered.

Therefore, APA is recommending that comparative effectiveness research focus on these five areas:

We encourage research that compares different behavioral and psychosocial interventions for the prevention and treatment of specific health conditions. This research is crucial given that the leading causes of chronic health problems and mortality in the United States—such as heart disease, diabetes, and many forms of cancer—are due to modifiable behavioral factors, such as smoking, improper diet, lack of physical activity, and excessive alcohol consumption, among others. In addition, mental disorders, such as depression, represent a significant disease burden in the U.S. and worldwide. Fortunately, effective behavioral and psychosocial interventions exist to reduce life-threatening behaviors and treat health conditions, such as depression, heart disease, chronic pain, and diabetes. Now is the time to test the comparative effectiveness of these interventions to improve the health of the public.

Next, we strongly encourage research that compares behavioral and psychosocial interventions with medical interventions, and combinations thereof. This type of research allows for an examination of the relative and combined effectiveness of behavioral and medical interventions for specific health conditions.

A classic example of the value of this form of comparative research comes from the randomized controlled trial of the Diabetes Prevention program, which found that intensive lifestyle intervention, as compared to placebo or medication, reduced the incidence of type 2 diabetes to half that of placebo, and was significantly more effective than medication alone. Enhanced outcomes have also been found for combined behavioral and pharmacological interventions for depression and smoking.

Next, we should pursue research that compares integrated systems of care comprised of interdisciplinary teams of medical and behavioral health providers versus routine medical care. There is some indication that co-locating medical and behavioral health providers improves patient access and health outcomes.

For example, the integrated care approach has shown the largest reduction in depression levels and highest patient satisfaction. Interestingly, mortality was reduced on one recent large trial of integrated, primary care-based treatment of depression.

We also believe that all health research studies should include measures of behavioral and psychosocial outcomes, such as life quality, adherence to treatment protocols, behavioral functioning, depression, and anxiety. Such attention to patient-centered care builds upon the IOM's own definition of evidence-based practice.

As new life-saving medical advances are developed, we must strive to maintain patient quality of life. For example, depression and anxiety have been shown to increase in heart disease patients using implantable cardioverter defibrillators. Both the positive and negative outcomes of medical procedures need to be considered and evaluated before they are adopted as standard practice.

And finally, research that examines health intervention outcomes across the lifespan and for different minority and gender groups is needed to understand the effectiveness of

interventions within and between population groups. This type of comparative research is important given the well documented health disparities that exist between different racial/ethnic, age, socioeconomic status, gender, and sexual minority groups, and because it is not clear if specific behavioral and medical interventions are equally effective across groups. This type of comparative research is critical as the U.S. population becomes more diverse.

Thank you for the opportunity to provide this brief statement. The American Psychological Association looks forward to the outcome of your deliberations.

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The ACC strongly supports investment in comparative effectiveness research (CER). Given the high prevalence of heart disease-related illnesses, along with the documented variability in the use of procedures used to treat and/or diagnose it, comparative effectiveness research could yield high returns in terms of improving patient outcomes and reducing costs.

Specifically, comparative effectiveness research is an essential building block to understanding the populations that may benefit from the many treatment options associated with cardiovascular disease, including medical therapy, stents, surgery and defibrillators. Understanding the comparative effectiveness of both diagnostic and treatment strategies in different patient populations, especially the elderly, is very important. Effective detection and risk assessment of coronary artery disease can help physicians determine the most appropriate care for their patients, whether it be more aggressive therapy and procedures or less intensive cardiac follow-up.

In particular, comparative effectiveness research of diagnostic imaging is a high priority for the ACC (see list of top CER priorities below). Understanding the comparative effectiveness of various cardiac imaging and diagnostic tests could help better target the use of these beneficial technologies and help inform policy decisions related to the use of these technologies. Randomized trials and registries will be important to understanding the role of imaging and other diagnostic tests in not only diagnosis but their impact on downstream treatment and outcomes.

Facilitating linkages of clinical and administrative databases is crucial to developing this research agenda (see infrastructure priorities below). Inpatient and outpatient registries could help track key elements of comparative effectiveness, including laboratory results, medication adherence and diagnosis decisions. Translation of the results of comparative effectiveness research will require transparency in terms of how users discuss certainty of the resulting evidence, the trade-off of different types of risks and benefits, and what it means for two or more strategies to be equally effective.

Cost-effectiveness must also be a critical priority for health reform given the reality of finite financial resources and rising costs. However, the College strongly believes comparative effectiveness research must remain strictly focused on comparative clinical science, such that decisions regarding cost effectiveness can be made sequentially later. This segregation of these important processes will be essential to ensuring physician and patient trust in the ethics and integrity of such work.

Comparative effectiveness research has the potential to make it much easier for patients and their doctors to choose the best treatment and avoid unnecessary treatment for not only heart disease, but other diseases a well, thus improving quality and ensuring greater patient value. The College looks forward to working with you on this endeavor.

Top Comparative Effectiveness Research Priorities

1. **Comparison of diagnostic tests for suspected Coronary Artery Disease (CAD) (Randomized Clinical Trial).** Compare the effectiveness of stress electrocardiography, stress echo, coronary computed tomography angiography (CCTA), and single-photon emission computed tomography (SPECT MPI) for the diagnosis and risk assessment of coronary artery disease in adult, intermediate pre-test probability patients with stable chest pain by assessing impact on detection and risk assessment, subsequent treatment (medical and procedures), prior and subsequent invasive and non-invasive cardiac imaging utilization, major adverse cardiac events, and cost. As several proposed trials were submitted to NHBLI in February, this project is "shovel ready."

2. **Comparison of diagnostic tests for Coronary Artery Disease (CAD) (Registry).** Compare the effectiveness of stress electrocardiography, stress echo, coronary computed tomography angiography (CCTA), and single-photon emission computed tomography (SPECT MPI) for diagnosis and risk assessment of coronary artery disease by assessing appropriate use patterns based on published criteria, prior and subsequent invasive and non-invasive cardiac imaging utilization, subsequent procedures, overall radiation dose and other safety issues, major adverse coronary events for normal studies, and testing and downstream costs.

3. **Compare preventive strategies guided by coronary artery calcium scoring versus usual care (RCT).** Compare the effectiveness of using a coronary calcium screening directed prevention strategy versus usual care in asymptomatic individuals who have low to intermediate coronary artery disease risk by assessing major adverse coronary events, medication usage, adoption of secondary prevention therapy, quality of life, and cost

4. **Linking STS, NCDR, and CMS databases.** By linking the clinical data from the Society of Thoracic Surgeons National Database and the ACC National Cardiovascular Data Registry with Centers for Medicare and Medicaid Services (CMS) administrative data, a powerful, longitudinal data set could be produced. Such a data set would contain process, outcomes, utilization, pharmacy, and cost data spanning perhaps a three to five year period. This linking project has the potential to cover the continuum of care for cardiovascular disease. Ultimately, the information obtained from this collaborative effort will aid in the analysis of the comparative effectiveness of coronary revascularization treatment strategies, such as coronary bypass rafting and stenting procedures.

5. **Ablation versus cardioversion.** Compare the effectiveness of ablation therapy for the treatment of atrial fibrillation versus electrical cardioversion by assessing cardiac

function, mortality, major adverse cardiac events, quality of life, and cost in a real world setting by paralleling the current randomized clinical trial.

Top CER Infrastructure Initiatives (What types of investments in infrastructure for comparative effectiveness research should the Coordinating Council consider?)

1. Creation of robust national registries for tracking both short- and long-term performance of therapeutic strategies, drugs, or devices
2. Clinical registry development, application, and networking
3. Clinical data pooling and mining support
4. Capacity to use electronic health records for safety and effectiveness monitoring
5. Clinical trials support (e.g., ad hoc collaborations)

Criteria for Setting Priorities (What criteria should the Coordinating Council consider when evaluating different investment options?)

1. variability in care
2. potential to act on the information once generated
3. disease burden
4. utility of the answer for decision-making
5. cost

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The focus of this testimony is on the contribution comparative effectiveness research can make to the extension of the newly developed consensus standards for treatment of substance use conditions, published by the National Quality Forum (NQF). The Treatment Research Institute and the UCLA Integrated Substance Abuse Program have been asked to provide leadership for the dissemination and adoption of the consensus standards by States financing treatment in the public sector.

Despite the knowledge that addiction to alcohol and drugs is a treatable health condition, the failure to provide care consonant with scientific evidence is manifest in the lack of ongoing care for substance dependence consistent with the condition's chronic nature. Scientific advances have resulted in a spectrum of evidence-based psychosocial and pharmacologic treatments for individuals with unhealthy use or dependence on alcohol and/or drugs----treatments whose results compare well with those obtained with treatments for other chronic illnesses. It is increasingly apparent that patients with more chronic forms of substance use disorders require and do well with appropriately tailored continuing care and clinical support as in other chronic illnesses such as cardiovascular diseases and diabetes.

There are gaps, however, in knowledge of which evidence-based therapies are better than others, how to treat multiple co-morbidities present in so many patients, and how to care for some population subgroups. Despite these gaps, there has been an impressive increase in the number and quality of studies on efficacious therapies for adolescents and adults. Yet, there remain large gaps in the research on the *effectiveness* of these treatments when delivered in usual settings of care, especially on how the costs of treatment are integrated into the research. In particular, there are significant gaps in the efficacy and effectiveness research related to individuals who are neither "unhealthy" but risky users of alcohol and/or drugs nor chronically and severely dependent. For this "middle" group comparative effectiveness research seems particularly critical.

Developing standards of care for addiction treatment in the public and private sectors is a relatively recent activity. Between 2005 and 2007, with funding from the Robert Wood Johnson Foundation and the Federal Center for Substance Abuse Treatment/SAMHSA, the National Quality Forum (NQF) conducted a consensus process to identify evidence-based organizational and clinical practices for treatment of substance use disorders. The basic principles outlined by the NQF and the specific standards and practices that were identified should serve as the basis for moving forward with comparative effectiveness research in addiction treatment. In addition to publishing the standards and practices, the NQF recommended additional research be conducted to improve the identified practices and the development and implementation of performance measures related to each practice standard.

There are differing views about the acceptability of various forms of evidence, what level of evidence is necessary for a practice to be endorsed as "evidence-based," and whether knowledge of evidence-based care for a population can be adapted to meet an individual's unique needs. Although the Agency for Healthcare Research and Quality has (AHRQ) identified sound methods for rating the strength of scientific evidence, its findings have not resolved debates about whether a given intervention is evidence-based, for whom, and under what conditions.

The focus on randomized clinical trials, while the gold standard for generating clinical evidence, cannot be relied upon exclusively to identify evidence-based care due to the sheer numbers of possible psychosocial and pharmacological interventions for substance use disorders. Furthermore, clinical trials do not generally include economic and cost analyses essential for comparative effectiveness research. Costs are borne not only by individuals and families, but by treatment organizations and, in the case of substance use disorders, almost entirely by the public sector. By 2014, the estimates made by a study of national expenditures funded by SAMHSA and published in *Health Affairs* (2008) show that we can expect about 85% of treatment expenditures for substance use disorders to be paid for with public financing—Federal, State, and local dollars.

Of critical importance to advancing the consensus standards identified by the NQF is a focus on the systematic analyses necessary to translate the evidence being generated in scientific research into clinically useful practice guidelines. Many of the numerous professional groups involved in treatment of substance use disorders have conducted their own reviews of the evidence and promulgated their own practice guidelines. The guidelines include little discussion of what might be included in comparative effectiveness research----the characteristics of the individuals

targeted for specific interventions, the structural and financing characteristics of organizations that are necessary for adoption of specific guidelines, the costs of the identified interventions to treatment organizations that are responsible for implementation related to training and staffing requirements, and the like. Numerous studies have identified clinicians' departures from evidence-based practice guidelines for opioid dependence and other substance use disorders.

If we expect improvement in the quality of care for treatment of substance use disorders, the clinical appropriateness of such variations needs become a focus of performance measurement. Performance measurement for addiction treatment at the treatment system level (health plans, States, and Counties) was first advanced by the Washington Circle Group (WCG). The WCG, a group of researchers, policy makers, States, and practitioners, since 1998 has worked to identify the processes of care necessary for addiction treatment, specify and test performance measures, and work with accrediting bodies and purchasers to adopt and utilize the measures. If we want an "uptake" in the use of evidence-based practices, measures are necessary, in addition to comparative effectiveness research, to be able to assure treatment organizations and clinicians that the evidence-based standards and practices they are being asked to adhere to have clear advantages in effectiveness and cost-effectiveness relative to the practices they are employing.

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Members of the Federal Coordinating Council (FCC), I am Andrew Sperling, Director of Legislative Advocacy for the National Alliance on Mental Illness (NAMI). NAMI is the largest national organization representing individuals living with serious mental illness and their families. Through our more than 1,100 affiliates in all 50 states NAMI is engaged in support, education and advocacy around serious mental illness.

NAMI believes strongly in the promise of comparative effectiveness research to improve quality and outcomes in health care. As a member of the Partnership to Improve Patient Care (PIPC), NAMI has endorsed a set of principles that we believe can help ensure that comparative effectiveness meets its full potential and does not become a blunt instrument that limits patient choice and results in cost becoming the dominant factor in guiding treatment decisions. Among these principles for ensuring that comparative effectiveness research is patient-centered:

- Defining CER as a tool to improve patient care;
- Focusing on communicating research results to the public, not making centralized coverage and payment decisions;
- Providing information on clinical value and patient health outcomes, not cost effectiveness assessments;
- Recognizing the diversity, including racial and ethnic diversity, of patient populations and communicating results in ways that reflect the differences in individual patient needs;

- Examining all aspects of health care – including medical interventions, care management, benefit design, and processes of care – that can improve care quality and reduce health care disparities; and
- Requiring open and transparent processes where all stakeholders have equal voice in governance and input into research priorities.

In moving forward to develop recommendations and research priorities for the Secretary, NAMI urges the Coordinating Council to think big and undertake research directed at the most important challenges facing our nation's health care system. The Coordinating Council should resist any focus on short-term clinical trials that simply compare two distinct interventions such as head-to-head comparisons of two medications. Rather, comparative effectiveness research should examine the range of issues that affect the quality of patient care (medical tests and treatments, health care delivery and organization, benefit designs and care management). All of these elements of health care affect patients' quality of care and health outcomes. These elements of care also have a significant impact on health care disparities. Research is needed to identify the best approaches to reducing disparities. In addition, sound comparative effectiveness research should include the different factors important to consumers, including quality of life, independence, productivity and recovery.

CER that starts with cost containment as a central goal will not lead to studies that answer these questions, and will likely result in misapplication of findings in order to achieve cost-cutting objectives. By contrast, CER that begins with the goal of quality improvement can help everyone in health care make better decisions and will ultimately lead to better health care value and greater cost efficiencies. This requires addressing the different factors that can help decide which treatment is optimal for the individual, such as the patient's particular medical condition, past treatment history and genetic variations.

Basing Public Policy Decisions on Comparative Effectiveness Has Limitations

NAMI would like to caution the Coordinating Council with regard to the limitations and difficulties associated with using existing comparative effectiveness studies that are now being used to drive policies related to treatment choice and prescribing decisions. There is no better example of this than the NIMH CATIE trial on antipsychotic medications. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) was the first large scale attempt to compare five different medications used to treat people living with schizophrenia. The study included both newer (atypical) and one older anti-psychotic medication. In general terms, the study found that there was relatively little difference in the effectiveness of any of the medications. Without regard to which medication was randomly assigned, patients discontinued the use of medications at similar rates due to intolerable side effects or failure to adequately control symptoms.

It is important to note that CATIE used discontinuation as a proxy for efficacy. Further, the protocols for the study required that patients be "randomized" to one of the five drugs. In NAMI's view, this randomization does not reflect best clinical practice which calls for a dialog between a medical professional and consumer that helps determine a best-choice medication based upon treatment goals and risk of side-effects. In addition, CATIE was only 18 months in

length, not enough time to accurately measure serious neurological side effects known as extrapyramidal symptoms (EPS) and movement disorders such as Tardive Dyskinesia associated with the older antipsychotic medications.

More importantly, CATIE is NOT the basis for any conclusion that "the older antipsychotic medications are just as good as the newer ones." In fact, 69% of the participants switched to a different medication at least once during the trial and just over half switched twice or more. If anything, CATIE supports a strong conclusion that there is no "one size fits all" in any aspect of schizophrenia treatment. At the systems level, patients and their support system should be skeptical of any attempt to change medications if treatment is demonstrating progress. NAMI believes that states should never engage in the practice of medicine.

Roles and Responsibilities for the Federal Coordinating Council

The announcement for this Listening Session in the Federal Register details 6 specific questions on which the Coordinating Council is seeking input from stakeholders and the general public. NAMI would like to address each of these questions separately

1. What types of investments in infrastructure for comparative effectiveness research should the Coordinating Council consider?

Investments in infrastructure of CER should be carefully considered. The $1.1 billion included in the ARRA is not a permanent authorization and it is uncertain whether Congress will continue to appropriate funding for CER beyond the 24 to 36 month time period authorized in the law. While investment in multi-site clinical trial networks and training for researchers and investigators are critical to furthering research and discovery, they cannot sustain themselves without ongoing funding from Congress over the long-term – far beyond the ARRA timeframe.

NAMI urges that these ongoing costs associated with high quality biomedical research continue to be a part of the NIH where they can be more appropriately maintained and developed over time.

2. What criteria should the Coordinating Council consider when evaluating different investment options?

As noted above, NAMI recommends investment of CER resources into the most difficult challenges facing our health care system, especially in the area of chronic disease management of conditions that represent the greatest public health burden. Investment in short-term head-to-head comparisons of specific interventions may be quicker and easier, but they will not help us move forward in addressing the most costly and difficult challenges such as the growing prevalence of obesity, diabetes heart disease, COPD, etc. The Coordinating Council should set forth criteria that prioritize examination of effective multi-systemic interventions in real world treatment settings among patients with multiple co-morbidities. NAMI would note for the record that adults with serious mental illness are experiencing significantly higher rates of the medical co-morbidities and experience (on average) as much as 25 years of lower life expectancy according to a 2006 study from the National Association of State Mental Health Program Directors (NASMHPD).

http://www.nasmhpd.org/general_files/publications/med_directors_pubs/Mortality%20and%20Morbidity%20Final%20Report%208.18.08.pdf

3. What Federal government activities in the area of comparative effectiveness research should the Coordinating Council focus its attention on?

NAMI urges the Coordinating Council to adhere to the activities set forth by Congress in establishing the Council as part of the ARRA, i.e. fostering coordination and advising the President and Congress. We note that the ARRA specifically bars the Coordinating Council from mandating coverage or reimbursement decisions or policies for both public and private payors. In addition, the ARRA explicitly states that Council recommendations shall not be construed as mandates or clinical guidelines for payment coverage or treatment.

4. How can the Coordinating Council best foster integration of these activities across the programs managed by the Departments of Health and Human Services, Defense, and Veterans Affairs?

NAMI urges regular meetings of the Coordinating Council and an open and transparent process that allows for maximum participation for all stakeholders, including patients. This should include the participation of disease advocacy organizations as the voice of patients, as opposed to the more general views of "consumer organizations." This distinction is critical since individuals living with chronic and life threatening illnesses (including serious mental illnesses) and their families are likely to offer unique perspectives on the importance of maintaining broad access to widest array of therapies and inventions. Inclusion of all stakeholders will also help ensure that unique needs of subpopulations, especially racial and ethnic minorities are integrated into these discussions. It is a perspective distinct from a "consumer" voice for the "average" patient.

5. What steps should the Coordinating Council consider to help ensure that public- and private-sector efforts in the area of comparative effectiveness research are mutually supportive?

Continuing regular public meetings such as this Listening Session will be critical to establishing a mutually supportive environment for public and private CER investments. NAMI also urged that, to the maximum extent possible, all Coordinating Council activities and meetings adhere to the standards in the Federal Advisory Council Act – advance public notice of meetings and meeting agendas, a public record, opportunity for public comment, etc.

6. What information on the Coordinating Council's activities would be most useful?

NAMI would be most interested in viewing information provided to the Coordinating Council by individual federal agencies and officials. It would therefore be helpful if any and all submissions from federal agencies be posted to the Council's website. Likewise NAMI recommends that all of the Committee's deliberations be conducted in public.

Submitted by
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Dear Dr. Conway:

The Suicide Prevention Action Network USA (SPAN USA) welcomes the opportunity to submit comments regarding the Federal Coordinating Council on Comparative Effectiveness Research (FCC-CER). SPAN USA is a 501(c)(3) organization dedicated to preventing suicide through public education and awareness, community action and federal, state and local grassroots advocacy. As you know well, suicide is the 11th leading cause of death in America and the third leading cause of death for younger Americans age 15-24. In addition, it is estimated that there are 800,000 suicide attempts each year. Reducing the number of suicides and suicide attempts among our nation's citizens is a criterion that the Coordinating Council should consider when evaluating different investment options.

As noted in the Federal Register Notice, there are investments in infrastructure for comparative effectiveness research that are needed. Currently, there is woefully inadequate data on suicide and suicide attempts in America. No government agency or private entity can determine exactly how many veterans die by suicide each year across America or how many murder-suicides have occurred. The National Violent Death Reporting System collects data from medical examiners, coroners, police, crime labs, and death certificates to understand the circumstances surrounding violent deaths including suicide. This information is important to develop, inform, and evaluate suicide prevention programs. However, the system does not operate in every state, but the Centers for Disease Control and Prevention (CDC) has the capability to continue expanding the system until all 50 states are covered. The Coordinating Council should consider investment in data systems infrastructure for suicides in order for comparative effectiveness research to be as useful as possible.

SPAN USA recommends focusing attention on government activities involving comparative effectiveness research on best practices for early intervention and prevention of suicide. The federal government has undertaken a number of activities to complete the goals and objectives of the National Strategy for Suicide Prevention. Unfortunately, at this time there are only 16 interventions listed in the Substance Abuse and Mental Health Services Administration's National Registry of Evidence-Based Programs and Practices. Additional research to determine evidence-based programs and practices that reduce suicide and suicide attempts are vital to reducing the public health problem of suicide.

For example, SPAN USA recommends a study to compare the safety and effectiveness of inpatient psychiatric hospitalization vs. the use of alternative service options (e.g., extended observation, partial hospital, and intensive outpatient care) for individuals following a suicide attempt. Following a suicide attempt, it is necessary to evaluate and monitor individuals in safe and risk-appropriate settings. An important research priority is to determine whether psychiatric inpatient hospitalization is the most cost-effective and least restrictive manner of providing care to acutely suicidal individuals, mindful of safety concerns. The use of alternative crisis services — e.g., extended observation beds, intensive outpatient services — may result in fewer repeat inpatient admissions while also allowing patients greater autonomy and increasing their collaboration with community-based treatments. Fear of adverse outcomes has hampered necessary, well-designed, risk-attentive comparative studies.

The Coordinating Council can foster integration of suicide prevention comparative effectiveness research activities across the programs managed by the Departments of Health and Human Services, Defense, and Veterans Affair by working with the Federal Working Group on Suicide Prevention that is co-chaired by staff from SAMHSA and the U.S. Marine Corps. Integration of suicide prevention research is already taking shape in the form of a $50M research study being conducted by the National Institute of Mental Health and the U.S. Department of Army. However, more research specific to comparative effectiveness for treatments, programs and practices to reduce suicide among veterans and military personnel is needed.

Once again, SPAN USA appreciates the opportunity to share our comments with the FCC-CER. Please do not hesitate to contact me at: baltman@spanusa.org or 202-449-3600 with any questions or concerns.

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On behalf of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), which together represent 4,000 practicing neurosurgeons across the United States, I would like to thank the Federal Coordinating Council for Comparative Effectiveness Research for giving us the opportunity to comment on comparative effective research priorities. My name is Rachel Groman, and I am the Senior Manager for Quality Improvement and Research in the AANS and CNS Washington Office.

Organized neurosurgery supports a ***well-designed*** comparative effectiveness research system that strengthens physician and patient decision-making, improves quality, and supports continued medical progress. Our members are committed to determining what medical treatments work best for their patients and our specialty is taking a variety of steps to ensure that the care neurosurgeons deliver is evidence-based. We have a robust practice guidelines development program and our specialty recently created a new clinical data registry entity called NeuroPoint Alliance. The NeuroPoint Alliance is partnering with Outcome Sciences, Inc. to build a database platform for a specialty-wide patient registry that will serve multiple purposes, including

Maintenance of Certification, clinical research, pay-for-performance and other quality improvement programs.

The AANS and CNS are very enthusiastic about partnering with the federal government, third party payers and others to conduct comparative effectiveness research that is important to neurosurgeons and their patients. To that end, we have identified a research priority that affects millions of American -- the treatment of common spinal disorders.

It is no secret that 75-85% of all Americans will experience back pain at some point in their lifetime and that management of chronic spinal conditions in the U.S. is estimated to cost nearly $85-100 billion each year. Despite advances in the surgical treatment of spinal diseases, which has dramatically expanded the treatment options available to patients, there is a deficiency of high quality clinical research to guide practice. This is largely due to the inherent difficulties of performing randomized controlled trials for surgical procedures and disorders characterized by significant heterogeneity, which often results in low patient compliance with randomized assignment. Consequently, many of the current clinical guidelines lack definitive guidance, resulting in marginal consensus among clinicians on what constitutes best practice and overall clinical uncertainty regarding the treatment of common spinal disorders. This has been reflected in significant regional variations in the treatment of neck and lower back degenerative diseases.

The AANS and CNS recently provided the Institute of Medicine (IOM) with specific clinical research recommendations focusing on two degenerative spinal diseases for which there is little high quality clinical research to guide practice: 1) low back pain without neurological deficit or spinal deformity; and 2) cervical spondylotic myelopathy. Low back pain is the fifth most common reason for seeing a physician in the United States, and cervical spondylotic myelopathy is the most common cause of spinal cord injury in both the United States and the world. Given the limitations of randomized clinical trials, we asked the IOM to consider the value of prospectively obtained data collected through patient registries to help identify specific patient characteristics that would serve as predictors of improved outcomes from different surgical and non-surgical approaches to these two diseases. We strongly encourage the Federal Coordinating Council to similarly consider the value of directing comparative effectiveness research funds to the creation and/or administration of a multi-center, prospective patient registry that could collect comparative data on different treatment approaches for degenerative spinal disorders. The AANS and CNS believe that the NeuroPoint Alliance is poised to serve as this registry, since it will produce meaningful data that will help refine indications, guide clinical decision-making, determine best practices, improve quality, and ultimately lower costs.

Thank you again for the opportunity to provide feedback on national comparative effectiveness research priorities. Organized neurosurgery looks forward to further exploring our registry project with the Federal Coordinating Council and to working with the federal government to collect the data needed to determine which treatments work best for neurosurgical patients.

Submitted by
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Dear Council Members:

The American Osteopathic Association (AOA) appreciates the opportunity to submit comments on comparative effectiveness research to the Federal Coordinating Council on Comparative Effectiveness Research as established by the American Recovery and Reinvestment Act of 2009. The AOA represents 64,000 osteopathic physicians nationwide, promotes public health, encourages scientific research, serves as the primary certifying body for D.O.s, and is the accrediting agency for all osteopathic medical colleges and health care facilities.

The purpose of our comments is to share our views on clinical and cost effectiveness research, inform the Council about AOA's guiding principles on comparative effectiveness research and its priority areas for comparative effectiveness research.

Clinical and Cost Effectiveness of Comparative Effectiveness Research

The AOA understands the purpose of the Federal Coordinating Council is to assist the offices and agencies of the Federal Government, including the Departments of Health and Human Services, Veterans Affairs, and Defense, and other Federal departments or agencies in coordinating the conduct or support of comparative effectiveness and related health services research; advise the President and Congress on strategies with respect to the infrastructure needs of comparative effectiveness research within the Federal Government; and assure optimum coordination of comparative effectiveness and related health services research conducted or supported by relevant Federal departments and agencies, with the goal of reducing duplicative efforts and encouraging coordinated and complementary use of resources.

A March 19, 2009 News Release of the Department of Health and Human Services states that the Council will help coordinate research and guide investments in comparative effectiveness research and will not recommend clinical guidelines for payment, coverage or treatment. Some Federal officials have stated that a portion of Recovery Act funds could be used for comparative effectiveness research that includes comparisons on the cost of treatments, but that the findings could not be used by Medicare as the basis of coverage decisions.

The AOA believes that it is in the best interests of the patient to exclude cost effectiveness of therapeutic or medical interventions from the decision-making process. Comparing the cost of interventions when the activity occurs between a patient and a physician with the final decision resting with the patient is entirely different from the use of cost effectiveness to deny coverage or treatment based on the cost of the intervention.

In our opinion, for comparative effectiveness research to realize its full potential, it must focus primarily on clinical efficacy. If the primary focus is on clinical efficacy, weighted against efficiency, physicians and patients will have relevant clinical information enabling them to make informed decisions on what is the best course of action. If clinical efficacy is removed as the primary focus, patients and physicians potentially may view such information from a negative perspective and the government's investment in comparative effectiveness research would fall short of our joint goals of improving quality, safety, and efficiency.

As stated in the following AOA Principles on Comparative Effectiveness Research, the physician-patient relationship must be protected. This includes the ability of physicians to provide individualized care using comparative effectiveness research as a recommended course of action, not a dictate and not to deny treatment based on cost effectiveness.

AOA Principles Regarding Comparative Effectiveness Research

Physicians and Patients

- Comparative effectiveness research should enhance the ability of osteopathic physicians (D.O.s) to provide the highest quality care to patients utilizing the best proven and widely accepted evidence based medical information at the time of treatment.
- Comparative effectiveness research should not be used to control medical decision-making authority or professional autonomy.
- Comparative effectiveness research should enhance, complement, and promote patient care, not impede it.
- Guidelines developed as a result of comparative effectiveness research studies should be advisory and not mandatory.
- Comparative effectiveness research should be viewed as a positive development for patients and physicians and a useful tool in the physician's armamentarium, working in concert with patients.
- Physicians in practice should be included in any discussions and decisions regarding comparative effectiveness research.
- Comparative effectiveness research should focus on clinical effectiveness, not cost effectiveness, and should not be used to deny coverage or payment.
- The physician/patient relationship must be protected and the needs of the patients should be paramount.

Location of a Comparative Effectiveness Research Institute

- The AOA would prefer that the Agency for Healthcare Research and Quality (AHRQ) be the home for comparative effectiveness research. Section 1013 of the Medicare Modernization Act (MMA) authorizes AHRQ to conduct comparative effectiveness research. AHRQ has been doing so since 2005. Under its Effective Health Care Program, AHRQ published studies on gastroesophageal reflux disease, renal artery stenosis, osteoporosis, osteoarthritis, rheumatoid arthritis, diabetes, depression, psychiatric disorders, hypertension, and prostate cancer.
- The AOA believes that AHRQ could collaborate with the National Institutes of Health (NIH) and other entities in cases where clinical trials or other resources are needed.

Funding

- The AOA believes that Congress should increase the current $50 million authorized in Section 1013 of MMA to a level commensurate with the funds necessary to carry out an expanded role in comparative effectiveness research.
- The AOA believes that there could be room for private funding provided that contributors are not in a position to influence study outcomes.

Governing Board

- The AOA believes that for comparative effectiveness research to be successful, all stakeholders (physicians, patients, researchers, government, and private sector) must be represented in the decision-making process.

AOA Comparative Effectiveness Research Priorities

On March 27, 2009, the AOA was pleased to submit the following research priorities to the Institute of Medicine (IOM) Committee on Comparative Effectiveness Research Priorities pursuant to the IOM's request for comment to its research priorities questionnaire:

- Compare the effectiveness of adding osteopathic manipulative treatment (OMT) to "best care" in low back pain in the primary care setting.

- Compare the effectiveness of coordinated care in the treatment of diabetics in the community versus standard care.

- Compare models of physician led community primary prevention in progression of glucose intolerance to diabetes.

The AOA thanks the Federal Coordinating Council on Comparative Effectiveness for considering our views.

Submitted by
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Comparative effectiveness research is imperative to better understand and improve the provision of care for children with asthma. We recommend prioritizing studies that compare, with respect to both cost savings and clinical outcomes, the effectiveness of an integrated asthma counselor/environmental mitigation chronic disease management model with a non-integrated episodic model for children with asthma. Childhood asthma is a significant chronic disease that has reached epidemic proportions in heavily disadvantaged communities, placing a disproportionate burden on low-income and minority families and communities. Childhood asthma carries high direct and indirect clinical, social, and economic costs - an estimated $20

billion in 2007 alone – in the form of preventable emergency department visits and inpatient hospital admissions, lost productivity, school absenteeism and family stress. Paradoxically, while much is known about effective integrated pediatric asthma management (including USPSTF recommendations for "home-based multi-trigger multi-component environmental interventions" for children with asthma), insurers continue to utilize coverage, cost sharing, and payment design strategies that treat asthma as an isolated episodic illness, and pediatric practice and public health have failed to systematically restructure their approach to emphasize an integrated chronic care/public health intervention.

A proposed model of comparison is an integrated asthma counselor/environmental mitigation chronic disease model with a non-integrated, episodic model of care. This can be accomplished through a range of health services research- including interventions specifically designed to better understand novel treatment pathways and comparisons of the standard of care/ usual care with new models as proposed above. This research should include children of all ages (young children and adolescents) and racial/ethnic minority groups.

The epidemic proportion of asthma among child populations at risk for social risk and heavy disease burden, coupled with the high costs associated with ineffective care, make asthma a prime candidate for comparative effectiveness research in pediatric health. The availability of a growing scientific and public health evidence-base, including appropriate models of integrated chronic disease management, also make asthma a priority where it is possible to improve the quality of life for children and families while reducing health care costs.

Submitted by
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The health professional educational system, particularly the education of physicians developed, over the last 100 years as a series of 'fixes' designed to ameliorate perceived gaps and deficiencies at specific points in time. This evolution took hold most notably with the publication of the AMA Council on Medical Education sponsored report of the Carnegie Foundation in 1910. The Flexnor report detailed the significant heterogeneity and inadequacy of physician training as the legacy of the 19th century. Since Flexnor, medical educators have put into place a cornucopia of solutions intended to assure the public that doctors and their care are of high quality care. These include, but are not limited to, medical school accreditation (LCME), residency program accreditation (ACGME), continuing medical education accreditation (ACCME, AMA PRA), board certification (ABMS), and state licensure (NBME, state licensure boards and FSMB).

Similar and parallel structures have developed in efforts to assure the public of the adequacy of nurses, pharmacists and other health professionals' education and maintenance of skills over a professional life. In addition, a concurrent system of public and private systems to evaluate and

accredit health care delivery systems has evolved.

Despite these efforts designed to assure high professional standards, it appears that the current educational systems for health professionals are inadequate in providing the requisite skills, knowledge and attitudes to assure the public of the highest standards of safe, quality care. This may be due in part to several factors. While not exhaustive, these include: the learning environment within professional schools, post graduate training programs and systems of continuing education, fragmentation of roles and responsibilities within the delivery system, financial incentives/disincentives which reward technical expertise and fail to penalize significantly for failure to measure, account and improve poor performance.

Unlike a heavy and sustained national investment in biomedical research, and more recently in health services research, there have not been significant resources devoted to developing and sustaining an infrastructure upon which to conduct meaningful and longitudinal research regarding the impact of innovation in health professional education. Limited resources have constrained our ability to understand the most effective methods by which to improve our educational systems and drive them toward expected educational outcomes. The limitation includes resources to conduct pilot, demonstration or multi-institutional collaborative projects, and longitudinal cohort studies of the impact of the educational continuum on practice attitudes, values, behaviors and outcomes. Further, despite the wealth of talent that resides within our institutions of higher education, little effort has been expended to capitalize on knowledge and learning from other disciplines which could reasonably be expected to have insight into methods to improve outcomes. Mechanisms designed to facilitate interdisciplinary research should be encouraged.

In sum, comparative effectiveness research funding should be considered broadly by the AHRQ and the oversight group. Comparative effectiveness of methods, mechanisms (i.e., tools) and outcomes from the health professional educational system, at all levels (i.e., pre and post degree) and across disciplines (i.e., medicine, nursing, pharmacy, other) should be considered at this time as part of the total research equation to best understand what works and does not work in the health delivery system.

Jibril M Hirsi
Executive Director
SomaliCAN
Somali Community Access Network
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I am the president of the Somali community in Ohio. I would like to suggest an increase in engagement and outreach services to help the Somali American community in the USA.

The Somali American community faces serious physical and mental health challenges including chronic medical problems, adjustment problems, nutrition issues and other hardships associated with the change in their environment. A basic outreach and community health education initiative can change the lives of many Somali Americans for the better.

Please consider this statement for inclusion in the hearing.

Submitted by
Theodore Chow, MD, FACC
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Dear Committee,

Real world clinical and cost effectiveness of ICDs are hard to extrapolate from clinical trials. Large health care networks are an ideal place to gather this information. For example, HCA owns hospitals that cross different geographies, practice patterns, and their patients are integrated into the community (as opposed to “captive” health systems). By linking their hospitals with a centralized patient tracking and outcome system, one can both measure treatment effectiveness, and test practice enhancements. This could serve as a test tube for what is possible through a fully integrated national electronic health record.

This registry could assess the effectiveness of ICD therapy and patient screening techniques. Microvolt T wave alternans (MTWA) is an inexpensive and non-invasive technique that has significant potential to fill this role, but will require government support to fully explore its potential. Many studies have shown MTWA to predict total and arrhythmic death, and patients most likely to benefit from ICD therapy. Recent “negative” MTWA studies, especially the MASTER Trial, have slowed adoption. However these negative studies have significant limitations that could invalidate the conclusions. Also, since MTWA is dynamic, chronic MTWA measurement (which has not been explored) could have additional benefit. More importantly, MTWA could serve as a means for optimizing medical treatment of CAD, heart failure, and arrhythmia—thereby reducing risk of costly hospitalization.

I propose an integrated data collection system within an organization like HCA to explore the "real world" impact of treatments, tests (including MTWA), and practice enhancements.

Submitted by
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Cancer Policy and Clinical Affairs
American Society of Clinical Oncology
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The American Society of Clinical Oncology (ASCO) is the leading specialty society in the United States and throughout the world for physicians who treat patients with cancer and conduct cancer research to improve patient outcomes. ASCO is committed to ensuring that high-quality,

evidence-based practices for the prevention, diagnosis and treatment of cancer are available to all Americans. This statement highlights both the importance of comparative effectiveness research in our community today, and offers suggestions for ways to enhance this science moving forward.

Because cancer is a complex illness that touches many aspects of the health care system, oncology can serve as an important laboratory for comparative effectiveness studies. Comparative clinical research is embedded in the culture of oncology. The extensive cancer clinical trials network across the U.S. has a long track record of pursuing comparative effectiveness research. Examples include:

- National prostate, lung, colorectal, and ovarian cancer screening trials;
- A large portfolio of trials and meta-analyses comparing different regimens used for adjuvant therapy of operable breast, colon, and lung cancer; and
- Correlative studies that compare relative effectiveness of alternative drug regimens or targeted agents in patient subgroups defined by presence or absence of specific biomarkers. An important point for this last example is that, for most of these studies, treatment occurred several years ago, outcomes are already known, and banked tumor tissue permitted subsequent evaluation of predictive biomarkers. This provides a useful model for comparative effectiveness research that can lead to individualized treatment choices.

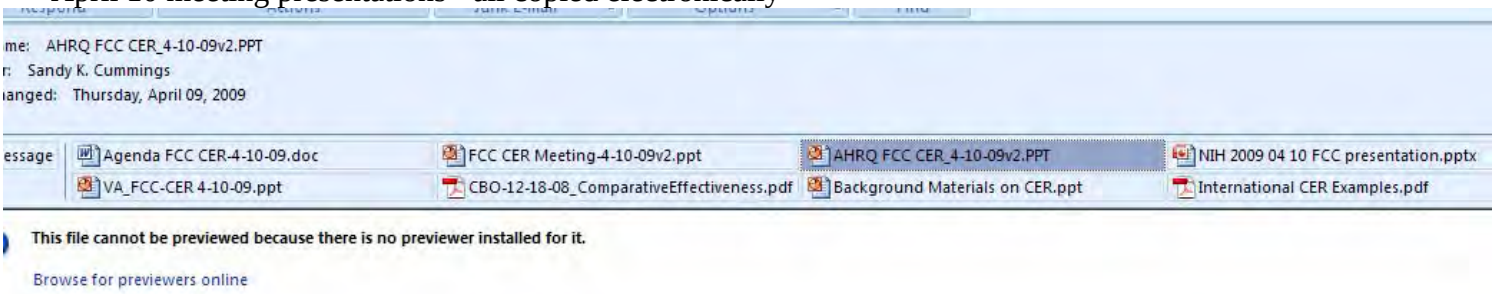
Much of this work has been possible because of our national cooperative group system, including disease site-specific scientific steering committees established by the National Cancer Institute's Coordinating Center for Clinical Trials, broad community involvement through the Community Clinical Oncology Program (CCOPs) and Cancer Trials Support Unit, a national registry program, and the multidisciplinary nature of our specialty. This network is already in place.

As you continue to work on shaping a national program on comparative effectiveness, we strongly recommend:

- Involvement of oncology experts in setting cancer-related priorities,
- Use and strengthening of existing oncology infrastructure to accomplish this work;
- Focus on areas where randomized clinical trials have established baseline data;
- Rigorous, standardized collection and storage of biospecimens in a way that allows broad access;
- Consideration of an oncology-specific evidence-based practice center; and
- Significant investment in expanding, strengthening, and linking national registries to include more robust data on individual patients' baseline characteristics, biomarker assay results, and specific treatment regimens.

Thank you for the opportunity to submit this statement. ASCO looks forward to working with you and others in the medical community as we move forward in this important area.

April 10 meeting presentations -all copied electronically



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Background Materials on CER

Federal Coordinating Council

Contents

- Definitions of CER
- Domestic Public Example - DERP
- Domestic Private example – Blue Cross Blue Shield Technology Evaluation Center

Definitions of CER

- CBO
  - Comparative effectiveness analysis is a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. Such a study may compare similar treatments, such as competing drugs, or it may analyze very different approaches, such as surgery and drug therapy. The analysis may focus only on the relative medical benefits and risks of each option, or it may also weigh both the costs and the benefits of those options. In some cases, a given treatment may prove to be more effective clinically or more cost-effective for a broad range of patients, but frequently a key issue is determining which specific types of patients would benefit most from it.

Definitions

- MedPAC
  - Comparative-effectiveness analysis evaluates the relative effectiveness, safety, and cost of medical services, drugs, devices, therapies, and procedures used to treat the same condition ... Effectiveness implies the “realworld” 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.

Definitions

- IOM
  - The terms ‘effectiveness’ and ‘clinical effectiveness’ refer to the extent to which a specific intervention, procedure, regimen, or service does what it what it is intended to do when it is used under real world circumstances …Recently, numerous proposals have called for a large expansion in the generation of comparative effectiveness information… These proposals call for systems to compare the impacts of different options for caring for a medical condition (e.g., prostate cancer) for a defined set of patients (e.g., men at high risk of prostate cancer recurrence). The comparison may be between similar treatments, such as competing prescription medications, or for very different treatment approaches, such as surgery or radiation therapy. Or, the comparison may be between using a specific intervention and its nonuse (sometimes called ‘watchful waiting’).

Definitions

- AHRQ
  - A type of health care research that compares the results of one approach for managing a disease to the results of other approaches. Comparative effectiveness usually compares two or more types of treatment, such as different drugs, for the same disease. Comparative effectiveness also can compare types of surgery or other kinds of medical procedures and tests. The results often are summarized in a systematic review. The kinds of results that are studied to compare drugs or procedures include relief of symptoms, length of life, or whether people need to go to the hospital. These results are called outcomes. Many other kinds of outcomes can also be compared.

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- Definitions of CER
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State Experience Using CER: DERP

- Drug Evidence Review Project
  - Initiated by state of Oregon in 2000
  - Collaboration of public entities, the Center for Evidence-based Policy and the Oregon Evidence-based Practice Center, who have joined together to produce systematic, evidence-based reviews of the comparative effectiveness and safety of drugs in many widely used drug classes, and to apply the findings to inform public policy and related activities in local settings
  - The DERP project produces systematic literature reviews of drug classes. Components of these reviews include Key Questions, Reports and Evidence Tables.

Source: Mark Gibson, Deputy Director of Center for Evidence-based Policy and DERP website

DERP Transparency

- Draft Key questions posted and comments incorporated
  - Full disclosure of methods and sources–Which studies included and why
  - Which studies not included and why
  - All industry submissions
- Universal peer review w/ comments public
- Final report in public domain

Source: Mark Gibson, Deputy Director of Center for Evidence-based Policy and DERP website

Reports Completed by DERP

- 2nd Generation Antidepressants
- 2nd Generation Antihistamines
- Alzheimer's Drugs
- Angiotensin Converting Enzyme Inhibitors
- Angiotensin II Receptor Antagonists
- Anti-Epileptic Drugs
- Anti-platelet Drugs
- Controller Drugs for Asthma
- Atypical Antipsychotics
- Quick Relief Medications for Asthma
- Beta Adrenergic Blockers
- Calcium Channel Blockers
- Combination Drugs for Hypertension & Hyperlipidemia
- Constipation Drugs
- Newer Diabetes Drugs
- Renin Angiotensin Aldosterone System Drugs
- Drugs to treat ADHD
- Hepatitis C Drugs
- Hormone Replacement therapy
- Long-acting Opiates
- MS Drugs
- Neuropathic Pain Drugs
- Newer Antiemetics
- Newer Insomnia Drugs
- NSAIDS
- Oral Hypoglycemics
- Proton Pump Inhibitors
- Statins
- 59 more updated reports

Source: Mark Gibson, Deputy Director of Center for Evidence-based Policy and DERP website

DERP Lessons Learned

- Publicly sponsored and governed project can produce highest quality evidence in U.S.
- Research informs not dictates policy
  - Structure of industry interface important–Need evidence not lobbying (independence)
  - Must be formal
  - Must be transparent
- Cost must be considered (policy process)
- Big gaps in evidence need filling

Source: Mark Gibson, Deputy Director of Center for Evidence-based Policy and DERP website

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BCBS TEC

- Started by BCBS in 1985
- Each TEC Assessment is a comprehensive evaluation of the clinical effectiveness and appropriateness of a given medical procedure, device or drug
- Averaging 20 to 25 assessments a year, TEC provides healthcare decision makers with timely, rigorous and credible information on clinical effectiveness

Source: BCBS

TEC Structure

- Core staff of research scientists
- Multidisciplinary support staff
- Medical Advisory Panel

TEC Criteria to Assess Whether a Technology improves health outcomes

1. The technology must have final approval from the appropriate governmental regulatory bodies.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.
3. The technology must improve the net health outcome.
4. The technology must be as beneficial as any established alternatives.
5. The improvement must be attainable outside the investigational settings.

TEC Collaboration and Reports

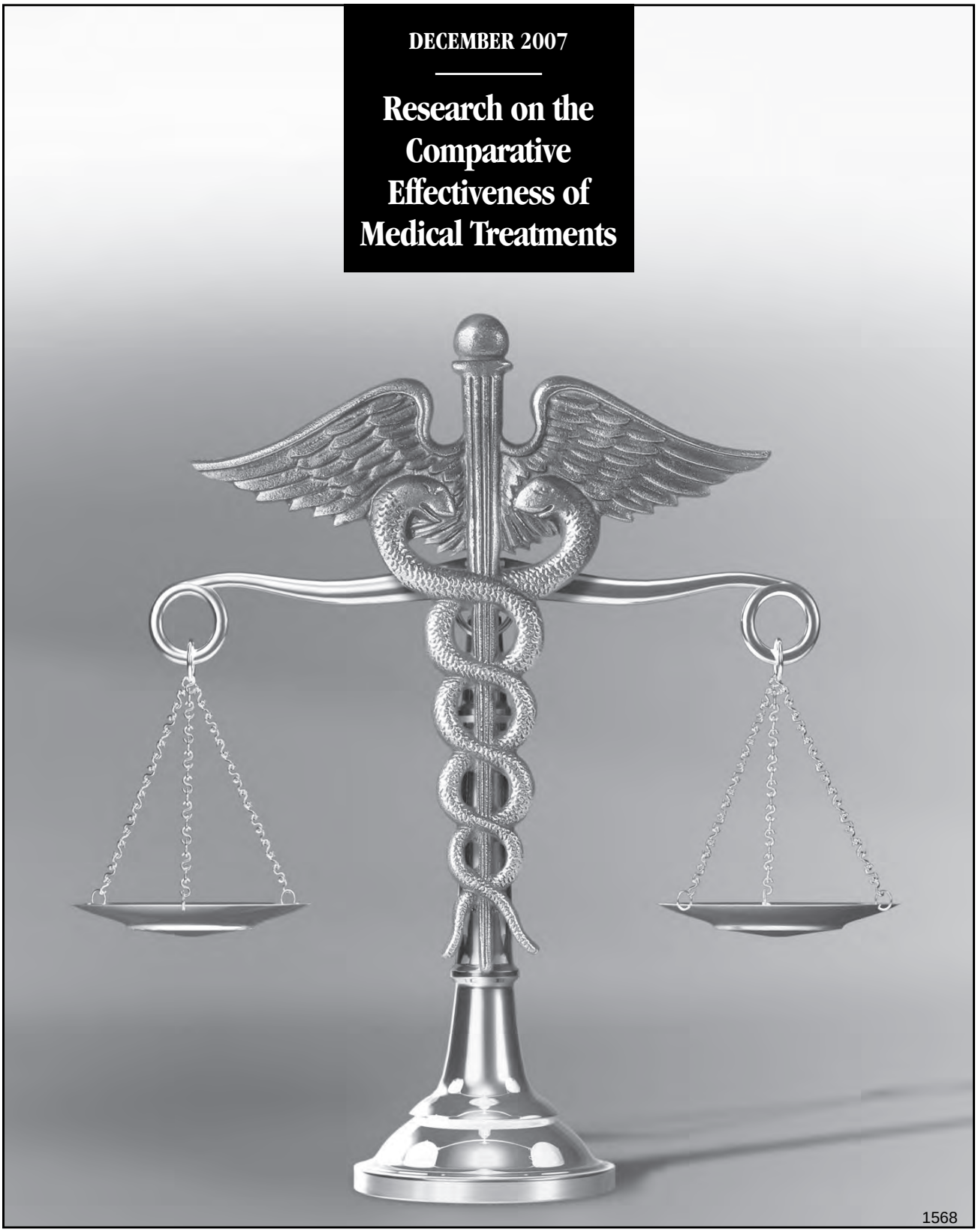
- TEC is an AHRQ Evidence-Based Practice Center
- Collaboration with Kaiser
- TEC assessments at: http://www.bcbs.com/blueresources/tec/tec-assessments.html

CONGRESS OF THE UNITED STATES
CONGRESSIONAL BUDGET OFFICE

A
CBO
PAPER

DECEMBER 2007

Research on the Comparative Effectiveness of Medical Treatments



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CBO

PAPER

Research on the Comparative Effectiveness of Medical Treatments: Issues and Options for an Expanded Federal Role

December 2007

The Congress of the United States ■ Congressional Budget Office

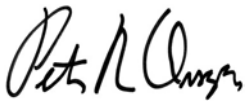
Preface

Rising costs for health care represent a central challenge both for the federal government and the private sector, but opportunities may exist to constrain costs in both sectors without adverse health consequences. Perhaps the most compelling evidence of those opportunities involves the significant geographic differences in spending on health care within the United States, which do not, on average, translate into higher life expectancy or substantial improvements in other health statistics in the higher-spending regions. At the same time, only a limited amount of evidence is available about which treatments work best for which patients and whether the added benefits of more-effective but more-expensive services are sufficient to warrant their added costs. Together, those findings suggest that generating better information about the costs and benefits of different treatment options—through research on the comparative effectiveness of those options—could help reduce health care spending without adversely affecting health overall.

This Congressional Budget Office (CBO) paper—prepared at the request of the Chairmen of the Senate Budget and Finance Committees—examines options for expanding federal support for research on comparative effectiveness. It reviews the current state of such research in both the public and private sectors and discusses several mechanisms for organizing and funding additional research efforts. It also discusses the different types of research that could be pursued and their likely benefits and costs. Finally, it considers the potential effects that such research could have on health care spending and the difficult steps that public and private insurers would probably have to take to achieve substantial savings on the basis of that research—in particular, changing the financial incentives for doctors and patients to reflect that information. In accordance with CBO's mandate to provide objective, impartial analysis, this paper contains no recommendations.

Philip Ellis of CBO's Health and Human Resources Division prepared the paper, with valuable contributions from Colin Baker and Morgan Hanger. The analysis benefited from comments by Dr. Alan Garber, Henry J. Kaiser Professor of Medicine at Stanford University, and Dr. Sean Tunis of the Center for Medical Technology Policy. (The assistance of external reviewers implies no responsibility for the final product, which rests solely with CBO.)

John Skeen edited the paper, and Maureen Costantino prepared it for publication and designed the cover. Lenny Skutnik printed the initial copies, Linda Schimmel handled the print distribution, and Simone Thomas prepared the electronic version for CBO's Web site (www.cbo.gov).



Peter R. Orszag
Director

December 2007

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Research on the Comparative Effectiveness of Medical Treatments

Summary and Introduction

Over the past 30 years, federal spending on Medicare and Medicaid has roughly tripled as a share of gross domestic product (GDP), rising from about 1.3 percent in 1975 to about 4 percent in 2007. According to the Congressional Budget Office's (CBO's) projections, under current policies such spending will reach about 12 percent of GDP by 2050—but substantial uncertainty surrounds that estimate.[1] If costs per enrollee continued growing over the next four decades as quickly as they have grown over the past four—about 2.5 percentage points faster than per capita GDP—then federal spending on those programs would reach about 17 percent of the economy. If, instead, costs per enrollee did not exceed the growth of GDP, those federal costs would reach about 6 percent of GDP in 2050 solely because of demographic changes (see Figure 1). As those figures indicate, the rate at which health care costs grow relative to income is the most important determinant of the country's long-term fiscal balance; it exerts a significantly larger influence on the budget over the long term than other commonly cited factors, such as the aging of the population or the coming retirement of the baby-boom generation.[2]

Rising health care costs represent a challenge not only for the federal government but also for private payers. Indeed, trends in both sectors reflect many of the same underlying forces—including the development and spread of new and more-expensive medical technologies—so controlling those federal costs over the long term will be difficult without addressing the forces that are also causing private costs for health care to rise. Total health care spending, which consumed about 8 percent of the U.S. economy in 1975, currently accounts for about 16 percent of GDP, and that share is projected to reach nearly 20 percent by 2016. About half of overall health spending in the United States is now publicly financed, and half is privately financed.

A variety of evidence suggests that opportunities exist to constrain health care costs both in the public programs and in the rest of the health system without adverse health consequences. Perhaps the most compelling evidence of those opportunities involves the substantial geographic differences in spending on health care—both among countries and within the United States—which do not translate into higher life expectancy or measured improvements in other health statistics in the higher-spending regions. For example, Medicare's costs per beneficiary vary significantly among different regions of the country, but much of the variation cannot be explained by differences in the population, and the higher-spending regions perform no better on available measures of average health outcomes than the lower-spending regions do.

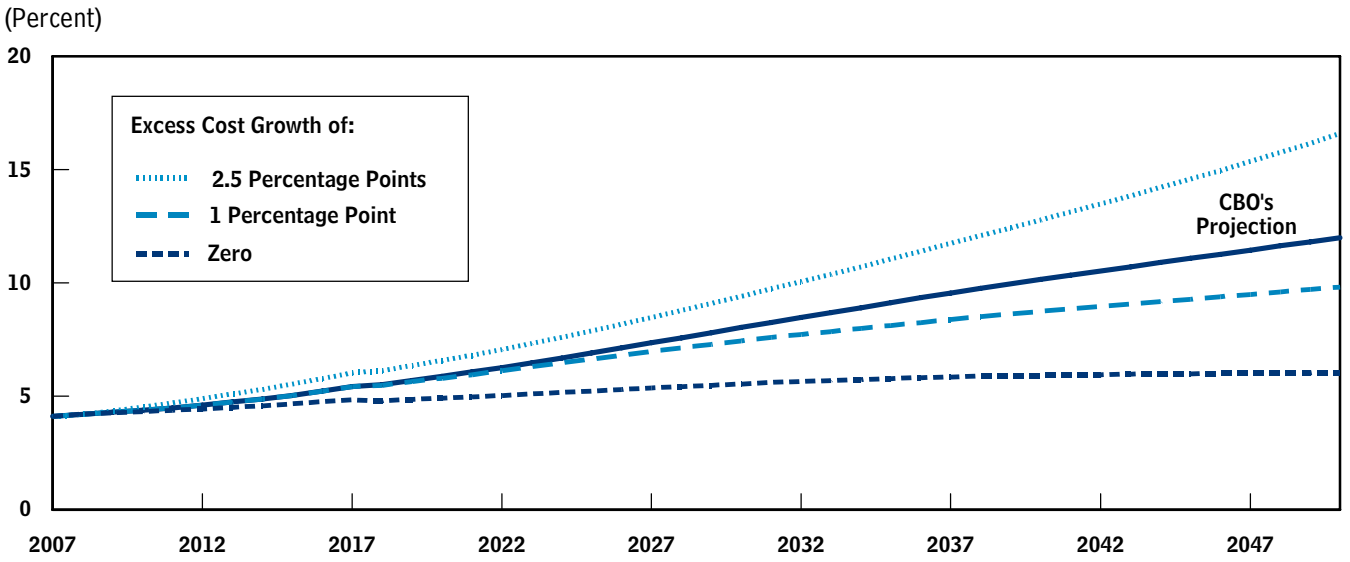
Furthermore, hard evidence is often unavailable about which treatments work best for which patients and whether the added benefits of more-effective but more-expensive services are sufficient to warrant their added costs—yet the current health system tends to adopt more-expensive treatments even in the absence of rigorous assessments of their impact. Indeed, the extent of the variation in treatments may be greatest when evidence about their relative effectiveness is lacking. Together, those findings suggest that better information about the costs, risks, and benefits of different treatment options,

1. Congressional Budget Office, *The Long-Term Outlook for Health Care Spending* (November 2007). The estimates of federal spending reflect Medicare's costs net of the premiums that enrollees pay and other offsetting receipts; the program's gross costs are about 15 percent higher than its net costs.

2. For additional discussion, see Congressional Budget Office, *The Long-Term Budget Outlook* (December 2007).

Figure 1.

Federal Spending for Medicare and Medicaid as a Percentage of Gross Domestic Product Under Different Assumptions About Excess Cost Growth



Source: Congressional Budget Office.

Note: Excess cost growth refers to the number of percentage points by which the growth of annual health care spending per beneficiary is assumed to exceed the growth of nominal gross domestic product per capita.

combined with new incentives reflecting the information, could eventually alter the way in which medicine is practiced and yield lower health care spending without having adverse effects on health. Over the long term, the potential reduction in spending below projected levels could be substantial.

Generating evidence that compares treatments is what research on "comparative effectiveness" does. This Congressional Budget Office (CBO) paper makes the following main points about the options that are available for an expanded federal role in supporting and organizing such research and about the impact that research could have on spending for health care:

- Because any private-sector entity (such as a health plan) has only a limited incentive to produce or pay for information that could benefit many entities—including its competitors—an argument can be made for a larger federal role in coordinating and funding research on comparative effectiveness. In addition, because federal health insurance programs play such a large role in financing medical care and account for such a large share of the budget, the federal government itself has an interest in generating evaluations of the effectiveness of different approaches to health care.

- If policymakers wanted to expand federal efforts to study comparative effectiveness, the endeavor could be organized in different ways—for instance, by augmenting an existing agency, by establishing a new agency, by supporting an existing quasi-governmental organization, or by creating a new public-private partnership. In choosing an organizational arrangement and a mechanism to provide federal funds to it, trade-offs could arise between the entity's independence from political pressure and its accountability to policymakers and other interested parties. Efforts to bolster comparative effectiveness research would be more likely to change medical practice if the organization coordinating the research was respected and trusted by doctors and other professionals in the health sector.

- The level of funding required for a new or augmented entity would depend largely on what its additional activities involved. Synthesizing existing studies or analyzing available data on medical claims would be less expensive than conducting new head-to-head clinical trials to compare treatments but could also yield

less definitive results—and therefore might have a smaller impact on medical practice. Clinical trials could be more persuasive but also more time-consuming, and there is probably a limit to how many comparative trials could be undertaken effectively at any given time. If privacy concerns could be addressed, having more health records available in electronic form would facilitate the use of such data for research.

- Studies might need to compare not only broadly different treatment options—such as surgery versus drug therapy—but also different approaches to the same basic treatment—such as different levels of follow-up care after surgery. Studies that included an analysis of cost-effectiveness would probably have a larger impact than ones that compared only clinical effectiveness, because they would highlight cases where more-expensive treatments or approaches provided added benefits that were modest compared with their added costs (at least for some types of patients).

- To affect medical treatment and reduce health care spending in a meaningful way, the results of comparative effectiveness analyses would not only have to be persuasive but also would have to be used in ways that changed the behavior of doctors, other health professionals, and patients. For example, the higher-value care identified by comparative effectiveness research could be promoted in the health system through financial incentives—the payments doctors receive or the cost sharing that patients face. Making substantial changes in payment policies or coverage rules under the Medicare program to reflect information on comparative effectiveness would almost certainly require legislation.

- Making such substantial changes in the delivery of health care could prove difficult and controversial for a number of reasons. To inform new systems of incentives—designed to discourage the use of more costly treatments that provided little or no added benefits—the results of effectiveness studies would have to be sufficiently robust to minimize the risk of overlooking subgroups of patients who could benefit greatly from a treatment. Even with an expanded evidence base, some patients and providers might object to the use of such incentives, and keeping pace with new treatments and procedures would be an ongoing challenge.

- Generating additional information about comparative effectiveness and making corresponding changes in incentives would seem likely to reduce health care spending over time—potentially to a significant degree. The precise impact, however, depends on several factors and is difficult to predict. Given the time necessary to conduct the research, to alter incentives in a manner reflecting the results, and to affect behavior through those changes, any potential for substantial cost savings from new research would probably take a decade or more to materialize. Even so, generating additional information comparing treatments would tend to reduce federal health spending somewhat in the near term—but that effect may not be large enough to offset the full costs of conducting the research over that same time period.

The Current State of Comparative Effectiveness Research

In weighing options to expand and reorganize research efforts, it is useful to define what comparative effectiveness research means and to consider the arguments for an expanded federal role in conducting such research. Related issues include the reasons why the current stock of research on comparative effectiveness is limited and why treatments and procedures can gain wide use even when evidence about their relative effectiveness is lacking. Reviewing past and current research efforts—by private and public organizations in the United States and by other countries—also sheds light on several issues and challenges likely to arise in any future U.S. efforts. To the extent that past and current efforts are seen as inadequate, careful consideration of those shortcomings would inform the choice of an organizational approach and funding mechanism for new federal activities.

What Is Comparative Effectiveness?

As applied in the health care sector, an analysis of comparative effectiveness is simply a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. Such a study may compare similar treatments, such as competing drugs, or it may analyze very different approaches, such as surgery and drug therapy. The analysis may focus only on the relative medical benefits and risks of each option, or it may also weigh both the costs and the benefits of those options. In some cases, a given treatment may prove to be more effective clinically or more cost-effective for a broad range of patients, but fre-

quently a key issue is determining which specific types of patients would benefit most from it. Related terms include cost–benefit analysis, technology assessment, and evidence-based medicine, although the latter concepts do not ordinarily take costs into account.

While some information about the effectiveness of new drugs, medical devices, and procedures is usually available, rigorous comparisons of different treatment options are less common. Drugs and devices must be certified as safe and effective by the Food and Drug Administration (FDA) before they can be marketed in the United States, but with certain exceptions the regulatory process for approving those products does not evaluate them relative to alternatives.[3] Furthermore, physicians commonly prescribe drugs for "off-label" uses—that is, for treatments that have not been certified by the FDA. For drug manufacturers, the costs of conducting additional trials to demonstrate safety and efficacy for a broader set of patients or conditions may outweigh the benefits from the increased sales that would result; in particular, the potential gains from finding a favorable result for a different population would have to be weighed against the risk that safety and efficacy could not be demonstrated conclusively.

Medical procedures, which account for a much larger share of total spending on health care than drugs and devices do, can achieve widespread use without extensive clinical evaluation. In many cases, it may be reasonable to assume that the benefits of a treatment will be similar for related conditions or a broader group of patients. Without hard evidence, however, decisions about what treatments to recommend often depend on the individual experience and judgment of physicians. Various reasons have been cited to explain why the use of new medical technologies can spread even in the absence of proof about their effectiveness and why health costs tend to increase as a result; those reasons include fee-for-service payment of physicians (common in the private sector and prevalent in Medicare, that payment method typically gives doctors a financial incentive to provide more-expensive care) as well as enthusiasm for the newest technology on the part of both doctors and patients.[4] Furthermore, patients with insurance typically pay only a small share of the costs of their treatments, so their incentives to weigh the costs against the benefits are limited—a trade-off inherent in having insurance protection.

A recent example of a comparative effectiveness study indicates that careful analysis can sometimes disprove widely held assumptions about the relative merits of different treatments. The study, which involved patients who had stable coronary artery disease, compared the effects of two treatments: an angioplasty with a metal stent combined with a drug regimen versus the drug regimen alone.[5] Patients were randomly assigned to receive the two treatments, and although the study found that patients treated with angioplasty and a stent had better blood flow and fewer symptoms of heart problems initially, the differences declined over time.[6] More importantly, it found no differences between the two groups in survival rates or the occurrence of heart attacks over a five-year period.

Other examples of studies comparing the clinical effectiveness of different treatment options illustrate the types of findings that they can generate:

3. Clinical trials of new drugs must compare them to alternative medications only when the manufacturer wants to make a claim of superiority in its FDA-approved marketing materials or when giving trial participants a placebo would be unethical (for example, in the case of a study of AIDS drugs).

4. See Mark R. Chassin, "Is Health Care Ready for Six Sigma Quality?" *The Milbank Quarterly,* vol. 76, no. 4 (November 1998), pp. 565–591.

5. Coronary artery disease, or a buildup of plaque in the heart's arteries, is considered stable if a patient experiences some chest pain (angina) but does not have worsening pain over time and has not had a heart attack. In an angioplasty, a small balloon is surgically inserted into a clogged artery and then inflated to expand the opening; a stent—a small wire mesh tube—is commonly added in an effort to keep the artery open.

6. William E. Boden and others, "Optimal Medical Therapy With or Without PCI for Stable Coronary Disease," *The New England Journal of Medicine,* vol. 356, no. 15 (April 12, 2007), pp.1503–1516. Other studies have found that angioplasty with a stent has clear medical benefits for patients who are undergoing a heart attack, illustrating the point that results for a given treatment may differ significantly among different types of patients.

- One recent trial found that older, relatively inexpensive drugs for treating high blood pressure (known as diuretics) were more effective in preventing cardiovascular disease in patients age 55 or older than commonly used newer drugs known as angiotensin-converting enzyme inhibitors and calcium channel blockers.[7]

- Another trial compared the effects of surgery to reduce lung volume for patients suffering from emphysema—a treatment that had anecdotal support but lacked hard evidence about its effectiveness—with standard medical therapy for that disease. For many patients, lung surgery increased their risk of death slightly and did not improve their functional status, but for patients with certain types of lung problems and a limited capacity for exercise, the surgery yielded small net improvements in their quality of life (though not in their survival rates).[8]

- A trial of two statin drugs, which was sponsored by the maker of one of those drugs, found that its competitor's product was more effective both at lowering cholesterol levels and at reducing the risk of mortality—illustrating the point that comparative trials can be risky for manufacturers to conduct.[9]

- Recent studies have found that magnetic resonance imaging combined with mammography is more effective than mammography alone in detecting breast cancer for women with certain genetic markers that indicate a substantial increased risk of contracting that disease; the impact of that difference on survival rates, however, could not be measured.[10]

The range of findings that those studies yielded highlights several characteristics of research on comparative effectiveness. First, studies can examine not only treatments for health problems but also different procedures to screen for the presence of a disease. Second, the findings may have broad applicability or may pertain only to a very specific subset of patients and may also vary in the outcomes considered—such as effects on mortality or other measures of health gains.

Third, studies are often based on clinical trials, in which eligible patients are randomly assigned to the treatments under review—but there are several other methods available to compare treatments, each with its own strengths and weaknesses. Clinical trials can yield persuasive findings but can also be relatively costly and time-consuming to conduct. In particular, a trial designed to determine whether two treatments differ in their effectiveness may require a large number of enrollees to be followed for an extended period in order to generate results that are statistically significant. Less expensive approaches include systematic reviews of the evidence about treatment options, which are essentially meta-analyses of all available studies, and studies that use medical claims data, which can be used to follow large groups of patients who have already received different treatments. The impact of systematic reviews can be limited, however, by the fact that they simply reflect existing evidence, and studies using claims data can be subject to bias because the treatments are not randomly assigned to comparable patients.

The studies cited above focus on relative clinical effects, and not cost-effectiveness. For reasons discussed below, gauging cost-effectiveness as well as clinical effectiveness is sometimes controversial, and some observers believe that the two considerations are in separate fields. But cost-effectiveness analysis appears to be well within the scope of research on comparative effectiveness—and

7. Officers and Coordinators for the ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) Collaborative Research Group, "Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs. Diuretic," *Journal of the American Medical Association*, vol. 288, no. 23 (December 18, 2002), pp. 2981–2997.

8. National Emphysema Treatment Trial Research Group, "A Randomized Trial Comparing Lung-Volume-Reduction Surgery with Medical Therapy for Severe Emphysema," *The New England Journal of Medicine*, vol. 348, no. 21 (May 22, 2003), pp. 2059–2073.

9. Christopher P. Cannon and others, "Intensive Versus Moderate Lipid Lowering with Statins After Acute Coronary Syndromes," *The New England Journal of Medicine*. vol. 350, no. 15 (April 8, 2004), pp. 1495–1504. Note that this study was undertaken in response to a similar one financed by the manufacturer of the other drug, which also showed that drug to be superior at lowering cholesterol levels but did not address mortality risks.

10. Ellen Warner and others, "Surveillance of BRCA1 and BRCA2 Mutation Carriers with Magnetic Resonance Imaging, Ultrasound, Mammography, and Clinical Breast Examination." *Journal of the American Medical Association,* vol. 292, no. 11 (September 15, 2004), pp. 1317–1325; and Mieke Kriege and others, "Efficacy of MRI and Mammography for Breast-Cancer Screening in Women with a Familial History or Genetic Predisposition," *The New England Journal of Medicine,* vol. 351, no. 5 (July 29, 2004), pp. 427–437.

Box 1.

Research on Comparative Effectiveness in Other Countries

Other developed countries also face challenges financing health care costs and have taken various steps to assess the comparative effectiveness of treatments. Unlike the United States, many of those countries establish overall budgets for their national health systems and regularly use the data on comparative effectiveness that are available to help determine the treatments and procedures to be covered and, in some cases, the payment rates. Despite differences in other countries' health insurance systems, the approaches that they have taken to organizing and funding those research and review activities could have lessons for any increased U.S. efforts.

Perhaps the best known example of an agency that assesses comparative effectiveness is the National Institute for Health and Clinical Excellence (NICE), which was established in 1999 as part of the United Kingdom's National Health Service (NHS). It analyzes both the clinical effectiveness and cost-effectiveness of new and existing medicines, procedures, and other technologies and provides guidance on appropriate treatments for specific diseases or types of patients. To date, NICE has published appraisals of over 100 specific technologies, guidance on the use of about 250 medical procedures, and about 60 sets of treatment guidelines—a substantial but not exhaustive list. If NICE approves a drug, device, or procedure, it must be covered by the NHS, but local health authorities make coverage decisions about treatments that NICE has not yet evaluated. With a staff of about 200 and an annual budget of about 30 million pounds (roughly $60 million), NICE does not fund new clinical trials or other forms of primary data collection. Instead, it commissions systematic reviews of existing research on clinical effectiveness and combines those findings with models of cost-effectiveness. Clinical trials are funded by the British Ministry of Health but (as in this country) data on total spending in the United Kingdom for research on comparative effectiveness are hard to come by.

Other countries such as Australia, Canada, France, and Germany have similar review processes, though the organizational and financing arrangements vary—and in several cases, the structures have recently been changed.[1] For example, France established a new agency in 2004 to bring together a number of related activities, including the evaluation of drugs, devices, and procedures, publication of clinical guidelines, accreditation of providers, and dissemination of medical information. Germany established a new agency in 2000 that conducts technology assessments and a new Institute for Quality and Efficiency

1. For additional information, see Institute of Medicine, *Learning What Works Best: The Nation's Need for Evidence on Comparative Effectiveness in Health Care* (September 2007), Appendix 2, available at www.iom.edu/ebm-effectiveness.

has been applied to many of to the treatments discussed above. For example, an additional analysis of lung-volume-reduction surgery, which focused on the patients likely to benefit from the surgery, found that it would be cost-effective if its benefits persisted for 10 years but might not be so if those benefits dissipated after three years.[11] (That study did not follow patients for a decade and therefore had to estimate the future benefits.) Similarly, another study examined the cost-effectiveness of more-expensive screening mechanisms for breast cancer and found that it varied substantially with the age of the patient.[12]

11. National Emphysema Treatment Trial Research Group, "Cost Effectiveness of Lung-Volume–Reduction Surgery for Patients with Severe Emphysema," *The New England Journal of Medicine*, vol. 348, no. 21 (May 22, 2003), pp. 2092–2102.

12. Sylvia K. Plevritis and others, "Cost-Effectiveness of Screening BRCA1/2 Mutation Carriers with Breast Magnetic Resonance Imaging," *Journal of the American Medical Association,* vol. 295, no. 20 (May 24/31, 2006), pp. 2374–2384.

Box 1.

Continued

in 2004 that evaluates health care services. Discussions about the use of comparative effectiveness in those countries sometimes focuses on their review processes for prescription drugs, but their efforts generally encompass all forms of acute medical care. (For all the attention they receive, drug costs represent less than 15 percent of health care spending in the United States—so research that focused only on medications would miss the vast majority of services and would not be able to compare drug therapy with surgical procedures or other interventions.)

Although those countries all have government-run health care systems, they have taken different approaches regarding the placement of and funding for their assessment bodies. In the United Kingdom and Australia, the agencies are part of the government's health departments; France and Canada have established independent not-for-profit organizations; and Germany has taken a mixed approach (the Institute for Quality and Efficiency is independent, but the technology assessment agency is an arm of the health ministry). Financing arrangements vary correspondingly: Funding in the United Kingdom and Australia comes from their health departments, whereas Germany's independent institute is funded by a levy on inpatient and outpatient health care services (which are mainly reimbursed by the country's regional health insurance funds), and the French agency gets its funding from a combination of taxes on promotional spending by drug companies, government subsidies, and accreditation fees. Health ministries in Australia, Canada, France, and Germany also help fund clinical trials and other forms of primary research, but total spending related to comparative effectiveness in those countries is also difficult to estimate.

Given the interest that has developed in many countries, it is not surprising that several international organizations have become involved in comparative effectiveness research. The best known may be the Cochrane Collaboration—a nonprofit organization that has a network of volunteers who conduct systematic reviews of treatments. Many of its activities are organized through centers located around the world, including one in the United States. Founded in 1993, the Cochrane Collaboration maintains an accessible database that now contains more than 4,500 reviews; its limited funding comes primarily from subscription fees for its quarterly journal. Any new or expanded U.S. entity that would organize and fund research on comparative effectiveness would probably draw upon Cochrane's findings and the results of research conducted in other countries (to the extent such research was applicable to U.S. patients).

More generally, the relative cost-effectiveness of treatment options is clear when a less expensive treatment yields comparable or superior health gains. In other cases, however, determining whether the additional medical benefits of a more expensive treatment warrant their added costs is complex. Typically, the benefits of different treatments are summarized as an increase in life expectancy or, more commonly, as an increase in quality-adjusted life years (QALYs) to account for effects on morbidity as well as mortality. That calculation reflects estimates of how much people value improving their health or avoiding various side effects, which are combined to create a single metric. By convention, cost-effectiveness analyses report results as the cost per QALY gained, so a lower dollar amount indicates a more cost-effective service. If that metric is used to determine whether specific health procedures are covered by an insurance program, choosing a cost-effectiveness threshold can be a controversial endeavor—but that need not be the manner in which such research is applied.

Research in the Private Sector

In the United States, most of the formal research that is done to examine the effects of drugs or medical devices is

conducted by the manufacturers of those products in the course of their development; as noted, however, it is the exception rather than the rule that those studies directly compare treatments or products.[13] Nevertheless, various other private organizations have also produced assessments and comparisons of some treatments. (Analyses conducted in other countries represent another source of information about treatments; see Box 1 on page 6.)

Several private-sector organizations exist primarily or exclusively to assess medical treatments and technologies. One prominent example is the Technology Evaluation Center that is part of the Blue Cross Blue Shield Association. Its analyses are based on systematic reviews of the available literature and therefore rely on clinical trials or other studies that have already been conducted. (In such reviews, more weight is given to studies that are judged to be of higher methodological quality.) The center produces about 20 to 25 new assessments of drugs, devices, and other technologies each year; the analyses consider clinical effectiveness but generally do not assess cost-effectiveness.

For-profit private-sector firms that specialize in technology assessments represent another source of analysis. Hayes, Inc., is one of the larger firms in the field. Such firms also conduct systematic reviews and evaluate medical and surgical procedures, drugs, and devices in return for a fee or on a subscription basis. Organizations that are similar but operate as nonprofit entities—sometimes affiliated with academic or medical centers—include the ECRI Institute and the Tufts-New England Medical Center's Cost-Effectiveness Analysis Registry (which provides an extensive list of the cost-effectiveness ratios that are available from published studies).

In addition, private health plans—most commonly, larger or more integrated ones—conduct their own reviews of evidence and sometimes undertake new analyses of comparative effectiveness using claims data for their enrollees.[14] Health plans may choose to publicize the results, or they may decide to keep their findings confidential and use them to shape their policies regarding coverage of and payment for the treatments in question. For example, health plans usually have an entity known as a pharmacy and therapeutic committee that considers the evidence regarding the relative effectiveness of different prescription drugs and makes recommendations about which ones should be covered (that is, included on formularies) or given preferred status. An example of a more public and collaborative effort is the HMO Research Network, a consortium of more than a dozen health maintenance organizations from different parts of the country; started in the mid-1990s, it brings together researchers to share findings and, in some cases, uses data from several plans as the basis for analysis.[15]

Notwithstanding those current efforts, the private sector generally will not produce as much research on comparative effectiveness as society would value. The knowledge created by such studies is costly to produce—but once it is produced, it can be disseminated at essentially no additional cost, and charging all users for access to that information is not always feasible. As a result, private insurers and other entities conducting research on comparative effectiveness often stand to capture only a portion of the resulting benefits and therefore do not invest as much in such research as they would if they took into account the benefits to all parties. In health plans that do not have exclusive provider networks, some of the benefits probably "spill over" to other health plans using the same doctors, because physicians tend to use a similar approach to care for all of their patients. Even if organizations could keep their findings confidential, so that they captured all of the benefits, some duplication of effort would probably occur. In such a situation, research constitutes a "public good," and economists have long recognized a role for government to increase the supply of such research toward the socially optimal level.

Another reason for the limited availability of information on comparative effectiveness is that public-sector health

13. In the limited number of instances in which manufacturers sponsor head-to-head trials, the comparisons tend to focus on the relative merits of products used to provide the same basic treatment. For example, a number of industry-sponsored trials have been conducted comparing different brands of coronary stents that are used during an angioplasty.

14. Although the Technology Evaluation Center discussed above is affiliated with the Blue Cross Blue Shield Association (which is an umbrella group that represents the Blue Cross and Blue Shield insurers from each state), that center does not work directly or exclusively for those insurers.

15. Medical specialty societies, such as the American Heart Association, represent another source of analysis of different treatment options—which typically take the form of treatment guidelines for various types of conditions and patients.

insurance programs—which collectively account for about 40 percent of all health care spending—have not sought to make extensive use of it. In particular, the Medicare program has made only limited use of comparative effectiveness data in making decisions about which treatments to cover and how much to pay for them. It stands to reason that the limited demand for such research from such a prominent payer has constrained the supply correspondingly. Conversely, increasing the amount of credible and objective research that was available could facilitate moving Medicare toward what former program administrator Mark McClellan has called a "fee-for-value" system rather than a fee-for-service one. (Options to incorporate research findings into Medicare's coverage and payment policies, along with the issues they raise, are discussed in the final section.)

Past and Current Federal Efforts

In the United States, the federal government has a rather long but somewhat checkered history of involvement in comparative effectiveness research and related efforts. Federal efforts date at least to the late 1970s and the short-lived National Center for Health Care Technology. Established in 1978 as part of the Department of Health, Education, and Welfare, it was given a broad mandate to conduct and promote research on health care technology, and it included an advisory board appointed by the Secretary to assist in setting research priorities. The center sponsored or cosponsored major evaluations of coronary artery bypass graft surgery, dental radiology, and cesarean delivery and made about 75 recommendations to the Medicare program about coverage. The center ceased operations at the end of 1981, however, reflecting changes in priorities for the new Administration and the Congress as well as opposition from some provider and industry groups.[16]

In that same period, the Office of Technology Assessment (OTA) was created as an advisory agency to the Congress, covering a broad set of issues, including health care. Given the agency's focus on evaluating technologies, much of its work would now be called research on comparative effectiveness; over the years, it studied a variety of health care topics, including the costs and benefits of screening tests for several diseases. OTA also produced an extensive review and analysis of the issues involved in and options for improving evidence about the clinical effectiveness and cost-effectiveness of medical treatments.[17] For a variety of reasons, however—having little to do with its health care studies specifically but instead reflecting broader questions about the agency's role—OTA was eliminated in 1995.

More recently, the Agency for Health Care Research and Quality (AHRQ) has been the most prominent federal agency supporting various types of research on the comparative effectiveness of medical treatments. Established in 1989 as the Agency for Health Care Policy and Research, AHRQ is an arm of the Department of Health and Human Services (HHS).[18] It currently has a staff of about 300 and an annual budget of over $300 million, which primarily funds research grants to and contracts with universities and other research organizations covering a wide range of topics in health services.

AHRQ has undertaken a number of initiatives related to comparative effectiveness. One such step—initially taken in collaboration with the American Medical Association and America's Health Insurance Plans, a coalition of insurance companies—has been the creation of a national clearinghouse for treatment guidelines, which are designed to summarize the available medical evidence on the appropriate treatments for various conditions. AHRQ has also endorsed about a dozen evidence-based practice centers around the country. Generally affiliated with a university, those centers analyze and synthesize existing evidence about treatments and technologies. Although many studies sponsored by AHRQ have examined only the relative clinical benefits of different treatments, some have also analyzed their cost-effectiveness. Research on comparative effectiveness has accounted for only a modest portion of AHRQ's budget, though.

As with other agencies examining the effectiveness of medical treatments or evaluating medical technologies, support for AHRQ has varied over time. In the mid-1990s, controversies arose after an agency-sponsored research team concluded that there was insufficient

16. See Seymour Perry, "The Brief Life of the National Center for Health Care Technology," *The New England Journal of Medicine*, vol. 307, no. 17 (October 21, 1982), pp. 1095–1100.

17. See Office of Technology Assessment, *Identifying Health Technologies that Work: Searching for Evidence,* OTA-H-608 (September 1994).

18. Prior to AHRQ's establishment as a separate agency, some of its functions were carried out by the National Center for Health Services Research within HHS.

Table 1.

Requested, Proposed, and Actual Funding for the Agency for Health Care Research and Quality

(Millions of dollars)

	Agency's Request	House Proposal	Senate Proposal	Appropriation
1991	109	88	138	115
1992	122	115	127	120
1993	125	118	130	128
1994	158	148	158	154
1995	171	154	166	162
1996	194	66	127	125
1997	144	125	144	143
1998	149	149	143	147
1999	171	171	171	171
2000	206	175	211	204
2001	250	224	270	270
2002	306	306	291	299
2003	250	0	314	304
2004	279	304	304	304
2005	304	304	319	319
2006	319	319	324	319

Source: Congressional Budget Office based on data from the Department of Health and Human Services, Agency for Health Care Research and Quality.

evidence to support certain spinal surgeries and, on the basis of that work, the agency issued practice guidelines for the treatment of back pain.[19] Strong opposition from back surgeons, along with broader questions about the value of the research that the agency had funded and other factors, led to proposals to eliminate the agency. Ultimately, the agency was retained, but its funding for fiscal year 1996 was reduced from prior levels (see Table 1). Since then, its overall budget has generally been maintained, at least in nominal terms, or increased. Again in 2002, however, the House of Representatives voted to cut off all funding for AHRQ, though in the end the agency received a small increase in its fiscal year 2003 appropriation.

Most recently, section 1013 of the Medicare Modernization Act of 2003 authorized AHRQ to spend up to $50 million in 2004 and additional amounts in future years to conduct and support research with a focus on "outcomes, comparative clinical effectiveness, and appropriateness of health care items and services (including prescription drugs)" for Medicare and Medicaid enrollees. The actual funding appropriated for that initiative has been $15 million per year. Using that funding, AHRQ has established an "Effective Health Care" program consisting of three main functions: reviewing and synthesizing existing evidence (using its evidence-based practice centers); generating new information using a set of approved research centers (such as the HMO Research Network) that have access to data from medical claims and electronic medical records; and publishing findings in formats that are geared to the differing needs of clinicians, patients, and policymakers.

Other federal agencies also engage in various activities related to comparative effectiveness research—efforts that receive less attention than AHRQ's activities but that are probably larger in dollar terms. The Department of Veterans Affairs (VA) has a very substantial research program that reviews evidence from the medical records of its patients, focusing particularly on the clinical effectiveness of treatments. The department also sponsors evidence reviews through a technology assessment program and helps fund clinical trials—including the study comparing

19. For a discussion, see Bradford H. Gray, Michael K. Gusmano, and Sara R. Collins, "AHCPR and the Changing Politics of Health Services Research," *Health Affairs,* Web Exclusive (June 25, 2003), pp. W3-283–W3-307.

stents to drug therapy mentioned above. Indeed, over the past 30 years, some of the most influential clinical trials have been supported by and conducted in the VA health system, including the first major trials that demonstrated the value of bypass surgery over medical therapy for some forms of coronary artery disease as well as head-to-head studies of drugs that treat prostate enlargement. Another source is the National Institutes of Health (NIH), part of HHS, which is the leading federal sponsor of medical research—primarily in the form of clinical trials. Although comparative effectiveness is not a focus of that research, over the years NIH has sponsored a number of trials that compare treatments directly.

The Centers for Medicare and Medicaid Services (CMS) has helped to sponsor a limited amount of research on comparative effectiveness (for example, it covered the medical costs of the study of lung-volume-reduction surgery). When making decisions about what services are covered, however, CMS generally considers only whether devices and procedures are clinically effective. It has sponsored some studies comparing the effectiveness of different treatments but has done so largely to determine whether to establish separate payment rates for similar treatments. For example, CMS is currently cosponsoring a trial with NIH that may eventually compare the effects of daily dialysis for kidney patients with the conventional treatment of dialysis three times per week.[20] If daily dialysis proves more effective for certain patients, CMS could modify its payment policy to cover the additional costs of more frequent treatment for those patients.

Estimating the total amount that is spent in the United States each year on research that compares the effectiveness of medical treatments is difficult. According to one recent analysis, the federal government spent about $1.5 billion in 2005 on all health services research, a broader category that includes some of the work on comparative effectiveness but also encompasses many other types of studies.[21] For example, that total included AHRQ's entire budget of roughly $300 million, whereas the funding devoted to the agency's effective health care program has been $15 million per year. At the same time, that aggregate figure may not include all federal funding for comparative trials or other efforts that are outside the traditional scope of health services research.

Estimating private expenditures is even more challenging. Although drug and device manufacturers spend billions of dollars each year on clinical trials aimed at demonstrating the safety and efficacy of new products, the vast majority of those efforts contribute to comparisons of treatments only indirectly. Data are simply not available on how much is spent by private organizations such a health plans, medical specialty societies, and technology assessment centers to compare medical treatments and procedures. Nevertheless, one recent study estimated that less that $2 billion is spent annually on comparative effectiveness research in this country—and even that rough estimate is subject to uncertainty.[22]

The Consequences of Limited Information

Whether the cause is limited supply or limited demand, the relative scarcity of rigorous data about comparative effectiveness has several effects. First and foremost, it means that decisions about what treatments to use often depend on anecdotal evidence, conjecture, and the experience and judgment of the individual physicians involved. In many cases, that basis may be sufficient; as some observers have noted, it is not necessary to conduct a randomized trial to determine whether to use a parachute when jumping out of an airplane. But if the benefits of a treatment—or risks of not providing it—are less obvious, the lack of hard data makes determining the appropriate choice of treatment difficult. Although estimates vary, some experts believe that less than half of all medical care is based on or supported by adequate evidence about its effectiveness.[23]

Evidence about treatments' effectiveness remains limited even though the number of rigorous studies has grown substantially in recent decades. To illustrate that point, one study simply examined the number of articles that were published each year in peer-reviewed medical journals that reported results from randomized trials.[24]

20. Initially, the study sought to test the feasibility of randomly assigning conventional or daily dialysis to a representative sample of patients.

21. AcademyHealth, *Placement, Coordination, and Funding of Health Services Research within the Federal Government* (September 2005), available at www.academyhealth.org/publications/placementreport.pdf.

22. See Institute of Medicine, *Learning What Works Best: The Nation's Need for Evidence on Comparative Effectiveness in Health Care* (September 2007), p. 8, available at www.iom.edu/ebm-effectiveness.

23. Institute of Medicine, *Learning What Works Best*, p. 2.

24. Mark R. Chassin, "Is Health Care Ready for Six Sigma Quality?"

Between 1966 and 1995, that number increased dramatically, from about 100 to nearly 10,000—with about half of the cumulative total over that period having been produced between 1990 and 1995. But even if the proportion of treatments based on hard evidence has increased as a result, the share remains relatively low. Furthermore, having the evidence base keep pace with the rapid development of new medical treatments and technologies will remain an ongoing challenge.

Another important effect of limited evidence—indeed, an indicator of that scarcity—is that the use of certain treatments and the types of care provided vary widely from one area of the country to another. For example, even after adjusting for differences in the age, sex, and race of Medicare enrollees, researchers at Dartmouth found about a fourfold variation in the share receiving a coronary artery bypass graft; and those differences were not correlated with rates of heart attacks in each region.[25] At the same time, those researchers found that overall surgery rates did not vary systematically; areas with above-average rates for certain procedures had below-average rates for others. Those differences in the use of treatments reflect at least in part the local practice norms that have arisen in each area, and the apparent variation in those norms indicates that there is not sufficient evidence to determine which approach is most appropriate.

Geographic differences in the types of care provided can remain substantial even among patients who turn out to be in their last six months of life. (Examining that period is an analytic approach that can be used in an effort to control for differences in the prevalence and severity of diseases patients have, on the grounds that large groups of patients who are nearing death are likely to have comparable health problems regardless of where they live.) For example, such patients spend nearly 20 days in the hospital over those last six months, on average, in the highest-use areas, compared with an average of about six hospital days in the lowest-use areas. Similarly, the average number of visits to physicians in that period is as high as 50 in some of the highest-use regions and as low as 16 in some of the lowest-use regions.[26]

The observed variations in the use of services correspond to substantial differences in Medicare spending per enrollee in different parts of the country (see Figure 2). In 2003, average costs ranged from about $4,500 in the areas with the lowest spending to nearly $12,000 in the areas with the highest spending (those averages were adjusted to account for differences in the age, sex, and race of Medicare beneficiaries in the various areas). Some of those differences in spending reflect varying rates of illness as well as differences in the prices that Medicare pays for the same service, which are adjusted on the basis of local costs for labor and equipment in the health sector. But according to the Dartmouth researchers, differences in illness rates account for less than 30 percent of the variation in spending among areas, and differences in prices can explain another 10 percent—indicating that more than 60 percent of the variation is due to other factors.[27] Other studies have found that a larger share of the variation in spending can be accounted for by differences in health status and demographic factors, but even so, the remaining differences are substantial in dollar terms.[28]

Of particular relevance to the issue of comparative effectiveness, there is some evidence that the degree of geographic variation in treatment patterns is greater when less consensus exists within the medical community about the best treatment to use. For example, patients who have fractured their hip need to be hospitalized, and there is relatively little variation in admission rates for Medicare beneficiaries with that diagnosis—but for hip replacements and for knee replacements, more discretion is involved and the surgery rates vary more widely

25. See John E. Wennberg, Elliott S. Fisher, and Jonathan S. Skinner, "Geography and the Debate Over Medicare Reform," *Health Affairs,* Web Exclusive (February 13, 2002), pp. w96–w97. The analysis divided the country into about 300 "hospital referral regions," which reflect where Medicare beneficiaries typically receive hospital care. In 2003, bypass surgery rates ranged from about 2 to 3 per 1,000 Medicare beneficiaries in the lowest-use regions to about 9 to 10 per 1,000 in the highest-use regions. Although higher rates of bypass surgery could reflect higher rates of heart attacks, higher surgery rates could also prevent some heart attacks—a factor that could help explain the lack of correlation between those two measures.

26. Based on data from 2000 to 2003, available from www.dartmouthatlas.org.

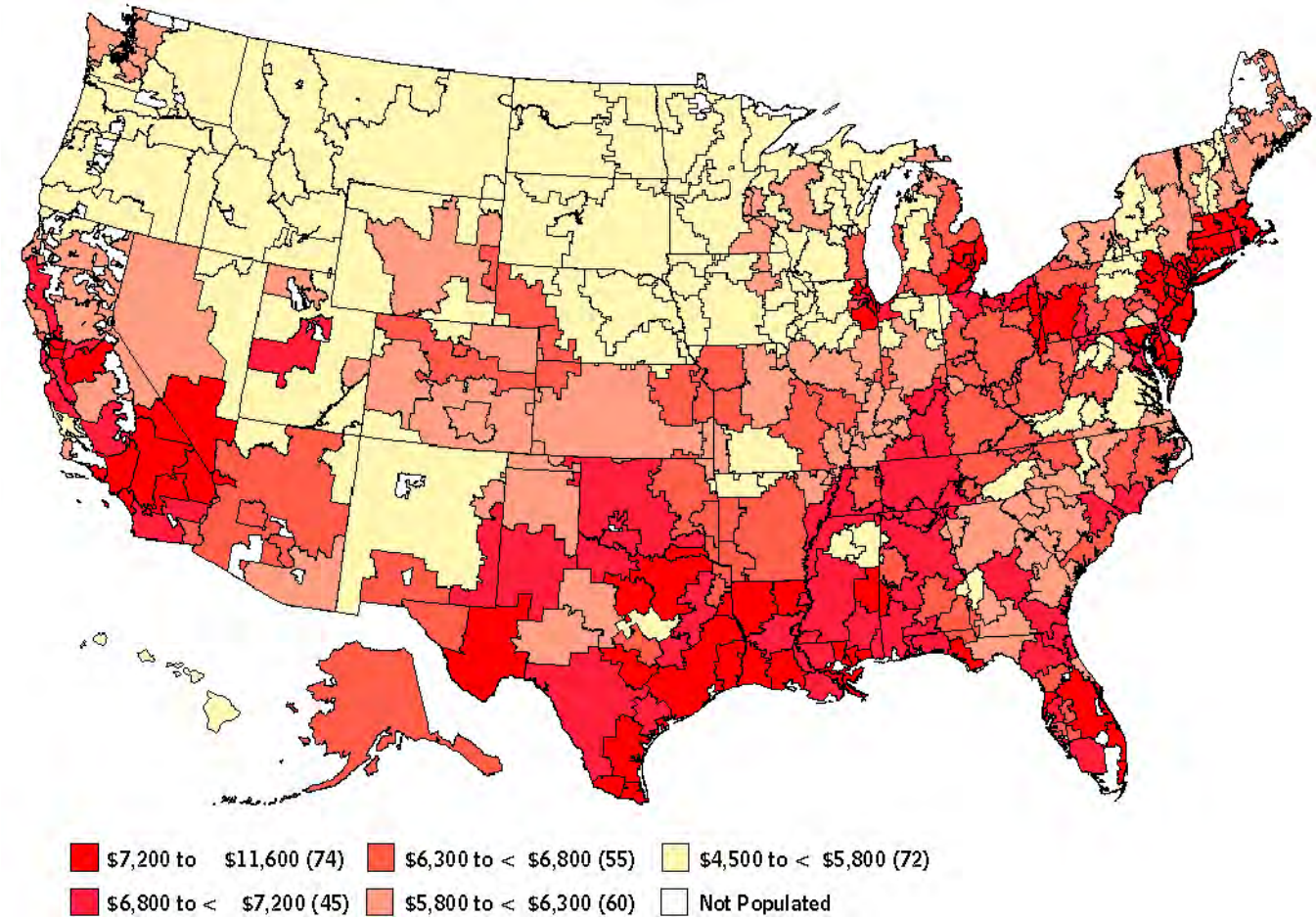
27. John E. Wennberg, Elliot S. Fisher, and Jonathan S. Skinner, "Geography and the Debate Over Medicare Reform"; and The Center for the Evaluative Clinical Sciences, Dartmouth Medical School, *The Dartmouth Atlas of Health Care 1999* (Dartmouth, N.H.: Health Forum, Inc., 1999), pp. 22–23.

28. David Cutler and Louise Sheiner, "The Geography of Medicare," *American Economic Review,* vol. 89, no. 2 (May 1999), pp. 228–233.

Figure 2.

Medicare Spending per Capita in the United States, by Hospital Referral Region, 2003

(Percent)



Source: *The Dartmouth Atlas of Health Care.*

Note: Numbers in parentheses refer to the number of hospital referral regions with per capita spending in each interval.

(see Figure 3). And there appears to be even more variation in the rates of back surgery—a treatment whose benefits have been the subject of substantial questions. Determining what share of any geographic variation in the use of procedures is due to differences in the treatments that doctors recommend and what share is due to differences in underlying illness rates is challenging, however, so the comparison of procedures may be sensitive to the manner in which the differences in illness rates are estimated.[29]

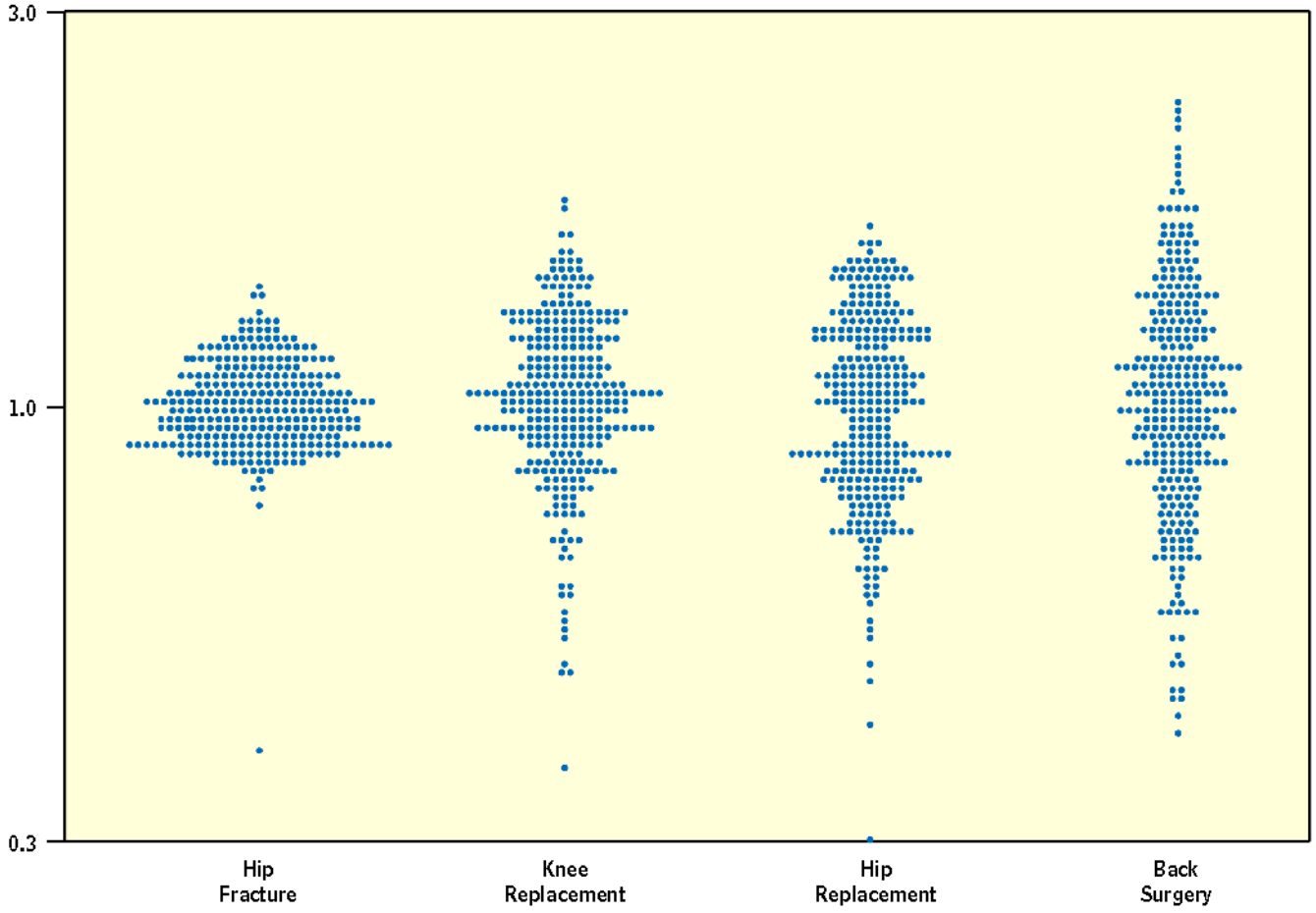
The implications of the observed variations in treatments and spending depend importantly on their relationship to health outcomes. If life expectancy and other measures were better in the areas with higher spending, that result would imply that increased spending in the low-cost areas would yield health benefits. One recent and well-

29. The data used in Figure 3 were adjusted to account for differences in illness rates among areas using data on five conditions, one of which was hip fracture. In the unadjusted data, the variation in knee and hip replacements is somewhat larger than the variation in hip fracture surgery—and variation in back surgery rates is larger still—but the differences are not as substantial. Whether the adjusted results were affected by including hip fracture rates both as an adjustment factor and in the comparison of procedures is not clear. Whether the prevalence of other diseases is correlated with the prevalence of those five conditions is also uncertain.

Figure 3.

Rates of Four Orthopedic Procedures Among Medicare Enrollees, 2002 and 2003

(Standardized discharge ratio, log scale)



Source: Dartmouth Atlas Project, *The Dartmouth Atlas of Health Care*.

Notes: In the figure, each point represents a hospital referral region; the country was divided into about 300 such regions on the basis of where Medicare enrollees typically receive their hospital care.

The points indicate how the rate at which the procedure is performed (per 1,000 Medicare enrollees) in each referral region compares with the national average rate (which has been normalized to 1.0). Differences in procedure rates were adjusted to account for differences among regions in the age, sex, and race of enrollees and for measures of illness rates.

designed study examined differences in hospital spending in Florida and found that areas with higher spending had lower mortality rates among Medicare patients who were treated in the emergency room for a heart attack.[30] Using data on Medicare enrollees nationwide, however, another study found that higher-spending regions did not, on average, have lower mortality rates than the lower-spending regions, even after adjustments to control for differing illness rates among patients and regions.[31] That study also found that higher spending did not slow the rate at which the elderly developed functional limitations (reflecting their ability to take care of themselves). Although more research is needed about the impact that differences in spending have on patients' morbidity and quality of life, perhaps using more-extensive measures of health outcomes, those findings suggest that spending in the high-cost areas could be reduced without adverse effects on the overall health of residents in those areas.

How much could spending be reduced? Some estimates of the potential savings from reducing the variations in treatments are quite large, although questions remain about what mechanisms could achieve those savings and what the effects on health would be. The Dartmouth researchers have suggested that Medicare spending—and perhaps all health spending in the country—could be cut by about 30 percent if the more conservative practice styles used in the lowest-spending one-fifth of the country could be adopted nationwide.[32] While they note the need for more research about the specific steps needed to reduce spending levels without harming health, their analysis indicates that the added spending is not contributing to better health outcomes. Other studies suggest that overall health might not suffer in the process of changing practice patterns but that patients who would benefit most from more-expensive treatments might be made worse off as a result, while patients who would do better with treatments that were less expensive would gain.[33]

Other studies of geographic variation indicate that there may be room to reduce spending without harming health in both high-use and low-use areas of the country. One older study, for example, had independent panels of doctors conduct after-the-fact reviews of the medical charts of Medicare enrollees who had had certain surgeries.[34] In areas with high use of the procedures, the study found that the share of surgeries that was clinically appropriate ranged from about 35 percent to about 70 percent; the remainder were either clinically inappropriate or of equivocal value. In low-use areas, the share considered appropriate ranged from about 40 percent to about 80 percent. In other words, the share of procedures deemed appropriate was slightly higher in the low-use areas, but that share was well below 100 percent in both high-use and low-use areas.

Options for Organizing and Funding New Federal Research Efforts

The approach that is taken for organizing and funding any increased federal efforts to support research on comparative effectiveness could play an important role in determining their impact. Some approaches would seek to insulate those efforts from political pressure by setting up an organization at "arm's length" from the government and by providing a dedicated source of financing. Many of the options that have been proposed seek to coordinate and centralize existing activities through one entity—which would tend to give any conclusions it reached more weight—but developing several competing sources of information about comparative effectiveness could also have value.

30. Joseph J. Doyle, Jr., "Returns to Local-Area Health Care Spending: Using Health Shocks to Patients Far From Home," NBER Working Paper 13301 (National Bureau of Economic Research, August 2007).

31. Elliott S. Fisher and others, "The Implications of Regional Variations in Medicare Spending, Part 2: Health Outcomes and Satisfaction with Care," *Annals of Internal Medicine*, vol. 138, no. 4 (February 18, 2003), pp. 288–298.

32. Elliott Fisher, "More Care is Not Better Care," *Expert Voices*, Issue 7 (National Institute for Health Care Management, January 2005), available at www.nihcm.org/publications/expert_voices.

33. Amitabh Chandra and Douglas O. Staiger, "Productivity Spillovers in Health Care: Evidence from the Treatment of Heart Attacks," *Journal of Political Economy,* vol. 115, no. 1 (February 2007), pp. 103–140.

34. Mark R. Chassin and others, "Does Inappropriate Use Explain Geographic Variations in the Use of Health Care Services? A Study of Three Procedures," *Journal of the American Medical Association,* vol. 258, no. 18 (November 13, 1987), pp. 2533–2537. The procedures studied were coronary angiography (which generally involves inserting a tube and special dyes into the heart to see how well blood flows through it), carotid endarterectomy (in which plaque is removed from the main artery that goes to the brain), and gastrointestinal endoscopy (in which a flexible tube with a small camera mounted on it is inserted into the intestines).

Specific options that have been put forward for organizing federal research on comparative effectiveness include the following (each of which could have many variants):[35]

- Expanding the role of an existing agency that already conducts or oversees research on health services generally—and comparative effectiveness specifically—such as AHRQ or NIH.

- Creating or "spinning off" a new agency, either within the Department of Health and Human Services or as an independent body that is part of either the executive or the legislative branch. The Federal Trade Commission and the Medicare Payment Advisory Commission (MedPAC) are potential models for such an option.

- Augmenting an existing quasi-governmental organization, such as the Institute of Medicine or the National Research Council. Such entities are often Congressionally chartered, but they are not subject to regular governmental oversight.[36] Even so, the Institute of Medicine receives most of its funding from government agencies, which is provided to finance specific studies that have been requested.

- Establishing a new public–private partnership to oversee and direct research. That option could be structured in various ways, but one such approach would be to set up a federally funded research and development center (FFRDC). FFRDCs are not-for-profit organizations that can accept some private payments but that get most of their funding from a federal agency that provides oversight and monitoring.

Regardless of the type of organization, several potential mechanisms (either individually or in combination) could be used to fund research on comparative effectiveness. Federal spending could be authorized and appropriated annually, as with other discretionary programs. Alternatively, funding could be drawn from Medicare's Hospital Insurance trust fund (which is financed primarily by payroll taxes) or specified as a percentage of mandatory federal outlays on health insurance programs.[37] Instead of or in addition to using existing sources of revenues, another option would be to require direct contributions from the health sector. For example, a new tax on health insurance premiums or other payments within the health sector could be established, with the resulting revenues dedicated to research on comparative effectiveness.

Trade-offs might arise between an entity's independence, credibility with the medical profession, and ability to reach controversial conclusions, on the one hand, and its accountability and responsiveness to policymakers and to other interested parties, on the other. For example, funding through appropriations would allow lawmakers to assess the new entity's contributions and accomplishments and to balance spending on those efforts against other federal priorities on an annual basis. But some observers have raised concerns that relying on annual appropriations would leave a new entity vulnerable to outside pressure and thus reluctant to undertake controversial studies or to reach conclusions that might generate opposition from affected groups. Indeed, the elimination of agencies engaged in such research that were funded by annual appropriations—or in the case of AHRQ, the occasional threat of elimination or substantial cuts in funding—may suggest the need for a different arrangement.

Alternatively, housing the new activities in an organization that was separate from the federal government and establishing automatic or dedicated funding mechanisms would give a new entity greater autonomy and potentially more influence on doctors and other health professionals. To be sure, lawmakers could change any funding formula that had been established—as is done frequently in Medicare—mitigating the degree to which the entity would lack oversight. Even with automatic funding, policymakers would want to periodically review the activities they

35. For a discussion of this issue, see Gail R. Wilnesky, "Developing a Center for Comparative Effectiveness Information," *Health Affairs,* Web Exclusive (November 7, 2006), pp. w572–w585.

36. Congressional Research Service, *The Quasi Government: Hybrid Organizations with Both Government and Private Sector Legal Characteristics,* RL30533 (updated February 13, 2007).

37. Current funding for AHRQ resembles a dedicated financing source in that it comes entirely from funds that are designated under the Public Health Service Act as available for evaluation activities. The total amount of funds available for such activities had been limited to 1 percent of certain expenditures (primarily those for research by NIH), but in recent years, that limit has been set at about 2 percent. As a practical matter, however, the agency's funding is like other discretionary appropriations. In previous years, some funding for AHRQ (and its predecessor agencies) came from regular appropriations, and a few million dollars was transferred from Medicare's trust funds.

were funding either to consider changes in the levels of spending or to adjust any funding formula to keep dedicated resources in line with spending trends—which could also provide a vehicle for pressure from interest groups. Nevertheless, automatic or dedicated funding mechanisms would tend to limit the influence of political pressure to some extent. But such mechanisms also would raise questions about how the entity set its priorities and allocated resources—and how it would be held accountable for those decisions. A nongovernmental organization might be able to act more quickly than a federal agency, but that speed could come at the expense of transparency.

Under any option, an advisory board (or governing council) could be established to serve several functions: providing guidance to the entity and establishing priorities for its research projects; creating an independent process for reviewing and possibly approving the findings that resulted from that research; and serving as a channel for interested parties to participate. For example, the board could include representatives of major federal health programs, private insurers, health care providers, advocacy groups for patients, and drug and device makers—as well as members of the general public and disinterested policy experts. Alternatively or in addition to including various stakeholders, a regular process could be established for getting input from interested parties. An example of that type of structure is the U.S. Preventive Services Task Force (see Box 2).

In designing such an oversight group, a number of issues would arise. The types of participants on any board and the manner in which members were chosen and replaced would have to be determined carefully to avoid giving one perspective undue influence. Similarly, conflict-of-interest rules governing the entity's staff would probably be needed. Trade-offs could exist between the extent to which many views and interests were represented and the ability of the council or board to make timely decisions or to reach consensus on contentious issues. Whether any oversight group was involved in reviewing or approving the results of research projects or focused instead on which projects to initiate and what those reviews entailed would also affect the entity's staffing requirements and the types of expertise that board members needed.

Another organizational issue is whether to establish a single or highly centralized entity or, instead, to design a more loosely coordinated system encompassing several distinct centers to produce independent analyses. Many of the options that have been proposed seek to centralize research activities through one entity—partly to address concerns about the lack of coordination among current U.S. efforts. An advantage of that centralized approach is that it would tend to give more weight to any conclusions reached. At the same time, that potential for having a greater impact could also lead the organization to adopt findings that were watered down to reach consensus; even if the entity did not have a formal approval process and instead simply released any results of approved projects, a single agency might be more reluctant to pursue research into more contentious questions. A decentralized approach could give individual research centers more latitude and encourage more competing perspectives to emerge. However, a more pluralistic approach could also involve some redundant efforts and, if it yielded any conflicting findings, would leave users with the task of reconciling the results.

An additional consideration—particularly if a new entity was created—would involve start-up costs and other implementation challenges. If funds were directed through an existing federal agency, some ongoing costs for additional staffing would be incurred, but the basic support infrastructure would largely exist already. By contrast, establishing a new agency or public–private partnership could require a greater effort before research could begin. At the same time, a quasi-governmental organization or public–private partnership could have more flexibility to develop and maintain its staff than a new or existing federal agency would have. Creating a new source of revenues (such as a tax on health insurance premiums) to help fund research on comparative effectiveness would also involve time and administrative costs.

Among existing organizations, their relative strengths and weaknesses could affect which one was best suited for new research efforts. NIH has extensive experience overseeing clinical trials but may not see research on comparative effectiveness as central to its mission of expanding the frontiers of biological and medical knowledge. AHRQ has substantial expertise in many areas of comparative effectiveness but has limited experience managing trials, and some observers have raised concerns about the impact that significantly expanded research about comparative effectiveness might have on that agency's other research endeavors. For its part, the Institute of Medicine is widely respected but does not have an extensive organizational capacity to conduct or oversee primary research,

Box 2.

The U.S. Preventive Services Task Force

The U.S. Preventive Services Task Force was established in 1984 by the Department of Health and Human Services to produce recommendations about which preventive health care services should be routinely provided to individuals who do not have any symptoms of a given disease. Such services include immunizations, tests to screen for the presence of diseases, and behavioral counseling (such as programs that encourage smokers to quit).[1]

The size and composition of the task force has varied over time, ranging from 10 to 20 members; the members are not federal employees but have generally been practicing clinicians. The task force's work is currently supported by the Agency for Health Care Research and Quality (AHRQ), with an annual budget of about $3 million. As a rule, the task force does not fund studies that evaluate preventive services but instead relies on existing evidence. Two research centers that AHRQ has designated generate summaries of that evidence—which are similar to but perhaps not as rigorous as systematic evidence reviews. Given the available time and resources, the task force has not sought to review all preventive services but instead has assigned priority to services that address significant health problems, that are likely to have new evidence available, or that have generated controversy about their use.

In developing its recommendations, the task force considers both the strength of the evidence and the magnitude of the expected benefits and risks. Risks can include adverse reactions to vaccines, false-positive test results that lead to unnecessary or even harmful follow-up care, and complications from invasive test procedures—which can have substantial aggregate effects even if their probabilities are low, because preventive services may be provided to very large numbers of people. The task force's recommendations cover which types of asymptomatic individuals should receive the services, taking into account how the risk of contracting a condition or disease varies by age, sex, and other factors.

1. For a general discussion, see Eileen Salinsky, *Clinical Preventive Services: When Is the Juice Worth the Squeeze?* Issue Brief No. 806 (Washington, D.C.: National Health Policy Forum, August 24, 2005).

and some observers believe its consensus-building process could make timely action difficult.

Among the options for a new entity, establishing an FFRDC has generated some interest, partly on the grounds that it would be somewhat insulated from political pressure. But most of an FFRDC's funding would have to come from a federal agency, so it is not clear why its activities (most of which, presumably, would also be contracted out to private researchers) would be subject to less pressure than the activities of an agency receiving direct funding. The argument is sometimes made that private contributions would make private payers more likely to accept and use the results of the research. If such contributions were voluntary, however, the incentives to make them would be modest because the benefits of the research would accrue to many parties. If such contributions were instead required, then the arrangement would be essentially equivalent to having the government collect the money and appropriate the funds via a federal agency.

More generally, competing perspectives exist about how the relative roles of public and private payers in funding research on comparative effectiveness would affect perceptions about the results of that research. In some quarters, the findings of research funded by the government are seen as reflecting political pressure, perhaps to accommodate the views of interest groups or to support budgetary objectives. Those concerns could be attenuated to some degree if the agency conducting the research was not also a payer for health care, such as CMS. At the same time, other observers have raised concerns about privately sponsored research, which is also seen as advancing cost-cutting objectives (if sponsored by insurers) or as promot-

Box 2.

Continued

The task force has presented its recommendations in a periodic series of reports, the most recent of which covers about 60 specific services. Those services are now given a letter grade, as follows:

- A, for services that are strongly recommended on the basis of solid evidence that the benefits of improved outcomes outweigh the risks of harm;
- B, for services that are recommended on the basis of reasonable evidence of net benefits;
- C, for services with no recommendation because the balance of benefits and risks is too close;
- D, for services that should not be routinely provided because the evidence indicates the services are ineffective or that the risks outweigh the benefits; and
- I, for services that do not have sufficient evidence on which to base a recommendation.

Initially, when formulating recommendations, the task force did not take into account the costs of providing preventive services or their cost-effectiveness.[2] According to one recent summary, however, the task force now "considers the total economic costs that result from providing a preventive service, both to individuals and to society, in making recommendations, but costs are not the first priority."[3] Although some immunizations against a disease have been shown to reduce total spending on health care, many other preventive services appear to increase spending on net—either because of the costs of providing those services to large segments of the population (only some of whom will be found to have the disease) or because the overall effects on treatment costs are modest. Analyses of cost-effectiveness would shed light on how the health benefits of preventive services compared with those increases in spending.

2. See Somnath Saha and others, "The Art and Science of Incorporating Cost-Effectiveness in Evidence-Based Recommendations for Clinical Preventive Services," *American Journal of Preventive Medicine*, vol. 20, no. 3 (April 2001), pp. 36–43.
3. Russell P. Harris and others, "Current Methods of the U.S. Preventive Services Task Force," *American Journal of Preventive Medicine*, vol. 20, no. 3 (April 2001), pp. 21–35.

ing the interests of drug and device manufacturers and of providers of health services.

Options for Comparing the Effectiveness of Treatments

The appropriate organizational form for any new or expanded federal entity, along with the mechanism and level of funding, may depend in large part on what activities it would carry out. For example, analyzing existing data would require a different set of skills, and would cost less, than overseeing new clinical trials that compared different treatments. In addition to setting priorities among the various methods of research, a new or expanded entity would have to define the scope of its analyses—both the types of comparisons it would commission and the questions that analyses would address. In particular, would the organization focus only on trying to determine which treatments conferred the greatest medical benefits, or would it also assess which treatments were most cost-effective? Whatever approach was taken, the manner in which the results were communicated to doctors, patients, and health insurers could play an important role in determining the impact on medical practice.

Methods of Research

Federal efforts to assess different treatment options could be pursued in a variety of ways. Options range from synthesizing existing research—a process known as a systematic review—to conducting new studies using data that are already available to funding new head-to-head clinical trials. Although those options are not mutually exclu-

sive—indeed, they could all be pursued at the same time—each one presents certain challenges, with potential trade-offs arising between the costs of the activities and the value of the information they provide.

Systematic Reviews of Existing Research. The approach that would probably be easiest to implement would be to review and summarize the results of existing studies in a systematic and rigorous way. For example, even though existing studies may only compare a single treatment to a placebo, the results of several studies of individual therapies could in some cases be combined to measure those treatments against one another. That effort could also critically assess the strengths and weaknesses of the available evidence and seek to reconcile conflicting findings or determine what the preponderance of the evidence indicated. Such reviews would be comparable to some of the work that AHRQ is already undertaking and to some current efforts based at universities or other public and private research centers such as ECRI and Hayes, Inc. One advantage of this approach is its relatively low expense; a single systematic review might cost a few hundred thousand dollars.

Because the evidence base for comparing treatment regimens is itself limited, however, how much additional insight can be gleaned from systematic reviews of existing research is not clear. Data from clinical trials that had already been conducted would naturally be the focus of any systematic review, because trials can provide the clearest evidence about a treatment's effects, but such studies also have limitations. Some analyses have indicated that clinical trials sponsored by interested parties—which is often the only source of such data—are more likely than independent studies to find favorable results.[38]

Another potential limitation is that existing information may not be sufficient to reach definitive conclusions. Studies may be difficult to compare or reconcile, either because they use different methodologies or analyze different populations of patients, or simply because they yield conflicting findings. For example, a number of independent studies have examined different screening techniques for colorectal cancer, each of which provides an estimate of the cost per enrollee for each increase in QALYs. But according to a recent review of those studies, the results varied to such an extent that reaching a definitive conclusion about which technique was most effective or most cost-effective was difficult (see Table 2).[39]

Available studies of treatments may have even more limitations than studies of screening tests, because trials of treatments for particular diseases frequently exclude patients with other health problems, elderly enrollees, or other populations that may be of considerable interest in gauging comparative effectiveness; as a result, determining how broadly the results apply or whether they will hold for other groups of patients is hard to do. The fundamental issue is that, no matter how rigorously a systematic review is conducted, its contribution is by definition constrained by the extent and quality of the underlying evidence.

A recent systematic review of drug treatments for one form of diabetes that was sponsored by AHRQ illustrates both the strengths and weaknesses of such research.[40] The review covered a large body of literature, consisting of over 200 reports, and it was able to reach a relatively clear conclusion: Older drugs were found to be at least as effective as newer drugs in controlling patients' blood sugar and cholesterol levels. Most of the studies that were reviewed had relatively short durations, however—two years or less—so they were not able to address the impact on mortality or other effects of diabetes on morbidity (which can take a long time to materialize). The studies also tended to focus on nonelderly white patients, so they could not address the effectiveness for other populations; indeed, the review recommended that several clinical trials be conducted to fill in those gaps. Moreover, study subjects typically had no other significant health problems, whereas most patients with diabetes also have other

38. See Justin E. Bekelman, Yan Li, and Cary P. Gross, "Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review," *Journal of the American Medical Association,* vol. 289, no. 4 (January 22/29, 2003), pp. 454–465; Stephan Heres and others, "Why Olanzapine Beats Risperidone, Risperidone Beats Quetiapine, and Quetiapine Beats Olanzapine: An Exploratory Analysis of Head-to-Head Comparison Studies of Second-Generation Antipsychotics," *American Journal of Psychiatry,* vol. 163, no. 2 (February 2006) pp. 185–194; and Jeffrey Peppercorn and others, "Association Between Pharmaceutical Involvement and Outcomes in Breast Cancer Clinical Trials," *Cancer,* vol. 109, no. 7 (April 2007), pp. 1239–1246.

39. Medicare Payment Advisory Commission, *Report to the Congress: Increasing the Value of Medicare* (June 2006), pp. 232–233.

40. See Shari Bolen and others, "Systematic Review: Comparative-Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus," *Annals of Internal Medicine*, vol. 146, no. 6. (September 18, 2007), pp. 386–399.

Table 2.

Cost-Effectiveness of Different Screening Methods for Colorectal Cancer

(Dollars)

Screening Method	Lowest	Highest
Colonoscopy		
Every 5 Years	17,316	36,612
Every 10 Years	10,633	26,693
Fecal Occult Blood Testing		
Annually	4,643	25,860
Every 3 Years	2,942	10,861
Sigmoidoscopy		
Annually	1,391 [a]	1,391 [a]
Every 3 Years	16,318	20,727
Every 5 Years	14,384 [b]	42,310

Source: Congressional Budget Office based on Medicare Payment Advisory Commission, *Review and Analysis of Cost-Effectiveness Analyses for Two Medicare-Covered Services* (prepared by the Institute for Clinical Research and Health Policy Studies, New England Medical Center, June 2006), available at www.medpac.org.

Note: The cost-effectiveness ratio is the estimated cost per one-year increase in quality-adjusted years of life expectancy, in comparison with the result of no screening.

a. Only one study was available for analysis.

b. One study found that screening every five years yielded lower costs and better health outcomes than no screening.

diseases, limiting the potential usefulness of the findings. In addition, the implication of the review—that older drugs for diabetes should be tried first—was already the protocol recommended by the American Diabetes Association. Thus, although the review was relatively inexpensive to conduct and may well have been worth its costs, its contribution was also limited.

In some cases, the existing evidence may permit more clear-cut determinations, but many systematic reviews are inconclusive—so views differ about their overall contribution. Britain's National Institute for Clinical Excellence (NICE) relies solely on systematic reviews of available studies. It has nonetheless been able to analyze many different treatments on the basis of their cost-effectiveness and to develop an extensive set of clinical guidelines and recommendations about using medical technologies.[41] Whether that record indicates the greater strength of the evidence on the reviewed treatments or a greater willingness on NICE's part to draw conclusions from that evidence is not clear. Typically, though, systematic reviews find that the available evidence is not adequate to address many important questions, so the primary value of such reviews may lie in clearly identifying the gaps in knowledge that should be the subject of future research.

Analyses of Claims Records. A somewhat more challenging approach than reviewing existing studies would be to fund new analyses comparing medical treatments using existing sources of data, such as health insurance claims records. An advantage of that approach is that it could provide new information to help resolve uncertainties about treatments at relatively low cost—using data on patients that had already been treated.

A central difficulty in such studies, however, is accounting for the differences in patients' health status that play a role in determining which treatment they get—which can make simple comparisons misleading. Insurance claims typically do not include any information about health status. Yet patients with more severe heart disease, for example, are more likely to receive invasive and expensive surgical procedures such as an angioplasty or a bypass operation. The greater severity of their condition may also make them more likely to have a subsequent heart attack and more likely to die. As a result, a comparison with patients receiving less aggressive treatments—who are probably not as sick, on average, to begin with—could understate the benefits of more aggressive treatments. In other settings, patients receiving more aggressive treatments may be healthier, so even well-designed observational studies can generate misleading findings regarding the benefits of those treatments. Studies of

41. To estimate cost-effectiveness, NICE generally combines the results of such reviews with its own models of the impact of different treatment options on the use of health services and health care spending.

cancer care, for instance, may be particularly susceptible to such confounding effects.[42]

To address such problems, researchers might be able to analyze geographic differences in treatment patterns to compare the impact of different treatments on comparable types of patients. For example, one study using claims data for Medicare enrollees sought to exploit the fact that patients living farther away from hospitals that treat a high volume of heart attacks were less likely to receive an intensive treatment for that condition (such as an angioplasty or a bypass operation).[43] At the same time, patients living farther from such hospitals appeared to be about as healthy as patients living nearby—so grouping patients by distance could address the analytic problem noted above whereby sicker patients get more intensive treatments. The study found that patients living closer to high-volume cardiac hospitals had slightly lower mortality rates, but the difference arose on the first day of admission and thus did not seem related to which procedure (if any) they ultimately received.

That example illustrates some of the challenges involved in using observational studies that are based on claims data. A key one is finding a factor that can be used in the analysis that is correlated with the treatment that patients receive but is not correlated with their underlying health status. (Economists refer to such factors as "instrumental" variables.) Even if such factors are available, proving that other confounding effects did not influence the results can be difficult. Whether that study's findings were persuasive enough to reduce the use of intensive medical treatments for heart attack patients, for example, is not clear. And the case of heart attacks—where urgent hospital care can mean the difference between life and death but where a range of potentially effective treatments are available—may be easier to analyze than other conditions.

Other issues surround the claims data themselves. First, maintaining the privacy of the patients whose records were being examined would be an important matter but could also present a barrier to conducting such studies. For statistical reasons, extracting meaningful results could require a large volume of claims data (as was the case in the study of heart attack treatments). Second, the quality of the study that could be conducted would depend on the level of detail that the data provided. Comparisons of the effects of treatments on mortality rates would be easier to generate because that information is relatively easy to obtain. Effects on morbidity or on the extent to which symptoms are relieved, however, might be more difficult to ascertain—depending on whether the relevant data were readily available. In addition, private health plans might have difficulty in conducting longer-term comparative effectiveness studies using claims data on their enrollees given the turnover in insurance coverage; if patients who changed plans were different from those who remained, statistical obstacles might undermine the comparison.

The expanded use of electronic health records could facilitate more-sophisticated analyses, if the issues of access and privacy could be addressed. In particular, those records could provide more comprehensive information both about the health histories of different patients and about their health outcomes. That additional information would make controlling for differences among patients receiving different treatments easier and would allow studies to address a broader set of outcomes than mortality. Some work of that nature is currently being conducted through the HMO Research Network and through a broader network of centers that have access to electronic databases that AHRQ established in 2005.[44] One challenge, however, is that the electronic records of different health plans are not always compatible, making aggregating data difficult.

42. See Alan M. Garber, "Cost-Effectiveness and Evidence Evaluation as Criteria for Coverage Policy," *Health Affairs,* Web Exclusive (May 19, 2004), pp. W4-284–W4-296. Some analyses have found similar results for observational studies and randomized controlled trials of the same treatment, but others have found important differences in the magnitude of the treatments' effects, particularly when the nonrandomized studies were done retrospectively. See Kjell Benson and Arthur J. Hartz, "A Comparison of Observational Studies and Randomized, Controlled Trials," *The New England Journal of Medicine,* vol. 342, no. 25 (June 22, 2000), pp. 1878–1886; and John P. A. Ioannidis and others, "Comparison of Evidence of Treatment Effects in Randomized and Nonrandomized Studies," *Journal of the American Medical Association,* vol. 286, no. 7 (August 15, 2001), pp. 821–830.

43. Mark McClellan, Barbara J. McNeil, and Joseph P. Newhouse, "Does More Intensive Treatment of Acute Myocardial Infarction in the Elderly Reduce Mortality? Analysis Using Instrumental Variables," *Journal of the American Medical Association*, vol. 272, no. 11 (September 21, 1994), pp. 859–866.

44. For a discussion of those efforts, see Lynn M. Etheredge, "A Rapid-Learning Health System," *Health Affairs,* Web Exclusive (January 26, 2007), pp. w107–w118; and related articles contained in that supplemental issue.

Medical Registries. Another option that could supplement or help improve analyses of claims data would be to establish medical registries, which generally track patients who have a particular disease or who have received a specific treatment. Registries collect additional information that is typically not contained in claims records, such as measures of health status or test results. In the United States, a number of registries—established or managed by various entities, including medical specialty societies and product manufacturers—have been used to help determine the clinical effectiveness or cost-effectiveness of various products and services.[45] Some health plans establish registries of their enrollees, although a centrally managed registry would have the advantage of being able to track patients if they moved or changed health plans.

Data from medical registries could help improve claims-based analyses both by allowing a broader set of outcomes to be measured and by providing information to control for differences among patients getting different treatments, including the severity of their illness. But a number of challenges and trade-offs would exist. One issue would be how to recruit patients and their providers to participate in and provide information to the registries and to retain them over time. Voluntary participation might be easy to implement but could introduce bias into analyses if patients choosing to participate differed in important ways from patients who had opted out. Some form of mandatory participation could avoid that problem but might raise objections from participants. Registries focused on specific treatments could also be subject to bias if those patients differed systematically from patients who did not receive those treatments—a problem that could be addressed by including a comparison group in the registries. Another trade-off concerns the data elements to collect; a more extensive list would permit richer analyses but would raise the burden of participation. More-extensive registries and registries involving more patients would also be more expensive to operate, although the annual costs of maintaining a typical registry are probably on the order of several million dollars.

The establishment of registries could affect medical practice in various ways. For example, CMS recently instituted a policy of "coverage with evidence development" for Medicare, to address treatments with potentially promising but uncertain medical benefits. Under that policy, Medicare now covers the costs of implantable cardioverter-defibrillators for a broader set of heart conditions than had previously been eligible—but only if those new patients are included in a registry that is supposed to track their progress.[46] If CMS would otherwise have decided not to cover that treatment for those patients, then the new policy means an increase in spending in the near term, but it also allows broader access to that technology in order to help generate the kind of evidence needed to reach a conclusion about its value. The registry may also help ensure, through its documentation requirements, that all patients meet the medical criteria required for Medicare coverage. Another example comes from Sweden, where a registry of patients undergoing hip replacement surgery has been used to provide periodic feedback to doctors about their surgical techniques and to track which specific models of artificial hip have the lowest rates of complications. That effort is credited with reducing health costs by avoiding repeat operations to fix faulty or poorly installed hips.[47]

Randomized Controlled Trials. The method of research that would probably yield the most-definitive results involves randomized controlled trials to compare treatments head to head, but that approach would also be the most expensive and would take the longest to conduct. The main advantage of random assignment is that it usually ensures that any differences in outcomes reflect true differences among treatments and not confounding differences among patients (such as their health status or other factors that are more difficult to observe). But detecting differences that are statistically significant—that is, unlikely to have arisen simply by chance—can require a substantial number of patients to participate, and in some cases, they must be followed for several years. Total costs for conducting an extensive trial can exceed

45. For more information, see Richard E. Gliklich and Nancy A. Dreyer, eds., *Registries for Evaluating Patient Outcomes: A User's Guide*, AHRQ Publication No. 07-EHC001-1 (Rockville, Md.: Agency for Healthcare Research and Quality, April 2007).

46. See Sean R. Tunis and Steven D. Pearson, "Coverage for Promising Technologies: Medicare's 'Coverage with Evidence Development,'" *Health Affairs,* vol. 25, no. 5 (September/October 2006), pp. 1218–1230. An implantable cardioverter-defibrillator (ICD) is a device designed to quickly detect a life-threatening rapid heartbeat and to deliver an electric shock that converts the rhythm back to normal. Apparently, CMS has not yet implemented the longitudinal registry for ICD patients.

47. See Henrik Malchau and others, "The Swedish Total Hip Replacement Register," *The Journal of Bone and Joint Surgery,* vol. 84, no. 11 (November 2002), pp. S2–S20.

$100 million over the course of the study, although many trials are less expensive, and some may cost only a few million dollars. (One factor affecting the costs of funding a trial is whether the health care services that the participants receive will be paid for by a third party, such as Medicare.)

Although the number of studies reporting results from randomized controlled trials has increased sharply, a number of questions have also been raised about the findings that can be derived from the existing stock of trial results. Many trials are aimed at demonstrating efficacy rather than effectiveness—the distinction being that efficacy reflects optimal conditions, whereas effectiveness requires a demonstration in real-world medical settings.[48] Partly as a result, patients with other health problems or groups such as the elderly are often excluded from trials. Further, many trials focus on demonstrating efficacy for a narrowly defined set of patients, so the results may not be generalizable; and combining studies in order to compare multiple treatment options may offer its own difficulties because of the differences among the patients studied. Finally, questions about the objectivity of industry-sponsored trials have also been raised.

To address those problems, some observers have recommended a greater emphasis on "practical" clinical trials.[49] The two key features of such trials are that they compare treatment choices that clinicians face and include a wide variety of study participants drawn from a range of practice settings. Traditionally structured trials, such as those typically sponsored by NIH, can involve a relatively large number of participants and relatively long periods of follow-up observation and analysis. As a result, they may be relatively costly to implement. Trials that are simpler and less expensive and that take less time to carry out could provide a greater "bang for the buck," but at some risk of reduced accuracy.[50]

Because their results can be persuasive, well-structured trials can have a noticeable effect on the use of treatments. For example, according to one report, the findings of the trial (discussed above) comparing the use of angioplasty and a metal stent with nonsurgical management of patients with stable coronary artery disease—which found minimal advantages of stenting—may have reduced the use of that procedure.[51] Determining the precise effect of the trial is difficult, however, in part because the downward trend in stenting procedures began about eight months before the trial's results were publicized. Another example comes from the trial that CMS sponsored assessing lung-volume-reduction surgery. Although that study identified some types of patients who would benefit from the procedure, and Medicare decided to cover it nationwide in those cases, the number of Medicare enrollees undergoing that surgery actually declined after the study was published (apparently reflecting the risks of undergoing the procedure that were discovered).[52] Such effects on medical practice may not be typical, however, and in any event, it took seven or eight years to complete those trials and release the results.

In addition to trials' relatively high costs and long durations, other constraints limit the number of trials that can

48. In other words, a finding of efficacy shows that a treatment can work for some patients in some circumstances, whereas a test of effectiveness determines whether the treatment usually works for a broader set of patients.

49. See Sean R. Tunis, Daniel B. Stryer, and Carolyn M. Clancy, "Practical Clinical Trials: Increasing the Value of Clinical Research for Decision Making in Clinical and Health Policy," *Journal of the American Medical Association,* vol. 290, no. 12 (September 24, 2003), pp. 1624–1632.

50. A recent example may illustrate the risks of drawing conclusions from trial results too quickly. In 2002, a trial of hormones used to treat menopause was halted abruptly when the initial findings indicated widespread increases in the risk of heart attack for participants. Subsequent analysis, however, found that the effects varied substantially depending on the ages of the patients and that some groups would benefit from hormone replacement therapy. See Tara Parker-Pope, "How NIH Misread Hormone Study in 2002," *The Wall Street Journal,* July 9, 2007. Even so, the trial's results indicated that observational comparisons had generally overstated the benefits of hormone replacement therapy because they did not adequately account for differences between the patients who received that treatment and the ones who did not.

51. See Keith J. Winstein, "Stent Implants Declined in April; Doctors Attribute Drop to Study Showing Drugs May Have Similar Benefits," *Wall Street Journal,* May 17, 2007. According to that report, total spending in the United States on angioplasties with stents was about $14 billion in 2006, but the number of stenting procedures began to decline in mid-2006.

52. Prior to the initiation of the trial, Medicare did not have a national policy regarding coverage of lung-volume-reduction surgery, but many of the local organizations that process Medicare claims had been approving it and paying for it under existing billing codes. See Tunis, "Coverage Options for Promising Technologies"; and Gina Kolata, "Medicare Says It Will Pay, but Patients Say 'No Thanks,'" *New York Times,* March 3, 2006.

feasibly be conducted at any given time. One is getting a sufficient number of patients to participate to allow valid statistical comparisons of treatment outcomes. For medical conditions that are common, that may not be a substantial challenge, but the difficulty increases the more narrowly the target population is defined—just because fewer patients meet the criteria for participation in the trial. Ethical issues can also arise if one set of participants is assigned a treatment that is generally considered less effective, although such concerns may be less likely to arise when significant uncertainty exists in the medical community about the relative benefits of different treatments. In light of those constraints, significantly expanding comparative effectiveness research is likely to require a combination of randomized trials and other research methods.

Modeling. Another approach that has been suggested—as an alternative or supplement to clinical trials—is the use of computer models to simulate the effects of treatments on different populations of patients. While many well-designed models exist, perhaps the most prominent one is known as Archimedes; its development has been led by Dr. David Eddy with the support of the Kaiser Permanente health plan.[53] One benefit of that approach is that, once such a model is developed, it can be used to answer questions about effectiveness at relatively low cost. Indeed, that approach can even have advantages over analyses of claims data, electronic health records, or medical registries: If the model can accurately predict the effects of a new treatment, waiting for those treatments to be used and then tracking their effects on actual patients over time can be avoided in some cases.

Achieving that objective may be quite difficult, however, and a particular obstacle is that models rich enough to simulate real-world medical care may not be transparent enough to generate confidence in or acceptance of their results. Archimedes, for example, is a highly complex model that seeks to capture not only the behavior of doctors and patients but also many of the biological processes of the human body. Tests of the model have shown that under certain conditions, it is able to predict the results of trials with high accuracy. In those tests, a set of trials is examined—and usually, about half of them are used to calibrate the model, while the rest are used to test its predictions. It is not clear, however, how well the model would do when starting with a less extensive evidence base, so its primary contribution might be to fill in some gaps between existing trial results and to permit modest extensions of completed trials at relatively low cost. For more ambitious efforts, it would not be possible to tell whether the model's predictions proved correct or incorrect until after the treatment in question had been used and analyzed via the other methods described above.

The Scope and Focus of Analyses and the Dissemination of Results

In addition to determining what types of research to conduct, any organization sponsoring research on comparative effectiveness would have to make a number of decisions about the scope and focus of that research—or policymakers might decide to set parameters for those decisions. One important question is whether federally sponsored research would seek to assess both the relative clinical benefits and the cost-effectiveness of treatments. A second is what balance to strike between evaluating treatments already being used widely and examining new treatments that seemed likely to become common—and more generally, how to keep up with the rapid pace of technological development in health care. Another issue is whether and to what extent the research would compare the performance of different providers or types of providers (such as high-volume and low-volume hospitals). Last but not least is the issue of how to communicate results to doctors, patients, and other interested parties.

Clinical Effectiveness or Cost-Effectiveness? There are arguments both for and against having federally sponsored research on comparative effectiveness consider cost-effectiveness as well as clinical effectiveness. Those arguments involve the practical steps needed to do the analysis and the ultimate effects of the research.

One practical reason a federal entity might not seek to assess which treatment was most cost-effective for a given type of patient is that the answer to that question might vary by health plan. Health insurance plans have different cost structures and may pay different prices for the same services, so there is an argument for giving insurers (and other interested parties) more information about the relative benefits of different treatments and letting those parties calculate which one was most cost-effective. Indeed, the prices of the inputs involved are often subject to

53. See David M. Eddy, "Linking Electronic Medical Records to Large-Scale Simulation Models: Can We Put Rapid Learning on Turbo?" *Health Affairs,* Web Exclusive (January 26, 2007), pp. w125–w136.

negotiation. But those negotiations could be influenced by objective comparisons of medical benefits. Australia's health agency, for example, calculates a price at which a new drug is cost-effective, given its clinical benefits relative to existing therapies. (That agency conducts the reviews of clinical effectiveness as well—but because it also administers that national health insurance program, the example may not shed light on this country's debate about whether and where to conduct cost-effectiveness analyses.)

More fundamentally, objections to considering cost-effectiveness reflect concerns that such efforts would at least taint the analysis of clinical effectiveness—and might ultimately be used to restrict access to valuable treatments. To the extent that federally funded analyses of clinical effectiveness facilitated calculations of cost-effectiveness by other parties, however, the same concerns about their ultimate impact would seem to arise. Moreover, well-designed studies would primarily affect treatments whose added benefits did not appear to justify their added costs, and access to treatments would depend largely on how the results were applied by public and private insurers. Thus, a more substantial concern about the research itself is that having the same organization fund analyses of both clinical effectiveness and cost-effectiveness could reduce the impact of any findings about the former—because those findings might be perceived as reflecting cost-control objectives.

An alternative view, however, holds that federal sponsorship of research addressing cost-effectiveness would give that research more credibility. Such sponsorship could help address concerns about the consistency of the methodologies used to calculate cost-effectiveness and about the transparency of the process by which those calculations were made.[54] In addition, some observers believe that federally sponsored analyses would be viewed with less suspicion than are studies conducted by private insurers. As a practical matter, having the federal entity develop or support an initial cost-effectiveness analysis, along with a template that insurers or others could use to modify the calculation using different prices, could also avoid some duplication of effort.

A more basic argument in favor of including cost-effectiveness is that achieving the greatest possible gains in the efficiency of the health sector ultimately would require assessing both the benefits and costs of different treatment options to see whether the added benefits of more-expensive options were worth their added costs. On balance, research that included an analysis of cost-effectiveness would probably have a larger effect on medical practice than research that analyzed only the comparative clinical effectiveness of different treatments—primarily because the results would sometimes highlight that benefits were small relative to the incremental costs.

Even so, extending the scope of research to include cost-effectiveness would raise a number of additional challenges. For example, the methods of calculating quality-adjusted life years could be a source of controversy. Although there may be substantial agreement within the scientific community about the relative benefits of avoiding different adverse outcomes—such as degrees of disability and risks and side-effects of surgery—converting those differences into the common metric of QALYs might nevertheless raise concerns among patients and other interested parties. Similarly, deciding how broadly or narrowly any findings applied would be a very important consideration, because some treatments might be more effective for certain subgroups of patients than for an average patient. That consideration would affect the design of studies and the comparisons that would be undertaken; that is, the studies would need to be sufficiently robust to examine the potential variation in benefits among subgroups of patients—in order to limit the risk of overlooking patients who could benefit greatly from a treatment.

Finally, the very practice of placing a dollar value (or range of values) on an additional year of life has generated controversy; many people find the notion uncomfortable if not objectionable, and the sentiment that no expense should be spared to extend a patient's life is often expressed. Nevertheless, researchers have developed estimates of that value reflecting choices that individuals are observed to make in other settings (for example, when they purchase life insurance or accept the risks of driving). Estimates of about $100,000 per year are commonly cited, though higher and lower figures are often used. An agency charged with analyzing cost-effectiveness would not, however, have to determine what the appropriate threshold or range was—that decision could be left to purchasers and other decisionmakers. Instead, the agency

54. Standards for conducting analyses of cost-effectiveness have already been developed; for a discussion, see M. C. Weinstein and others, "Recommendations of the Panel on Cost-Effectiveness in Health and Medicine," *Journal of the American Medical Association,* vol. 276, no. 15 (October 16, 1996), pp. 1253–1258.

could estimate cost-effectiveness ratios and rank treatment options on that basis.

Other Questions of Scope and Focus. In addition to choosing which methods of research to pursue and whether to consider cost-effectiveness, a new or expanded agency would need to consider several other questions of scope and focus as well. Would it make recommendations about coverage of treatments as well? On which treatments would it focus attention, and how would it set those priorities? Would it compare different ways of providing a given treatment or concentrate on assessing broadly different options? Would it also try to assess doctors and other providers in terms of their effectiveness? And should it take explicit steps to expand the capacity for comparative research or anticipate that supply would grow to meet demand?

The question is whether the new or expanded federal entity would make recommendations about which treatments should be covered by insurance—either generally or for public programs—is related to but separate from the issue of whether to assess cost-effectiveness. Some observers have suggested that a U.S. entity focusing on comparative effectiveness should steer clear of making such recommendations because they would be controversial in themselves and because they might be seen as tainting findings about relative medical benefits. As a practical matter, furthermore, the entity would not have to make formal recommendations in order for its research to affect the use of medical care, as long as its findings on clinical effectiveness or cost-effectiveness were considered credible by doctors and other health professionals and could be easily used by insurers and other parties.

A more pressing issue is how a new or expanded entity would choose the specific treatments on which to focus its attention. Selecting broad areas of treatment (such as cardiovascular disease) might be relatively easy, but tradeoffs could arise between focusing on specific treatments that were widespread, expensive, and had uncertain benefits or, instead, on emerging treatments and technologies that promised to be expensive and might be adopted widely but had not yet become common practice. In the former case, data might be more readily available, but changing ingrained practice patterns might be difficult (short of producing evidence of actual harm). In the latter case, analyses might be more difficult to conduct given the limited claims data that would be available, while generating new data via clinical trials would take several years and thus might not be timely. A related question is how frequently to reassess treatments or variations on them; according to one study, systematic reviews typically require revision after about five years.[55]

An additional issue is whether to expand the scope and structure of comparisons so that they analyzed degrees of service use within a given treatment approach, not just broadly different approaches. As noted above, the literature on geographic variations in health care indicates that overall surgery rates do not vary systematically or in a manner that is strongly correlated with the variation in total Medicare spending. Rather, spending differences reflect more intensive use of hospital and physician services (as well as more use of ancillary services like tests). Therefore, future studies might need to examine different approaches to providing the same basic treatment, such as the extent of follow-up care provided or the frequency of using tests and imaging services—in addition to the "either/or" question of whether a given type of imaging or test was informative. Such analysis could also be applied to structured programs of care coordination or disease management, in order to assess their impact on health and their cost-effectiveness.

Another question is whether assessments would be limited to procedures and treatments or would also seek to evaluate the performance of individual doctors. In particular, the data from medical records that were used to compare the effectiveness of different treatments for a given type of patient could also be used to analyze the quality with which doctors provided each treatment. The potential gains from such analysis would include identifying doctors who delivered high-quality care and encouraging doctors who were not performing as well to improve—and doing both on the basis of objective evidence. At the same time, concerns could arise that evaluating doctors would detract from the focus on identifying effective procedures. Further, controlling for differences among patients that could affect the ratings of numerous individual doctors could be even more challenging than controlling for differences in patients when comparing a small set of treatments. Although such an approach could

55. See Karen J. Shojania and others, "How Quickly Do Systematic Reviews Go Out of Date? A Survival Analysis," *Annals of Internal Medicine*, vol. 147, no. 4 (August 21, 2007), pp. 224–233.

have a larger impact on health care than examining treatments alone, it could also be highly controversial.[56]

A final question regarding the scope of the activities funded revolves around the capacity to conduct research on comparative effectiveness. Several observers have indicated that the capacity is currently rather limited, which could serve as an important constraint on any expansion of federally funded efforts. In particular, some recent discussions have suggested that federal spending on that research should increase by billions of dollars per year, but it is not at all clear that such sums could be spent in an effective way in the near term.[57] At a minimum, additional research efforts would probably reach a point of diminishing returns. The entity that oversaw those efforts might therefore want to consider the option of using some funds to expand the pool of skilled researchers and to encourage steps that would make it easier to incorporate comparisons of effectiveness into the routine practice of medical care.[58]

The Dissemination of Results. Whatever types of results were produced, any new or augmented entity focused on comparative effectiveness would want to consider carefully how those results were communicated to doctors, patients, and other interested parties. (Such communication efforts represent an important element of AHRQ's program on effective health care.) Providing information to both technical and general audiences that was both useful and accurate would be challenging, though; a particular difficulty might be conveying the degree of uncertainty surrounding conclusions. A useful first step might be to conduct a critical assessment of past dissemination efforts in order to identify their strengths and weaknesses.

The mechanisms by which the results of comparative studies were disseminated could have important implications for their impact on medical practice. In particular, one such pathway could be the incorporation of any findings into computerized decision-support tools that some physicians and health plans now employ. Rather than having to recall any relevant evidence from memory, physicians could call up the results of comparative effectiveness research for a given patient's symptoms—or be presented with those findings (or their practical implications) automatically. The limited infrastructure for information technology that currently characterizes the health system, however, presents an obstacle to capturing the full potential of this approach. Alternatively, a few studies have found that presenting patients with comparative information about the benefits and risks of treatment alternatives—particularly in cases when elective surgery is one of the options being considered and when patients may vary in their valuation of the benefits and risks—leads them to choose less intensive treatments for certain conditions.[59] What process is most effective for presenting such information to patients, however, and how broadly those findings apply are less clear.

Implications for Health Care Spending

To affect medical treatment and reduce health care spending, the results of comparative effectiveness analyses would ultimately have to change the behavior of doctors and patients. For any large-scale changes to occur, the new or expanded entity would have to generate new findings for a substantial number of medical conditions—which would take many years. To have the maximum effect on behavior, those findings would then have to be incorporated into the incentives for providers and patients, a process of adjustment that might also take time. Although some patients and providers might object to such changes, over the long term the combination of

56. CMS has taken some initial steps toward assessing the quality of care that individual doctors provide. The Tax Relief and Health Care Act of 2006 provided for modest bonus payments under Medicare to doctors who elect to report information on certain measures of the care they provide in 2007. Although CMS will be able to provide feedback to doctors on how their performance compares to their peers', the payments do not depend on that performance. Furthermore, the measures that have been chosen cover areas of substantial consensus in the medical community about appropriate treatment protocols (for example, prescribing drugs known as beta blockers to patients who have had a heart attack). For a broader discussion, see Government Accountability Office, *Medicare: Focus on Physician Practice Patterns Can Lead to Greater Program Efficiency,* GAO-07-307 (April 2007).

57. The Health Industry Forum, *Comparative Effectiveness Forum: Executive Summary* (summary of a conference, Washington, D.C., November 30, 2006), available at http://healthforum.brandeis.edu/meetings/materials/2006-30-Nov./ExecBrief.pdf.

58. For a discussion, see Sean A. Tunis, "A Clinical Research Strategy to Support Shared Decision Making," *Health Affairs*, vol. 24, no. 1 (January/February 2005), pp. 180–184.

59. See Annette M. O'Connor, Hilary A. Llewellyn-Thomas, and Ann Barry Flood, "Modifying Unwarranted Variations in Health Care: Shared Decision Making Using Patient Decision Aids," *Health Affairs,* Web Exclusive (October 7, 2004), pp. VAR-63–VAR72.

additional information and revised incentives would tend to reduce spending for health care below currently projected levels, potentially to a substantial degree.

Currently, Medicare is effectively precluded from taking costs into account when making decisions about coverage and would probably need new legal authority to adjust payments to providers or cost-sharing requirements for enrollees to encourage the use of more cost-effective care. For their part, private insurers might not face legal barriers to limiting coverage of or altering payments for treatments that were shown to be less effective but still might be reluctant to do so if Medicare did not alter its own policies regarding coverage and payment. Thus, beyond conducting the analyses themselves, many difficult steps would probably need to be taken before spending on comparative effectiveness research translated into substantial savings for federal programs and the health care system. Even so, additional information comparing treatments would tend to reduce federal health spending in the near term—but probably not by enough to offset the full costs of conducting that research over the same period.

The Potential for Savings on Health Care

Predicting the impact that research on comparative effectiveness could have on health care spending is difficult because it is hard to know what that research will show. In some cases, the research could provide clearer evidence than exists today that the benefits of an expensive treatment outweighed the costs—in which case spending on such treatments could increase. Some observers have therefore suggested that comparative effectiveness research could also cause spending to increase on treatments already considered effective but not used as extensively as recommended protocols indicate.[60] By itself, however, new research on comparative effectiveness seems unlikely to increase the use of services that are already deemed effective, for two reasons. First, that research is unlikely to focus on such cases—instead, it would presumably target treatments of uncertain value. Second, even if it did address those types of care, an additional finding of effectiveness would be unlikely to have much impact on the use of already-recommended services without corresponding changes in the incentives to use them.

Although spending increases in some areas would be possible, current incentives already favor the adoption and spread of more-expensive treatments, so new research that found those treatments to be more effective or more cost-effective would probably increase their use only modestly. As a general rule, the fee-for-service reimbursement system by which health care is primarily financed in the United States—especially but not exclusively in Medicare—typically provides financial incentives for doctors and hospitals to adopt new treatments and procedures broadly even if hard evidence about their effectiveness is not available. For their part, insured individuals generally face only a portion of the costs of their care and, consequently, have only limited financial incentives to seek a lower-cost treatment. Although private health insurers have incentives to limit the use of ineffective care, they are currently constrained both by a lack of information and by public concerns about overly aggressive management (as was evident in a recent "backlash" against managed care plans).

Conversely, credible and well-designed studies that found that more-expensive treatments and approaches to care yielded little or no additional health benefits would have a greater potential to affect health care spending. Moreover, the evidence that additional spending and use of services in some parts of the country is not producing better health suggests that additional comparative research would be more likely to question than to support the value of more-expensive services. Research that affected the demand for treatments would also affect their supply; in particular, if the developers of new medical products and procedures had to demonstrate their value more clearly, those parties would not only have incentives to produce more evidence but also would be encouraged to focus their developmental efforts on approaches that were more clinically effective or more cost-effective. Over the long term, therefore, generating additional objective information about the relative costs and benefits of treatments seems much more likely to reduce total health care spending than to raise it—particularly if public and private insurers incorporated the findings into their coverage and payment policies.

Getting to the point at which additional research on comparative effectiveness could have a noticeable impact on health care spending would take several years. In addi-

60. One recent study found that patients typically received about half of recommended services, whether for preventive care, treatment of acute conditions, or treatment of chronic conditions. See Elizabeth A. McGlynn and others, "The Quality of Health Care Delivered to Adults in the United States," *The New England Journal of Medicine*, vol. 348, no. 26 (June 26, 2003), pp. 2635–2645.

tion to the time required to get the new activities under way, a lag would exist before results were generated, particularly if they depended upon the completion of new clinical trials. Initially, the available results would probably address a relatively small number of medical treatments and procedures; additional time would elapse before a substantial body of results was amassed. And in areas of medicine with significant levels of spending, many studies could be needed before a consensus emerged about the appropriate conclusions to be drawn—even if those studies did not generate conflicting results. For all of those reasons, it would probably be a decade or more before new research on comparative effectiveness had the potential to reduce health care spending in a substantial way.

The magnitude of that impact in the long term would depend primarily on how private and public insurers used that information and whether and how the results were incorporated into the incentives facing providers and patients. But additional information could have a modest effect on health care spending in the near term even if those incentive systems remained largely unchanged. The information would primarily affect spending in the private sector, where the scope for using comparative information is currently greater, but some "spillover" effects for enrollees in public programs would also be likely because doctors are inclined to provide similar care to all of their patients.

Possible Responses by Private and Public Insurance Plans

To affect medical treatment and reduce health care spending, the results of comparative effectiveness analyses would ultimately have to change the behavior of doctors and patients—that is, to get them to use fewer services or less intensive and less expensive services than are currently projected. Bringing about those changes would probably require action by public and private insurers to incorporate comparative effectiveness information into some combination of their coverage and payment policies. Those steps, however, could be difficult and controversial.

Private Insurers. One option for private insurers would be to not cover drugs, devices, or procedures that were found to be less effective or less cost-effective. That approach might prove to be particularly controversial, however, and the insurers would have a number of additional options as well. They could simply provide more information to providers and patients, which could improve compliance with treatment guidelines. For example, the use of medicines known as beta blockers, which is recommended following a heart attack to prevent a recurrence, has grown substantially in recent years—apparently as a result of reporting on the share of patients who receive prescriptions for them.[61] The availability of that information may have encouraged individuals to seek health plans whose doctors were more likely to prescribe beta blockers and may have encouraged doctors to prescribe them.

Alternatively, insurers could require enrollees to pay some or all of the additional costs of more-expensive treatments that were shown to be less effective or less cost-effective (in which case enrollees would have to decide whether the added benefits were worth the added costs); that approach is sometimes called value-based insurance design.[62] Or insurers could adjust payments to doctors and hospitals to encourage the use of more-effective care. According to one recent study, private insurers will currently cover a more effective treatment in nearly all cases—even if it is more costly—but it is also common for them to require that more costly treatments receive prior authorization before they are used or that patients try a less costly intervention first.[63] Research on comparative effectiveness could be used to determine when to apply those requirements.

Making substantial changes to insurance design and reimbursement would not be easy. Some patients, providers, and other interested parties would probably object to such arrangements or to the manner in which insurers established them. A particular concern would be that the average effects found by studies might not apply

61. Since 1996, the National Committee for Quality Assurance (NCQA), a not-for-profit organization that provides information about health care quality, has required private health care plans to report that information in order to receive accreditation. The average share increased from 63 percent in 1996 to 95 percent in 2005, and as a result, NCQA has now adopted a more stringent measure (which tracks actual use of those drugs). See Thomas H. Lee, "Eulogy for a Quality Measure," *The New England Journal of Medicine,* vol. 357, no. 12 (September 20, 2007), pp. 1175–1177.

62. See Michael E. Chernew, Allison B. Rosen, and A. Mark Fendrick, "Value-Based Insurance Design," *Health Affairs*, Web Exclusive (January 30, 2007), pp. w195–w203.

63. Garber, "Cost-Effectiveness and Evidence Evaluation as Criteria for Coverage Policy."

to all types of patients that were considered—so that subgroups of patients who could benefit greatly from a treatment might be overlooked. And as discussed above, having research studies keep pace with the development of new technologies would be an ongoing challenge. Consequently, any new incentive systems would probably be applied only in areas of care where the evidence was convincing.

Making such changes would also generate some new costs for insurers. Some administrative costs would be incurred to monitor whether patients met the medical criteria for which a given treatment had been proved effective or cost-effective. An exception or appeals process might also be needed to permit case-by-case reviews, and negotiating more complex reimbursement arrangements with providers would entail some costs. Those costs would probably be small in comparison to the change in health spending, given that insurers already monitor the use of treatments to ensure that they are medically necessary and generally have appeals processes in place. In addition, providing stronger incentives for patients and providers to use effective care would probably increase the use of services that are already deemed effective. The types of effective care that studies find are underprovided, however, tend to be relatively inexpensive screening and monitoring services for chronic health problems.

The steps that private insurers took could both affect public spending and be affected by public programs' responses to additional information about comparative effectiveness. To the extent that changes instituted by private insurers affected doctors' methods, there would probably be some "spillover" benefits for public programs. However, private insurers might be more reluctant to pursue such approaches aggressively, at least in the short term, if public insurance programs were not adopting similar methods.

Medicare. To reduce spending substantially under Medicare on the basis of comparative effectiveness research would probably require additional legislative authority to allow the program to consider relative benefits and costs in a more extensive way and to modify the financial incentives facing doctors and enrollees accordingly. Under current law, Medicare does not have clear authority to take costs into account when making decisions about what treatments are covered and has made only limited use of information about relative clinical effectiveness. Federal law does not explicitly prohibit Medicare from considering costs, but the Medicare statute provides that the program will pay for items or services if they are deemed "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."[64] A regulation was proposed in 1989 that would have included cost-effectiveness as a factor in determining whether a treatment was reasonable and necessary, but that proposed regulation generated considerable opposition and was eventually withdrawn.[65]

Most recently, Medicare officials sought to clarify the definition of "reasonable and necessary" for the purpose of determining whether a new treatment or procedure would be covered. In 2000, they issued a "notice of intent" to publish a proposed rule on that topic.[66] Under the concept outlined in that notice, Medicare would generally require new treatments to provide "added value," which was defined in the following way:

- A "breakthrough" technology (one conferring substantially more benefits than existing treatments) would be covered without regard to its cost.
- A new item or service that had some medical benefits would be covered regardless of its cost if no other medically beneficial alternative was available or if the alternative treatment used a different "clinical modality." (That term was not defined precisely, but drug therapy and surgery would clearly be treated as different modalities.)
- An item or service equivalent in its benefits to a similar currently covered service (using the same modality) would be covered only if its costs were comparable to or lower than the cost of the currently covered service.

64. See section 1862(a)(1)(A) of the Social Security Act.

65. See Peter J. Neumann and others, "Medicare and Cost-Effectiveness Analysis," *The New England Journal of Medicine*, vol. 353, no. 14 (October 6, 2005), pp. 1516–1522.

66. Health Care Financing Administration, "Criteria for Making Coverage Decisions," *Federal Register,* vol. 65, no. 95 (May 16, 2000), pp. 31124–31129.

That nascent proposal also generated opposition, however, and to date, CMS has not taken the next step of issuing a proposed rule.[67]

As a practical matter, therefore, under current policy and law, Medicare generally covers any treatment or procedure that has net medical benefits—that is, benefits that outweigh the risks of the procedure—regardless of its cost or its effectiveness relative to alternative therapies. As noted earlier, Medicare officials recently developed an initiative that provides provisional coverage for new treatments that have uncertain medical benefits—but also requires the resulting evidence about their effects to be analyzed so that a more informed final decision on coverage can be made using those data. That initiative, however, may not involve comparing different treatments to see which is more effective and does not appear to take the costs of treatments into account. At the same time, CMS officials have given some indications that they will consider whether a new treatment is as good or better (on purely medical grounds) than currently covered alternatives when making coverage decisions, and a recent decision not to cover artificial spinal discs took into account a comparison of that option with other spinal surgeries that are covered.

Medicare currently has somewhat more flexibility regarding the payments it makes for covered services, which can take comparative medical benefits—and, in some cases, costs—into account on a limited basis. For example, in order for a hospital to receive an additional payment for using a new device during a covered procedure (known as a "pass-through" payment), the device must be shown to provide a substantial clinical improvement for Medicare beneficiaries compared with the current technology. Over time, however, Medicare's payments to hospitals are adjusted to account for the costs of new technologies (on an aggregate basis) without requiring an explicit analysis of their effectiveness. Similarly, CMS requires evidence that a new procedure or device offers improved medical benefits compared with similar items or services in order to qualify for a new procedure code (which is then assigned a payment rate). As noted above, CMS has been supporting research to determine whether more frequent dialysis for certain kidney patients has clinical advantages; if so, the agency could establish a new procedure code and payment amount for that service.

Although Medicare has not generally used information about effectiveness to set payment levels, a recent exception is its policy that bases payment rates on the "least costly alternative" for certain types of items. Under that policy, Medicare will not cover the additional cost of a more expensive product if a clinically comparable one is available that costs less; in other words, the program's payment rate for both products is set at the level of the least expensive one. That policy has been applied to payments for durable medical equipment and to certain comparable drugs, but wider application to products that are not very close substitutes would probably require additional statutory authority.[68]

Even those limited steps toward using information about comparative effectiveness have proven controversial, however. Medicare's decision to apply the least costly alternative policy to set the payment rate for certain drugs that treat prostate cancer, for example, has raised concerns about whether the policy has been administered consistently and questions about whether that approach has been superseded by a new system that sets the reimbursement rate for each drug as a function of its market price.[69] Similarly, CMS set the payment rate for a new antianemia drug equal to the rate for two existing drugs on the grounds that the products were "functionally equivalent"—but then the Medicare Modernization Act of 2003 prohibited CMS from applying a standard of functional equivalence in any future case involving Medicare's payments to hospital outpatient departments. (CMS's decision regarding antianemia drugs was not overturned.) Similarly, the provisions of that act governing AHRQ's research on comparative clinical effectiveness also specified that the CMS administrator could not use the results to withhold coverage of a prescription drug—although the private drug plans administering that benefit could presumably use relevant findings when designing their formularies.

67. For a further discussion, see Susan Bartlett Foote, "Why Medicare Cannot Promulgate a National Coverage Rule: A Case of *Regula Mortis*," *Journal of Health Politics, Policy and Law*, vol. 27, no. 5 (October 2002), pp. 707–730.

68. For further discussion about Medicare's current use of information on comparative effectiveness, see Medicare Payment Advisory Commission, *Report to the Congress: Issues in a Modernized Medicare Program* (June 2005), pp. 180–182.

69. For a discussion of the least costly alternative policy, see Medicare Payment Advisory Commission, *Report to the Congress: Impact of Changes in Medicare Payments for Part B Drugs* (January 2007), pp. 10–11.

If changes in law were made, Medicare could use information about comparative effectiveness to promote the use of more-effective care. It could, for example, choose not to cover treatments that were less effective or less cost-effective or it could exclude extremely inefficient providers from participating in the program—just as private insurers may do today. Alternatively, Medicare could tie its payments to providers to the cost of the most effective or most efficient treatment. If that payment was less than the cost of providing a more expensive service, then doctors and hospitals would probably elect not to provide it—so the change in Medicare's payment policy could have the same practical effect as a coverage decision. Even so, patients and providers might object more strongly to a decision not to cover a treatment than they would to a change in Medicare's payment for it. Alternatively, enrollees could be required to pay for the additional costs of less effective procedures (although the impact on patients' incentives and their use of care would depend on whether and to what extent they had supplemental insurance coverage that paid some or all of Medicare's cost-sharing requirements).

More modest steps that Medicare could take would include smaller-scale financial inducements to doctors and patients to encourage the use of cost-effective care. Doctors and hospitals could receive bonuses for practicing effective care or reductions in their payments for using less effective treatments (although the evidence to date about the effect of such pay-for-performance initiatives on health care spending is somewhat mixed).[70] Likewise, enrollees could be asked to pay only a portion of the additional costs of less efficient procedures. Or Medicare could simply provide information to doctors and their patients about their patterns of practice, which would create some pressure for doctors to use more-efficient approaches and could encourage patients to select more-efficient doctors. Adopting more modest measures to incorporate the findings of comparative effectiveness research, however, would probably yield smaller savings for the program.

Medicaid. As for Medicaid, state officials generally determine what specific services are covered—subject to broad federal requirements—and are reimbursed by the federal government for a portion of the reported costs using formulas specified in law. Because enrollees have low income, options for adjusting cost-sharing requirements to encourage the use of cost-effective care may be limited. Furthermore, a substantial portion of Medicaid spending pays for long-term care services such as nursing home care for elderly and disabled enrollees, which may be less amenable to comparative effectiveness research. At the same time, most of the poor mothers and children enrolled in the program receive their care through a private health insurance plan under contract to Medicaid, so spending for them would be directly affected by any changes that private insurers made. Another portion of Medicaid spending goes to cover cost-sharing requirements and payments of premiums for enrollees who are also on Medicare, so the impact on that spending would depend largely on what the Medicare program did.

An additional issue in applying the results of comparative effectiveness studies in Medicaid relates to the sharing of program costs between the federal and state governments. Federal matching rates under Medicaid currently range across states from 50 percent up to about 75 percent, and, by CBO's estimates, the federal government now covers 57 percent of the reported costs of health services provided by that program across the nation as a whole. At least in principle, those financing arrangements reduce the incentives for state Medicaid officials to limit coverage of less effective services—because, on net, states would face only a portion of those costs currently and would see only a portion of the savings that resulted from a programmatic change. Some coordination between state and federal officials might therefore be required to incorporate the results of comparative effectiveness research.

At the same time, many states recognize the growing fiscal burden posed by Medicaid costs, and several of them have already expressed interest in comparative effectiveness research. For example, more than a dozen state Medicaid programs are involved in a project (affiliated with the Oregon Health and Sciences University) assessing evidence about the relative safety and effectiveness of competing drugs in the same class. Similarly, the state of Washington has recently initiated a program to provide independent assessments of health technologies; a committee of physicians and other providers will review that evidence and make decisions about what treatments will be covered under the state's Medicaid program and other state-run health care programs. Oregon tried a broadly similar approach in its Medicaid program the 1990s (although controversies about the ranking of medical ser-

70. See Congressional Research Service, *Pay-for-Performance in Health Care*, CRS Report RL33713 (December 12, 2006).

vices according to their overall cost-effectiveness ultimately limited the impact of that experiment).[71]

Potential Effects on Research and Development. If public and private insurers incorporated the results of comparative effectiveness research into their coverage and payment policies, the types of new medical technologies that were supplied could be affected. Developers of new drugs, devices, and procedures would have clearer incentives than currently exist to generate products and services that yielded substantial health gains relative to current treatments or that could replicate the benefits of current care at a lower cost. Either outcome would tend to improve the efficiency of the health sector.

One potential concern is that the results of comparative research might enable the manufacturers of products with patent protection (such as prescription drugs) to charge higher prices, if their product was shown to be superior. But those same results would put downward pressure on the prices of competing products, which in turn could dampen the incentive to increase the price of the "winner." What is more, research that could establish the superiority of a specific product—rather than comparing broadly different treatment options—is more likely to be undertaken by the private sector, so the added impact of any federally sponsored studies in such circumstances might be modest. Overall, during the period of patent protection, prices of products found to be clinically more effective might rise, and those found to be less effective might fall relative to the current situation in which less is known about the comparative effectiveness of different products. The result would be relative prices that more appropriately reflected the relative values of products in terms of patients' health outcomes. Such a situation would signal producers to place a greater emphasis on developing products with greater clinical effectiveness.

Perhaps a greater concern is that extensive use of information about comparative effectiveness would discourage medical innovation and thus reduce the flow of new products and treatments—but the types most likely to be forgone are those that would have modest expected benefits or poor prospects for demonstrating cost-effectiveness. A particular concern may involve poorly constructed studies, which could provide inaccurate information about the relative merits of treatments and thus, in turn, skew research incentives; that possibility reinforces the importance of having new studies use rigorous methodologies. Overall, greater emphasis on using rigorous data about comparative effectiveness would seem likely to alter incentives for product development in ways that improved the efficiency of the health sector both at a point in time and over time.

71. See Thomas Bodenheimer, "The Oregon Health Plan—Lessons for the Nation," *The New England Journal of Medicine*, vol. 337. no. 9 (August 28, 1997), pp. 651–655; and Jonathan Oberlander, "Health Reform Interrupted: The Unraveling of the Oregon Health Plan," *Health Affairs,* Web Exclusive (December 19, 2006), pp. w96–w105.

Estimated Effects of a Recent Proposal

The near-term effects on health care spending that expanded federal research on comparative effectiveness could have are illustrated by CBO's estimate regarding a provision in legislation that was recently passed by the House of Representatives. Section 904 of H.R. 3162, the Children's Health and Medicare Protection Act of 2007, would do the following:

- Establish within AHRQ a Center for Comparative Effectiveness Research, which would fund research comparing the clinical effectiveness of treatments—using clinical trials, systematic reviews, observational studies, medical registries, and other methods. The center would develop methodological standards for conducting studies of comparative clinical "value" but would not fund studies that analyzed treatments' cost-effectiveness.

- Create a commission to oversee the center's activities, consisting of the Director of AHRQ, the Chief Medical Officer of CMS, and up to 15 additional members who would have relevant expertise and would represent clinicians, patients, researchers, insurers, and employers. The Comptroller General of the United States, in consultation with certain Members of Congress, would appoint those 15 members to multiyear terms.

- Provide authority to spend $300 million from 2008 to 2010 and $375 million per year thereafter, funded primarily by an annual per capita fee of about $2 imposed on private health insurance premiums that would start in 2011.

The provision would not change any of Medicare's or Medicaid's rules about which procedures and treatments were covered or how much was paid for them. Thus, any

impact that the resulting research would have on federal spending for health care would have to come primarily from changes such research induced in doctors' patterns of practice or patients' choices of treatments. Those changes—encouraged in some cases by private health insurers—would primarily affect private health spending, but some changes in treatment patterns would also be likely for enrollees in public programs because doctors tend to treat their patients in a similar manner regardless of their source of insurance.

To a lesser extent, some federal savings might also occur through changes in coverage that could be implemented under current law (although CBO did not make explicit assumptions about what those changes would be). For example, if research on comparative effectiveness determined that a service covered by Medicare did not confer any health benefits for certain types of patients or involved risks that outweighed the expected benefits, under its current coverage policies CMS would have clear authority to decide not to cover that service for those patients.

As discussed, evaluating the precise effect of new research is difficult because it is hard to know which studies will be undertaken and what they will find, but CBO estimates that such research would probably reduce spending for health care somewhat. Any impact of a given research study is likely to be felt over many years, so the change in spending in any given year would reflect the cumulative effects of past studies. Little evidence is available with which to estimate the precise magnitudes of the annual effects, although one comprehensive review of the issue indicated that additional information about the effectiveness of treatment options could "succeed in improving health care while paying for its own research-related costs through targeted health system cost reductions."[72] In estimating the effects of section 904, CBO assumed that the annual federal savings on health care would eventually reach a point at which they roughly equaled the annual outlays for research on comparative effectiveness—a process that would take about a decade.

Under H.R. 3162, budget authority for the Center for Comparative Effectiveness Research would be $1.1 billion over the 2008–2012 period and $2.9 billion over the 2008–2017 period. Because spending those funds would take some time, CBO estimates that outlays would amount to about $600 million over five years and $2.4 billion over 10 years. Direct spending by the federal government—mostly for Medicare and Medicaid—would be reduced by $0.1 billion over the 2008–2012 period and $1.3 billion over the 2008–2017 period. (Those amounts would constitute a very small fraction of cumulative federal outlays for those programs—less than one one-hundredth of 1 percent.) Thus, the net effect of enacting section 904 would be to increase federal direct spending by $0.5 billion over five years and $1.1 billion over 10 years, CBO estimates.

The impact on total spending on health care in the United States would be about five times as large as the effect on federal outlays, CBO estimates. Some of that effect would be seen in lower costs for providing health insurance to workers—costs that are excluded from income and payroll taxes. In turn, some of those savings on private insurance premiums would go to increase the taxable compensation of workers; by itself, that change would lead to a small increase in expected federal revenues. At the same time, the new fees on health insurance that would be used to finance the research would generate corresponding increases in health care costs for workers, which would tend to reduce taxable compensation modestly. Overall, those indirect effects of section 904 on revenues would be small.

72. Office of Technology Assessment, *Identifying Health Technologies that Work: Searching for Evidence*, p. 6.

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CER Work Group

July 2, 2009

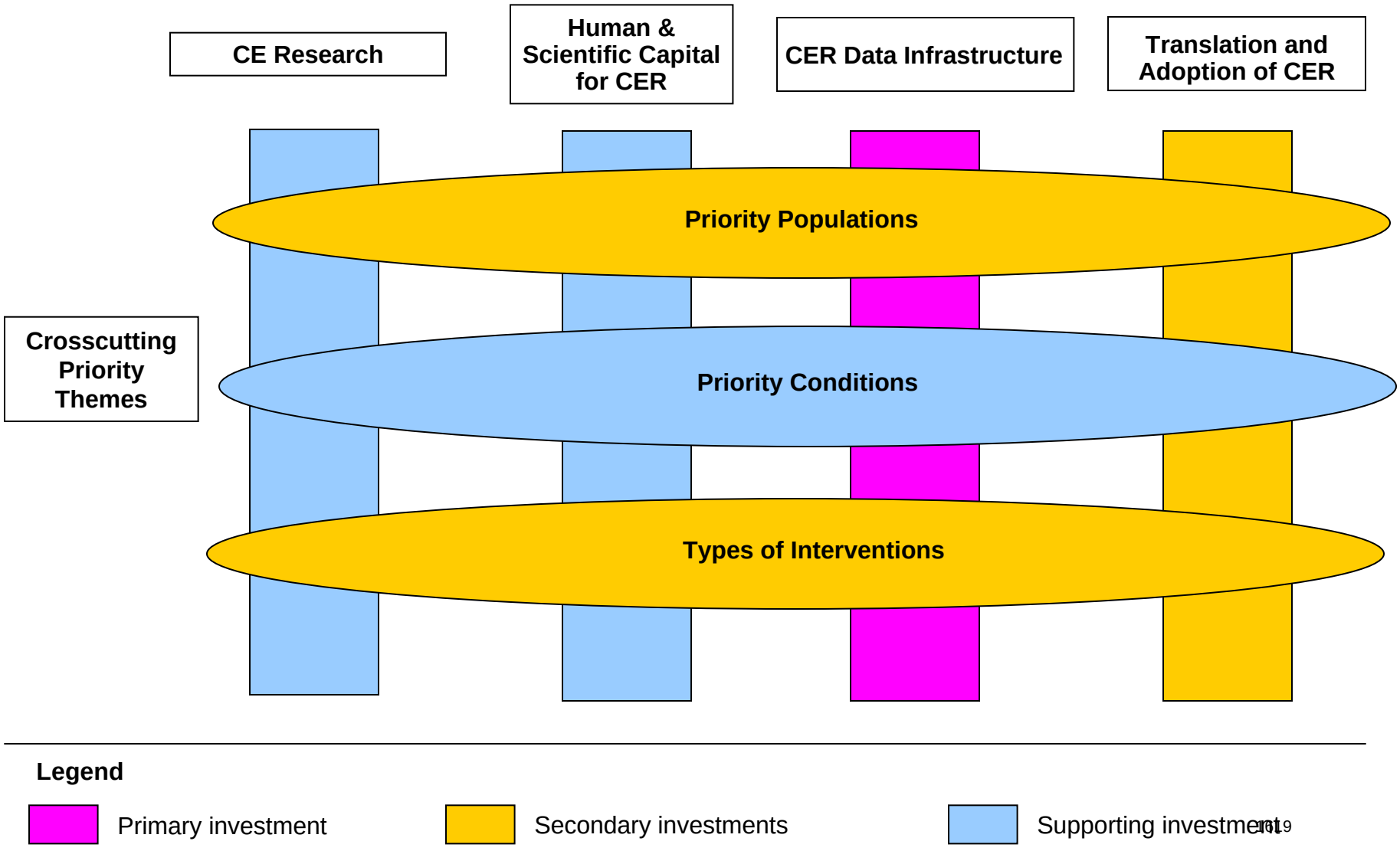
AGENDA

- Review several new proposals
- Discuss Potential Subcategories of strategic framework for evaluation
- Survey Results
- Discuss individual/groups of proposals
  - By evaluation criteria
  - General

New Proposals

- Patient-centered dissemination strategies
- Provider-centered dissemination strategies
- Expand Chronic Care Model networks and create registry for patients with multiple chronic conditions
- Creation of all-payer, all-claims database

Strategic Framework



Subcategories for Investment

- Infrastructure
  - Longitudinal claims data
  - Distributed Data Networks
  - Patient Registries
  - Surveys
- Dissemination and Translation
  - Federal delivery system
  - Non-Federal delivery system

Subcategories for Investment

- Interventions
  - Medications
  - Medical and Assistive Devices
  - Procedures and Surgeries
  - Diagnostic Testing
  - Behavioral Change
  - Delivery System Strategies
  - Prevention Strategies

Infrastructure

- LONGITUDINAL CLAIMS DATABASE-Research database that links claim data for single patients over a long period of time
- DISTRIBUTED DATA NETWORK-funding for patient registry networks, health information exchanges, and clinical EHR data networks for CER purposes
- PATIENT REGISTRY-databases that collect clinical data on patients with a specific disease or on a specific test or procedure
- SURVEYS-large scale surveys of patients or providers about health or health system related topics

Dissemination and Translation

- FEDERAL PROVIDER SYSTEMS-Support implementation of CER findings into practice in provider systems run by the Federal government, e.g., DoD, VA, IHS

- NON-FEDERAL PROVIDER SYSTEMS-Support communication, translation, and dissemination of CER to consumer, providers, and other decision makers outside of the Federal system

Interventions

-MEDICAL AND ASSISTIVE DEVICES (e.g., comparing rehabilitative devices)

-PROCEDURES AND SURGERIES (e.g., evaluating surgical options or surgery versus medical management)

-MEDICATIONS (e.g., comparing the effectiveness of 2 drugs from different classes on a specific disease)

-DIAGNOSTIC TESTING (e.g. comparing imaging modalities for evaluating certain types of cancer)

-BEHAVIORAL CHANGE (e.g., developing and assessing smoking cessation programs)

-DELIVERY SYSTEM STRATEGIES (e.g., testing two different discharge process care models on readmission rates

-PREVENTION (e.g., comparing two interventions to prevent or decrease obesity)

Minimum Threshold Criteria

- Included within statutory limits of Recovery Act and the Council's definition of CER
- Potential to inform decision-making by patients, clinicians, and other stakeholders
- Responsiveness to expressed needs of patients, clinicians, and other stakeholders
- Feasibility of research topic (including time necessary for research)

Prioritization Criteria

- Potential impact (based on prevalence of condition, burden of disease, variability in outcomes, costs, potential for increased patient benefit or decreased harm)
- Potential to evaluate comparative effectiveness in diverse populations and patient sub-groups and engage communities in research
- Uncertainty within the clinical and public health communities regarding management decisions and variability in practice
- Addresses need or gap unlikely to be addressed through other organizations
- Potential for multiplicative effect (e.g. lays foundation for future CER such as data infrastructure and methods development and training, or generates additional investment outside government)

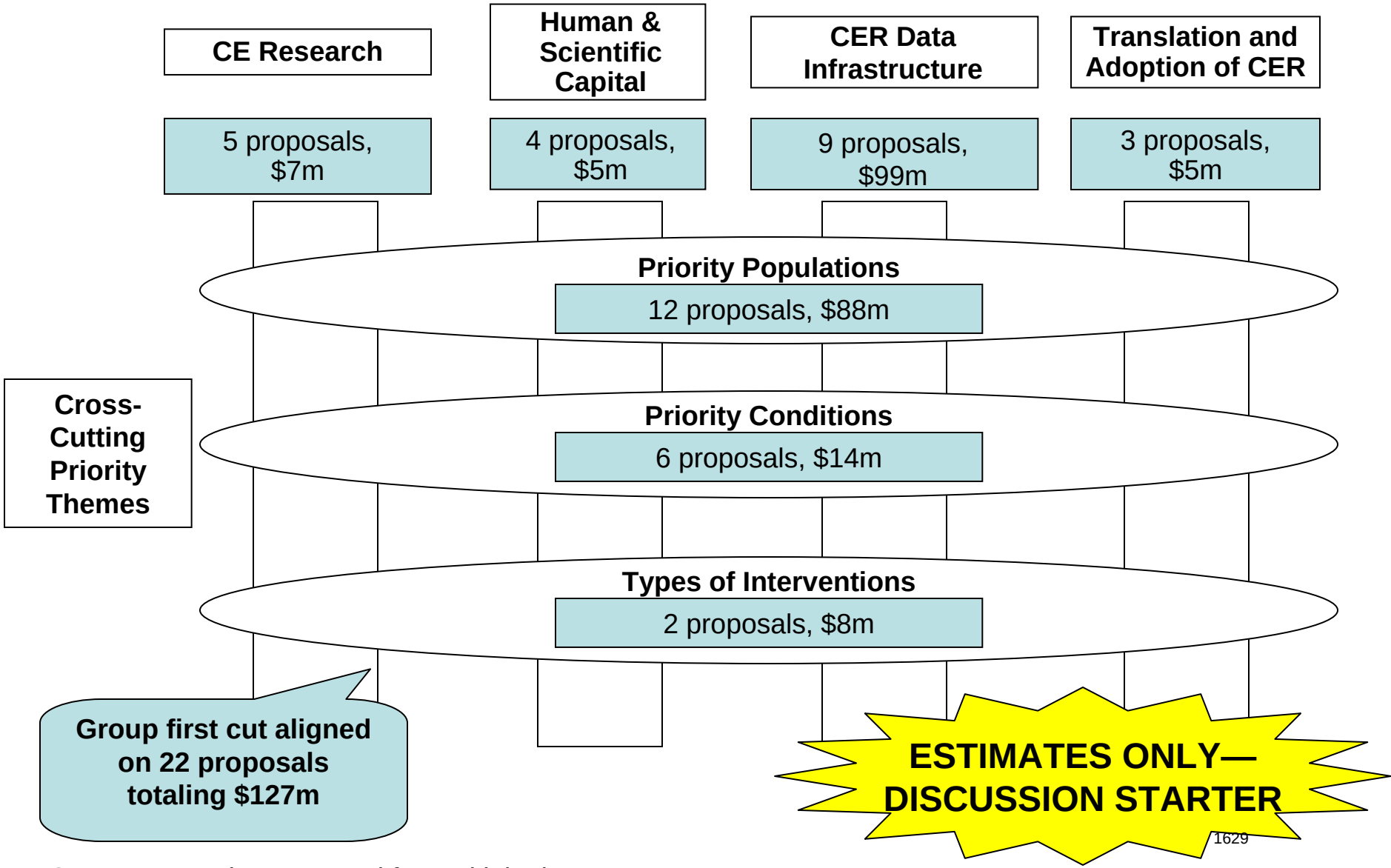
Potential Criteria for Overall Portfolio

- Balance across the strategic framework
- Balance of time to impact (short term vs. long term gains)
- Cost
- Balance of mechanisms (e.g. contracts, grants, public-private partnerships)
- Number of FTEs

Survey results summary

- 25 complete responses
- Group believes all 4 types of infrastructure investments are important, with maximum funding going towards longitudinal claims databases
- Efforts in translation and dissemination should be balanced across Federal and non-Federal provider systems, being sure to include public health providers in both groups
- The group agreed with the Council's recommendations that devices, procedures, diagnostics, behavioral change, delivery systems strategies, and prevention were the top priority types of interventions
- Majority agreed that 22 projects totaling ~$130m should receive requested funding or more than the requested funding
- Projects selected roughly correlate with Council recommendations, though relatively fewer investments in translation and more in research
- New proposals for this week and next address results of subcategory prioritization

Summary of "survey portfolio"



Note: Some proposals accounted for multiple times

Survey portfolio

Linked HHS longitudinal claims and clinical data sets
CER research standards
Clinicaltrials.gov expansion
HHS Summit meeting
Longitudinal ICD registry
Enhance availability and use of Medicare data to support CER
Medicaid analytic extract (MAX) data repository for CHIP and Medicaid populations
Data mining efforts
Centers of Excellence for Cultural and Linguistic Competency in Healthcare
Integration of Primary Care and Behavioral Health Services for Racial and Ethnic Minority Populations, Technical Assistance Center
Supporting Dissemination and Use of Behavioral Health Comparative Effectiveness (CE) Research in "Real World" Settings
Pediatric Research in Office Settings (PROS)
Depression Intervention and Comparative Effectiveness

Depression Intervention and Comparative Effectiveness
Expanding and Evaluating the Health Information Technology to Improve Care within the IHS
Using HIT to Examine HIS Medical and Pharmacy Utilization and Related Costs for Diabetes and other Co-Morbidities
Comparative Effectiveness of combinations of therapies for treating diabetes and associated co-morbidities in AIAN.
Comparing Effectiveness and Costs of Intervention models to Prevent and Treat Diabetes within Indian Communities
Advanced Pharmacy Practice Model
Compare effectiveness of locally applied models of health epidemiology in American Indian and Alaska Native communities
Develop a toolkit for comparing effectiveness of new models for managing and caring for patients with chronic health conditions
Developmental activities in support of a strategy for expanding CER
Clinically Enhanced State Data for Analysis and Tracking of Comparative Effectiveness Impact

Group's "Pick 5" portfolio (number of votes)

Group believes this proposal should request more funds—how much more? What should they go towards?

- Linked HHS longitudinal claims (11)
- Enhance availability for Medicare data to support CER (8)
- Medicaid MAX expansion (8)
- Distributed data networks (7)
- Surveys measuring impact on provider practice (6)

Proposals with a plurality of “Do not fund” recommendations

- Orthopedic joint registry (42% DNF)
- HIV/AIDS Oral Health (42% DNF)
- Developmental activities in support of a CER strategy (35%)
- Reducing Oral Health Disparities (47%)

Group was strongly divided on this proposal

How can we strengthen these proposals? What do they need to get over the line?

Proposals to fund for “less than the requested amount”

•10. Partnership in applied CE science for medical products (PACES) ($13)

•12. Accelerating Adoption of CER results by Providers & Patients ($45)

•13. Centers of Excellence for Cultural and Linguistic Competency in Healthcare ($5.5)

•14. Integration of Primary Care and Behavioral Health Services for Racial and Ethnic Minority Populations, Technical Assistance Center ($4)

•15. Use of Public Health Outreach Workers (PHOW) to Improve Clinical Outcomes. ($6.5)

•17. Effective Use of Regionalized Emergency Care Delivery ($2)

•18. Pediatric Emergency Care Applied Research Network (PECARN) ($8.8)

•21. The Health Center Consortia and Comparative Effectiveness ($4)

•22. Health Center Controlled Networks: Infrastructure Models for CER ($7.9)

•23. ADAP HIV/AIDS Drug Registry and HIV Care Models and CAREWare ($6.8)

•34. Informing clinical and public health approaches to chronic disease prevention using the foundation and the network of the prevention research centers (PRCs) ($20)

•35. Performing high-quality new synthesis of CER through the Guide to Community Preventive Services ($30)

•37. Assessing and Accelerating Implemenation Stragegies in AHRQ Networks ($17.8)

•40. Surveys Measuring the Impact of Comparative Effectiveness Research Findings on Medical Provider Practice and Patient Outcomes ($30.1)

Why should these proposals receive less funding? What is the right size? What should be cut?

BACKUP-Raw survey results

Evaluate each of the following subcategories for CER Data Infrastructure, 1 being should not receive funding, 6 being should receive maximal funding.

Answer Options	1	2	3	4	5	6	Response Count
Longitudinal claims databases	0	2	3	2	6	12	25
Distributed data networks	0	2	3	4	10	6	25
Patient registries	0	1	4	5	8	6	24
Surveys	4	3	1	7	6	1	22
Other	0	0	0	0	0	1	1

Evaluate each of the following subcategories for CER Translation and Dissemination, 1 being should not receive funding, 6 being should receive maximum possible funding.

Answer Options	1	2	3	4	5	6	Response Count
Federal provider systems	0	2	1	4	8	9	24
Non-federal provider systems	0	1	3	5	7	7	23
Other	0	0	0	1	0	0	1

Evaluate each of the following subcategories for Types of Interventions, 1 being should not receive funding, 6 being should receive maximum possible funding.

Answer Options	1	2	3	4	5	6	Response Count
Drugs	1	1	2	8	5	8	25
Medical and assistive devices	0	1	6	5	7	6	25
Procedures and surgeries	0	0	2	7	7	9	25
Diagnostic testing	0	1	1	7	10	6	25
Behavioral change	0	0	3	4	10	6	23
Delivery system strategies	0	0	4	2	7	11	24
Prevention	0	2	1	3	5	14	25
Other	0	0	0	0	0	0	0

Answer Options	Do not fund	Fund for less than the requested amount	Fund for the requested amount	Fund for greater that the requested amount	Response Count
1. Distributed clinical data networks ($40)	0	9	8	2	19
2. Linked HHS longitudinal claims and clinical data sets	1	2	12	4	19
3. CER research standards ($2)	2	5	9	3	19
4. Clinicaltrials.gov expansion ($2)	0	6	10	3	19
5. HHS Summit meeting ($0.3)	4	4	6	4	18
6. Orthopedic joint registry ($4)	8	5	3	3	19
7. Longitudinal ICD registry ($4)	2	4	10	3	19
8. Enhance availability and use of Medicare data to	1	5	6	9	21
9. Medicaid analytic extract (MAX) data repository for	0	7	9	5	21
10. Partnership in applied CE science for medical	3	9	7	0	19
11. Data mining efforts ($4.5)	2	5	7	3	17
12. Accelerating Adoption of CER results by Providers &	0	13	3	3	19
13. Centers of Excellence for Cultural and Linguistic	6	6	6	1	19
14. Integration of Primary Care and Behavioral Health	4	6	8	1	19
15. Use of Public Health Outreach Workers (PHOW) to	3	11	5	0	19
16. Supporting Dissemination and Use of Behavioral	2	7	9	1	19
17. Effective Use of Regionalized Emergency Care	3	9	6	1	19
18. Pediatric Emergency Care Applied Research	1	11	6	1	19
19. Pediatric Research in Office Settings (PROS) ($1.9)	2	7	9	1	19
20. Depression Intervention and Comparative	3	5	11	0	19
21. The Health Center Consortia and Comparative	4	9	6	0	19
22. Health Center Controlled Networks: Infrastructure	4	9	5	0	18
23. ADAP HIV/AIDS Drug Registry and HIV Care Models	6	7	5	0	18
24. HIV/AIDS Oral Health ($0.5)	8	5	3	3	19
25. Expanding and Evaluating the Health Information	2	3	14	0	19
26. Using HIT to Examine HIS Medical and Pharmacy	4	5	10	0	19
27. Comparative Effectiveness of combinations of	1	4	11	3	19
28. Comparing Effectiveness and Costs of Intervention	1	4	11	3	19
29. Advanced Pharmacy Practice Model ($4)	5	4	10	0	19
30. Compare effectiveness of locally applied models of	3	6	8	2	19
31. Develop a toolkit for comparing effectiveness of	2	2	12	3	19
32. Enhancing clinicaltrials.gov ($4)	4	5	7	3	19
33. Developmental activities in support of a strategy for	7	3	7	3	20
34. Informing clinical and public health approaches to	2	12	4	2	20
35. Performing high-quality new synthesis of CER	6	8	5	1	20
36. Reducing Oral Health Disparities:Fluoride and	9	3	5	2	19
37. Assessing and Accelerating Implemenation	1	10	8	0	19
38. Clinically Enhanced State Data for Analysis and	0	9	9	1	19
39. Clinicall Enhanced All Payer All Claims (APAC) Data	0	9	9	1	19
40. Surveys Measuring the Impact of Comparative	4	9	5	2	20

Please select the five proposals you believe are most deserving of funding.

Answer Options	Response Percent	Response Count
1. Distributed clinical data networks	29.2%	7
2. Linked HHS longitudinal claims and clinical data sets	50.0%	12
3. CER research standards	12.5%	3
4. Clinicaltrials.gov expansion	16.7%	4
5. HHS Summit meeting	8.3%	2
6. Orthopedic joint registry	12.5%	3
7. Longitudinal ICD registry	12.5%	3
8. Enhance availability and use of Medicare data to	33.3%	8
9. Medicaid analytic extract (MAX) data repository for	33.3%	8
10. Partnership in applied CE science for medical	4.2%	1
11. Data mining efforts	16.7%	4
12. Accelerating Adoption of CER results by Providers &	12.5%	3
13. Centers of Excellence for Cultural and Linguistic	12.5%	3
14. Integration of Primary Care and Behavioral Health	16.7%	4
15. Use of Public Health Outreach Workers (PHOW) to	16.7%	4
16. Supporting Dissemination and Use of Behavioral	12.5%	3
17. Effective Use of Regionalized Emergency Care	4.2%	1
18. Pediatric Emergency Care Applied Research	4.2%	1
19. Pediatric Research in Office Settings (PROS)	4.2%	1
20. Depression Intervention and Comparative	8.3%	2
21. The Health Center Consortia and Comparative	4.2%	1
22. Health Center Controlled Networks: Infrastructure	4.2%	1
23. ADAP HIV/AIDS Drug Registry and HIV Care Models	0.0%	0
24. HIV/AIDS Oral Health	4.2%	1
25. Expanding and Evaluating the Health Information	0.0%	0
26. Using HIT to Examine HIS Medical and Pharmacy	0.0%	0
27. Comparative Effectiveness of combinations of	4.2%	1
28. Comparing Effectiveness and Costs of Intervention	4.2%	1
29. Advanced Pharmacy Practice Model	4.2%	1
30. Compare effectiveness of locally applied models of	0.0%	0
31. Develop a toolkit for comparing effectiveness of	4.2%	1
32. Enhancing clinicaltrials.gov	8.3%	2
33. Developmental activities in support of a strategy for	4.2%	1
34. Informing clinical and public health approaches to	12.5%	3
35. Performing high-quality new synthesis of CER	12.5%	3
36. Reducing Oral Health Disparities:Fluoride and	12.5%	3
37. Assessing and Accelerating Implemenation	16.7%	4
38. Clinically Enhanced State Data for Analysis and	4.2%	1
39. Clinicall Enhanced All Payer All Claims (APAC) Data	4.2%	1
40. Surveys Measuring the Impact of Comparative	29.2%	7

FEDERAL COORDINATING COUNCIL FOR
COMPARATIVE EFFECTIVENESS RESEARCH

REPORT TO THE PRESIDENT AND THE CONGRESS

JUNE 30, 2009

US DEPARTMENT OF HEALTH AND HUMAN SERVICES

Federal Coordinating Council for Comparative Effectiveness Research

Report to the President and the Congress

June 30, 2009

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EXECUTIVE SUMMARY

Across the United States, clinicians and patients confront important health care decisions without adequate information. What is the best pain management regimen for disabling arthritis in an elderly African-American woman with heart disease? For neurologically impaired children with special health care needs, what care coordination approach is most effective at preventing hospital readmissions? What treatments are most beneficial for patients with depression who have other medical illnesses? Can physicians tailor therapy to specific groups of patients using their history or special diagnostic tests? What interventions work best to prevent obesity or tobacco use? Unfortunately, the answer to these types of comparative, patient-centered questions in health care is often, "We don't really know."

Thousands of health care decisions are made daily; patient-centered comparative effectiveness research focuses on filling gaps in evidence needed by clinicians and patients to make informed decisions. Physicians and other clinicians see patients every day with common ailments, and they sometimes are unsure of the best treatment because limited or no evidence comparing treatment options for the condition exists. As a result, patients seen by different clinicians may get different treatments and unknowingly be receiving less effective care. Patients and their caregivers search in vain on the Internet or elsewhere for evidence to help guide their decisions. They often fail to find this information either because it does not exist or because it has never been collected and synthesized to inform patients and/or their caregivers in patient-friendly language. When they do find information, it may be informed by marketing objectives, not the best evidence.[1]

Due to astonishing achievements in biomedical science, clinicians and patients often have a plethora of choices when making decisions about diagnosis, treatment, and prevention, but it is frequently unclear which therapeutic choice works best for whom, when, and in what circumstances. The purpose of comparative effectiveness research (CER) is to provide information that helps clinicians and patients choose which option best fits an individual patient's needs and preferences. It also can inform the health choices of those Americans who cannot or choose not to access the health care system.[2] Clinicians and patients need to know not only that a treatment works on average but also which interventions work best for specific types of patients (e.g. the elderly, racial and ethnic minorities). Policy makers and public health professionals need to know what approaches work to address the prevention needs of those Americans who do not access health care. This information is essential to translating new discoveries into better health outcomes for Americans, accelerating the application of beneficial innovations, and delivering the right treatment to the right patient at the right time.

Examples of successful CER include summaries of evidence from the Agency for Healthcare Research and Quality (AHRQ) on numerous conditions, such as prostate cancer and osteoporosis, as well as the National Institutes of Health (NIH) diabetes prevention trial that demonstrated lifestyle change was superior to metformin and placebo in preventing onset of type 2 diabetes. Additionally, the Veterans Affairs (VA) COURAGE trial demonstrated that patients treated with optimal medical therapy alone did just as well as patients who received percutaneous coronary intervention plus medical therapy in preventing heart attack and death. These exemplars show the power of CER to inform patient and clinician decisions and improve health outcomes.

Patients increasingly and appropriately want to take responsibility for their care. Therefore we have a responsibility to provide comparative information to enable informed decision-making. This patient-

[1] Lee TH, Brennan TA. N Engl J Med. 2002;346:529-531.
[2] Green LA, et al. N Engl J Med. 2001; 344:2021-5.

centered, pragmatic, "real world" research is a fundamental requirement for improving care for all Americans.

Comparative effectiveness differs from efficacy research because it is ultimately applicable to real-world needs and decisions faced by patients, clinicians, and other decision makers. In efficacy research, such as a drug trial for the U.S. Food and Drug Administration (FDA) approval, the question is typically whether the treatment is efficacious under ideal, rather than real-world, settings. The results of such studies are therefore not necessarily generalizable to any given patient or situation. But what patients and clinicians often need to know in practice is which treatment is the best choice for a particular patient. In this way, comparative effectiveness is much more patient-centered. Comparative effectiveness has even been called patient-centered health research or patient-centered outcomes research to illustrate its focus on patient needs.

The American Recovery and Reinvestment Act (ARRA) provided $1.1 billion for comparative effectiveness research. The Act allocated $400 million to the Office of the Secretary in the U.S. Department of Health and Human Services (HHS), $400 million to the National Institutes of Health (NIH), and $300 million to the HHS Agency for Healthcare Research and Quality. It also established the Federal Coordinating Council for Comparative Effectiveness Research (the Council) to foster optimum coordination of CER conducted or supported by Federal departments and agencies. Furthermore, the legislation indicated that "the Council shall submit to the President and the Congress a report containing information describing current Federal activities on comparative effectiveness research and recommendations for such research conducted or supported from funds made available for allotment by the Secretary for comparative effectiveness research in this Act" by June 30, 2009.

Transparent, Open Process Seeking Public Input

From the outset, the Council recognized the importance of establishing a transparent, collaborative process for making recommendations and sought the input of the American people on this important topic. The Council held three public listening sessions, two in the District of Columbia and one in Chicago. The Council also received comments for two months on its public Web site. Importantly, the open process allowed the Council to hear from hundreds of diverse stakeholders who represent views across the spectrum. Many patients expressed their need for this type of research; one of the most emotional and moving testimonies came from the mother of a child with a seizure disorder in Chicago who had struggled to find the best treatment for her child. A physician from the American Board of Orthopedics summarized many physicians' testimony by saying, "developing high quality, objective information will improve informed patient choice, shared decision-making, and the clinical effectiveness of physician treatment recommendations." The Council heard repeatedly at the listening sessions that the Federal Government must use this investment to lay the foundation for informing decisions and improving the quality of health care. In addition, the Council posted interim working documents for feedback, including the definition of CER, the prioritization criteria, and the strategic framework, and modified these based on the feedback. Comments from the listening sessions and via the Web site significantly influenced Council discussion and decisions. Indeed, this entire report is influenced by the public input—and Appendix A elaborates on the key themes that ran through the public comments.

Vision

The Council's vision for the investment in comparative effectiveness research focuses on laying the foundation for this type of research to develop and prosper so it can inform decisions by patients and clinicians. This research is critical to transforming our health care system to deliver higher quality and more value to all Americans. The Council specifically focused on recommendations for use of the

Office of Secretary (OS) funds to fill high priority gaps that were less likely to be funded by other organizations and therefore represent unique opportunities for these funds.

Early in the process, the Council set the following objectives consistent with ARRA:

1. Develop a definition, establish prioritization criteria, create a strategic framework, and identify priorities that lay the foundation for CER.

2. Foster optimum coordination of comparative effectiveness research conducted or supported by relevant Federal departments.

3. Formulate recommendations for investing the $400 million appropriated to the HHS Office of Secretary as part of this Report to Congress.

Definition and Criteria
The Council first established a definition, building on previous definitions, for comparative effectiveness research:

> Comparative effectiveness research is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in "real world" settings. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.
>
> - To provide this information, comparative effectiveness research must assess a comprehensive array of health-related outcomes for diverse patient populations and sub-groups.
> - Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
> - This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and actively disseminate the results.

The Council needed explicit criteria to make recommendations for priorities. Therefore, the Council's second step was to establish minimum threshold criteria that must be met and prioritization criteria.

Minimum Threshold Criteria (i.e. must meet these to be considered):

- Included within statutory limits of Recovery Act and the Council's definition of CER
- Potential to inform decision-making by patients, clinicians, or other stakeholders
- Responsiveness to expressed needs of patients, clinicians, or other stakeholders
- Feasibility of research topic (including time necessary for research)

The prioritization criteria for scientifically meritorious research and investments are:

- Potential impact (based on prevalence of condition, burden of disease, variability in outcomes, costs, potential for increased patient benefit or decreased harm)

- Potential to evaluate comparative effectiveness in diverse populations and patient sub-groups and engage communities in research
- Uncertainty within the clinical and public health communities regarding management decisions and variability in practice
- Addresses need or gap unlikely to be addressed through other organizations
- Potential for multiplicative effect (e.g. lays foundation for future CER such as data infrastructure and methods development and training, or generates additional investment outside government)

Importance of Priority Populations and Patient Sub-Groups
One important consideration for comparative effectiveness research is addressing the needs of priority populations and sub-groups, i.e., those often underrepresented in research. The priority populations specifically include, but are not limited to, racial and ethnic minorities, persons with disabilities, children, the elderly, and patients with multiple chronic conditions. These groups have been traditionally under-represented in medical research.

In addition, comparative effectiveness should complement the trend in medicine to develop personalized medicine—the ability to customize a drug and dose based on individual patient and disease characteristics. One of the advantages of large comparative effectiveness studies is the power to investigate effects at the sub-group level that often cannot be determined in a randomized trial. This power needs to be harnessed so personalized medicine and comparative effectiveness complement each other.

Strategic Framework
After completing the draft definition and criteria for prioritization of potential CER investments, the Council recognized the need to develop a strategic framework for CER activity and investments to categorize current activity, identify gaps, and inform decisions on high-priority recommendations. This framework represents a comprehensive, coordinated approach to CER priorities. It is intended to support immediate decisions for investment in CER priorities and to provide a comprehensive foundation for longer-term strategic decisions on CER priorities and the related infrastructure. At the framework's core is responsiveness to expressed needs for comparative effectiveness research to inform health care decision-making by patients, clinicians, and others in the clinical and public health communities.

Types of CER investments and activities can be grouped into four major categories:

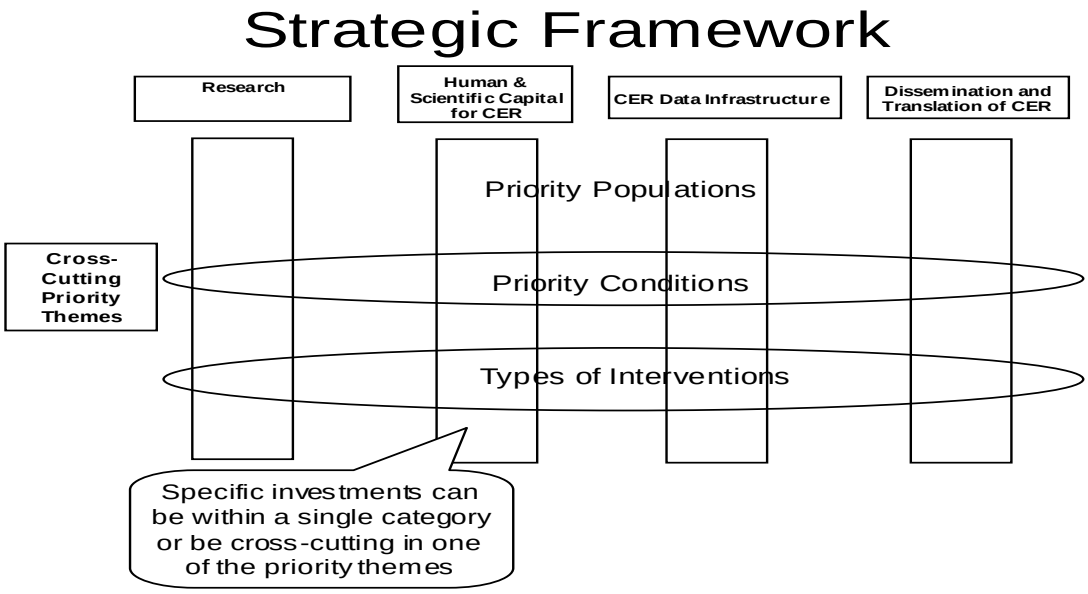
- **Research** (e.g., comparing medicines for a specific condition or discharge process A to discharge process B for readmissions)
- **Human and Scientific Capital** (e.g., training new researchers to conduct CER, developing CER methodology)
- **CER Data Infrastructure** (e.g., developing a distributed practice-based data network, longitudinal linked administrative or Electronic Health Record (EHR) databases, or patient registries)
- **Dissemination and Translation of CER** (e.g., building tools and methods to disseminate CER findings to clinicians and patients and translate CER into practice)

Furthermore, investments or activities related to a specific theme can cut across one or more categories and may include research, human and scientific capital, CER data infrastructure, and/or translation and adoption. These themes could include:

- **Conditions** (e.g., cancer, heart failure)
- **Patient populations** (e.g., elderly, minorities, children, persons with disabilities)
- **Type of intervention** (e.g., devices, behavioral change, delivery system)

Together, these activities and themes make up the "CER Strategic Framework" (Figure A)

Figure A



CER Inventory and Priority-Setting Process

The Council also conducted an inventory of CER and data infrastructure to help identify gaps in the current CER landscape. Maintaining that inventory and ongoing evaluation of government and private sector (where possible) CER investments and programs across these activities and themes is critical to this framework's value for decision-making. The first draft Federal Government inventory of CER and data infrastructure is included in this report, but it is critical to note that evaluation of current activities and the identification of gaps in order to inform priority-setting must be iterative and continue in the future.

As noted above, the Council's priority-setting process was informed by public input, and that input had a substantial influence on how the Council formulated its framework and priorities for CER. CER is an important mechanism to improve health and continued public input is vital for agenda setting.

Priority Recommendations

In developing its recommendations for how to invest the OS ARRA funding of $400 million, the Council sought to respond to patient and physician needs for CER, to balance achieving near-term results with building longer-term opportunities, and to capture the unique value that the Secretary's ARRA funds could play in filling gaps and building the foundation for future CER. The Council recommended that, among the four major activities and three cross-cutting themes in the CER

framework, the primary investment for this funding should be data infrastructure. Data infrastructure could include linking current data sources to enable answering CER questions, development of distributed electronic data networks and patient registries, and partnerships with the private sector.

Secondary areas of investment are dissemination and translation of CER findings, priority populations, and priority types of interventions. The priority populations identified that could be the focus of cross-cutting themes were racial and ethnic minorities, persons with disabilities, persons with multiple chronic conditions (including co-existing mental illness), the elderly, and children. CER will be an important tool to inform decisions for these populations and reduce health disparities. High-priority interventions for OS to consider supporting include medical and assistive devices, procedures/surgery, behavioral change, prevention, and delivery systems. For example, behavioral change and prevention have the potential to decrease obesity, decrease smoking rates, increase adherence to medical therapies, and improve many other factors that determine health. Delivery system interventions, such as comparing different discharge and transitions of care processes on hospital readmissions, community-based care models, or testing the effect of different medical home models on health have substantial potential to drive better health outcomes for patients.

The OS funds may also play a supporting role in research and human and scientific capital. Because the Council anticipates that AHRQ, NIH, and VA will likely continue to play a major role in these essential activities for the CER enterprise, OS funding would likely only fill gaps in these areas.

Longer-Term Outlook and Next Steps
This report and an Institute of Medicine report funded by the Department will inform the priority-setting process for CER-related funding. The most immediate next step will be the development of a specific plan, to be submitted by July 30, 2009, from the Secretary of Health and Human Services for the combined $1.1 billion of ARRA CER funding. In addition, an annual report from the Council is required under the ARRA legislation.

It will be important for this funding both to accomplish short-term successes and to build the foundation for future CER. The CER activity and investments should be coordinated across the Federal Government and avoid duplicative effort. In addition, the funding should complement and link to activities and funding in the private sector to maximize the benefits to the American people.

Clinicians, patients, and other stakeholders greatly need comparative effectiveness research to inform health care decisions. One private citizen unaffiliated with any health care group summarized, “It is more important than ever to engage in robust research on what treatments work and what do not. Doing so empowers doctors and patients, and helps make our practice of medicine more evidence-based.”

This is a unique opportunity to invest in the fundamental building blocks for transformation of health care in the United States to improve the quality and value of health care for all Americans. Physicians and patients deserve the best patient-centered evidence on what works, so Americans can have the highest quality care and achieve the best possible outcomes.

I. INTRODUCTION

The American Recovery and Reinvestment Act of 2009 (ARRA), Pub. L. 111-5, made available to the Department of Health and Human Services $1.1 billion for comparative effectiveness research (CER). Of this amount, $300 million was allocated to the Agency for Healthcare Research and Quality (AHRQ), $400 million to the National Institutes of Health (NIH), and $400 million was allocated to the Office of the Secretary (OS) for disbursement.

These and all Federal agencies distributing ARRA funds must do so in accordance with all nondiscrimination and equal opportunity statutes, regulations, and Executive Orders that apply to the distribution of funds under the Recovery Act. Agencies that grant funds also must ensure that their recipients comply with Title VI of the Civil Rights Act of 1964 (prohibiting race, color, and national origin discrimination), Section 504 of the Rehabilitation Act of 1973 (prohibiting disability discrimination), Title IX of the Education Amendments of 1972 (prohibiting sex discrimination in education and training programs), the Age Discrimination Act of 1975 (prohibiting age discrimination in the provision of services), and a variety of program-specific statues with nondiscrimination requirements.[3]

ARRA provides further guidance on how funds appropriated to the Office of the Secretary are to be allocated:

> … the funding appropriated in this paragraph shall be used to accelerate the development and dissemination of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that: (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions; and (2) encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data.

Section 804 of ARRA authorizes the establishment of the Federal Coordinating Council for Comparative Effectiveness Research (the Council). The Council is composed of senior Federal officials with responsibility for health-related programs. Most of the members are physicians and many have research expertise. The members represent not only the Department of Health and Human Services but also the Department of Veterans Affairs and the Department of Defense. Members of the Council come from a broad range of backgrounds, including the Office of Minority Health, the Office on Disability, community health centers, mental health, HIV and other infectious diseases, prevention, and others. The Council's purpose is to coordinate comparative effectiveness research and related health services research across the Federal Government with the intent of reducing duplication and encouraging the complementary use of resources. The Council is also charged with advising the President and Congress on strategies to address the infrastructure needs for CER within the Federal Government and organizational expenditures for CER by relevant Federal Departments and agencies.

[3] Memorandum from the Acting Assistant Attorney General for Civil Rights. 4 March 2009

The 15-member Council was announced by HHS via website on March 19, 2009, and has been meeting regularly since then.[4] One of the Council's responsibilities is to submit to the President and Congress an initial report describing current Federal activities on comparative effectiveness research and recommendations for CER conducted or otherwise supported from the $400 million made available for CER to be allocated by the Secretary. This report meets that requirement.

Rationale for Comparative Effectiveness Research

When patients ask clinicians about the evidence supporting one treatment choice, diagnostic plan, or prevention modality over another, the answer too often is that the evidence is unclear. Even when evidence exists, it is often from a trial that may not apply to the specific patient and/or situation under consideration, such as an elderly African-American woman with multiple comorbidities. When specific evidence is lacking, clinicians have to rely on their clinical experience to make the best treatment decisions possible. Nevertheless, these decisions can result in less than optimal, and sometimes inappropriate, treatment choices.

Due largely to government and scientific leadership accompanied by astonishing achievements in biomedical science, clinicians and patients often have a plethora of choices when making decisions about diagnosis, treatment, and prevention. Total investment in health services research, which includes CER, accounts for only 1.5 percent of medical research expenditures.[5] The Recovery Act greatly increased funding for CER and the prominence and important of such research. The purpose of CER is to provide information that helps clinicians and patients choose which option best fits an individual patient's needs and preferences. The amazing biomedical discoveries made in the United States to date can now support CER to routinely compare commonly used therapies or test which interventions work best for particular patients. This information is essential to translate new discoveries into better health outcomes for Americans.[6] We must generate this knowledge to be able to deliver the right treatment to the right patient at the right time. Patients increasingly and appropriately want to take responsibility for their care; therefore, we have an obligation to provide the comparative information that enables informed decisions.

No standardized Federal definition of comparative effectiveness research existed prior to the Council's definition. However, several government entities had developed individual definitions for CER. For example, the Congressional Budget Office has described comparative effectiveness research as "rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients." The Institute of Medicine refers to comparative effectiveness as "the extent to which a specific intervention, procedure, regimen, or service does what it is intended to do when it is used under real world circumstances." The Council's definition builds on these concepts and highlights key aspects of the ARRA CER provisions. The Council defined CER broadly, asserting that it is patient-centered, "real world" research that can help patients, clinicians, and other decision makers

[4] See Appendix D for Council membership.
[5] Moses III H, Dorsey EK, Matheson DHM, et al. Financial Anatomy of Biomedical Research. JAMA 2005; 294:1333-42
[6] Dougherty, D, Conway PH. The "3 T's" Roadmap to Transform U.S. Health Care: The "How" of High Quality Care. JAMA. 2008 May 21;299(19):2319-21

assess the relative benefits and harms of strategies to prevent, diagnose, treat, manage, or monitor health conditions and the systems in which they are made.[7] This definition will form the foundation of the common Federal definition.

The Department of Health and Human Services' ARRA appropriation for CER is a significant investment. CER and activities that support CER have been undertaken by a wide range of stakeholders both inside and outside the public sector. However, despite diverse activities across the Federal Government,[8] funds exclusively appropriated for CER have until now been funded under authorized by section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 for the Agency for Healthcare Research and Quality, which the Agency makes available for projects through its Effective Health Care Program. Since 2005, Congress has appropriated a total of $125 million for the program, including $50 million for comparative effectiveness in FY 2009.

The ARRA funding reflects the heightened interest in CER among the nation's clinicians, patients, policy makers and researchers and broader recognition of its potential to improve outcomes that matter to patients, including morbidity, mortality, and quality of life. CER has the ability to assess these very patient-centered outcomes in a comprehensive way. Furthermore, patients increasingly play an active role in their health care and expect to be active participants in decisions about their health care. These interests are rooted in the strong desire for better evidence upon which to make clinical and other health-related decisions at a time of heightened focus on the quality and variability of care delivered.

A health system guided by better information about "what works" would have benefits for all who have a stake in the nation's health system. Consumers and patients would develop more confidence that the increasingly complex array of treatments and interventions could be tailored to meet their individual needs; health professionals would have more certainty that their clinical decisions were evidence-based and serving patients well. Consequences of the lack of such information include wide geographic variations in treatments typically received for specific conditions and, with these variations, sizeable differences in related health care spending not accompanied by proportional differences in outcomes.

Noted medical author Dr. Atul Gawande recently summarized this issue, "In situations where the right thing to do is well established, physicians from high- and low-cost cities make the same decisions. But in cases where the science is more unclear, some physicians pursue the maximum possible amount of testing and procedures; some pursue the minimum. And what kind of doctor they are depends on where they came from. In case after uncertain case, more was not necessarily better… We will need to do in-depth research on what makes the best systems successful… and disseminate what we learn. Congress has provided vital funding for research that compares the effectiveness of different treatments, and this should help reduce uncertainty about which treatments are best. But we also need to fund research that compares the effectiveness of different systems of care—to reduce our uncertainty about which systems work best for communities. These are empirical, not ideological, questions."[9] This variation in care

[7] See Chapter 3 for the Council's definition of CER.
[8] See Chapter 6 for a comprehensive listing of CER activities across the Federal Government.
[9] Atul Gawande. "The Cost Conundrum." The New Yorker. June 1, 2009.

documented by Wennberg[10], Fisher[11] and others, means that Americans in one part of the country who are seeing particular clinicians may get vastly different care with potentially worse outcomes than Americans somewhere else. The health system can no longer produce highly variable results and tolerate low quality and inefficiency. The care delivered should be based on evidence and best practices, not on which physician a patient was referred to or where a patient lives. The Council believes that bringing to bear careful research across the continuum of care, from prevention, to diagnosis, to treatment, to delivery systems, will yield improved care for both individuals and for populations.

Current Comparative Effectiveness Research Landscape

In order to inform recommendations for comparative effectiveness research, the Council conducted an inventory of current CER activity. Section 6 summarizes CER activity in the Department of Health and Human Services, the Department of Veterans Affairs and the Department of Defense. Several examples of these activities are discussed below.

AHRQ has an established CER program as described above. As an example, an AHRQ Comparative Effectiveness Review in 2008 examined treatments for localized prostate cancer. There are a number of treatment options available for prostate cancer, each with its own potential for risks and benefits, so it is important that men understand what is known about the effectiveness of these treatments. Key findings from the report included:

- There is a lack of comparative studies across major modalities of treatment (e.g. surgery, radiation, watchful waiting).
- There were no randomized trials evaluating cryotherapy, laparascopic or robotic prostatectomy, primary androgen deprivation therapy, high-intensity focused ultrasound (HIFU), proton beam therapy, and intensity modulated radiation therapy (IMRT). While these therapies have become increasingly of interest for men considering treatments for prostate cancer, it is impossible to evaluate whether these therapies are more or less effective than other options.
- Of men who had surgery, those undergoing a radical prostatectomy were less likely to experience urinary incontinence and other complications if the operation was done by an experienced surgeon in a hospital that does many of the procedures.

NIH has funded numerous comparative trials with huge implications for the practice of medicine. For example, the Diabetes Prevention Program was a major multicenter trial to evaluate the comparative effectiveness of intensive lifestyle changes (diet and exercise), a pill for diabetes (Metformin), or a placebo in preventing the onset of type 2 diabetes in adults with pre-diabetes. This landmark trial found that while both lifestyle changes and Metformin reduced the risk of developing diabetes compared to a placebo, lifestyle changes were significantly more effective than Metformin. This effect was seen in men and women, and in all ethnic groups. With the increasing incidence of pre-diabetes in this country, the results of this trial were critical in informing patients and physicians about prevention strategies for diabetes. Similarly, the BARI

[10] Wennberg J, Gittelsohn A. Small area variations in health care delivery. Science. 1973; 182:1102-8.
[11] Fisher ES, Wennberg J. Health Care Quality, Geographic Variations, and the Challenge of Supply-Sensitive Care Perspectives in Biology and Medicine. 2003; 46(1): 69-79

2D trial compared optimal medical management with revascularization for preventing premature death in Type 2 diabetes and found medical management to deliver equivalent outcomes.[12]

VA also has a very strong history of conducting CER. For example, the COURAGE trial, published in 2007, compared the effectiveness of percutaneous coronary intervention (PCI, or angioplasty) plus optimal medical therapy with optimal medical therapy alone in the prevention of heart attack or death in veteran patients with stable heart disease. The results showed that patients treated with optimal medical therapy alone did just as well as patients who received PCI plus medical therapy. This trial can inform patients and clinicians about the most efficient use of PCI in patients with stable angina.

In addition to Federal activities, state level, private sector, and non-profit sector CER efforts are currently underway across the country.[13,14] For example, 14 states participate in the Drug Effectiveness Review Project (DERP), based at the Center for Evidence-Based Policy (EPC) at the Oregon Health & Science University. The project is a collaboration between the Oregon EPC and the Oregon Center for Evidence-Based Policy. Together, they produce evidence-based reviews of the comparative effectiveness and safety of drugs in many drug classes, and then make this information publicly available.

Large insurers and health organizations such as Aetna, CIGNA, UnitedHealthcare, and Humana have developed the capacity to conduct evidence reviews in-house. These payers may also commission external studies from entities such as the Blue Cross and Blue Shield Association Technology Evaluation Center, which has been conducting evidence-based technology assessments for more than thirty years. Pharmaceutical, biotechnology, and medical device companies may sponsor studies that share some of the attributes of CER. In the non-profit sector, organizations synthesize and publicize CER, rather than generating new evidence. For example, Consumers Union relies on DERP reports to provide information for its *Best Buy Drugs* Web site.

Although there are a number of institutions, both public and private, involved in CER, a number of challenges remain unaddressed. Much of the CER underway is fragmented, and not aligned with a common set of priorities or definition of what constitutes CER. Databases and patient registries that are invaluable for comparative effectiveness analysis are similarly fragmented and often limited in numbers of patients or of variable or unknown data quality. Some resources, such as privately maintained claims databases and Medicare claims data, are difficult for researchers to access due to licensing and cost issues. Furthermore, there are a number of gaps in the content of the research being conducted. Studies often do not include participants of sub-groups, such as racial minorities or people with disabilities, and generally focus on therapeutics at the expense of other types of interventions (e.g., devices or the delivery system). Many effective interventions for improving health are likely to involve prevention and community

[12] BARI 2D study group et al. N Engl J Med. 2009; 360(24):2570-2.

13 Academy Health. A First look at the Volume and Cost of Comparative Effectiveness Research in the United States. Available at: http://www.academyhealth.org/files/FileDownloads/AH_Monograph_09FINAL7.pdf. Accessed June 17, 2009.

[14] The following paragraphs draw on information contained in an environmental scan prepared by the Lewin Group for the Federal Coordinating Council on Comparative Effectiveness Research.

intervention, but these areas are currently understudied. CER should identify interventions that yield the most health improvement and represent the best value wherever and however the interventions are delivered.

The OS ARRA funds are a unique opportunity to address some of these gaps. The following box summarizes gaps in CER landscape:

Major Gaps in CER Landscape

- **Coordination across the CER framework**
  - Substantial CER assets exist across the Federal Government, but coordination is necessary to capture their full value
- **Research**
  - Many comparative, patient-centered research questions remain unanswered
- **Human and Scientific Capital**
  - CER methods development needed
  - Limited trained researchers for conducting CER
- **CER Data Infrastructure**
  - Fragmented data
  - Data sources limited in terms of clinical robustness of data and longitudinal data capture
  - Data capture and feedback loop at point of care often lacking
- **Dissemination and Translation of CER**
  - Suboptimal dissemination and translation of CER findings to patients and clinicians
  - Limited linkages between CER findings and directly improving patient outcomes
- **Priority populations**
  - Limited information on many priority populations and sub-groups
- **Priority Interventions**
  - Less information on certain comparative interventions such as behavioral change, procedures, devices, delivery system strategies, and prevention

<u>Opportunity Provided by ARRA Funds</u>

Within this context of national and international activity, the ARRA CER funds offer an extraordinary opportunity to complement ongoing research in the public and private sectors by establishing a solid infrastructure for future CER. Such investments could include development of data and methods, training of researchers who could accelerate the conduct of future studies, and rapid dissemination of results to patients and clinicians. For example, enhancing existing data resources and learning better how to maximize their utility could expand the types of questions addressed as well as identify high-impact opportunities for research. In addition, ARRA's investment in CER coincides with expected increases in the adoption of health information technology to improve health care quality and safety. That technology also offers the promise of including care delivery in the conduct of research (what some have termed a "learning health care system") and offering a platform for rapid dissemination of results to the

point of care to inform physician and patient decisions.[15] The field of CER is not entirely new, but increased availability of clinical electronic data resulting from diffusion of information technology demands improved methods and a cadre of researchers ready to take advantage of these expanding data resources.

As CER becomes a more integrated resource for health care decision-making, we must assure public trust by ensuring the privacy and security of health information and by maintaining access to appropriate care options. CER should not be used as a sole criterion for denying or awarding care or as justification for making care choices based on cost without consideration of effectiveness, safety, and convenience for an individual patient. CER has the potential to offer tremendous benefits to Americans so long as we apply its conclusions appropriately and protect the individual health information that informs it.

The Council believes that there is much to be learned about how research results can be incorporated into the everyday practice of medicine and inform consumer health care choices. The Council's hope is that ARRA funding has the potential to form a firm base for the Federal Government's future investments in CER and lay the foundation for a productive CER enterprise that improves care for all Americans.

II. VISION AND COUNCIL OBJECTIVES

Comparative effectiveness research has the potential to catalyze a patient-centered transformation of the U.S. health care system. By equipping patients and clinicians with the information needed to make joint medical decisions, and by optimizing the system in which the patient/clinician team makes these decisions, CER can improve the quality, safety, and value of care delivered while increasing patient satisfaction.[16] By passing ARRA, Congress recognized this vision and the need for CER, and also highlighted the need for an unbiased, cross-functional Council to "foster optimum coordination" of the Federal Government's CER efforts.

Given the Council's distinct role and the unprecedented resources available to the Secretary, the Council has a unique opportunity to begin working toward this vision for CER. The Council sees the following as potential accomplishments at the end of the ARRA funding period:

1. Establishment of a process for CER priority-setting that maximizes the value of Federal investments in CER through responsiveness to patient and other stakeholder needs, transparency, and effective coordination.

2. Development of a robust, foundational infrastructure for CER.

3. Implementation of a strategy to support rapid, systematic dissemination of CER results to empower patients, clinicians, and other stakeholders to make more informed decisions and increase the quality of care.

[15] Conway PH, Clancy C. Transformation of Health Care at the Front Line. JAMA. 2009 Feb 18;301(7):763-5.
[16] Naik AD, Peterson LA. The Neglected Purpose of Comparative Effectiveness Research. NEJM. 2009 May 7; 360(19):1929-31.

To accomplish this vision, the Council outlined three specific, near-term objectives that build on those established in ARRA:

1. Develop a definition, establish prioritization criteria, create a strategic framework, and identify priorities that lay the foundation for CER.

2. Foster optimum coordination of comparative effectiveness research conducted or supported by relevant Federal departments.

3. Formulate recommendations for investing the $400 million appropriated to the HHS Office of Secretary as part of this Report to Congress.

III. COMPARATIVE EFFECTIVENESS RESEARCH DEFINITION AND CRITERIA

One of the first activities of the Council was to build on previous definitions of comparative effectiveness research, including IOM, CBO, and others, to develop a definition of comparative effectiveness research for the Council. After much discussion and sharing with the public for feedback, the Council established the following definition.

Definition

Comparative effectiveness research is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in "real world" settings. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.

- *To provide this information, comparative effectiveness research must assess a comprehensive array of health-related outcomes for diverse patient populations and sub-groups.*
- *Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.*
- *This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and actively disseminate the results.*

The definition above is not meant to exclude randomized trials; however, these trials would need comparator arms other than placebo and be representative of populations seen in "real world" practice.

Once a definition was established, the Council drafted threshold criteria for consideration and prioritization criteria for comparative effectiveness research and related investment. These criteria were posted on a public Web site, feedback was received, and modifications were made. The following are the current Council criteria.

Prioritization Criteria for Comparative Effectiveness Research Related Investments

Minimum Threshold Criteria (i.e. must meet these to be considered):

- Included within statutory limits of Recovery Act and FCC definition of CER
- Potential to inform decision-making by patients, clinicians, or other stakeholders
- Responsiveness to expressed needs of patients, clinicians, or other stakeholders
- Feasibility of research topic (including time necessary for research)

The prioritization criteria for scientifically meritorious research and investments are:

- Potential impact (based on prevalence of condition, burden of disease, variability in outcomes, costs, potential for increased patient benefit or decreased harm)
- Potential to evaluate comparative effectiveness in diverse populations and patient sub-groups and engage communities in research
- Uncertainty within the clinical and public health communities regarding management decisions and variability in practice
- Addresses need or gap unlikely to be addressed through other organizations
- Potential for multiplicative effect (e.g. lays foundation for future CER such as data infrastructure and methods development and training, or generates additional investment outside government)

This definition and criteria guided the Council as it considered potential priority recommendations for the OS funds and will guide AHRQ and NIH in allocating their CER funds.

IV. IMPORTANCE OF PRIORITY POPULATIONS AND SUB-GROUP ANALYSIS

As the United States has grown in its diversity, there has remained a persistent under-representation of women, the elderly, persons with disabilities, and racial and ethnic minorities in clinical and other research studies. While the NIH has a policy of inclusion of women and racial and ethnic minorities in all NIH-funded clinical trials,[17] the majority of research conducted in the U.S. does not require the inclusion of these and other priority populations. The lack of adequate representation of important patient populations in many research studies presents a major challenge in applying the results of these studies to important populations and sub-groups. In recognition of this fact, the ARRA legislation notes that "research conducted with funds appropriated shall be consistent with Departmental policies related to the inclusion of women and minorities." This criterion is critically important for ensuring that information gained from comparative effectiveness research improves the quality of care for all Americans.

[17] http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

Indeed, focused attention is needed on priority populations,[18] including racial and ethnic minorities, individuals with disabilities, children, persons with multiple chronic conditions, and the elderly, not only because of their under-representation in current research but also because of the increased disease burden and health disparities faced by these sub-groups.

The following sections highlight some of the challenges facing our health system as it relates to priority populations. Disparities in health care and health outcomes for these populations persist, affecting an ever-increasing proportion of residents of the United States. Also outlined are some of the research challenges that exist for priority populations, followed by recommendations to address these issues.

Growth in Priority Populations

Priority populations not only account for a large proportion of current health services utilization, but their numbers are growing; their need for health care services will likewise continue to grow. The most recent U.S. Census Bureau data reveal that over 100 million people living in the United States belong to a racial or ethnic minority group; this equates to 34 percent of the total U.S. population, and these minorities will likely become the majority of the U.S. population within 30 years.[19] Similarly, the number of elderly Americans is growing, with that segment of the population expected to increase from 35 million today to 71 million by 2030— or nearly 20 percent of the overall U.S. population. The population over the age of 85 is projected to grow from 5.3 million today to 21 million by 2050.

Health Disparities

A number of important reports have highlighted disparate disease prevalence, progression, and health outcomes for racial and ethnic minorities, elderly Americans, individuals with disabilities people of low socioeconomic status, people with mental illness, and others.[20,21] In this context, health disparities are defined as significant gaps or differences in the overall rate of disease incidence, prevalence, morbidity, mortality, or survival rates in the priority population as compared to the health status of the general population.[22] For example, African-American women are 34 percent more likely to die from breast cancer, even though they are diagnosed with the disease 10 percent less frequently than white women; Hispanics in the U.S. are 50 percent more likely than whites to suffer from diabetes; and the incidence of diabetes among

[18] Priority populations are defined in Sec. 901 of the Healthcare Research Act of 1999, S. 580.
[19] U.S. Census Bureau. Minority Population Tops 100 Million: Press Release. Available at: *http://www.census.gov/Press-Release/www/releases/archives/population/010048.html*. Accessed April 1, 2009.

[20] Report of the Secretary's Task Force on Black and Minority Health. U.S. Department of Health and Human Services. 1985.

[21] Brown ER et al. Racial and Ethnic Disparities in Access to Health Insurance and Health Care. UCLA Center for Health Policy Research and the Henry J Kaiser Family Foundation. 2000.

[22] Minority Health and Health Disparities Research and Education Act of 2000. Public Law 106-525. November 20, 2008.

Native Americans is more than twice that for whites. Elderly Americans also face particular health challenges, from greater susceptibility to multiple chronic conditions to a lower likelihood of obtaining preventive treatments, including mammograms and immunizations. In addition, approximately 42 percent of individuals over the age of 65 report a functional limitation.[23]

Persons with Disabilities

According to the 2007 Institute of Medicine report *The Future of Disability in America,* from 40 to 54 million people in the United States have disabilities. These numbers will grow considerably in coming decades as baby boomers age and as new medical interventions extend the lives of young persons with significant impairments who would once otherwise have died. Although rates are lower in children, disability prevalence is rising at younger ages. According to figures from the National Health Interview Survey, childhood disability has risen by 350 percent during the last 40 years, with the largest increase occurring during the past decade.

Across the lifespan, disabilities are clinically and functionally heterogeneous, encompassing diverse cognitive, sensory, physical, and mental health impairments. Traditionally patients with disabilities have been excluded from clinical trials, yet they have the same risk for diseases as non-disabled persons. Future clinical trials should exclude persons with disabilities only if there are clear and compelling reasons to do so.

Comparative effectiveness research relating to persons with disabilities is important in a number of areas.

First, research would be beneficial about the most effective interventions to prevent or mitigate disability and the disabling effects of chronic diseases. All research including comparative effectiveness research relating to disability should include outcome measures that address functional abilities, people's abilities to participate in daily activities, and quality of life. This is critical as the world's population is growing older at a very fast pace and this has serious implications due to expected increasing rates of chronic conditions. Moreover, with the advances in science and technology, lifespan has increased considerably; this is also true for persons with disabilities.

Second, future comparative effectiveness research should look into community-based models of care for persons with disabilities. Following the Supreme Court *Olmstead v. L.C. ex rel. Zimring, 527 U.S. 581 (1999) Decision*, traditionally institutionalized individuals with disabilities or those at risk of being placed in institutions are increasingly being cared for in their own homes and/or communities. Underscored by the *Olmstead Decision* states now have to consider civil rights when developing their programs. Effective care coordination/care management is critical to help persons with disabilities live independently in their communities with added years of quality life. Care coordination/care management is even more important for those individuals with multiple chronic conditions, which are often associated with certain levels of disability. While care

[23] Federal Interagency Forum on Aging-Related Statistics. Older Americans 2008: Key Indicators of Well Being. Federal Interagency Forum on Aging-Related Statistics. Washington, DC: U.S. Government Printing Office. March 2008

coordination/care management is the current state-of-the-art, it is still considered to be in its early stage. This represents a major opportunity for building the infrastructure to support future CER studies. In addition, because the definition of care coordination varies according to settings and models of care, its effectiveness has not been clearly established, particularly as it relates to the role support services play and how better integration of health and support services can lead to improved health outcomes for persons with disabilities and reduced health care costs for our nation.

Third, persons with disabilities are at increased risk for developing secondary conditions that are associated with their primary disabling condition. For example, without preventive measures, individuals with spinal cord injuries may acquire a number of adverse health conditions, including cardiovascular disease, genitourinary tract disorders, depression, obesity, and pressure sores. Comparative effectiveness studies should determine which interventions are most likely to prevent secondary conditions or ameliorate their consequences.

Fourth, studies should investigate the comparative effectiveness of rehabilitation interventions to restore or maintain functioning or minimize its loss. For example, much more research is needed to identify effective speech-language, physical, and occupational therapy interventions. This research could include a comparison of conventional treatments to newer interventions or a comparison of various systems of care. More research is also required about various assistive devices, medical equipment, and technologies, including technologies addressing sensory deficits, communication impairments, and physical and motor limitations.

Fifth, comparative effectiveness studies of therapeutic and preventive interventions need to address explicitly the needs of children with disabilities and be sensitive to the developmental stage of the child. For many children with disabilities and complex health care needs, the transitions through adolescence and into adulthood are complicated by the absence of comprehensive care programs that fully address their needs. Comparative effectiveness studies should examine different care models to determine which ones offer the best care coordination and generate the greatest patient and family satisfaction and health outcomes.

Other underrepresented populations

Children represent another group that can benefit tremendously from comparative effectiveness research. Evidence cannot simply be extrapolated from adults to the pediatric population. There is a dearth of information to inform decisions by children and their families, especially since outcomes, such as quality of life and functioning, are often more subtle. In addition, comparative preventive interventions (e.g. for obesity) will often have the most long-term effects if started in the pediatric population.

At the other end of the continuum, the elderly represent another group for which there exists little information about best care practices. As our population ages, knowledge about the best and most effective treatments for this group will become essential. Other important areas of focus for the elderly include home health care strategies and optimal approaches to delivery of care within nursing facilities.

Veterans and service members often have many conditions for which CER could be informative. They have a number of special considerations in deployment-related illness such as post traumatic stress disorder, traumatic brain injury, exposures, infectious diseases, disabilities and others. CER provides a vital opportunity to glean additional information necessary for clinicians to make informed decisions about particular veterans needs and information to assist veterans in their participation in care decisions.

Finally, research to compare the effectiveness of prevention strategies, treatments, diagnostics, and care delivery for patients with multiple chronic conditions is essential. Again, as our population ages, patients increasingly have several comorbidities which may impact their response to treatment. The majority of clinical research to date excludes such patients, so the applicability of "standard" treatments to this population is unclear. A physician advising a 45-year-old woman with asthma and HIV about treatment for breast cancer simply does not have the evidence necessary to factor her comorbidities into her patient's treatment decision. By utilizing varied and robust research methodologies, CER affords the opportunity to target treatments and other interventions to improve the quality of life and overall health of this important group of patients.

Personalized Medicine and Patient Sub-groups

The need to identify and address the needs of emerging patient sub-groups, and indeed the very concept of sub-categories of conditions to which medical products are applied, is expected to change and grow as our understanding of genomics and molecular medicine increases and becomes an integral part of health care. Better understanding of an individual's genomic and other individual biological characteristics will enable us to recognize and respond to human variability with a new degree of specificity. Understanding biological differences at the molecular level promises a significant leap in our ability to use and develop medical technologies more effectively, targeting interventions at more defined groups of individuals with greater precision. This potential, sometimes referred to as personalized medicine, has strong bearing on comparative effectiveness research.[24] Many drugs prescribed in the United States today are effective in fewer than 60 percent of treated patients. This is not a fault of the drugs, but reflects the variability of metabolism or other factors from person to person.[25]

Unfortunately, it remains common medical practice to follow a trial-and-error approach in selecting medical interventions for patients to achieve a satisfactory therapeutic outcome. In the case of breast cancer, for example, while chemotherapy can be an important positive treatment for some patients, we have few tools today to successfully predict which patients will benefit– and the result is that many women who are treated with chemotherapy today are receiving treatments that may not be effective for their condition.

Personalized medicine aims to make medical care more precise and effective. Increased understanding of our individual genomic profiles and other individual biological characteristics

[24] Willard HW: Organization, Variation and Expression of the Human Genome as a Foundation of Genomic and Personalized Medicine. In *Genomic and Personalized Medicine. Volume 1.* Edited by Willard HW and Ginsburg GS. London: Academic Press; 2009:4-21.
[25] Spear BB, Heath-Chiozzi M, Huff J. Trends Mol Med. 2001 May; 7(5):201-4.

will enable us both to use more effectively the therapies we have now and to identify significant areas where research and development of new products may be needed. Pharmacogenomics, the use of genetic information or other biomarkers to assist in accurate medical therapy decision-making, is expected to be a hallmark of this approach.

CER can be an important partner in helping to bring about this new level of medical effectiveness, personalization, and innovation. At the same time that CER is being used to identify which interventions and strategies work best on average, it can also help to identify different responses by different groups of patients. In some cases, different existing therapies may be identified as most effective for specific sub-groups. In other cases, CER may help to identify significant sub-groups for whom effective therapies do not yet exist. CER may also help steer research efforts toward the development of products and strategies for areas of significant need.

Research Challenges

Multiple research challenges exist for priority populations. Examples include a need for increased diversity in research populations, expanded data sources for evidence-based studies in diverse populations, enhanced collection of racial and ethnic health data, a better understanding of the effectiveness of interventions in the context of comorbidities, and a greater focus on implementation research.

Generalizations that result from comparative effectiveness research that fail to consider sub-groups and individual differences may have limited applicability. Currently there are gaps in knowledge about whether specific treatment strategies work across different sub-groups under a variety of circumstances. Recognizing that there might be variations in the effectiveness of specific interventions in the elderly, racial and ethnic minorities, individuals with disabilities, and other priority populations is key to designing evidence-based strategies to successfully improve the quality of care that is delivered. Infrastructure investments that capture priority populations and patient sub-groups will be critical to overcoming these challenges.

Strategies to Strengthen Comparative Effectiveness Research for Priority Populations

In light of the aforementioned challenges, comparative effectiveness research presents an opportunity to be more inclusive of minorities, the elderly, persons with disabilities, and other priority populations. This feature of CER is especially true in the context of conducting specific studies that take into account health conditions and linguistic and cultural attributes in order to develop the most appropriate and effective interventions.

Investments in CER can be used to address the needs of priority populations by doing the following:

Evaluating and identifying interventions that are tailored for priority populations. To explore which interventions are most effective for addressing the needs of priority populations, specific studies are needed to look at interventions that target diseases with a high prevalence in racial and ethnic minority communities, the elderly, and individuals with disabilities. These

studies may need to simultaneously address several diseases/conditions, or assess combinations of interventions (e.g., behavioral and physical treatments/interventions) that are most effective in promoting desired outcomes for these populations. Studies examining care delivery interventions tailored for priority populations are also needed in order to ensure that care is delivered to these individuals through effective approaches that are targeted to their needs. To ensure effective communication with the priority populations both in conducting the research and implementing its results, investigators should ensure that those language and communication services are available for those with limited English proficiency or disabilities.

Creating and enhancing potential databases looking at interventions in priority populations. Successfully examining and evaluating a range of interventions that are effective for priority populations will require a broad range of potential data sources and infrastructure investments. In addition to traditional patient registries and systematic reviews, the inclusion of distributed data networks that utilize community-based infrastructure, such as Federally Qualified Health Centers, will be an important asset in broadening the tools to evaluate effectiveness in various priority populations. CER studies should routinely perform and report sub-group analyses to examine possible differences in effectiveness for important racial and ethnic groups, and should over-sample such groups whenever there is existing evidence to suggest differences in effects or outcomes in any priority population. Standardized reporting and analysis of priority population sub-groups will also permit pooling of research results across studies to explore sub-group differences.

In addition, efforts should be made to build capacity and infrastructure within traditionally underserved racial/ethnic communities to allow for standardization of data collection and to enable the seamless integration of such data with larger databases/systems currently in use by the research community. This will allow for more accurate downstream comparisons to pre-existing and future majority data sets, producing more comprehensive and reliable CER study results.

Finally, this infrastructure for CER in priority populations is particularly important for developing and implementing Clinical Preventive Services Guidelines and recommendations for the U.S. Preventive Services Task Force. According to the IOM, CER data on priority populations is often unavailable for developing guidelines, and what information is available is often insufficient for making conclusions on how to treat priority populations.

Increasing the number of community-based studies, including community-based participatory research (CBPR) studies. CBPR is defined as a collaborative research approach in which communities and researchers are equally involved in the design and conduct of research that is conducted in their communities. Successful and effective CBPR studies result in the development of research tools, strategies, and interventions that are effective in creating sustainable and positive behavior changes and outcomes among priority populations within communities. Because CBPR studies are conducted with substantial input from the community, interventions are typically tailored to fit the needs and characteristics of the community. Furthermore, communities become “owners” of the research, which results in sustainable research outcomes.

Increasing cultural competency. Understanding the linguistic, cultural, social, and environmental attributes of priority populations is essential in designing interventions and promoting strategies that are effective in addressing the needs of these populations. Specifically, doing so allows for the development of culturally and linguistically appropriate interventions. For example, an obesity/diabetes intervention involving diet and/or physical activity would require an understanding and assessment of the populations' cultural attributes (e.g., food preferences), social attributes (e.g., competing family and work demands), and environmental attributes (e.g., access to 'healthy' foods and safe walkways) that support or inhibit adhering to a diet and/or physical activity intervention.

Building workforce capacity. Racial/ethnic minorities, individuals with disabilities, and women are underrepresented in the research and medical communities. The lack of a diverse and linguistically competent scientific workforce adds to disparities in research development, service delivery, and quality of care. Initial CER investments in workforce capacity could create opportunities to engage researchers and providers from diverse backgrounds. For example, 90 percent of minority physicians educated at Historically Black Medical Colleges live and serve in minority communities. Hispanic-Serving Institutions (HSIs) also play a major role in educating Hispanics researchers. Approximately 49 percent of all Hispanic students attend an HSI. A special focus on priority populations could provide an avenue for engaging Historically Black Colleges and Universities and HSIs in the conduct of CER among priority populations.

Developing and implementing outreach strategies to various racial, ethnic, and health disparity populations for participation in research protocols. In order to strengthen CER, effective outreach strategies must be developed and implemented that will increase the participation of priority populations in clinical research protocols. Developing appropriate strategies to reach out to various priority communities requires an understanding of the history of these populations in research and the identification and recruitment of trusted community members who can champion the research benefits and inform communities about risks. Community health workers can be important partners in addressing and advocating for the needs and concerns of priority populations. In addition, clinicians and providers will need to be educated on the benefits and implications of CER and the utilization of evidence-based interventions.

Dissemination, translation and adoption of research results is one of the biggest challenges within comparative effectiveness research, particularly as applied to priority populations, but also as applied to the population as a whole. The young science of implementation research focuses on the acceleration of translation of evidence into everyday care, and affords an opportunity to build a more coordinated approach to improving the quality of health care of priority populations. This is not a one-way transfer of knowledge. Racial and ethnic minorities, persons with disabilities, children, and the elderly, can offer insights into how best to engage their communities. Active listening and thoughtful planning of the dissemination process can create better health outcomes for all Americans.

Making CER investments that are responsive to the needs of priority populations and sub-groups is critical to ensuring that the benefits of CER reach those with the greatest needs. Such

investments, however, can also benefit the population as a whole by validating new strategies and approaches for comparative research and implementation.

V. STRATEGIC FRAMEWORK FOR CER

There are countless opportunities for action and investment in CER. Many Federal, state, and private institutions are already involved in CER and have made choices about which of these activities and investments to pursue. After completing the draft definition and criteria for prioritization of potential CER investments, the Council recognized the need to develop a strategic framework for CER activity and investments to categorize current activity, identify gaps, and inform decisions on high-priority recommendations.

This framework represents a comprehensive, coordinated approach to CER priorities. It is intended to support immediate decisions for investment in CER priorities and to provide a comprehensive foundation for longer-term strategic decisions on CER priorities and the related infrastructure. At the framework's core is responsiveness to expressed needs for comparative effectiveness research to inform health care decision-making by patients, clinicians, and others in the clinical and public health communities. The framework will be supported by detailed inventories of Federal CER activities and research/data infrastructure, and a priority-setting approach. This organizing framework fosters consideration of the balance of activities and priority themes, focuses on the most pressing needs expressed by patients and clinicians, and allows for identifying and addressing gaps in the current landscape of CER.

CER activities and investments made by the government or other institutions can be grouped into four major Core Categories:

- **Research** includes activities or investments in primary research or meta-analysis. Organizations involved in this group of activities may be funding research, conducting research themselves, or helping to establish a common set of research priorities to create momentum around the most critical research topics.

- **Human and Scientific Capital** includes activities or investments that enhance the United States' capacity for CER by expanding and strengthening relevant research skills or by advancing CER approaches and methodologies. Organizations involved in this group of activities may be directly involved in training and workforce development, developing new CER methods, validating results of CER, or driving consensus on valid approaches to CER.

- **CER Data Infrastructure** includes activities or investments that develop, build, or maintain data infrastructure, systems, or tools. These investments could include the creation of new research data sets and repositories, aggregation of existing data sources, development of new tools to query and analyze existing data sets, or creation of standards for new data collection.

• **Dissemination and Translation of CER** includes activities or investments that disseminate CER findings and put them into practice. Activities and investments range from dissemination and distribution of CER information to improving processes and outcomes in health care and public health delivery systems through CER translation and adoption.

Table 1
Example Activities in Each Major Category

Activity	Examples
Research	Comparing outcomes of treatments or care delivery for a specific condition
Human & Scientific Capital	Training new researchers to conduct CER or developing CER methodology and standards
CER Data Infrastructure	Developing a distributed practice-based data network, linked administrative or EHR databases, or patient registries
Dissemination and Translation of CER	Building tools and methods to disseminate findings and translate CER into practice to improve health outcomes for patients

Furthermore, investments or activities focused on a specific priority theme can cut across these categories. The potential themes include:

•**Conditions.** Organizing investments and activities around a condition or disease state is common in research and reflects the organization of medical practice. Focusing on a single disease state across all four major categories of activity (e.g., funding primary CER in oncology, developing new methodologies for CER in palliative care settings, expanding the Surveillance, Epidemiology, and End Result database (SEER), and partnering with an academic cancer center to pilot CER implementation strategies) could result in significantly improved patient-centered outcomes in that disease area.

•**Patient populations.** While clinical research is relevant to the patient population it is designed to address, it often provides little information relevant to patient groups not typically enrolled in clinical studies. In private-sector-funded trials, this often includes the elderly, racial and ethnic minorities, children, and persons with disabilities. The NIH, however, already requires that all publicly funded trials include appropriate numbers of women and racial and ethnic minorities. Cross-cutting activities and investments that facilitate studies responsive to the needs of these populations can ensure that all Americans benefit from CER.

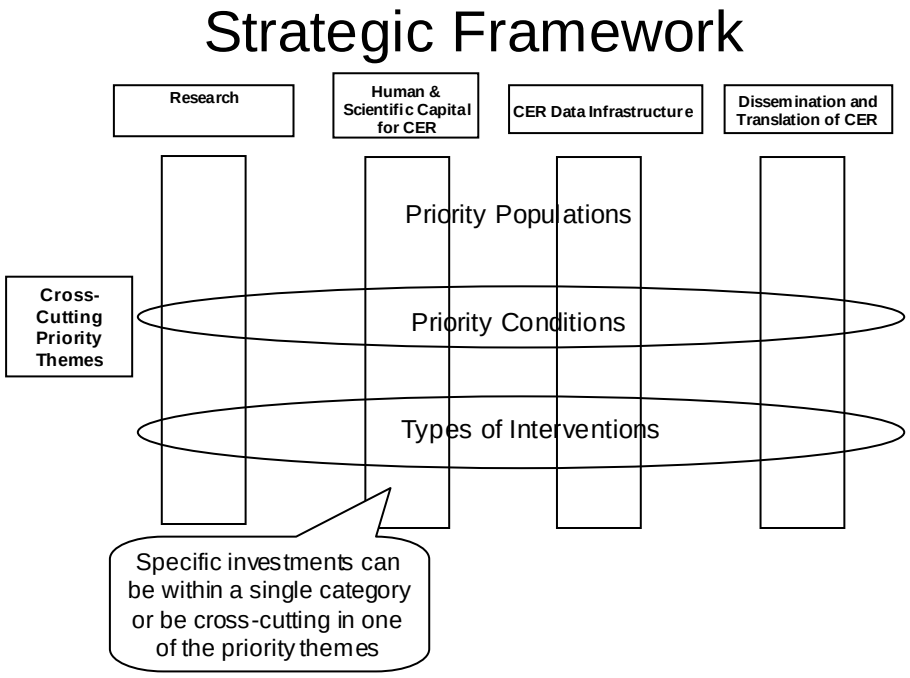
•**Type of intervention.** Several potential areas of focus emerge from studying interventions by type. In defining CER, the Council specifically included the following types of interventions: medications, medical and assistive devices, procedures, behavioral change, diagnostic testing, and delivery system strategies. Each of these has unique opportunities for coordinated investment in data infrastructure, research, building

research capacity, and translation. In addition, one could focus on interventions at a stage of the disease (i.e., prevention, diagnosis, treatment, and management).

Together, these activities and themes make up the CER strategic framework (Figure 1).

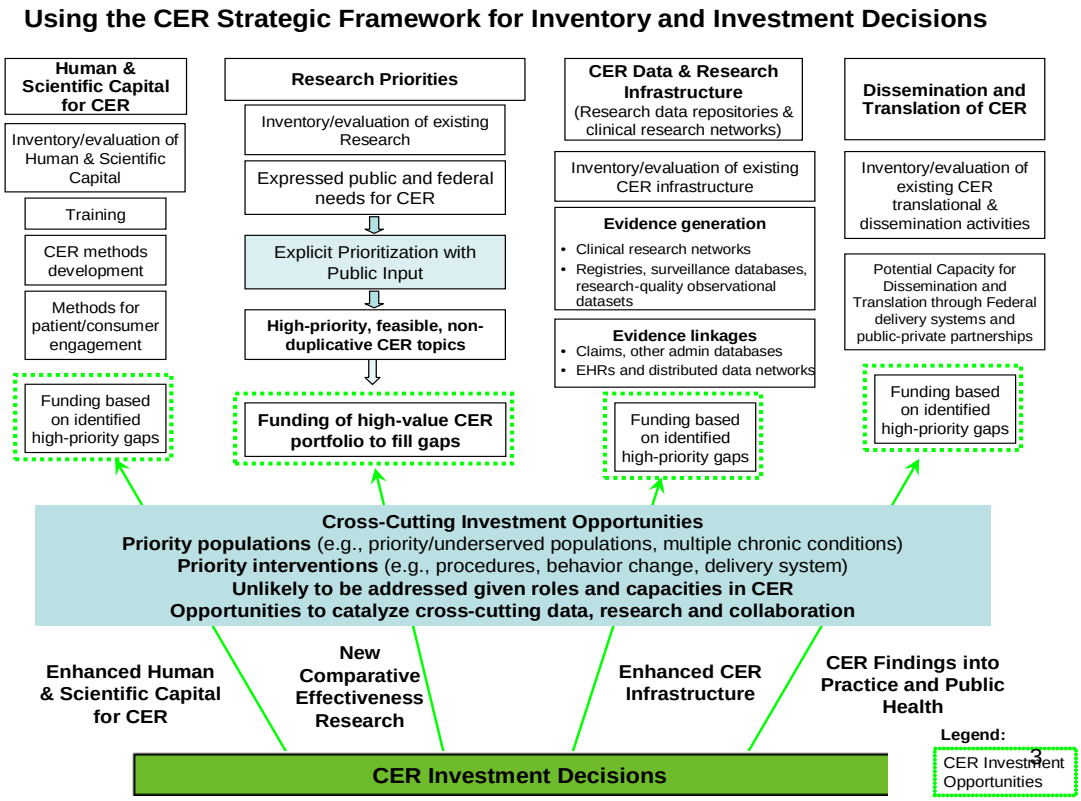
Agencies or organizations that are engaged in CER will often make investments in one group of activities or across multiple groups within a cross-cutting theme. The pattern of activity and investment for a single organization highlights its strategy. For example, a medical information database company may concentrate its CER activities in data infrastructure, whereas the National Cancer Institute is involved in multiple types of activities with a focus on cancer. When patterns of activity for the most critical agencies and organizations involved in CER are viewed in aggregate, the CER framework reveals gaps in CER activities and investments. These gaps are potential areas of opportunity and impact for the Secretary's ARRA funds. As such, the framework is useful for determining what investments are appropriate for ARRA funds and for future Federal investments in CER, as well as for codifying the ongoing activities of Federal agencies involved in comparative effectiveness research.

Figure 1



Creating and maintaining an inventory summarizing current and past Federal efforts across the CER framework is critical to its value in decision-making. This inventory of Federally-sponsored CER activities will also be a critical component of future Council annual reports. This process of inventory-taking, gap analysis, and establishing priorities for investment should be iterative. The process for developing the inventory and aligning findings from that process with CER investment decisions is outlined in Figure 2.

Figure 2



Overall, the CER framework is a useful strategic and analytic tool to help organize ongoing CER activities of Federal agencies, to facilitate development of a strategy for the Secretary's ARRA investments, and to continually monitor progress in CER across the different dimensions of the framework.

VI. CURRENT CER INVENTORY AND CER DATA INFRASTRUCTURE

The following CER inventory and data infrastructure was collected for the first time and on a very short timeline. The counts of CER studies are based primarily on electronically accessible sources, informed in part by interviews of senior agency staff. Attributes of the research reported here (study designs, types of interventions studied, etc.) were determined from study summaries or abstracts rather than inspection of full-text reports of these studies.

As described below, providing a high-confidence estimate of the number of Federally-funded CER studies underway for a given fiscal year is not currently feasible. Prospective identification of CER studies using keywords or other "tagging" in one or more readily searchable electronic databases would enable tracking of completed and ongoing CER. Therefore, this preliminary inventory is informed by a convenience sample and should be viewed as a rough estimate of what will be an iterative process going forward.

Although ARRA is the first coordinated Federal CER effort, several Federal agencies have been conducting comparative effectiveness research and maintaining data and infrastructure for CER. Most of this activity has been conducted independently within the given agency. The agencies most active in CER include AHRQ, NIH, and the Veterans Health Administration (VHA). But many other agencies conduct or have resources related to CER to a lesser degree, such as comparative effectiveness research studies, related data infrastructure, or the potential to be effector arms for research dissemination and translation. Finally, it is important to note that this inventory does not include CER conducted by private or not-for-profit organizations.

CER Inventory

Table 2 provides information about the numbers of studies for these agencies. There is no standard, systematic means of reporting on CER studies and funding across Federal agencies. It is not possible at this time to estimate the total number of primary or secondary CER studies conducted by the Federal Government. Other than AHRQ, by virtue of its dedicated Effective Health Care Program, agencies have limited ability to track CER studies and spending, reflecting that CER is a relatively new field of inquiry, has no standard definition, and is not "tagged" or readily searchable in biomedical or health services research databases. AHRQ tracks its funding and number of studies by fiscal year. Funding for CER studies for AHRQ ranges from 12 million to 35 million per fiscal year since FY 2006, with 12-18 studies funded per year. Estimates for the number of CER studies and funding for DoD and VHA are approximations per year rather than specific numbers for particular years. For example, DoD estimates its funding to be approximately $125,000 to $500,000 per year for 5-10 studies per year; the VHA estimates are 50 million to 70 million per year for 40-50 studies per year.

As part of its large portfolio of biomedical research, the CER funded by NIH makes that agency the single largest sponsor of primary comparative effectiveness research. These studies are difficult to identify, however, as they are not "tagged" or otherwise readily searchable as CER in such databases as ClinicalTrials.gov or CRISP (Computer Retrieval of Information on Scientific Projects, a database of biomedical research funded by NIH).

For purposes of this pilot inventory, a keyword search of ClinicalTrials.gov yielded an initial set of 1,800 NIH-funded trials during the years 2006-2009 that were candidates for CER. Subsequently, in cooperation with NIH, a sample set of 463 NIH CER studies for 2008 was identified, starting with a new searching process under development by NIH to track CER studies and spending.[26]

[26] NIH recently developed an initial process involving a keyword searching software algorithm based on consensus among several experts regarding which studies from among those funded by NIH qualify as CER. NIH applied this algorithm to all studies funded by NIH in 2008, which yielded more than 800 studies with a score above a certain threshold—tagging them as potential CER. Inspection of all of the records of all of these studies in CRISP by staff supporting the Coordinating Council identified the set of 443 that appeared to qualify as CER. This set of 443 does not necessarily represent the full set of CER studies funded by NIH in 2008.

Table 2: Estimated CER Grant/Study Counts FY 2006 – FY 2009[1]

Agency	CER Grants/Studies FY2006-FY 2009 (YTD)
AHRQ	144
DoD	25
VHA	96
NIH[2]	463

[1]As of June 2009, based on review of agency/department websites and agency/department generated lists

[2]NIH is in process of cataloging CER. This primarily represents FY 2008.

CER studies conducted or sponsored by VHA and DoD often focus on the particular populations they serve. These include CER studies involving patient groups that fall within designated U.S. priority populations (e.g., the elderly, racial and ethnic minorities, patients with multiple chronic conditions, persons with disabilities).

The main findings from analyses of Federal CER for fiscal years 2006-2009 include the following:

- In this initial compilation, the inventory of CER that could be confirmed independently for those agencies that perform or sponsor it was generally comparable to the inventory as described in interviews with agency staff. The main exception was NIH, where the volume of CER is acknowledged to be large yet remains to be quantified.
- Other than that for AHRQ, agency budgets for CER are not well defined. Agency staff typically described rough percentages of total research budgets or approximate ranges of annual expenditures on CER, but generally could not cite budget amounts allocated to CER (e.g., by Federal fiscal year).
- Excluding AHRQ, which could cite studies in its Effective Health Care program as at least a core set of CER, agency staff could not specify the number of CER studies conducted per year or other period. Three main factors account for this. First, there has not been a standard definition of CER. Second, while agencies may have a sense of expenditures or relative emphasis of CER, individual studies are typically not titled, given keywords, or otherwise "tagged" in a manner for identification as CER. Third, the time frame for CER study counts is not standardized; some agencies provided counts in terms of studies underway during a given year, others provided counts of studies initiated in a given year. Thus, providing a high-confidence estimate of the number of Federally-funded CER studies underway for a given fiscal year is currently not feasible. Clear identification of CER studies, particularly prospectively, would better enable tracking of completed and ongoing CER.
- Combined Federal CER is broadly distributed across study types (i.e., primary versus secondary studies). The volume of primary CER sponsored by NIH, particularly Randomized Controlled Trials (RCTs) and other trials, accounts for the largest general type of CER.
- The greatest concentrations of Federal CER are systematic reviews by AHRQ, RCTs by NIH, and RCTs by VHA (Table 3).

- Most AHRQ CER comprises secondary research (i.e., systematic reviews and other syntheses) and VHA supports secondary research through its Evidence-based Synthesis Program. Otherwise there is little emphasis on secondary research. Moreover, mathematical modeling is infrequently used in Federal CER (Table 3).
- Most primary research is done through RCTs (Table 3).
- Without careful inspection on a trial-by-trial basis, reliable detection of "practical" (or "pragmatic") trials among the primary CER studies is not possible. As a group, the VHA trials appear to have more such "practical" characteristics than trials sponsored by other agencies.
- Relative to the RCT volume from NIH and VHA, the use of observational analyses, including those involving large patient-level databases, is relatively infrequent.
- The locus of research varies by agency. All CER funded by VHA and most by DoD is intramural. Most CER funded by AHRQ is extramural. Although NIH conducts some intramural primary research, most CER is done extramurally.
- The interventions studied most often in Federal CER are pharmacologic, which account for the majority of the interventions studied by AHRQ and NIH. These are followed by studies of the health care delivery system, led by VHA, and behavioral interventions (which are often compared to pharmacologic interventions), led by NIH and VHA (Table 4).
- Roughly 86 percent of the CER studies in this sample across agencies focus on at least one priority disease/condition. The leading categories among these are depression and other mental health disorders, substance abuse, cardiovascular disease, and diabetes (Appendix C).
- The distribution of priority diseases/conditions studied by DoD and VHA largely reflects the respective populations they serve. For DoD, they are cancer, functional limitations and disability, and depression and other mental health disorders. For VHA, they are cardiovascular disease, and depression and other mental health disorders (Appendix C).

Table 3: Estimated Types of CER by Agency/Department

Study Type[1]	AHRQ	NIH[2]	DoD	VHA	Total
Primary Research					
Randomized Controlled Trial	11%	79%	0%	77%	60%
Practical/Pragmatic Controlled Trial[3]	3%	1%	16%	1%	2%
Other Non-Randomized Controlled Trial	2%	2%	32%	0%	3%
Observational Study (natural experiment)	1%	2%	0%	4%	2%
Observational Study (Prospective/Registry)	4%	3%	16%	6%	4%
Observational Study (Retrospective)	9%	5%	6%	4%	6%
Secondary Research					
Systematic Review	58%	0%	13%	0%	14%
Meta-Analysis	3%	0%	0%	0%	1%
Mathematical Model	4%	3%	3%	3%	3%
Research Training	n/a[4]	0%	13%	0%	1%
Other Capacity Building	n/a[4]	0%	0%	1%	0%
Other	2%	2%	0%	3%	2%

[1] Some studies include more than one study design, totals may not equal 100% due to rounding.
[2] NIH 2008 (based on sample of 443 studies) plus NIH multi-year (based on 30 studies across years).
[3] Rough estimate given no standard definition for pragmatic trial.
[4]AHRQ has been heavily involved in development of human and scientific capital for CER. It provides career development (K) grants for CER as well as a T and R grant for CER capability building. It also has funded numerous methodology studies for CER. These will be more fully quantified in the completed inventory.

Table 4: Estimated Types of Interventions Included in Studies

Study Intervention Type[1]	AHRQ	NIH[2]	DoD	VHA	Total
Pharmacologic Treatment	35%	68%	24%	10%	34%
Biologic Treatment	1%	1%	10%	4%	4%
Alternative Medicine	2%		8%	1%	2%
Medical Device/Equipment	17%	6%	0%	7%	11%
Surgical Procedure	11%		3%	9%	9%
Behavioral Intervention	11%	24%	11%	24%	16%
Public Health Intervention	2%	1%	17%	3%	3%
Delivery System	11%		19%	41%	20%
Other	10%		8%	1%	2%

[1] Some studies include multiple types of interventions and may not total 100% due to rounding
[2] NIH multi-year. Will need to be updated once inventory based on types of NIH interventions is complete.

The involvement of priority populations in CER sponsored by Federal agencies is varied. While several studies do not explicitly focus on a priority population, investigators sometimes report on analyses of one or more specific sub-groups:

- About half of CER studies across these Federal agencies involve a priority population, with nearly 60 percent of VHA studies doing so. Many studies focus on more than one population group. In part consistent with their respective missions, the agencies exhibit different distributions of emphasis on priority populations.
- Among those studies that do involve priority populations, those involving patients requiring chronic care, and those who are elderly are the most common. While no studies specifically indicate a focus on low-income groups, such individuals often comprise some of the patients studied, including the elderly, those with multiple chronic conditions, and minority groups.
- Studies vary as to whether there is sufficient representation of one or more priority groups in the study population to enable sub-group analysis, even if the study does not focus on a priority population as a principal objective. Particularly at AHRQ, in cases where studies do not have as their primary focus a priority population, sufficient numbers of members of priority groups may not be present for sub-group analyses, especially in the case of systematic reviews.
- Future iterations of the inventory will need to drill down on the representation of priority populations in studies.

CER Data Infrastructure

Substantial Federal and private sector infrastructures exist that could be used to identify potential CER priorities, to support the conduct and improve the productivity of CER, and to enable the translation of research findings into actionable information. However, the current infrastructure for CER is fragmented, and it is not coordinated or mobilized in a way that would enable providing coherent and targeted support for CER.

Patient-level Databases and Databases to Support Researchers

Federal agencies support or have access to substantial patient- and person-level databases that could support CER. Additional databases in the private sector can also deliver specialized content for CER. For example, these Federal and private sector databases can support or enable:

- Analyses preparatory to CER, such as.:
    - Disease prevalence and burden to help determine priority areas for comparative effectiveness research.
    - Utilization and distribution (e.g., geographic) of alternative interventions to help identify variations in practice and candidate interventions for CER.

    - Patient characteristics, socioeconomic attributes, comorbidities, and so forth, to determine the availability of certain patient populations for clinical trials, registries, and other person-level studies.
- Observational studies and retrospective data analysis (e.g., mining data from natural experiments).
- Support for prospective studies, including efficient development of registries and objective collection of treatment detail.

Important considerations for investing in and applying patient/person level databases to CER include:

- Potential to link to other databases that enrich the person/patient view, such as databases containing socioeconomic characteristics of individuals and mortality information (e.g., the Social Security Deathmaster or the CDC National Death Index).
- Potential to link databases that contain clinical information to those with transactional information (e.g., linking claims databases that have chemotherapy detail on cancer patients to electronic health records or registries for the same patients that have clinical data such as cancer stage, histology, and patient status).
- Research readiness of the databases (e.g., requiring minimal time on the part of the researcher to learn database attributes and develop special programs for data clean-up and access).
- Requirement to maintain security and privacy for any personally identifiable health information.

Appendix C lists some key patient-level databases with potential applications for CER. Among the ones available through Federal agencies are the major administrative databases maintained by CMS, the medical records databases at VHA, targeted databases maintained by AHRQ and NIH focused on service areas (e.g., HCUP on hospital-based care), and the NIH's SEER cancer registry.

Key private sector databases for CER include large administrative databases with longitudinal health care detail on millions of patients, and consolidated databases on EHRs. To the extent that these repositories can be linked (for which many have the potential), they can be highly valuable assets for CER, particularly because they account for commercially insured populations that are not captured in Federal and state databases.

In supporting research activities, the following Federal data infrastructure assets can speed communication among researchers and expedite identification of researchers with special skills:

- AHRQ: the DEcIDE Network, the CERTs (Centers for Education & Research on Therapeutics), and group of EPCs (Evidence-Based Practice Centers).
- NIH Clinical Translational Research Awards (CTSAs) recipients.
- CDC: Evaluation of Genomic Applications in Practice and Prevention (EGAPP) workgroup.
- HRSA research networks: Pediatric Research in Office Settings (PROS) and Emergency Medical Services for Children (EMSC) groups, among others

- SAMHSA: National Child Traumatic Stress Network
- VA Research Center of Excellence

Other databases for supporting researchers include:

- ClinicalTrials.gov (Federally and privately supported clinical trials).
- MEDLINE/PubMed (biomedical journal literature), HSRProj (Health Services Research Projects in Progress).
- CRISP (biomedical research funded by NIH, including clinical trials and other studies).
- Disease-oriented databases, surveys and Web sites, including the Longitudinal Studies on Aging (NCHS and NIA) and the Cardiovascular Health Study (NHLBI).
- Survey of Mental Health Organizations, General Hospitals Mental Health Services, and Managed Care Organizations (SAMHSA).
- Numerous CDC disease and research data assets and sites, including the NCHS surveillance systems, cancer registries, and vaccine registries.

None of these databases with actual or potential applications in CER were developed for the explicit purpose of comparative effectiveness research. Furthermore, they generally have not been organized or indexed to enable searching for CER. For example, careful record-by-record inspection of such research study databases as ClinicalTrials.gov and CRISP is required to identify CER. In order to assess current gaps and support translation and adoption of CER findings efficiently, these databases would require "tagging" of records or related searching functions that would enable accurate identification of CER.[27]

Dissemination and Translation Infrastructure

A few agencies, notably AHRQ, VHA, NIH, and SAMHSA, have capacities to translate CER into actionable information for practitioners, patients, and other target audiences. The VHA's capabilities for translation and adoption are inherent in its integration of research and patient care at VHA treatment centers. Additional agencies also have capabilities for disseminating information to segments of consumers and practitioners. All of these agencies have the potential to influence adoption of CER findings.

There are, however, minimal formal mechanisms to disseminate and translate CER from research agencies such as AHRQ and NIH into the delivery system side of HHS (e.g., HRSA, IHS, SAMHSA, CMS QIO's). In addition, given the current expansion of CER and the increased emphasis on achieving impact from its findings, the current dissemination and translation capacity of the relevant agencies involved in CER is likely to be insufficient for achieving CER's potential.

Some of the key elements that can be leveraged in a comprehensive and articulated CER dissemination and translation strategy are outlined below.

[27] In MEDLINE, for example, indexing tags for particular "publication types," such as Randomized Controlled Trial, Clinical Trial, Phase III, Meta-Analysis, and Review, would readily enable searching for journal articles that report such studies.

- AHRQ
  - CER methods guides, tools, and resources made available via the AHRQ Web site, Web conferences, public service announcements, advertising campaigns, online audio guides available to public, and other means for informing consumers, clinicians, and policymakers.
  - The John M. Eisenberg Clinical Decisions and Communications Science Center, which focuses on translation of research to various target audiences.
  - AHRQ Publications Clearinghouse.
  - AHRQ dissemination partnerships, including with health professional societies, patient advocate groups, and non-profit organizations focused on particular diseases/conditions.
  - Effective Health Care Program Stakeholder Group, which helps to identify important information gaps, ensure transparency, and provide feedback on reports.

- CDC
  - Information to monitor the adoption of CER recommendations and to track the effects from changes in clinical practices and policies on the following process and outcomes measures: clinical management of specific conditions, including the use of medications and other specific services, and intermediate health-related outcomes, such as test results; incidence and prevalence of specific conditions; personal behaviors, health status, and functioning; and births and deaths.
  - Public use data from NCHS surveys available through the CDC/NCHS Web site and internal confidential data available for researchers through the NCHS Research Data Centers.
  - NCHS/CDC reports, including Data Briefs and E-Stats, and other analyses available through the Web site, and articles in the peer-reviewed literature.
  - Dissemination by and with collaborators, including sponsors of specific data collection and analysis.

- DoD
  - Searchable publication libraries, including the Military Health System Publication Search.
  - DeployMed Research Link, which informs Service members, researchers, health care providers, military leaders, and others about DoD and other Federally funded medical research related to deployments since 1990.

- NIH
  - Clinical and Translational Science Awards (CTSAs), which are NIH-funded academic centers that translate research into practice.
  - Nation Cancer Institute's Physician Data Query, an online database that summarizes study results in prevention, screening and management of cancer in versions appropriate for physicians and for patients.
  - Research databases, including MEDLINE/PubMed, HSRProj, CRISP, and ClinicalTrials.gov.

- Public health campaigns, such as Red Dress (women's heart health) and Small Steps Big Rewards (weight loss).
- NIH Consensus Development Conference program, which summarizes knowledge about a variety of clinical and public health interventions.

- VHA
  - QUERI (Quality Enhancement Research Initiative) program for enhancing the uptake of evidence within VHA.
  - Periodic research summaries and issues briefs for senior VHA clinical and policy leaders, and related research results disseminated to researchers.
  - CME programs for nurses and other health professionals that incorporate recent research findings.
  - Print and online patient education tools, including the MyHealthE Vet Web site, for dissemination to patients.
  - Point-of-service decision-support tools and reminders to clinicians within the VHA EHR system guiding practice toward the most effective treatment, including a Web portal for clinicians to access clinical practice guidelines.

- SAMHSA
  - National Registry of Evidence-based Programs and Practices (NREPP) and the Technical Assistance Centers can serve as translation vehicles. NREPP is a searchable online registry of approximately 140 mental health and substance abuse interventions and targeted outcomes; it provides quality of research and "readiness for dissemination" ratings.
  - The Addiction Technology Transfer Center (ATTC) Network is comprised of 14 Regional Centers and a national office which facilitates alliances among providers, administrators, and recovery and treatment communities, and connects them to the latest research and information through activities such as skills training, academic education, online and distance education, conferences, workshops, and publications.
  - The National Centers for the Application of Prevention Technologies (CAPT) work to bring research to practice by assisting States/Jurisdictions and community-based organizations in the application of the latest evidence-based knowledge to their substance abuse prevention programs, practices, and policies.
  - The SAMHSA Health Information Network (SHIN) provides a one-stop, quick access point that connects the behavioral health workforce and the general public with the latest information on the prevention and treatment of mental and substance abuse disorders.

- FDA
  - Web site provides news and other information to physicians and consumers on drugs, biologics, and devices.

- Office of Public Health and Science (OPHS)
  - Comprises 12 core public health offices and the Commissioned Corps, some of whom work with population and community-based networks to disseminate health information (e.g., Office of Disease Prevention and Health Promotion, Office of

Minority Health (OMH), Office on Women's Health). OMH, for example, has cooperative agreements and other partnerships to disseminate research findings (though not CER to date) to minority populations.

- Office of the National Coordinator for Health Information Technology (ONC)
  - Efforts to develop and implement a nationwide, interoperable health information technology infrastructure could provide a means for incorporating CER into decision-support systems for clinicians and other applications in health care.

- HRSA
  - Among multiple dissemination vehicles, the AIDS Education and Training Centers Program and the Ryan White HIV/AIDS Program support a network of 11 regional centers and more than 130 associated sites that conduct targeted, multidisciplinary education and training programs for health care providers treating people living with HIV/AIDS.
  - HRSA's Maternal and Child Health Bureau disseminates information using cooperative agreements with professional organizations and academic institutions, and funds grants for continuing education to academic centers across the country, specifically for the purpose of translating research into practice.

There is virtually no capacity to track the impact of CER dissemination, translation, and adoption activities. As a result, this limits the ability to measure the impact of CER and to conduct research on effective approaches. Claims databases could be one resource for tracking changes in practice over time and their impact.

Human and Scientific Capital

The future workforce engaged in CER should include experts from a wide array of disciplines, including biostatistics, epidemiology, mathematics, economics, and ethics. To date, however, there has been little focus on human and scientific capital infrastructure for CER. The principal exception is the close affiliation of certain AHRQ activities involving academic centers and other organizations, including the DEcIDE network, CERTs, EPCs, the Eisenberg Center, and various awards to researchers. AHRQ funding of DEcIDE network members and EPCs supports research trainees at those organizations. AHRQ also provides career development (K) grants focusing on generation of new scientific evidence and analytic tools that enable the prioritization of evidence-based services and goals for patients with multiple comorbidities.[28] In addition, AHRQ has sponsored other scientific and methodological activities, including development of methods guides, training seminars, and related events (e.g., at AcademyHealth and other professional conferences), and various workshops and support materials on MEPS, HCUP, and other data sets.

NIH provides significant training opportunities that could incorporate CER, including support for medical students interested in research, clinical fellowships, workshops for researchers, training grants, and consensus conferences. The CTSA program at NIH provides translational development support at academic and other research centers, some of which addresses evidence-

[28] http://grants.nih.gov/grants/guide/notice-files/NOT-HS-08-004.html.

based medicine approaches, if not CER in particular. The NIH K30 Clinical Research Curriculum Awards support training in design of clinical research projects, hypothesis development, biostatistics, epidemiology, disease mechanisms, medical technology, human genetics, and the legal, ethical, and regulatory issues related to clinical research.[29]

Although DoD has an extensive training and professional education infrastructure, it does not focus on CER.

A small number of training programs at academic centers focus on areas that address methodologies and study designs related to CER. Among these are the Clinical Research Training (CREST) program at Boston University, which provides training in clinical research that includes epidemiology, clinical epidemiology, health services research, biobehavioral research, and translational research,[30] and the Duke Clinical Research Training Program, which provides training in quantitative and methodological principles of clinical research, including research design, research management, medical genomics, and statistical analysis.[31]

Several agencies draw on the considerable scientific and methodological expertise resident in the FDA, but there is little emphasis on comparative effectiveness research at that agency. These informal links to scientific expertise could be formalized; also, specific CER expertise could be housed in selected agencies with an expectation of a cross-agency role. FDA expertise would be of exceptional value in, for example, understanding the respective merits of alternative study designs for assessing efficacy vs. effectiveness and for collecting and assessing adverse event data, strengths and limitations of using surrogate endpoints and other biomarkers in CER, incorporation of genomics and other aspects of personalized medicine into CER. Phase III and phase IV studies could also generate evidence on comparative effectiveness, as well as on other scientific and methodological aspects of CER.

Despite the promise of "practical" or "pragmatic" trials for CER, methodological gaps and threats to internal and external validity remain. Real world trials must deal with confounders, including confounding by indication and presence of comorbidities, selection bias, and other factors that impede the assessment of cause and effect. Focused research to improve the validity of practical trials and interpretation of their findings could enhance the use of these study designs.

Further development of mathematical modeling approaches and retrospective data analysis capabilities would also provide alternative means of analyzing comparative effectiveness, as well as generating viable research hypotheses and providing input for designing primary and secondary CER.

Gaps in the Current CER Landscape and Investment Opportunities

The inventories of CER and CER data and research infrastructure reveal gaps and other challenges for achieving the potential of comparative effectiveness research.

[29] http://grants.nih.gov/training/K30.htm.
[30] http://www.bumc.bu.edu/clinepi/crest/general-info/
[31] http://crtp.mc.duke.edu/content.asp?page=about

Coordination across the CER framework: Substantial CER assets exist across the Federal Government, but coordination is necessary to capture their full value. Several challenges exist in achieving this:

- Prior to this report, there was no standardized Federal definition for CER; aligning organizations around this definition will be necessary for identifying, cataloging, and disseminating CER in a coordinated manner
- Difficulty in setting national CER priorities.
- Structural barriers that limit collaborations among agencies.
- Limited coordination with private sector CER efforts. This includes lack of integration of existing data sets across payers, suboptimal development of CER data infrastructure, an inability to track populations and treatments across payers, and suboptimal translation and adoption of CER findings.
- Unrealized benefits of stakeholder involvement. Greater involvement of stakeholders (e.g., patient advocates, health professionals, researchers, technology manufacturers, payers) in CER processes can help to achieve the goals of CER, including more informed priority setting, input on certain aspects of study design (e.g., identification of important subgroups and patient-centered outcomes), and identification of target audiences for CER and strategies to reach them.

Research: Despite the comparative effectiveness research to date, there are many unanswered questions.

- Those who sponsor and design clinical trials continue to face challenges in tradeoffs between internal validity of CER for causal effects of interventions on outcomes and external validity of CER to heterogeneous patient groups and routine health care settings.
- Increased emphasis on well-conducted pragmatic trials could increase acceptance of CER findings.
- May research questions for important clinical health care decisions remain unanswered

Human and scientific capital: Due in part to the increasing interest in comparative effectiveness research, continued investment in human and scientific capital for the field is needed.

- Greater investment is needed in developing education and training programs to support the development of professional talent, the development of methods for linking and using databases for CER, the development of new methodologies for pragmatic trials, effective translation and adoption of CER findings into practice, modeling approaches for CER, and evaluation of the impact of CER
- More methods work is needed to advance the state-of-the-art for pragmatic trials and to provide training for using these study designs.
- Recent growth in training for the related fields of health technology assessment, outcomes research, and health economics, among others, has helped to yield a cohort of researchers who are well-positioned to become more expert in CER, along with

educational curricula and materials that can be adapted for training in comparative effectiveness research.

CER Data Infrastructure: The scope and scale of CER requires data infrastructure that may outstrip current capabilities.

- Current data sources are fragmented and limited in terms of clinical robustness and longitudinal data capture.
- An evolving inventory of CER data infrastructure is needed to track the capacity of this infrastructure and provide a basis for its further development; this inventory should include observational databases, registries, claims and other administrative data, pharmacy and laboratory data, adverse events registries, EHR networks, and other health information technology.
- In addition to one or more inventories, greater understanding is needed regarding the strengths and limitations of these data sources, and areas for their further development. An example of a relevant resource is the 2007 *Registries for Evaluating Patient Outcomes: A User's Guide*, produced by the AHRQ's DEcIDE Research Center.
- Investment in linking such data sources is more likely to be realized by establishing clear information policies and technical standards, standardized terminology, improved platform capability, novel search algorithms, mechanisms to maintain patient privacy, and controls to access data, and by reducing and coordinating data processing times.[32]
- There are few searchable electronic inventories or related databases of CER and CER infrastructure. While sources like ClinicalTrials.gov, CRISP, MEDLINE, and HSRProj contain information about completed and ongoing CER, but they are not presently configured or linked to serve the needs of CER.
- Absence of an inventory of CER limits the ability to assess the magnitude and nature of the current portfolio of completed and ongoing CER, to identify CER on particular topics, and to inform priority-setting for CER.
- A comprehensive inventory of CER infrastructure would improve the ability to conduct CER and to allocate resources to develop the national capacity to conduct CER.

CER Dissemination and Translation: Many findings to date from CER have not yet been fully integrated into clinical practice or made accessible to patients in easy-to-understand language.

- Certain effective dissemination avenues are in place, including among some of the agencies engaged in CER. Except for AHRQ, however, these agencies are not yet oriented to CER and do not adequately extend beyond dissemination alone to translation and adoption of CER into practice.
- Tools and mechanisms to support clinicians and patients in incorporating available CER information are lacking. This information needs to be delivered to the front line of care where health decisions are made and results measured.

[32] See, for example: Diamond CC, Mostashari F, Shirky C. Collecting and sharing data for population health: a new paradigm. Health Aff (Millwood) 2009;28(2):454-66.

Priority populations and other sub-groups: At present, the agencies have largely separate approaches to addressing these groups. A better-coordinated Federal approach is needed to address priority populations and priority conditions, including sub-groups with multiple chronic conditions.

- Greater attention on designing studies with sufficient power to discern treatment effects and other impacts of interventions among patient sub-groups (e.g. accounting for heterogeneity of treatment effects) will better serve clinical decision-making, enabling more individualized, patient-specific care.
- Improved partnerships with Federal grantees serving priority populations, such as Community Health Centers, will enhance their engagement with CER.
- Improved access to and utilization of Federally sponsored databases that include priority populations can significantly enhance the inclusion of sub-groups into CER.

Types of interventions: To date, CER has been disproportionately focused on pharmacologic treatments rather than the full spectrum of intervention types. This likely derives in part because of the relative emphases of the research agendas of agencies that sponsor CER and the focus of the private sector is primarily on new drugs and biologics. The emphasis on pharmacologic treatments has meant fewer resources for other interventions, including behavioral, procedures, prevention, and delivery system interventions, that can have major impacts on health outcomes.

VII. PRIORITY-SETTING PROCESS

The Council actively sought public input throughout this process, and this input significantly influenced all Council decisions. To help guide the Council's deliberations on the definition, framework, and priorities for comparative effectiveness research, the Council held three listening sessions and solicited additional public comments online. The Council heard from over 300 stakeholders representing health care associations; consumer, community, and advocacy organizations; academia and think tanks; patients; providers; hospitals and hospital systems; payers; pharmaceutical companies; foundations, public health entities; and private sector companies engaged in the health care field. One U.S. Senator also submitted comments.

Several respondents honed in directly on the reason why investments in CER are important. One person, for example, said that CER is crucial to reforming the practice of medicine to increase the quality, safety, value, and effectiveness of what providers bring to patients on a daily basis. Other respondents addressed a wide range of interrelated issues, including priorities for the research agenda, collaboration, infrastructure development, research methodology, transparency, care delivery, cost, and knowledge transfer. Many patients expressed their need for this type of research; one of the most emotional and moving testimonies came from the mother of a child with a seizure disorder in Chicago who had struggled to find the best treatment for her child. A physician from the American Board of Orthopedics summarized many physicians' testimony by saying, "developing high quality, objective information will improve informed patient choice, shared decision-making, and the clinical effectiveness of physician treatment recommendations."

The public input has been extremely valuable in informing the Council's deliberations, and many of the major thematic threads that run thought the public comments are reflected in the strategic framework, focus, and recommendations for priorities for OS CER funds. Details about what the public had to say are contained in Appendix A.

The Council also conducted a first draft inventory of CER and data infrastructure (outlined above) to help identify gaps in the current CER landscape. For the Office of Secretary funding recommendations, the Council proceeded through structured deliberations informed by public input, developed an inventory of current activities, established prioritization criteria and a strategic framework, and discussed the unique role for OS funds to fill gaps and build the foundation for future CER. In the future, the Council should continually and actively engage stakeholders inside and outside the government, including patients, providers, payers, employers, industry, academia, and others. This critical component of the priority-setting process could take the form of even more active participation by external stakeholders in the future.

VIII. PRIORITY RECOMMENDATIONS FOR OFFICE OF SECRETARY CER FUNDS

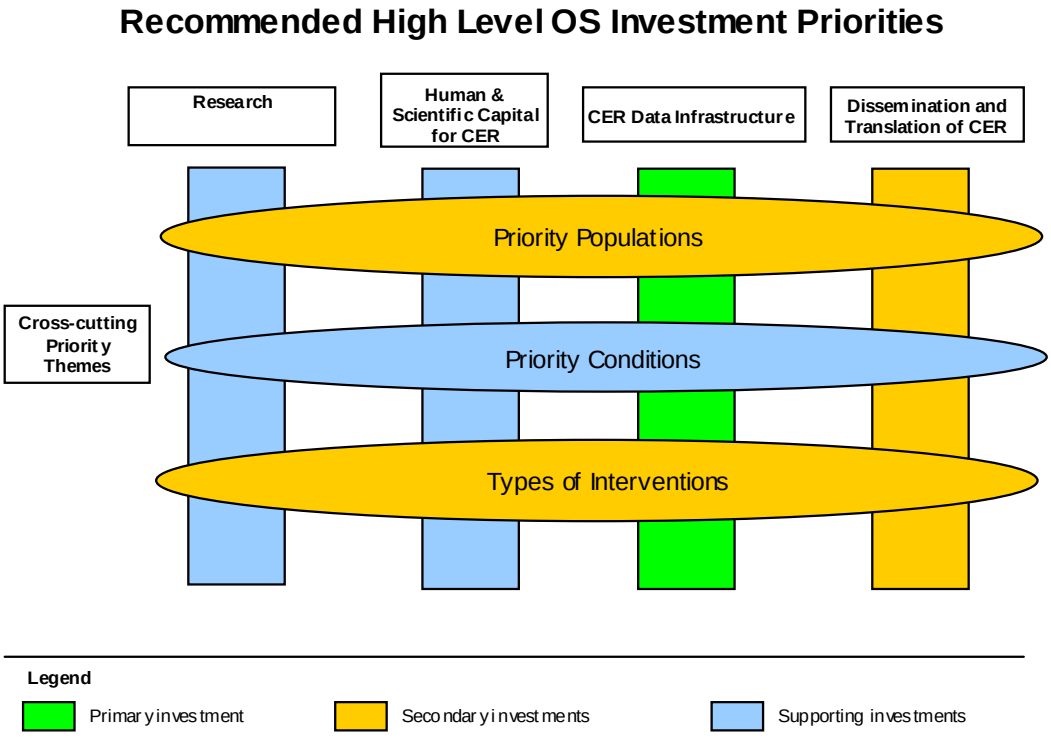
Using the strategic framework for CER discussed in Section V, and taking into consideration the unique role that OS funds can play in addressing high priority gaps, the Council developed a recommended high-level investment strategy for the use of the OS ARRA funds. The strategy has three different levels of priority recommendations for OS fund investments in the Core Activities and Cross-cutting Priority Themes in the CER framework (Figure 3).

- **Primary investment.** This area of investment should represent a large portion of the OS funds. It best fulfills the full range of prioritization criteria and requires scaled investment in order to be successful. The Council recommends that CER Data Infrastructure be the primary investment.

- **Secondary investments.** These areas should also receive significant investment. They are as critical to success in CER as the primary focus, but individually may require a smaller amount of funding to be successful. The Council recommends that Dissemination and Translation of CER, Priority Populations, and Priority Types of Intervention be secondary investments.

- **Supporting investments.** These areas should not be the major focus of OS funding as they do not fulfill the prioritization criteria as well as primary and secondary investments, but some funding may be necessary to support and enable investments in higher priority areas and fill identified gaps. The Council recommends that Human and Scientific Capital, Research, and Conditions receive supporting investments. It is important to note that these recommendations pertain only to OS funds; AHRQ, NIH, and VA have a history of significant investments in Research, Human and Scientific Capital, and Conditions.

Figure 3



The Council believes that this strategy and distribution of investments will best position the Secretary to:

- Respond to patient and physician demand for CER.
- Balance achieving near-term results with building longer-term opportunities.
- Capture the distinctive value of the Secretary's ARRA funds.

While it is the responsibility of the Office of the Secretary to operationalize this strategy, the Council's rationale for these recommendations is designed to help guide the Secretary in making specific investment decisions. The Council based its rationale for each level of investment in the strategy on the prioritization criteria described above, as well as representative examples of investment in each area proposed through the public comment process and by Federal agencies.

Primary investment

CER data infrastructure development is the most distinctive opportunity for OS ARRA funding. It requires a large, up-front infusion of capital to be successful that is unlikely to come from any source other than OS ARRA funds, making it ideal for this funding mechanism. It has broad potential impact, with the ability for resulting research to address conditions and populations captured in the primary data. Given the absence of comprehensive databases and data evaluation

tools (See Section VI), there is significant demand from the patient, clinical, and public health communities for new, expanded data infrastructure and data access to support decision-making. Finally, investments in data infrastructure have the potential to generate significant additional investments in two ways. First, some of these investments could take the form of public-private partnerships. Second, data infrastructure is a tool that, once developed, will result in new research conducted and/or funded by entities such as biomedical research organizations, payers, foundations, and health care providers.

The Council received proposals on a number of potentially promising initiatives related to data infrastructure, including but not limited to:

- Building, expanding, and linking longitudinal administrative claims databases.
- Linking administrative data with EHR-based or registry data.
- Expanding high-impact patient registries, (e.g., collaborations with specialty organizations, SEER).
- Distributed data networks populated by EHRs in practice and provider settings.
- Expanding analysis of FDA and private sector data on drug and device trials and safety.

As the Office of the Secretary identifies specific opportunities in data infrastructure, the Council recommends that it consider most carefully those that:

- Expand access to existing resources, especially those currently managed by Federal agencies.
- Create scaled platforms by leveraging existing data and capabilities in the private sector.
- Capitalize on linkages between health IT investments and the potential for CER infrastructure to develop evidence to inform decision-making.
- Ensure that infrastructure is responsive to needs of patients, providers, and other decision-makers—and not driven by what is most feasible.

The Council appreciates the relationship and need for coordination between CER and health IT (e.g. through a distributed network of EHRs) investments. As the Secretary develops HHS's full portfolio of ARRA investments, it will be critical to consider both CER and health IT holistically, not as policy silos, recognizing that success in CER is largely dependent on success in health IT and vice versa.

With all data infrastructure investments, the government will need to ensure data security and privacy. Protecting security and privacy is key to maintaining the public's trust.

Secondary investments
Secondary investments include a core area of investment—Dissemination and Translation of CER—and two cross-cutting themes—Priority Populations and Types of Intervention.

Dissemination, translation and adoption of CER is about realizing the benefits that comparative effectiveness research has to offer both patients and providers. While the breadth and depth of the near-term impact depends on what types of pilot programs the OS supports, the lessons and tools for translation developed by those pilots will be relevant to all.

The lack of reliable success in disseminating findings from CER in ways that translate into better health outcomes highlights the uncertainty and difficulty of this enterprise. However, dissemination and translation is essential to improving outcomes for patients and the link between evidence production and how best to get this information to physicians and patients in a way they understand is critical to capitalizing on the CER investment. Despite important efforts by the Federal Government, especially AHRQ, NIH, VA and DoD, the majority of current funding goes to building evidence as opposed to ensuring that the existing evidence base is utilized in patient care and health systems management. This creates a unique role for OS ARRA funding. Investments in dissemination and translation programs also have the potential to generate additional investments, especially from providers, if private institutions elect to implement similar efforts or partner with the Federal Government on translation efforts.

There are a wide range of potential dissemination, translation and adoption programs that the OS could support, including:

- Investing in dissemination and translation of CER findings throughout the Federal delivery system.
- Dissemination and translation through partnerships with provider and/or patient organizations.
- Decision support and shared decision-making tools to provide information to clinicians and patients at the point of care.
- Developing standards for communication tools for patients and providers, (e.g., a patient-friendly simple scoring system).
- Partnering with an existing consumer media channel (e.g., Internet search engine or health information site) to expand patient access to existing CER data.
- Creating a National Patient Library with a primary focus on providing evidence to patients in easy-to-use and understandable formats.

The Council recommends that the Office of the Secretary consider the following in making investments in dissemination and translation:

- Investing in better understanding the most effective methods to disseminate and translate research findings to improve patient outcomes.
- Identifying opportunities both to develop tools for translation and to pilot implementation of these tools.
- Partnering with provider organizations in Federal agencies, as well as in states and the private sector.
- Accounting for potential surrogate decision-makers (e.g., families) and the context for decisions in patient-focused tools.
- Ensuring that programs address a specific need articulated by the implementing organization or the partner to ensure success and the sustainability of dissemination activities.
- Focusing on developing standards for communication.
- Increasing understanding of the most effective methods to disseminate findings to clinicians and patients to inform decision-making

From an operational perspective, investments in the cross-cutting themes are somewhat distinct from investments in the core areas. Whereas funding for a core area might go to a project or organization focused on a specific activity, funding for a cross-cutting theme requires multiple coordinated investments and activities to be successful. Investments in these themes could cover some or all of the four core activities: research, data infrastructure, human and scientific capital, and dissemination and translation. These investments could involve a coordinated investment across HHS or the Federal Government, or they could be focused in academic centers, integrated delivery system organizations, private industry, or other non-governmental entities. Collaborative efforts to inform and transform care will be essential to achieving meaningful impact across these cross-cutting themes.

Investments in specific populations, meanwhile, will help ensure that the benefits of CER are available to all. It can also focus CER efforts on populations with existing health disparities and worse outcomes. CER has the potential in some populations, such as racial and ethnic minorities, to fill critical gaps that, historically, efficacy research has left unaddressed.

The Council identified several populations for whom the Secretary should consider allocating CER funds:

- Racial and ethnic minorities
- Persons with disabilities
- Elderly
- Children
- Patients with multiple chronic conditions

Investment in specific types of interventions in a cross-cutting manner also presents a unique opportunity for the nation's health system. The Council has identified six specific interventions for the Secretary to consider that address large and varied populations, resulting in high potential impact, are areas of high clinical uncertainty, and are not being adequately addressed by other entities. They are:

- Medical and assistive devices (e.g., comparing rehabilitative devices).
- Procedures and surgery (e.g., evaluating surgical options or surgery versus medical management).
- Diagnostic Testing (e.g. comparing imaging modalities for evaluating certain types of cancer)
- Behavioral change (e.g., developing and assessing smoking cessation programs).
- Delivery system strategies (e.g., testing two different discharge process care models on readmission rates or testing two different medical home models on preventing hospital admissions and improving quality of life).
- Prevention (e.g., comparing two interventions to prevent or decrease obesity, comparing strategies for reaching populations that do not access the health care system with prevention efforts).

Furthermore, the Council recommends that the Office of the Secretary consider the following in making investments in the cross-cutting themes of priority populations and types of interventions:

- Focusing on immediate, specific patient needs that can generate results.
- Concentrating on areas with cross-cutting gaps in research, data infrastructure, scientific capital, and/or translation.
- Building on promising systems and practices already in place, both within the government and in the private sector, and measuring results when scaled up and disseminated.
- Strongly encouraging coordination across the government and with entities outside of the government.

Supporting investments

The Council recommends that the OS reserve some ARRA funding for Research, Human & Scientific Capital, and the Conditions cross-cutting theme. Because these investments and topics are the major foci of CER activities at NIH and AHRQ, both of which will likely utilize ARRA funds administered by those organizations for these purposes, they do not represent distinctive investment for OS funds. However, there will likely be targeted investments in these areas that could support other OS ARRA efforts, such as training new researchers in CER methods or addressing gaps not addressed elsewhere in the Federal Government.

In making these targeted investments, the Council recommends the Office of the Secretary consider:

- Focusing on areas that maximize the value of the Secretary's investments in other areas.
- Avoiding duplication of efforts with other agencies.

For all of the above investments, the Council recommends that the Office of the Secretary consider the portfolio of investments and where synergies exist to leverage one investment into multiple areas. For example, a data infrastructure investment that can also be used for a cross-cutting priority theme would be of higher value than an investment that has more limited applications. Doing so will help to ensure that the funds allocated to the Office of the Secretary for CER will have a significant positive impact on the quality of patient care in the near term, and lay the foundations for continued improvements going forward.

IX. LONGER-TERM OUTLOOK AND NEXT STEPS

Outlook

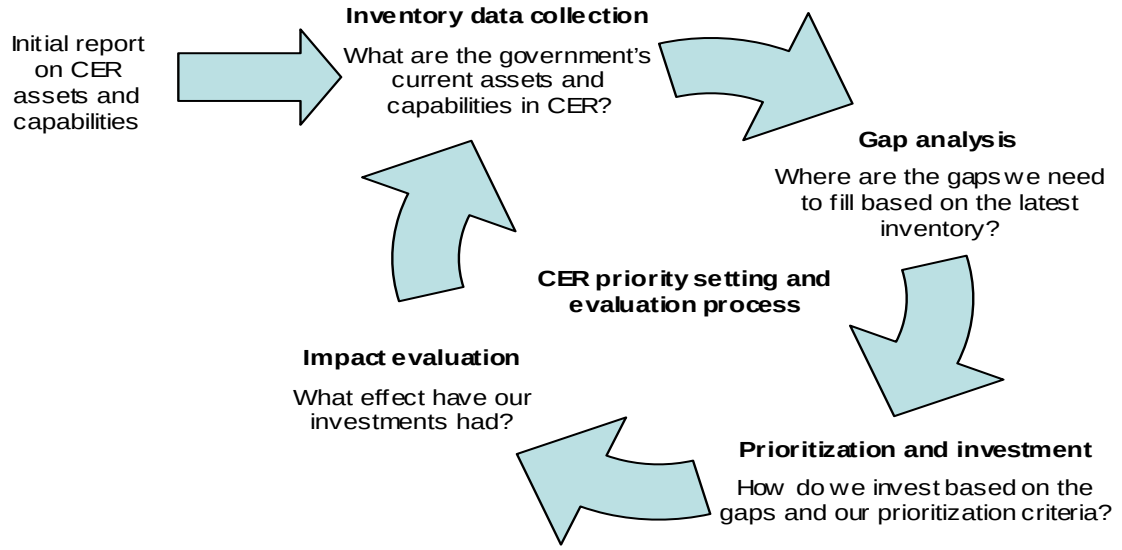
The CER investment strategy recommended in the previous section, if implemented successfully, has the potential to further a number of elements of the Council's vision for improved patient care. In the near term:

- CER dissemination and translation pilots in Federal health care delivery systems could help empower patients and their physicians to make better decisions now about their care and serve as models for expansion to private delivery systems. Moreover, a time limited investment can support establishment of a systematic strategy for translating the products of all relevant research to benefit patients served by Federal programs.
- An increased emphasis on CER for priority populations could ensure that all will benefit from comparative effectiveness research.
- Improved access for researchers to existing Federal data sources, and development and enhancement of distributed data networks and patient registries outside of the Federal Government, could jump-start a new wave of CER in the areas that matter most to patients.
- The inventory of Federal activities in CER will help reduce duplicative or uncoordinated investments among Federal agencies and help create transparency for patients.

It will be essential that a continuous cycle of CER priority-setting and evaluation of impact take place. The four critical steps in this cycle are inventory of CER and infrastructure; gap analysis; priority setting; and evaluation of impact. Figure 4 below depicts this process.

Figure 4

Continuous Evaluation of CER Inventory, Gaps, Priority Setting, and Impact



The strategic framework for comparative effectiveness research is intended to lay the groundwork for longer-term initiatives, such as innovative public-private partnerships to build data infrastructure and conduct CER. The goal of this investment is to generate some near-term results and momentum for the future. This strategy allows the government to facilitate the building of needed infrastructure, to expand access to existing infrastructure, and to demonstrate proof of concept for implementation efforts. These efforts are only a first step, however, to

achieving the vision of improved quality, safety, efficiency, equity, and patient satisfaction through improved medical decision-making and an optimized health care delivery system.

Indeed, a number of clear issues and challenges will remain for Federal CER efforts in the near term:

- **Listening and Engaging External Stakeholders.** While the Council has worked to create transparency and responsiveness in this process to date, it is critical that it continue to have a patient-centered focus going forward. In the future, the Federal Government may want to consider the options of listening and engaging stakeholders with representatives including, at minimum, patients, providers, payers, employers, and industry representatives, to guide CER or broader patient-centered outcome efforts.
- **Continued Coordination.** The Council laid the groundwork for coordination, but coordination will need to become embedded across the Federal Government. As the government makes investments in CER, there must be a mechanism in place to track and coordinate these investments and avoid duplication of efforts.
- **Building Scientific and Human Capital.** To maximize the potential benefit of investments in CER, the nation needs more researchers trained in the applicable research methods and further development of these methodologies. This presents both a short-term and a long-term challenge.
- **Maintaining Gains.** These investments represent only the beginning of CER efforts. New research findings will need to be disseminated and successful translation of evidence efforts should be expanded. New databases and data sets need to be maintained and kept current, and the catalog of Federal activities and data infrastructure in CER needs to become a living document.
- **Building Leverage.** The Federal Government is now a major funding source of CER, but the private sector still represents a majority of the investment in biomedical research. The government needs to find innovative ways of partnering with the private sector to leverage government investments and help private-sector investment better serve patients.
- **Keeping it Current.** There are no widely accepted and applied common standards or approaches for periodically re-evaluating CER to ensure that previous conclusions still hold. A system must be developed to ensure that the conclusions from CER remain valid over time.

These issues reflect both the fact that comparative effectiveness research remains in its infancy and that it must be seen as a continuous and iterative process that needs to constantly evolve based on the changing needs of the patient.

Next steps

There are a number of next steps leading to the Secretary's integrated strategy and spend plan for CER on July 30, 2009, and several requirements for the success in implementation of that strategy. Most importantly, it is critical to the success of CER and health care transformation that the plan is coordinated across the ARRA CER funding allocated to the Secretary, AHRQ, and NIH. Furthermore, the Secretary should develop the plan as part of HHS's broader portfolio of ARRA investments, not as a stand-alone program.

The following steps are needed to finalize the CER operational strategy prior to the July 30 deadline mandated by Congress:

- Integrate IOM and Council strategic recommendations and leverage the investments, resources, and capacity identified through the initial inventory effort.
- Provide more specific recommendations for a portfolio of initiatives for all of HHS' ARRA funds within the framework outlined in the report.
- Define metrics for evaluating success.
- Coordinate the submission of the CER ARRA spend plans to ensure that they cover the gaps in CER outlined in this report, and that the agencies' investments leverage the strengths of each agency and are complementary, not duplicative.
- Maintain transparency and engagement with the public.

The Federal Government will need to continue its work to coordinate CER investments and assure Americans that these resources are being invested wisely. ARRA required that the Council submit an annual report regarding its activities and recommendations concerning the infrastructure needs, organizational expenditures, and opportunities for better coordination of comparative effectiveness research by relevant Federal departments and agencies. The first annual report will likely be in June 2010.

Comparative effectiveness research is being considered as a key piece of health reform, and the Federal Government must demonstrate its capability to coordinate that investment, achieve impact, and measure the results. This report outlines the priorities and path forward. Now the Federal Government must make progress and deliver results for the American people.

APPENDICES

Appendix A. LISTENING SESSIONS AND PUBLIC COMMENT SUMMARY

Overview

In order to help guide the Council's thinking on the definition, framework, and priorities for comparative effectiveness research (CER), the Council held three listening sessions (April 14 in Washington, D.C.; May 13 in Chicago; and June 10 in Washington, D.C.) and solicited public comments through the hhs.gov/recovery Web site. The response was strong:

- 92 panelists testified
- Greater than 300 individuals and organizations submitted comments

A breakdown of the responses by stakeholder type reveals that over half of the comments came from three groups: health care associations; academia and think tanks; and consumer, community-based, and advocacy organizations. Additional comments were received from patients, providers, payers, hospital and health systems, pharmaceutical companies, foundations, public health entities, and private sector companies in the health care field. One U.S. Senator also submitted comments.

More important than the diversity of respondents is what individuals and organizations had to say. Respondents provided a wide range of opinions and offered recommendations on everything from stakeholder participation to how to prioritize investments in CER to specific areas of focus to knowledge transfer and dissemination.

Without question, the public input has been extremely valuable in informing the Council's deliberations; many of the major thematic threads that run through the public comments are reflected in the Council's strategic framework, focus, and recommendations for priorities for OS CER funds. Of particular value to the Council was the opportunity to engage with panelists at the listening sessions. This back-and-forth discussion enabled Council members to refine their ideas and solicit further feedback.

Before summarizing the key themes, it is useful to note that several respondents honed in directly on the reason why investments in comparative effectiveness research are important—CER matters. For example, one respondent talked about the value of and application of CER for everyone's health and health care. Another talked about how funding is crucial to reforming the practice of medicine to increase the quality, safety, cost benefits, and real world effectiveness of what providers bring to patients on a daily basis.

One theme that wove through many of the comments was the need for greater collaboration among Federal agencies, among organizations at the Federal, state and local levels, and between the public and private sectors. One respondent stated that because expertise on comparative effectiveness research resides in both public and private entities, every effort should be made to encourage public-private collaboration in the design, conduct, analysis, and reporting of CER. This discussion about collaboration dovetailed with the question of stakeholder input, including the need to ensure that patients have a defined and central role in the CER process.

Key Themes

Some respondents recommended targeted research topics; these ranged from testing the total effects of medication on the frail elderly, to testing the efficacy of a diet to treat children with seizures, to informing prescribing physicians on a wide range of what does and doesn't work well for patients with various complex conditions.

Most of the comments, however, fell into several broad categories—prioritizing the agenda, infrastructure development, research methodology and conduct, care delivery, knowledge transfer, cost, and health disparities and personalized medicine. A number of key themes and specific comments are summarized below.

Prioritizing the Agenda

A number of respondents tried to step back and look broadly at the question of how to prioritize the agenda for comparative effectiveness research and what criteria should guide decision-making in this arena. An overarching theme that echoed through many of these comments was the need to think big and look system-wide. One respondent stated that CER that is localized to a single disease may be less of a priority than questions that cross over diseases. Another talked about the need for CER to be undertaken for quality, efficiency, effectiveness, and other appropriate dimensions for health care delivery systems along the entire spectrum of systems integration, adding that the spectrum should include integrated delivery systems, multi-specialty group practices, single-specialty groups, "virtual" groups, and small medical practices.

A number of recommended areas of focus emerged. Many respondents talked about focusing on areas of major clinical significance and the greatest impact on health care delivery, including chronic conditions. One respondent specifically noted that CER on chronic diseases should focus on all relevant health care services, including medical and surgical procedures, diagnostics, and medical devices. Another respondent said that more attention is needed in the areas of post-acute and long-term care. Still others talked about the need for comparative effectiveness research on emergency care processes, and CER to evaluate regional differences in trauma care. A few people talked about studying the role of alternative treatments, including homeopathic treatments for chronic and acute disease states. Several respondents also talked about looking at conditions with the greatest impact on morbidity, and a few about doing research on conditions with the greatest impact on cost.

A few respondents discussed the need to ensure that the priorities of state and local jurisdictions be given consideration in evaluating various CER strategies. For example, one participant noted that many jurisdictions have on-going investigative agendas designed to improve program effectiveness that can be considerably amplified by Federal support, adding that such efforts would extend beyond purely clinical protocols to include the evaluation of public health, community-based, and behavioral strategies that may enhance the effectiveness of public programs.

One respondent suggested that significant resources be devoted to population-level interventions as well as patient-level effectiveness. Another respondent talked about the need for comparative effectiveness priority research areas to include critical cross-cutting research questions and cited

several examples (clinical decision-making, human-technology partnership, team coordination and continuity of care).

In addition, respondents talked about the need for Federal investments in CER to focus on health disparities and understudied sub-groups. Many of the respondents who addressed this topic talked about under-sampling of minorities in clinical trials and stressed the need for research that looks at the impact of various treatments on specific sub-groups, including women, minorities, people in rural communities, persons with disabilities, and children.

Infrastructure Development

A number of respondents honed in on the need to scale up the capacity to do comparative effectiveness research. As one respondent put it: "All healthcare reform proposals are predicated on the presumption that a robust and well-developed quality infrastructure exists. However, this is not uniformly the case."

Infrastructure capacity, as framed by the public comments, incorporates three components: human and scientific capital, organizational capacity, and data capacity.

Regarding human and scientific capital, respondents said that investments are greatly needed to enhance the skills, supply, and diversity of the research work force. One respondent pointed specifically to a dearth of researchers focused on mental health and substance abuse and treatment. Another respondent talked specifically about the need to increase the number of Hispanic health professional researchers, and suggested that HHS target Hispanic health professional, students, residents, and graduate students interested in serving in their communities.

Regarding organizational capacity, many of the comments focused on building capacity at the regional and local level. For example, one respondent talked about the role that health improvement collaboratives and chartered value exchanges can play in maintaining patient registries and other databases, and about using the information for performance reporting. A second respondent talked about the role that more community organizations could play in helping to address racial and ethnic health disparities were they to have the appropriate infrastructure and capacity.

The third critical subset of infrastructure development is data. A number of respondents talked about the need for both better data and access to data for comparative effectiveness research and decision-making. They urged the Council to access as much available data as possible, including clinical trials data, electronic health record systems, health care claims systems, administrative data, and Federal health data (including data from Medicare and Medicaid and that collected by the Veterans Health Administration). Respondents also talked about the need to invest in a coordinated effort to link public and private sector databases, as well as the need for standardized data available from the point of patient care.

Several respondents also talked about the value of registries, and the need to link data sets in order to provide valuable sources of data to examine appropriate use, effectiveness of care, cost of care, value-based health care, and other criteria. Another respondent stressed the need for

research that involves collaboration in different data environments and research that explores the use of different types of electronic health care data.

Research Methodology and Conduct

How should CER be undertaken? This is another theme that ran through many of the comments. Those who tackled this question addressed key issues that ranged from the enterprise level to guidance on study design. At the broader level, one respondent talked about the need for a broad Federal CER enterprise that spans treatment, prevention, promotion, and health-determinant interventions designed for both people and populations. Another respondent recommended adopting value of information principles and tools to prioritize CER investments on those studies where there is a greater likelihood that the research will lead to changes in practice. A third person spoke about the opportunity to fund research into "the science of CER" to build a foundation for this work.

Others talked about the scope of CER, noting that much of the research is conducted in single settings of care. One respondent, for example, noted that this poses a challenge for "generalizability," and suggested that many of the questions that remain unanswered relate to uncommon conditions or outcomes that have proven challenging to study. He recommended the use of multi-center research networks to address this issue.

Looking more closely at study design, one respondent noted that CER should continue to use a variety of study designs to generate evidence about the comparative effectiveness, comparative safety, and cost effectiveness of medical interventions. A second respondent talked about the limitations of randomized clinical trials, suggesting that the Council should also consider designs that are more common for evaluating comprehensive population-focused interventions, such as observational cross-sectional studies, quasi-experimental designs, and time series analyses. Another respondent stressed that clinical trial design and CER infrastructures must accommodate the goal of addressing health disparities. Another respondent pointed out that comparative effectiveness can at times be determined by assessing technology and using quantitative metrics rather than via an expensive and sometimes-lengthy clinical trial. A fourth respondent talked about the need to include utilization of laboratory services in order to effectively compare treatments and outcomes for major chronic disease cost drivers.

Several respondents also addressed the need for greater transparency throughout the process. They talked about the critical importance of transparency for reducing bias and rebuilding trust, and they recommended that researchers show results prior to adjustments as well as adjusted results. Respondents who tackled the issue of transparency also talked about the need to disclose in detail the methods and metrics used in any research. One respondent stressed that patients and providers need to know all the inputs that go into a research analysis so that they can weigh the costs, safety, and quality issues appropriately in each instance.

A corollary to transparency is addressing potential conflicts of interest. Respondents talked about the need to develop a strong and clear policy for conflicts of interest in both research and publishing, and suggested that funding decisions for CER should favor researchers and institutions that are focused on the public interest and do not have current conflicts. They also talked about the need for 100-percent disclosure and transparency at the outset of all conflicts by

individual researchers and institutions. One respondent specifically said that the ARRA expenditures on CER offer an opportunity to move to a platform where research funding is completely independent of other sources of funds in order to get to research that is independent, unbiased, untainted, and neither methodologically flawed nor influenced by industry.

Care Delivery

Several respondents pointed out that care delivery is critical, and that investments in CER are needed to look at how the health care delivery system should be organized and the best models for delivering care to patients. One respondent recommended that the Council invest in research that looks at optimal practice models for delivering patient care along with strategies for using information technology and clinical decision support tools to implement research findings into clinical practice. Another respondent suggested that CER is needed to look at the organization, design, and management of patient care. A third said that CER should focus on medical delivery systems and operations, resulting in information that can be leveraged to foster better clinical and cost outcomes.

Much of the discussion on care delivery was focused on people with one or more chronic conditions (e.g., diabetes). One respondent, for example, talked about the need for CER studies that compare current, more traditional models of chronic care delivery with team-based, patient-centers models that include patient education and self-care. Another respondent emphasized the need to focus research on the impact of non-medical services (e.g., providing housing) on cost-effective and clinical outcomes for chronically medically ill populations. A third person talked about CER around the role of support services (e.g., case management) in the health outcomes of people with HIV/AIDS; a fourth, about the need for CER on crisis residential services as an alternative to psychiatric hospitalization. Yet another respondent talked about the need to study the cost-effectiveness of community health worker interventions.

One respondent talked about the need to study care models that integrate primary and tertiary care. Another respondent suggested that there was a need for research into how to deliver care in a way that helps patients get the care they need, adhere to proposed treatment regimes, and prevent subsequent untoward effects of chronic diseases. Regarding adherence to treatment regimes, one respondent specifically noted that patient compliance is a seldom-accounted-for variable in CER, and he talked about the value of electronic verification devices to track compliance. Another respondent talked about the need to compare palliative care models to understand which processes of care and specific program interventions and models are the most effective.

One respondent noted that much of the literature on the impact of electronic medical records is anecdotal, and he expressed concern that people are considering the value of electronic health records without understanding the totality of what an effective system does for health care delivery. As a result, he urged that research be done to evaluate the comparative effectiveness of different types of EHR-mediated interventions. A second respondent likewise talked about the needs for research on how health information technology and EHR exchanges can be used to create more robust data sources and to help evaluate comparative effectiveness issues across a broader range of settings.

Knowledge Transfer

A number of respondents pointed out that all the data is meaningless if the information is not disseminated effectively. One respondent, for example, stressed that knowledge translation research must not be overlooked, while another respondent pointed out that both research and dissemination of research findings are essential to realizing the quality improvements and returns-on-investment that are integral to the success of comparative effectiveness research.

While respondents had different recommendations for how to approach knowledge transfer, there was a consensus that this work is critical. One respondent noted that the evidence base that is developed around clinical comparative effectiveness offers a substantial opportunity to improve value in health care if the information is disseminated and applied by physicians and patients. Others talked about the need to identify what approaches and incentives to dissemination and adoption are most effective (and under what circumstances), and when dissemination should target change at the organizational level, the community level, or the individual level. One respondent talked about cultural competence and health literacy research, and the need for both in order to change behaviors and improve lifestyles.

One respondent noted that while technology (including electronic health records) is one avenue for dissemination, other effective dissemination and translation techniques are also needed. She noted that while many strategies have been used to enhance the rate and extent of adoption of evidence-based best practices (including clinical guidelines, continuing education for health care professionals, patient education tools, and academic detailing), the approaches have not been well studied and the results are variable.

One respondent suggested that an independent body be established to disseminate comparative effectiveness research findings; others took the approach that everyone—including providers, payers, consumers, and employers—has a role to play in disseminating research results. Another respondent suggested creating a national citizens' advisory board to help HHS better understand the perspectives and values of the general public when designing and disseminating CER. Another respondent talked about the need not only to provide the evidence base for best disease prevention, health promotion, and/or clinical interventions, but also to look at how these findings can be implemented in "real-world, complex organizational settings."

Cost

Two distinct opinions about cost emerged: (1) that it should be a factor in comparative effectiveness research or (2) that it has no place in the discussion.

Those opposed to factoring cost into CER expressed concern that too often people put cost into a separate silo and make decisions without regard to efficacy, and they suggested that a focus on costs could lead to limiting access and benefits. For example, one respondent said that comparative effectiveness research should not be focused on looking for cheaper treatments, and it should not be the basis for coverage decisions. Another talked about the fear that CER results might impact physician reimbursement rates. Several respondents also expressed concern that CER could be used to restrict access to care, to deny coverage, or to reduce payments for interventions, thus undermining physician/patient decision-making and limiting patient access to treatment options.

On the flip side, other respondents felt equally strongly that cost was an integral component of informed decision-making. For example, one respondent said that information about costs enables understanding not only of the direct differences in terms of clinical outcomes but also of the value of interventions and whether they represent an efficient use of resources. Another respondent suggested that, if costs are not considered, the tradeoff in terms of lost health benefits would be too steep. Others stressed that a wide range of stakeholders—including employers, policymakers, and state and local public health departments—have said that they need cost information to make decisions.

Health Disparities and Personalized Medicine

Several respondents spoke about the related topics of the need to address health disparities within CER and support for the growth of personalized medicine. Inclusion of and attention to underrepresented sub-groups was spoken of as a means to address the problem of disparities in care. Others spoke of the importance of fostering the application of personalized medicine.

Respondents cited the need for more CER in the areas of preventive care, pediatric care and children's health, behavioral health interventions, addiction, mental disorders, and suicide prevention. One respondent pointed out that CER is needed to understand the cost and quality implications to the overall health system of continuing to under-treat conditions in systems that are siloed and distinct from mainstream health and health care. Another respondent specifically noted that the aim of personalized medicine and the mapping of the human genome is to achieve disease interventions much earlier (ideally at the point of preventing the disease from ever taking hold, he said).

One respondent stressed that CER must be mobilized to improve the health outcomes of various racial and ethnic minorities in order to close the gap that exists between the health status of some minority populations and other Americans. Others warned about relying on small, narrowly focused studies, suggesting that understanding and addressing health disparities requires a broader approach; conversely, respondents also cautioned against "one-size-fits-all" approaches that could decrease access to treatments. One respondent specifically talked about the need for research that examines health intervention outcomes across the lifespan, and for different minority and gender groups, in order to understand the effectiveness of interventions within and between population groups.

Several people talked about the need to design studies that appropriately include minority populations (see also *Prioritizing the Agenda*, above). For example, one respondent said that the design of studies must reflect the diversity of patient populations, including racial and ethnic diversity, and must communicate results in ways that reflect the differences in individual patient needs. Another respondent stressed that clinical trial design and CER infrastructures must accommodate the goal of addressing health disparities. There was also discussion more broadly about the need to build the infrastructure to address health disparities relating to people of color.

One respondent pointed to the dichotomy between studying populations and the promise of personalized medicine, asking: How can CER at a broad population level be balanced with the

goals and rapid scientific advancements in the area of personalized and stratified medicine in order to encourage the development of targeted therapies for sub-groups?

One respondent talking about personalized medicine recommended that CER studies include the evaluation of approaches to health care delivery and care management that foster the effective application of personalized medicine.

Appendix B: SUMMARY OF THE COUNCIL'S MEETINGS AND DELIBERATIONS

The following contains a summary of the Council's deliberations as they unfolded once the Council was officially convened.

April 10, 2009

The Council was presented with background information on comparative effectiveness research and briefed on CER activity at AHRQ, NIH, and VA. The Council also discussed the scope of their work and objectives.

Next, the Council began discussion of the components of the definition of CER and potential criteria for prioritization. The Council also discussed how CER and data infrastructure for CER might be categorized. Finally, the Council reviewed the timeline and discussed plan for listening sessions, including the first listening session on April 14, 2009.

April 22, 2009

The Council met to discuss what they had heard at the April 14 listening session. Members identified several key themes, including the need to outline a clear, well-delineated definition of comparative effectiveness research. They noted that participants had also talked about the need to prioritize methodology, and the fact that CER should be inclusive of all components of medical care.

Council members also noted that they had heard, loud and clear, that the Council's governance and processes must be transparent, and that the Council must incorporate input from all stakeholders to gain credibility and build trust.

Other themes that emerged from the listening session include the need to focus on patients and outcomes; the importance of incorporating diverse populations and multiple research methods; and the need for investments in infrastructure. Regarding the focus on patients and outcomes, Council members noted that participants had talked about the importance of considering patient input from the start and the fact that the results must be framed and disseminated in ways that are relevant to patients and providers. Regarding diverse populations, Council members observed that there was discussion about the need to include sub-groups with multiple chronic conditions, and the need more broadly to make CER relevant to sub-groups. Members also noted that participants had talked about the need to use a multitude of different research methodologies (not just randomized clinical trials), and to look at the Department of Veterans Affairs' experience using registries.

Regarding infrastructure, Council members observed that participants had stressed there was a need to expand, improve, and build on existing information and registries, and that perhaps this investment could lay the foundation for distributed data networks with the capability to answer many future CER questions. Members also noted that there had been discussion about the need to make data monitoring easier and more routine.

Finally, Council members talked about how they could tweak the listening session format to allow for a more robust conversation with participants.

May 1, 2009

The Council looked at the timetable for its work and the due dates for its key deliverable. The Report to Congress is due June 30, and the preliminary timetable builds in time for HHS and OMB clearance, comments, and suggested edits. The Council also briefly discussed the upcoming second listening session, slated for May 13 in Chicago.

Next, the Council briefly discussed the process for compiling the CER and data infrastructure inventories, and agreed that members would identify primary contacts in their division or agency who can work with the contractor to drive that process.

The Council's next goal was to arrive at consensus on a draft definition of comparative effectiveness research, prioritization criteria, and a categorization framework for CER. Once complete, the Council agreed to post the draft language on the hhs.gov/recovery Web site and to solicit public feedback.

To begin that work, the Council tackled the draft definition. There was considerable discussion about what the definition of CER should be. Members expressed the belief that the definition needed to be inclusive of the multiple stakeholders in the health care arena, including communities, and they also looked at what types of interventions should be called out. The Council ultimately came to consensus that they wanted a definition that was broad-based and inclusive, but that was not so detailed as to inadvertently narrow the scope of comparative effectiveness research.

The Council next turned its attention to the prioritization criteria. Before doing so, however, the Council first wrestled with the question of whether the criteria should be focused broadly or more narrowly targeted to provide guidance to the Office of the Secretary in allocating its Recovery Act funds. The Council generally felt that the criteria should be broad enough to allow the Council to make recommendations on overall funding and funding criteria.

Next, Council members discussed how to prioritize the CER criteria, including whether impact should be listed first, with feasibility and scientific merit second. One person spoke out about the need to keep the criterion on diverse populations and patient sub-groups within the top five. There was also discussion about whether knowledge gap was a criterion, or whether it should perhaps be wrapped into the criterion on impact.

The Council also looked at several potential frameworks for comparative effectiveness research, including categorization by type of CER investment, by patient sub-groups, by condition, and by type of intervention. The aim of developing a framework was to help categorize current CER activity and to identify gaps for potential future investments in CER. Council members also discussed CER centers, and agreed that Recovery Act funding could be used to support this work. One member suggested that the Council, at a future date, should discuss how to coordinate interest in CER centers across agencies.

Finally, the Council received a presentation on enhancing the inclusion of minority and other underserved populations in comparative effectiveness research. As a result, the Council agreed to establish a small workgroup co-led by NIH, AHRQ, the HHS Office of Minority Health, and the HHS Office on Disability. The workgroup will have two key tasks: (1) to develop recommendations for the inclusion of minority and other underrepresented populations in the expanded comparative effectiveness research agenda, and (2) to receive input from non-Federal groups on targeted actions.

May 8, 2009

The Council reviewed a revised definition of comparative effectiveness research and agreed to post the definition on the hhs.gov/recovery Web site on or about May 15.

Next, the Council resumed its discussion of the prioritization criteria. There was considerable discussion about whether "scientific rigor and validity" needed to be included in the threshold minimal criteria, with some members saying that it was implicit (and something already being done) and others expressing concerned about including a yes/no component to the threshold minimal criteria. The consensus of the Council was that scientific rigor and validity be included as part of a concept statement.

The Council then looked at a first draft outline of the Report to Congress. It included (1) Introduction, (2) Objectives, (3) Definition and Criteria, (4) Framework for CER, (5) Current CER and CER data infrastructure, (6) Recommendations for Priorities for OS CER Funds, and (7) Longer-term Vision and Opportunities.

Council members discussed a number of items that they believed needed to either be included or called out in the report, including concrete examples of what CER is and why it matters as well as a discussion about the full range of CER activities (and not just randomized clinical trials). There was also discussion about having a stand-alone section on high level priorities; the need to call out the roll of public/private partnerships; including a sub-section on the need for CER data to be synthesized and operationalized, along with some mechanisms for achieving this outcome; and the need to add language on sub-groups. Members also agreed to add a new section, Summary of the Listening Sessions, and to include a high-level Executive Summary.

Next, the Council began its discussion of CER priorities. To frame their discussion, members looked at four categories: primary research, dissemination of results, data infrastructure, and cross-cutting coordinated investments. One member asked, "What are the gaps that no one else can fill?" The Council agreed to continue its discussion at its next meeting.

May 22, 2009

The Council opened its meeting with a debrief from the May 13 listening session in Chicago. Members said they found the meeting both useful and exciting, and cited some themes they had heard that particularly struck them. These included the need to study chronic diseases (and to include sex, ethnicity, and race in the analysis); the idea of using theoretical models to assess how to approach a study (and to ensure the information is useable); the inclusion of mental health as a priority area; the importance of CER on pediatric populations; the importance of CER on prevention; and the need for training, and for starting to build the pipeline early.

The Council then briefly addressed next steps on the Report to Congress, including the fact that certain members would be assigned to draft specific sections of the report.

Next, the Council resumed its discussion of CER priorities where it had left off: looking at research, dissemination, data infrastructure, and cross-cutting investments. There was general consensus that OS funds should focus primarily on the latter three areas (as AHRQ and NIH are likely to make CER investments in research); there was also discussion about how to frame the priorities, including whether they should be framed around the type of CER investment or around types of diseases (e.g., people with multiple chronic illnesses, or people with disabilities and chronic illnesses). There was also specific discussion about the need to improve dissemination of research results—and a related topic, impacting practice. "If we just talk about dissemination," said one Council member, "we won't get anywhere. We need to look at the best methods for impacting practice."

There was also discussion around the question of how the Council should think about structuring its Report to Congress. At issue was whether the report should focus primarily on guidance to the HHS Secretary on how to allocate the $400 million in OS funds. In addition, the Council discussed the research time horizon, and whether ARRA monies could be used to fund projects that will have a time horizon longer than two years. One member suggested that one way to think about the question was to reframe it and ask, "Can we think about creating research centers that will be great resources into the future?"

Council members also stressed the need for the Council to address in its report the *process* for its deliberations and its recommendations, including making clear that CER investments are weighted to public health needs and responsive to the needs of decision makers. Council members suggested that some of the discussion about impacting practice might be linked to the discussion about data infrastructure investments.

May 29, 2009

The Council honed in on the details of the strategic framework for comparative effectiveness research, and the fact that it represents a comprehensive, coordinated approach to Federal investment in CER priorities that is intended to support immediate decisions for investments in CER priorities and to provide a comprehensive basis for longer-term CER investment decisions.

The Council discussed a framework that includes four major categories of activity (research, human and scientific capital, data and research infrastructure, and translation and adoption). The framework is designed to allow for investments within a single category or to cross-cut priority

themes. The Council agreed upon the categories. The Council's next step will be to determine the recommended mix among the major activities for OS funds.

The Council agreed to post on the hhs.gov/recovery Web site a copy of the broad framework diagram as well as a more detailed version to inform the public and to seek feedback on the strategic framework.

Next, the Council looked at some examples of the types of investments that might be made in the areas of infrastructure and translation and adoption. The idea of the discussion was to enable members to think about what types of projects might address gaps and further the CER enterprise.

The Council also looked briefly at an updated draft outline for the Report to Congress, and then members heard a presentation on three possible categories for investments in disability comparative effectiveness research.

June 5, 2009

The Council discussed the first draft of the Report to Congress. There was consensus that the Executive Summary needed to better frame the conversation around the value of CER to inform patients, clinicians, and other stakeholders. There was also discussion about setting out, early in the body of the report, why CER matters and how it matters to each stakeholder group. In addition, the Council agreed to add an additional appendix that contains a summary of its meetings and deliberations.

Next, the Council took up its recommendations for priorities. The discussion revolved around four key issues: the balance in spending priorities among the major activities versus cross-cutting themes; the distribution of spend priorities across the four major activities; what themes should be prioritized (and what the distribution of spend priorities should be across those themes); and whether the overall distribution makes sense vis-à-vis the prioritization criteria.

Regarding the distribution of spend priorities across the four major activities, Council members generally agreed that the majority of funding (e.g. 60 percent) should be spent on activities rather than themes. At the same time, there were lingering questions about the need to identify research gaps, implementation gaps, or both.

Regarding the distribution of spend priorities across the four major activities, the Council supported a breakdown that focuses the bulk of the funding in the areas of infrastructure (e.g. 60 percent) and translation (e.g. 20 percent). Members noted that there is a unique opportunity with ARRA funds to make significant investments in infrastructure.

Regarding potential priorities, members looked at draft lists of both priority populations and types of interventions. On the populations side, one Council member said that all of the proposed priority populations share in common that they have not traditionally been enrolled in clinical trials. There was also discussion about the need to include veterans as well as people with co-occurrence of mental health disorders along with physical comorbidities. On the interventions side, there was some discussion about the inclusion of delivery systems, and that

CER on delivery systems offers an opportunity to look at promising practices and how they might be scaled up and disseminated.

Finally, the Council was divided as to whether the bulk of OS funds should be used primarily for investments in populations or in interventions—or whether they should be equally important priorities.

June 12, 2009

The Council debriefed on what was heard in the third listening session. This generated enhancement to the common themes and some new information to be incorporated. The Council then revised the definition, threshold and prioritization criteria, and strategic framework based on the feedback from the session and the feedback received online. The Council then further discussed priority recommendations and the Report to Congress. The Council suggested edits for the Report prior to it going into clearance the next week.

Appendix C. PRELIMINARY DATA INFRASTRUCTURE AND CER BY CONDITION

The following is a preliminary inventory of examples of CER data infrastructure and CER by condition.

Person-Level Health Care Research Databases from First Inventory

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
US Federal							
Healthcare Cost and Utilization Project (HCUP)	AHRQ	Hospital information system	—	All	Y	N	Y
HIV Cost and Services Utilization Study (HCSUS)	AHRQ	Surevy & records abatsraction	2,864	HIV	Y	N	Y
AIDS Cost and Services Utilization Study (ACSUS)	AHRQ	Hospital information system	1,900	AIDS	Y	N	Y
National Vital Statistics	CDC	Surveillance program/registry data	—	All	n/a	N	N

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
National Vital Statistics—Natality	CDC	Surveillance program/registry data	4 million	All	n/a	N	Y
National Health Interview Survey	CDC	Survey	87,000	All	n/a	Y	Y
National Health and Nutrition Examination Survey	CDC	Survey	5,000	All	n/a	Y	Y
National Ambulatory Medical Care Survey	CDC	Survey and records abstraction	n/a	All	N	Y	Y
National Hospital Ambulatory Medical Care Survey	CDC	Survey and records abstraction	n/a	All	N	Y	Y
National Hospital Discharge Survey	CDC	Survey and records abstraction	n/a	All	N	Y	Y
National Nursing Home Survey	CDC	Survey and records abstraction	13,507	All	N	Y	Y
National Home and Hospice Care Survey	CDC	Survey and records abstraction	9,416	All	N	Y	Y
Chronic Condition Data Warehouse	CMS	Administrative claims database, enrollment data, health assessment data, prescription drug event data	45 million	All	Y	Y	Y
Hospice Standard Analytical File (Hospice SAF)	CMS	Administrative claims database	—	All	Y	Y	?

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
Medicaid Statistical Information System Personal Summary File (MSIS Personal Summary File)	CMS	Administrative claims database, EMR/EHR system	—	All	Y	Y	Y
National Claims History (NCH) 100% Nearline Fil	CMS	Administrative claims database	—	All	Y	Y	?
MEDPAR Claims Data	CMS	Administrative claims database	—	All	Y	Y	Y
MMA Part D Claims Data	CMS	Pharmacy claims database	25 million	All	Y	Y	Y
Sentinel System	FDA	Surveillance program/registry data	N/A	n/a	N	Y	N
SEER (Surveillance Epidemiology and End Results)	NCI	Surveillance program/registry data	11.4 million	Cancer	Y	N	Y
SEER-Medicare database	NCI, CMS	Administrative claims database, Surveillance program/registry data	3.3 million	Cancer	Y	Y	N
Cancer Research Network (CRN)	NCI, AHRQ	Administrative claims database, EMR/EHR system	—	Cancer	Y	Y	N
Computerized Patient Record System (CPRS)	VA	EMR/EHR system	4.2 million	All	Y	N	N
Diabetes Epidemi-ology Cohort	VA	Surveillance program/registry data	> 4,800	Diabetes	Y	Y	Y

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
Hepatitis C Registry	VA	Surveillance program/registry data	>60 K	Hepatitis C	Y	N	Y
Immunological Case Registry	VA	Surveillance program/registry data	>15 K	HIV	Y	N	Y
Dementia Registry	VA	Surveillance program/registry data	>150 K	Dementia	Y	N	N
National Surgery Quality Improvement Program	VA	Surveillance program/registry data	>1 Million	All major surgery	Y	Y	Y
Scientific Registry of Transplant Recipients (SRTR)	HRSA	Transplant registry and outcomes data		Organ specific	Y	Y	Y
Pediatric Emergency Care Applied Research Network (PECARN) CDMCC*	HRSA	Emergency medical services for children	800,000 + patients	Emergency Services to Children	Y	Y	Y
AIDS Drug Assistance Program (ADAP)	HRSA	Care Program Registry Data	—	HIV/AIDS	Y	Y	N
US Private Sector							
National Oncologic PET Registry (NOPR)	Academy of Molecular Imaging	Intervention program data	>100,000	Cancer	Y	Y	?
Cerner Health Facts Database	Cerner	EMR/EHR system	—	All	Y	Y	Y
GE Centricity	GE	EMR/EHR system	10 million	All	Y	N	Y

* Central Data Management and Coordinating Center

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
Ingenix Research Data Mart (RDM) Database	Ingenix	Administrative claims database	>39 million	All	Y	Y	Y
Premier Perspective Data Warehouse	Premier	Administrative claims database	—	All	Y	Y	Y
MarketScan Data Warehouse	Thomson-Reuters	EMR/EHR system	—	All	Y	N	N
International Databases							
General Practice Research Database (GPRD)	NHS (UK)	EMR/EHR system	> 3.6 million	All	Y	Y	Y
NHS Care Records Service (CRS)	NHS (UK)	EMR/EHR system	2 million	All	Y	N	Y
The Health Improvement Network (THIN)	INPS and EPIC (UK)	EMR/EHR system	—	All	Y	Y	Y

Priority Diseases/Conditions in CER

Priority Diseases/Conditions	AHRQ (n=178)	NIH (n=513)	DoD (n=26)	VHA (n=106)	Total (n=823)
Arthritis and non-traumatic joint disorders	6%	1%	0%	3%	**2%**
Cancer	10%	7%	23%	7%	**8%**
Cardiovascular disease, including stroke and hypertension	20%	10%	4%	23%	**13%**
Dementia, including Alzheimer's Disease	1%	1%	0%	3%	**1%**
Depression and other mental health disorders	8%	16%	8%	18%	**14%**
Developmental delays, attention-deficit hyperactivity disorder, and autism	4%	1%	0%	0%	**1%**
Diabetes mellitus	11%	11%	0%	8%	**10%**
Functional limitations and disability	8%	4%	15%	7%	**5%**

Infectious diseases including HIV/AIDS	3%	11%	0%	6%	**8%**
Obesity	1%	3%	0%	2%	**3%**
Peptic ulcer disease and dyspepsia	0%	0%	0%	0%	**0%**
Pregnancy, including preterm birth	1%	4%	0%	0%	**2%**
Pulmonary disease/asthma	5%	3%	0%	4%	**3%**
Substance abuse	2%	19%	0%	9%	**14%**
Other	20%	11%	50%	12%	**14%**

*Studies focusing on patients with more than one priority disease or condition are counted in applicable rows..
**NIH 2008 plus NIH multi-year sample.

Appendix D. COUNCIL LIST AND STAFF SUPPORT

1. Carolyn Clancy, MD	AHRQ
2. Peter Delaney, PhD, LCSW-C	SAMHSA
3. Ezekiel Emanuel, MD, PhD	OMB
4. Jesse Goodman, MD, MPH	FDA
5. Garth Graham, MD, MPH	Office of Minority Health
6. Anne Haddix, PhD	CDC
7. Deborah Hopson, PhD, RN	HRSA
8. David Hunt, MD	ONC
9. Michael Kilpatrick, MD	Dept of Defense
10. Joel Kupersmith, MD	Dept of VA
11. Michael Marge, Ed.D.	Office of Disability
12. Elizabeth Nabel, MD	NIH
13. James Scanlon, PhD	ASPE
14. Neera Tanden, JD	Office of the Secretary
15. Tom Valuck, MD, MHSA, JD	CMS

Executive Director: Patrick Conway, MD, MSc
Deputy Executive Director: Cecilia Rivera Casale, PhD

Alternates to the Council participating: Kelley Brix, Margaret Cary, Rosaly Correa-de-Araujo (replaced Michael Marge on Council June 12th), Elisabeth Handley, Lynn Hudson, Michael Millman

Contributors to Council and Report: Kate Goodrich, Lauren Hunt, John Poelman, Daria Steigman, Caroline Taplin, Jordan VanLare.

Appendix E. THE AMERICAN RECOVERY AND REINVESTMENT ACT STATUTE RELATED TO CER AND COUNCIL

Appropriations

For an additional amount for 'Healthcare Research and Quality' to carry out titles III and IX of the Public Health Service Act, part A of title XI of the Social Security Act, and section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, $700,000,000 for comparative effectiveness research: *Provided,* That of the amount appropriated in this paragraph, $400,000,000 shall be transferred to the Office of the Director of the National Institutes of Health ('Office of the Director') to conduct or support comparative effectiveness research under section 301 and title IV of the Public Health Service Act: *Provided further,* That funds transferred to the Office of the Director may be transferred to the Institutes and Centers of the National Institutes of Health and to the Common Fund established under section 402A(c)(1) of the Public Health Service Act: *Provided further,* That this transfer authority is in addition to any other transfer authority available to the National Institutes of Health: *Provided further,* That within the amount available in this paragraph for the Agency for Healthcare Research and Quality, not more than 1 percent shall be made available for additional full-time equivalents.

In addition, $400,000,000 shall be available for comparative effectiveness research to be allocated at the discretion of the Secretary of Health and Human Services ('Secretary'): *Provided,* That the funding appropriated in this paragraph shall be used to accelerate the development and dissemination of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that: (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions; and (2) encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data: *Provided further,* That the Secretary shall enter into a contract with the Institute of Medicine, for which no more than $1,500,000 shall be made available from funds provided in this paragraph, to produce and submit a report to the Congress and the Secretary by not later than June 30, 2009, that includes recommendations on the national priorities for comparative effectiveness research to be conducted or supported with the funds provided in this paragraph and that considers input from stakeholders: *Provided further,* That the Secretary shall consider any recommendations of the Federal Coordinating Council for Comparative Effectiveness Research established by section 804 of this Act and any recommendations included in the Institute of Medicine report pursuant to the preceding proviso in designating activities to receive funds provided in this paragraph and may make grants and contracts with appropriate entities, which may include agencies within the Department of Health and Human Services and other governmental agencies, as well as private sector entities, that have demonstrated experience and capacity to achieve the goals of comparative effectiveness research: *Provided further,* That the Secretary shall publish information on grants and contracts awarded with the funds provided under this heading within a reasonable time of the obligation of funds for such grants and contracts and shall disseminate research findings from such grants and contracts to clinicians, patients, and the general public, as appropriate: *Provided further,* That, to the extent feasible, the Secretary shall ensure that the recipients of the funds provided by this paragraph offer an opportunity for public comment on

the research: *Provided further,* That research conducted with funds appropriated under this paragraph shall be consistent with Departmental policies relating to the inclusion of women and minorities in research: *Provided further,* That the Secretary shall provide the Committees on Appropriations of the House of Representatives and the Senate, the Committee on Energy and Commerce and the Committee on Ways and Means of the House of Representatives, and the Committee on Health, Education, Labor, and Pensions and the Committee on Finance of the Senate with an annual report on the research conducted or supported through the funds provided under this heading: *Provided further,* That the Secretary, jointly with the Directors of the Agency for Healthcare Research and Quality and the National Institutes of Health, shall provide the Committees on Appropriations of the House of Representatives and the Senate a fiscal year 2009 operating plan for the funds appropriated under this heading prior to making any Federal obligations of such funds in fiscal year 2009, but not later than July 30, 2009, and a fiscal year 2010 operating plan for such funds prior to making any Federal obligations of such funds in fiscal year 2010, but not later than November 1, 2009, that detail the type of research being conducted or supported, including the priority conditions addressed; and specify the allocation of resources within the Department of Health and Human Services: *Provided further,* That the Secretary, jointly with the Directors of the Agency for Healthcare Research and Quality and the National Institutes of Health, shall provide to the Committees on Appropriations of the House of Representatives and the Senate a report on the actual obligations, expenditures, and unobligated balances for each activity funded under this heading not later than November 1, 2009, and every 6 months thereafter as long as funding provided under this heading is available for obligation or expenditure.

Sec. 804. Federal Coordinating Council for Comparative Effectiveness Research

(a) ESTABLISHMENT— There is hereby established a Federal Coordinating Council for Comparative Effectiveness Research (in this section referred to as the 'Council').

(b) PURPOSE— The Council shall foster optimum coordination of comparative effectiveness and related health services research conducted or supported by relevant Federal departments and agencies, with the goal of reducing duplicative efforts and encouraging coordinated and complementary use of resources.

(c) DUTIES— The Council shall—

(1) assist the offices and agencies of the Federal Government, including the Departments of Health and Human Services, Veterans Affairs, and Defense, and other Federal departments or agencies, to coordinate the conduct or support of comparative effectiveness and related health services research; and

(2) advise the President and Congress on—
(A) strategies with respect to the infrastructure needs of comparative effectiveness research within the Federal Government; and
(B) organizational expenditures for comparative effectiveness research by relevant Federal departments and agencies.

(d) MEMBERSHIP—

(1) NUMBER AND APPOINTMENT— The Council shall be composed of not more than 15 members, all of whom are senior Federal officers or employees with responsibility for health-related programs, appointed by the President, acting through the Secretary of Health and Human Services (in this section referred to as the 'Secretary'). Members shall first be appointed to the Council not later than 30 days after the date of the enactment of this Act.

(2) MEMBERS—
(A) IN GENERAL— The members of the Council shall include one senior officer or employee from each of the following agencies:
(i) The Agency for Healthcare Research and Quality.
(ii) The Centers for Medicare and Medicaid Services.
(iii) The National Institutes of Health.
(iv) The Office of the National Coordinator for Health Information Technology.
(v) The Food and Drug Administration.
(vi) The Veterans Health Administration within the Department of Veterans Affairs.
(vii) The office within the Department of Defense responsible for management of the Department of Defense Military Health Care System.
(B) QUALIFICATIONS— At least half of the members of the Council shall be physicians or other experts with clinical expertise.
(3) CHAIRMAN; VICE CHAIRMAN— The Secretary shall serve as Chairman of the Council and shall designate a member to serve as Vice Chairman.

(e) REPORTS—

(1) INITIAL REPORT— Not later than June 30, 2009, the Council shall submit to the President and the Congress a report containing information describing current Federal activities on comparative effectiveness research and recommendations for such research conducted or supported from funds made available for allotment by the Secretary for comparative effectiveness research in this Act.

(2) ANNUAL REPORT— The Council shall submit to the President and Congress an annual report regarding its activities and recommendations concerning the infrastructure needs, organizational expenditures and opportunities for better coordination of comparative effectiveness research by relevant Federal departments and agencies.

(f) STAFFING; SUPPORT— From funds made available for allotment by the Secretary for comparative effectiveness research in this Act, the Secretary shall make available not more than 1 percent to the Council for staff and administrative support.

(g) RULES OF CONSTRUCTION—

(1) COVERAGE— Nothing in this section shall be construed to permit the Council to mandate coverage, reimbursement, or other policies for any public or private payer.

(2) REPORTS AND RECOMMENDATIONS— None of the reports submitted under this section or recommendations made by the Council shall be construed as mandates or clinical guidelines for payment, coverage, or treatment.

Title VIII—Departments of Labor, Health And Human Services, and Education, and Related Agencies

200 INDEPENDENCE AVENUE, S.W.

WASHINGTON, DC 20201

Federal Coordinating Council for Comparative Effectiveness Research

April 10, 2009

Agenda

1. Comparative Effectiveness Research Background and Draft Initial Framework
2. Comparative Effectiveness Research Current Portfolios and Future Plans for CER
   - AHRQ
   - NIH
   - VA
3. Listening Session Format
4. Other

Statute Description of Comparative Effectiveness Research

- Statute states that CER funding “shall be used to accelerate the development and dissemination of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that:
  - (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions;
  - (2) encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data.”

Potential Interventions in CER

- Interventions include at least the following:
  - Medications
  - Devices
  - Surgery or procedures
  - Behavioral interventions (e.g. for smoking)
  - System interventions (e.g. discharge process A vs. B from hospital) – included in CER? how to scope?
- Reasonable to compare across categories at times (e.g. medication vs. surgery or behavioral intervention vs. medication)

Outcomes

- Examples of Potential Outcomes
  - Clinical endpoints (e.g. mortality and morbidity, adverse events)
  - Surrogate endpoints (HbA1c, biomarkers)
  - Functional endpoints (e.g. quality of life, symptom severity, and patient satisfaction)
  - Economic outcomes (e.g. cost effectiveness)

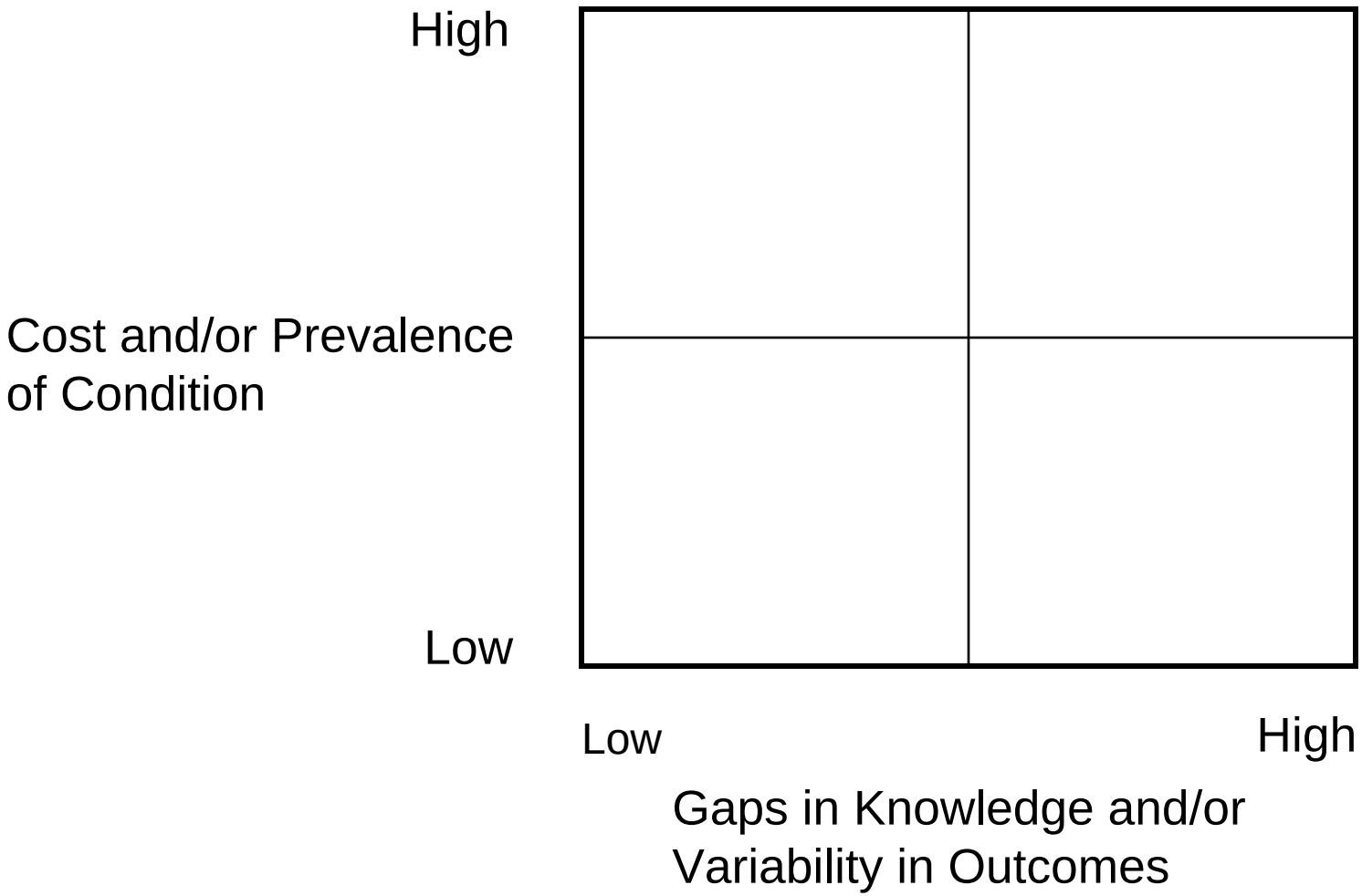
Objectives for FCC

1. Foster optimum coordination of comparative effectiveness research conducted or supported by relevant Federal departments.
2. Formulate recommendations for how best to spend the $400 million appropriated to Office of Secretary as part of Report to Congress.

Need:

1. Framework for setting priorities
2. Categorization scheme for current CER and to help evaluate future investments to fill gaps

Draft Simplified Framework for Priority Setting



Other Criteria for Priority Setting

- Responsiveness to expressed needs / preferences of patients and clinicians
- Potential to evaluate comparative effectiveness in diverse patient populations and patient segments
- Cost of investment versus potential importance of finding(s)
- Balance of short term and longer term projects
- Other?

Types of CER Investment

- Consistent with ARRA
  1. Comparative Effectiveness Research
  2. Investment in electronic clinical data networks and registries that support evaluation of outcomes and comparative effectiveness
- Strategic issue for Council: Balance of investment in specific research projects vs. investment in electronic data resources

Major Categories of CER

Category	Advantage	Disadvantage
Evidence Synthesis/Systematic Reviews	• Least time and cost • Summary of Evidence	• Need substantial primary evidence to summarize
Observational Studies - Administrative data - Electronic clinical data	• Less time and cost than RCT's • Evaluate large volumes of data so easier to investigate patient subgroups (e.g. elderly Hispanic patients) • "Real world" effectiveness	• Potential for bias in results
Randomized Controlled Trials	• No selection bias so most definitive results	• Sometimes exclude or fail to have sufficient numbers to inform decisions for patient sub-populations • Expensive and long time

Example Potential Priority Investments and Time Needed for Results

Potential Investment	Relative Time Horizon
R1: Evidence Synthesis	Short
R2: Observational studies	Medium
R3: RCT	Long
I1: Linked administrative data	Short
I2: Electronic Clinical Data Networks	Medium - Long
I3: Patient Registries (e.g. transplant, patients with devices)	Medium

Major Strategic Issues

- Balance of investments (e.g. research vs. data infrastructure; and type of investment within categories)
- Scheme for Priority Setting
- Coordination of OS funding with other investments in HHS and across Federal govt
- Other?

Agenda for Listening Session

1.	Background on Council and CER	2:00 – 2:15
2.	Panel 1 (10 panelists for 3 min comment each, Council questions)	2:15 – 3:00
3.	Panel 2 (10 panelists for 3 min comment each, Council questions)	3:00 – 3:45
4.	Panel 3 (10 panelists for 3 min comment each, Council questions)	3:45 – 4:30
5.	Time for Open Public Comment	4:30 – 4:55
6.	Closing	4:55 – 5:00

Format for Listening Session

- Room 800 Humphrey, overflow in Great Hall, 14th 2-5pm
- Webcast and call-in capability
- 3 panels of 10 pre-selected panelists and then open public comment (volunteer at registration desk on day of session – 7 open slots max)
- Press table set-up
- Council will ask questions of panelists (not vice-versa)
- Strict 3 minute time limit for each public comment and then 15 minutes or less of Council questions
- Will assign primary 5 Council member group to be responsible for asking questions of each panel but any Council member can ask a question

Reminder Activities and Timeline

Activity	Description	Date
Opening Meeting	Introductions, Scope, Objectives Discussion	March 27th
1st Working meeting	Presentation and Discussion of NIH, AHRQ, and VA CER work-to-date and future plans	April 10th
1st Listening Session (DC)	3 hours to hear external stakeholders	April 14th
2nd Working meeting	Outline of Report to Congress Beginning presentation and discussion of proposals for OS funds from CER workgroup	May 1st
2nd Listening Session (DC)	2-3 hours to hear external stakeholders	May 6th
3rd Listening Session (midwest - chicago?)	3 hours (core of interested Council members could travel) Could coordinate with Regional/State Office (e.g. Governor)	May 14th
3rd Working Meeting	Discussion of Inventory of current CER within strategic framework Presentation of proposals for OS funds	May 29th
4th Working Meeting	Final presentation of proposals Begin Discussion of Proposals and funding priority recommendations	June 12th
5th Working Meeting	Review and Suggest Edits for Draft Report to Congress on Current CER and recommendations for OS funding of CER	June 26th
Finalize Report	Final Draft of Report to Congress	Week of June 30th
Monthly Meetings	Updates on Progress and further Recommendations on CER funding and priorities. Review overall funding within strategic framework to ensure addressing gaps	July 10th and ongoing

Federal Coordinating Council for Comparative Effectiveness Research

July 17, 2009

Agenda

1. Debrief on FCC Report Release
2. Debrief on IOM report and cross-walk process
3. Discussion of process for OS funding and combined CER operational plan
4. Other?

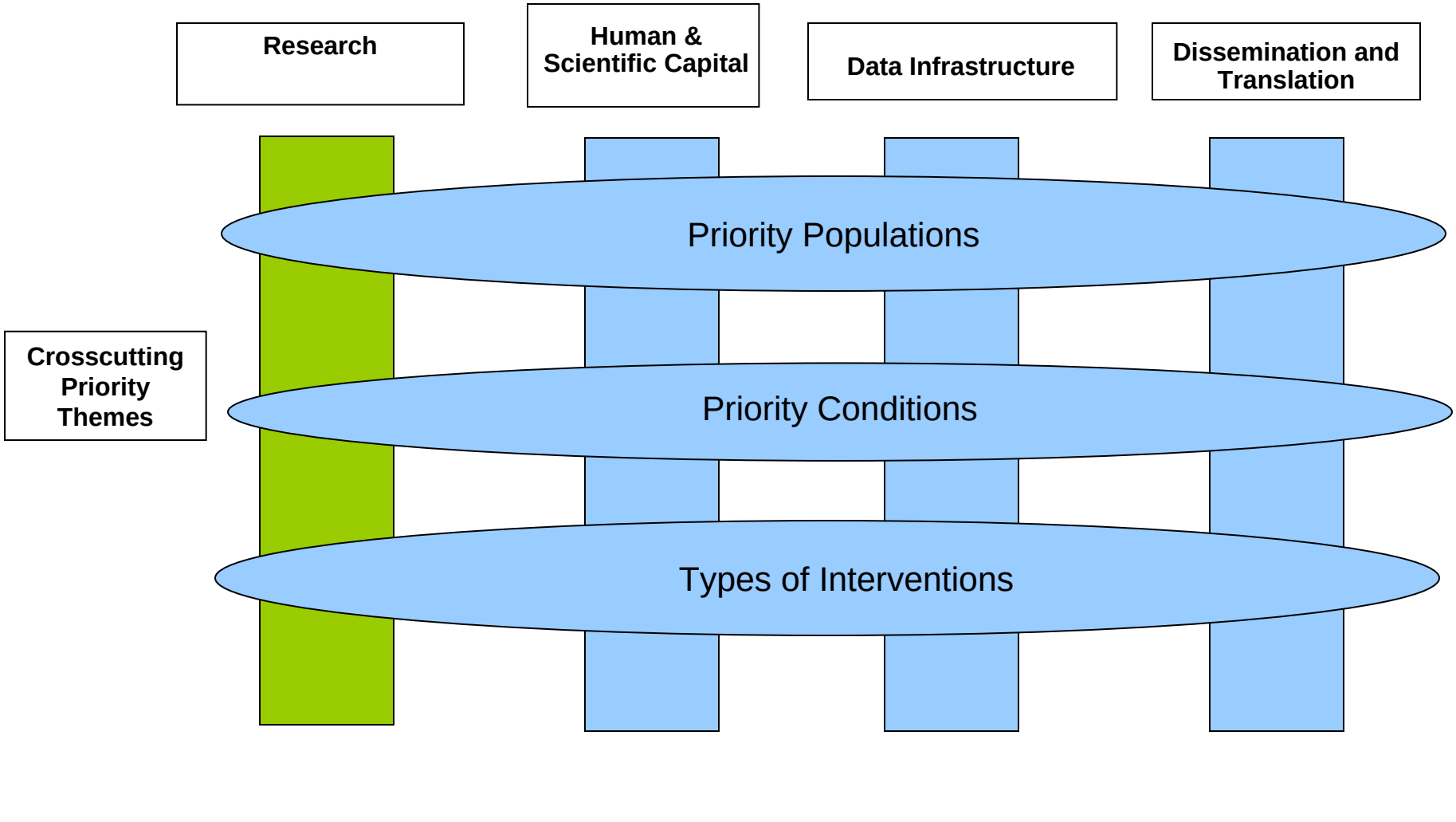
Debrief FCC report

- Hill briefings on June 29th
- Press call on June 29th
- Reaction thus far positive
- Thoughts?

Debrief IOM report

- Reactions from IOM briefing?

IOM Recommendations for CER



IOM General Recommendations

- Prioritization of CER topics should be sustained and continuous and informed by topic briefs, such as current state of research
- Obtain public input and maintain transparent processes
- Regular reporting of activities and recommendations is necessary
- HHS Secretary should establish a mechanism—such as a coordinating advisory body – to strategize, organize, monitor, and evaluate the implementation and impact of the CER program.
- CER program should involve consumers, patients, and caregivers
- Devote sufficient resources to methods
- Develop and promote robust data and information systems
- Develop and support the CER workforce
- Promote rapid adoption of CER findings and conduct research to identify the most effective strategies for dissemination

IOM cross-walk

- We are in process of cross-walking IOM 100 research topics to completed, ongoing, and planned CER (most of these fall under purview of AHRQ and NIH)

OS funding

- Based on Council recommendations, IOM report, public input, and work done within HHS by ARRA CER workgroup, portfolio of funding options presented for Secretary's consideration
- These directly link to strategic framework and Council recommendations

Combined CER plan

- Secretary is to submit combined operational plan for $1.1 billion of CER funding by July 30th to Congress
- Draft of this plan is under review within the Department and then will be shared with OMB
- Once finalized, it will also be shared with Council

Council Next Steps

- ARRA stated that, “The Council shall submit to the President and Congress an annual report regarding its activities and recommendations concerning the infrastructure needs, organizational expenditures and opportunities for better coordination of comparative effectiveness research by relevant Federal departments and agencies.”
- This will require intermittent updates and meetings. The frequency of updates remains to be determined.
- Potential next meeting, likely in August, would be presentation of ARRA CER funding

Comparative Effectiveness (CE)

Kalipso Chalkidou
Gerard Anderson

What Will Be Different?

- How do other countries operate their comparative effectiveness programs?
- What are the differences between the US CE program and CE programs in other countries?
- What are the important lessons for the US?

Counties We Studied

- Australia
- Brazil
- Canada
- **England and Wales**
- France
- **Germany**
- Russian Federation
- South Korea
- Sweden
- Turkey

Focus In Other Countries

- Drugs and devices
- Surgical interventions
- Diagnostic tests
- NOT
  - Public health interventions (UK only)
  - Alternative delivery systems

US Focus still to be determined
-Some delegation to IOM

CE entities were established as part of a comprehensive strategy and are integrated into the overall system

- US will provide money to AHRQ, NIH and Office of Secretary
- No new entities created aside from Federal Coordinating Council
- Not clear how it will be integrated into overall system aside from the fact that it cannot “ mandate coverage or reimbursement” or “clinical guidelines”

Examples of System Integration

- Australia part of drug coverage process
- UK part of larger reform initiative preceding increased spending on health care
- Germany part of initiative to revise health insurance system
- France part of effort to rationalize spending, improve quality, promote adoption of cost effectiveness

Australia - Pharmaceuticals Benefits Scheme (PBS)

- First established to provide drugs to WWI veterans returning to Australia
- Formulary established(1953)
  - Determination solely on clinical need
- Senior public servants initially ran program and made all decisions
- Membership expanded to include clinical and academic communities in 1970s
- Costs first included in 1993
- PBS is independent committee – clinicians, epidemiologists, economists and consumers
- Reports to Ministry of Health

NICE Responsibilities

- Part of UK's National Health Service
- Determines what does and does not work
- Best value for money
- Reduce unreasonable geographic variation

Separate entities conduct:

- Horizon scanning for emerging technologies
- NHS research on clinical and cost effectiveness of health technologies

Institute for Quality and Efficiency in Healthcare (IQWiG) Responsibilities

- Part of German social insurance system
- Cost and clinical effectiveness as conditions for evaluation coverage and reimbursement of coverage
- Identify quality standards

Reports to Joint Federal Committee (providers and sickness funds) that actually make the decisions

French High Health Authority

- Established 2005
- Independent public body
- Responsibilities
  - Provider accreditation
  - Guideline development
  - Definition of basic benefit package
  - Promotion of information technology

Independence from government is common

- Even when part of government no direct line reporting responsibilities
  - Australia evolved from part of bureaucracy to greater independence over time
  - Most countries the CE entity is a separate government agency, private entity, or public private partnership
- US government activity
  - Federal coordinating council all civil servants

Organizational Models

- Typically independent agency
- US will be part of DHHS

National Institute For Health and Clinical Excellence

- NICE is special health authority
  - 12 Directors
  - Independent appointments commission
  - Partners council (stakeholders)
  - Funding from NHS
  - Many groups participate in process

Germany

- IQWiG is advisory to Joint Federal Committee (providers and insurers)
  - 30 member board of trustees
  - Scientific board
  - Steering Committee

Some CE entities set standards while others only recommend

- Set Standard
  - NICE – mandatory for primary care and hospital trusts (technologies)
- Recommend Standard
  - IQWiG – recommended to Joint Federal Committee (JFC) – JFC must explain if disagree with IQWiG recommendations

US – Strictly advisory

Political Endorsement is Critical

- All the CE entities have made numerous controversial decisions
- Politicians come under tremendous pressure to overturn decisions
- In many countries this has happened only once because the politicians recognized that they would be brought into every decision and it would eviscerate the CE entity
- In US remember demise of OTA and near death of AHRQ

Size and Budget

- Generally small
  - NICE - 270 staff and $70 million
  - IQWiG – 90 staff and $30 million
- Most of cost is in other entities that conduct the research
- US much larger
  - $1.1 billion
  - Staff uncertain

Appeals Process

- Necessary if standards are binding
- NICE appeals on 3 grounds
  - Perverse – no reasonable person
  - Violation of NICE rules
  - Exceeds scope of responsibilities
  - 1/3 decisions appealed and ½ upheld

US -If not binding then no appeals process necessary

Methods

- Topic selection
- Assessment
  - Evidence synthesis
  - Prospective evidence generation
- Appraisal
- Costs

Topic Selection

- NICE:
  - Independent horizon scanning; web-based suggestions; field consultants; regular evidence review by IS teams
  - Multi stakeholder panels led by top UK clinician
  - Final ratification by SoS; gradually passed on to NICE to speed up process
- IQWIG: JFC as the main client, refers topics – IQWIG decides “patient information” topics
- PBS: (mostly) manufacturer driven – all new drugs

Collecting the evidence

- NICE: mostly outsourced: universities and professional groups
- IQWIG: in-house and outsourced
- HAS: mostly in-house
- PBS: outsourced

Types of evidence

- Mostly evidence synthesis
- NICE:
  - methods research; prospective trials
  - no hierarchies of evidence (RCTs vs. claims data)
  - Conditional coverage and risk sharing
- IQWIG:
  - strong focus on published RCTs– Cochrane model
- OHTAC (Canada): prospective studies

Prospective studies: NICE

- Direct Access: 10-15 PCTs; registries and prospective cohorts between 2007-2008 from Research Recommendations (NIHR)
- Only In Research: conditional coverage to reduce uncertainty whist allowing access (NIHR; industry)
- Risk Sharing/Patient Access Schemes: pricing deals
- Value-based pricing
- More to come: diagnostics; surgery

Who pays for bringing the evidence together?

- IQWIG: providers/insurers
- NICE: tax-payers/manufacturers
- PBS: tax-payers/manufacturers
- OHTAC: tax-payers
- US : taxpayers

Appraisal

- Separate from evidence synthesis or generation in all agencies
- Multi stakeholder process
- Inclusiveness; transparency; regular review and contestability (appeal)
- Value judgments included to different extents and in different ways
  - CDR: strict threshold
  - NICE: additional considerations but high "fudge factor"
  - IQWIG: no threshold

Costs

- PBS (1993), NICE (1999), IQWIG (2008), HAS (2008)
- PBS, NICE: Reference Case: CEA, preferred outcome measure (QALY)
- IQWIG: efficiency frontier…
- Value for money matters! – cost-minimization not enough…

Dissemination

- PBS recommends to health ministry but a no is a no but a yes is a maybe
- IQWiG recommends to JFC
- NICE
  - Included in benefit package
  - Local health authorities must cover
  - May soon be part of rights of British citizens

US - unclear

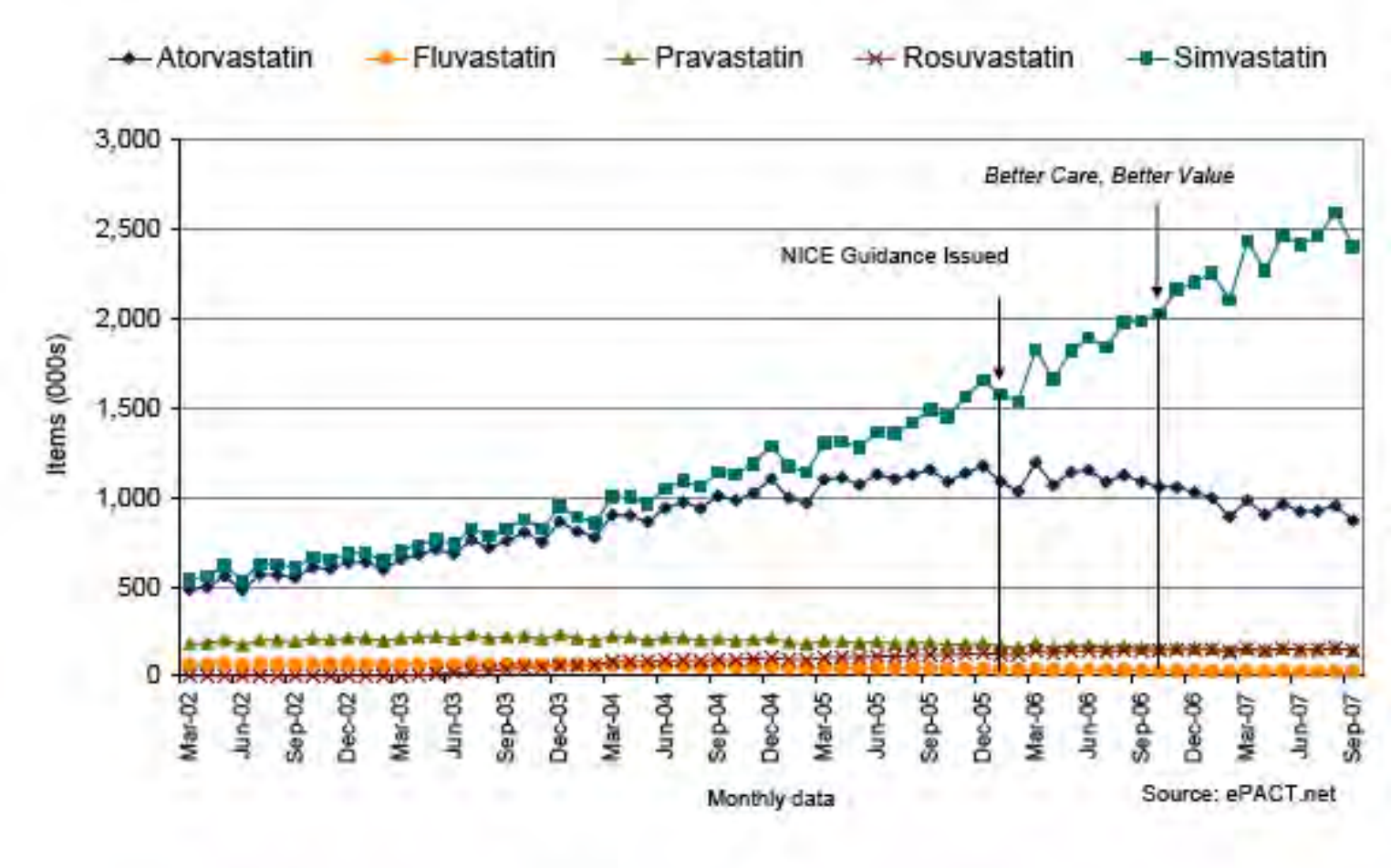
Impact

- Very difficult to assess – many moving parts
- None of them were designed to be cost saving
- NICE has shown some impact on compliance and reducing regional variation
- IQWiG greater transparency by sickness funds

Evidence of impact at NICE

- 50% increase in uptake of cancer drugs reviewed by NICE over 18 months; more than halving of variation in uptake across England
- 95% of hospitals compliant with NICE guidance in 2007; up from 84% in 2005
- 96% of academics working on NICE appraisals reported their work has an impact compared to 60% in control group

Statin uptake



Impact

How will we know if the CE entity in the US is working?

Federal Coordinating Council for Comparative Effectiveness Research

Report to the President and the Congress

June 30, 2009

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EXECUTIVE SUMMARY

Across the United States, clinicians and patients confront important health care decisions without adequate information. What is the best pain management regimen for disabling arthritis in an elderly African-American woman with heart disease? For neurologically impaired children with special health care needs, what care coordination approach is most effective at preventing hospital readmissions? What treatments are most beneficial for patients with depression who have other medical illnesses? Can physicians tailor therapy to specific groups of patients using their history or special diagnostic tests? What interventions work best to prevent obesity or tobacco use? Unfortunately, the answer to these types of comparative, patient-centered questions in health care is often, "We don't really know."

Thousands of health care decisions are made daily; patient-centered comparative effectiveness research focuses on filling gaps in evidence needed by clinicians and patients to make informed decisions. Physicians and other clinicians see patients every day with common ailments, and they sometimes are unsure of the best treatment because limited or no evidence comparing treatment options for the condition exists. As a result, patients seen by different clinicians may get different treatments and unknowingly be receiving less effective care. Patients and their caregivers search in vain on the Internet or elsewhere for evidence to help guide their decisions. They often fail to find this information either because it does not exist or because it has never been collected and synthesized to inform patients and/or their caregivers in patient-friendly language. When they do find information, it may be informed by marketing objectives, not the best evidence.[1]

Due to astonishing achievements in biomedical science, clinicians and patients often have a plethora of choices when making decisions about diagnosis, treatment, and prevention, but it is frequently unclear which therapeutic choice works best for whom, when, and in what circumstances. The purpose of comparative effectiveness research (CER) is to provide information that helps clinicians and patients choose which option best fits an individual patient's needs and preferences. It also can inform the health choices of those Americans who cannot or choose not to access the health care system.[2] Clinicians and patients need to know not only that a treatment works on average but also which interventions work best for specific types of patients (e.g. the elderly, racial and ethnic minorities). Policy makers and public health professionals need to know what approaches work to address the prevention needs of those Americans who do not access health care. This information is essential to translating new discoveries into better health outcomes for Americans, accelerating the application of beneficial innovations, and delivering the right treatment to the right patient at the right time.

Examples of successful CER include summaries of evidence from the Agency for Healthcare Research and Quality (AHRQ) on numerous conditions, such as prostate cancer and osteoporosis, as well as the National Institutes of Health (NIH) diabetes prevention trial that demonstrated lifestyle change was superior to metformin and placebo in preventing onset of type 2 diabetes. Additionally, the Veterans Affairs (VA) COURAGE trial demonstrated that patients treated with optimal medical therapy alone did just as well as patients who received percutaneous coronary intervention plus medical therapy in preventing heart attack and death. These exemplars show the power of CER to inform patient and clinician decisions and improve health outcomes.

Patients increasingly and appropriately want to take responsibility for their care. Therefore we have a responsibility to provide comparative information to enable informed decision-making. This patient-

[1] Lee TH, Brennan TA. N Engl J Med. 2002;346:529-531.
[2] Green LA, et al. N Engl J Med. 2001; 344:2021-5.

centered, pragmatic, "real world" research is a fundamental requirement for improving care for all Americans.

Comparative effectiveness differs from efficacy research because it is ultimately applicable to real-world needs and decisions faced by patients, clinicians, and other decision makers. In efficacy research, such as a drug trial for the U.S. Food and Drug Administration (FDA) approval, the question is typically whether the treatment is efficacious under ideal, rather than real-world, settings. The results of such studies are therefore not necessarily generalizable to any given patient or situation. But what patients and clinicians often need to know in practice is which treatment is the best choice for a particular patient. In this way, comparative effectiveness is much more patient-centered. Comparative effectiveness has even been called patient-centered health research or patient-centered outcomes research to illustrate its focus on patient needs.

The American Recovery and Reinvestment Act (ARRA) provided $1.1 billion for comparative effectiveness research. The Act allocated $400 million to the Office of the Secretary in the U.S. Department of Health and Human Services (HHS), $400 million to the National Institutes of Health (NIH), and $300 million to the HHS Agency for Healthcare Research and Quality. It also established the Federal Coordinating Council for Comparative Effectiveness Research (the Council) to foster optimum coordination of CER conducted or supported by Federal departments and agencies. Furthermore, the legislation indicated that "the Council shall submit to the President and the Congress a report containing information describing current Federal activities on comparative effectiveness research and recommendations for such research conducted or supported from funds made available for allotment by the Secretary for comparative effectiveness research in this Act" by June 30, 2009.

Transparent, Open Process Seeking Public Input

From the outset, the Council recognized the importance of establishing a transparent, collaborative process for making recommendations and sought the input of the American people on this important topic. The Council held three public listening sessions, two in the District of Columbia and one in Chicago. The Council also received comments for two months on its public Web site. Importantly, the open process allowed the Council to hear from hundreds of diverse stakeholders who represent views across the spectrum. Many patients expressed their need for this type of research; one of the most emotional and moving testimonies came from the mother of a child with a seizure disorder in Chicago who had struggled to find the best treatment for her child. A physician from the American Board of Orthopedics summarized many physicians' testimony by saying, "developing high quality, objective information will improve informed patient choice, shared decision-making, and the clinical effectiveness of physician treatment recommendations." The Council heard repeatedly at the listening sessions that the Federal Government must use this investment to lay the foundation for informing decisions and improving the quality of health care. In addition, the Council posted interim working documents for feedback, including the definition of CER, the prioritization criteria, and the strategic framework, and modified these based on the feedback. Comments from the listening sessions and via the Web site significantly influenced Council discussion and decisions. Indeed, this entire report is influenced by the public input—and Appendix A elaborates on the key themes that ran through the public comments.

Vision

The Council's vision for the investment in comparative effectiveness research focuses on laying the foundation for this type of research to develop and prosper so it can inform decisions by patients and clinicians. This research is critical to transforming our health care system to deliver higher quality and more value to all Americans. The Council specifically focused on recommendations for use of the

Office of Secretary (OS) funds to fill high priority gaps that were less likely to be funded by other organizations and therefore represent unique opportunities for these funds.

Early in the process, the Council set the following objectives consistent with ARRA:

1. Develop a definition, establish prioritization criteria, create a strategic framework, and identify priorities that lay the foundation for CER.

2. Foster optimum coordination of comparative effectiveness research conducted or supported by relevant Federal departments.

3. Formulate recommendations for investing the $400 million appropriated to the HHS Office of Secretary as part of this Report to Congress.

Definition and Criteria
The Council first established a definition, building on previous definitions, for comparative effectiveness research:

> Comparative effectiveness research is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in "real world" settings. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.
>
> - To provide this information, comparative effectiveness research must assess a comprehensive array of health-related outcomes for diverse patient populations and sub-groups.
> - Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
> - This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and actively disseminate the results.

The Council needed explicit criteria to make recommendations for priorities. Therefore, the Council's second step was to establish minimum threshold criteria that must be met and prioritization criteria.

Minimum Threshold Criteria (i.e. must meet these to be considered):

- Included within statutory limits of Recovery Act and the Council's definition of CER
- Potential to inform decision-making by patients, clinicians, or other stakeholders
- Responsiveness to expressed needs of patients, clinicians, or other stakeholders
- Feasibility of research topic (including time necessary for research)

The prioritization criteria for scientifically meritorious research and investments are:

- Potential impact (based on prevalence of condition, burden of disease, variability in outcomes, costs, potential for increased patient benefit or decreased harm)

- Potential to evaluate comparative effectiveness in diverse populations and patient sub-groups and engage communities in research
- Uncertainty within the clinical and public health communities regarding management decisions and variability in practice
- Addresses need or gap unlikely to be addressed through other organizations
- Potential for multiplicative effect (e.g. lays foundation for future CER such as data infrastructure and methods development and training, or generates additional investment outside government)

Importance of Priority Populations and Patient Sub-Groups
One important consideration for comparative effectiveness research is addressing the needs of priority populations and sub-groups, i.e., those often underrepresented in research. The priority populations specifically include, but are not limited to, racial and ethnic minorities, persons with disabilities, children, the elderly, and patients with multiple chronic conditions. These groups have been traditionally under-represented in medical research.

In addition, comparative effectiveness should complement the trend in medicine to develop personalized medicine—the ability to customize a drug and dose based on individual patient and disease characteristics. One of the advantages of large comparative effectiveness studies is the power to investigate effects at the sub-group level that often cannot be determined in a randomized trial. This power needs to be harnessed so personalized medicine and comparative effectiveness complement each other.

Strategic Framework
After completing the draft definition and criteria for prioritization of potential CER investments, the Council recognized the need to develop a strategic framework for CER activity and investments to categorize current activity, identify gaps, and inform decisions on high-priority recommendations. This framework represents a comprehensive, coordinated approach to CER priorities. It is intended to support immediate decisions for investment in CER priorities and to provide a comprehensive foundation for longer-term strategic decisions on CER priorities and the related infrastructure. At the framework's core is responsiveness to expressed needs for comparative effectiveness research to inform health care decision-making by patients, clinicians, and others in the clinical and public health communities.

Types of CER investments and activities can be grouped into four major categories:

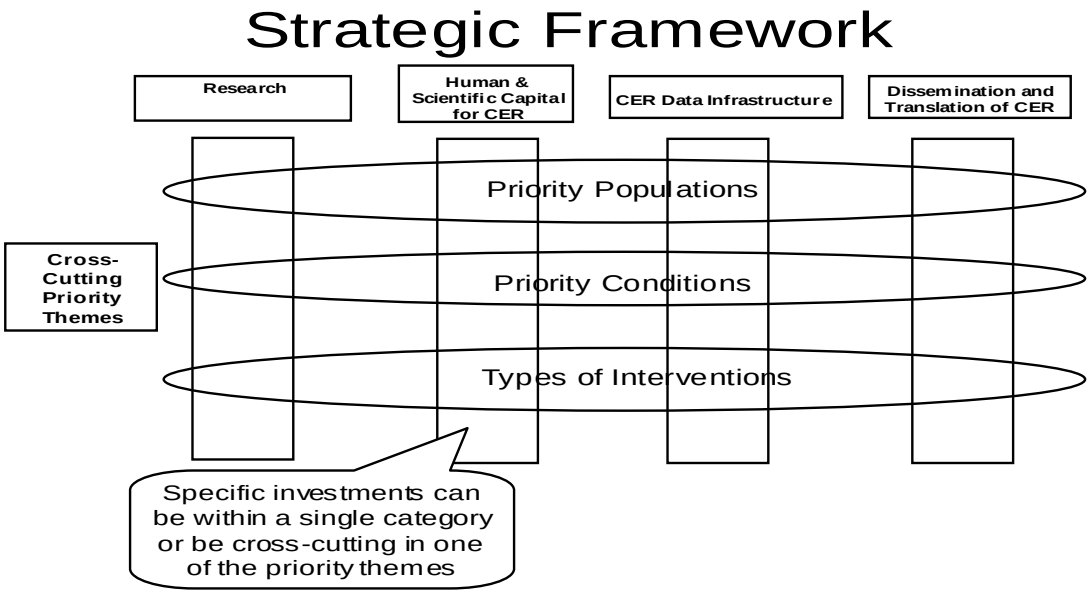
- **Research** (e.g., comparing medicines for a specific condition or discharge process A to discharge process B for readmissions)
- **Human and Scientific Capital** (e.g., training new researchers to conduct CER, developing CER methodology)
- **CER Data Infrastructure** (e.g., developing a distributed practice-based data network, longitudinal linked administrative or Electronic Health Record (EHR) databases, or patient registries)
- **Dissemination and Translation of CER** (e.g., building tools and methods to disseminate CER findings to clinicians and patients and translate CER into practice)

Furthermore, investments or activities related to a specific theme can cut across one or more categories and may include research, human and scientific capital, CER data infrastructure, and/or translation and adoption. These themes could include:

- **Conditions** (e.g., cancer, heart failure)
- **Patient populations** (e.g., elderly, minorities, children, persons with disabilities)
- **Type of intervention** (e.g., devices, behavioral change, delivery system)

Together, these activities and themes make up the "CER Strategic Framework" (Figure A)

Figure A



CER Inventory and Priority-Setting Process

The Council also conducted an inventory of CER and data infrastructure to help identify gaps in the current CER landscape. Maintaining that inventory and ongoing evaluation of government and private sector (where possible) CER investments and programs across these activities and themes is critical to this framework's value for decision-making. The first draft Federal Government inventory of CER and data infrastructure is included in this report, but it is critical to note that evaluation of current activities and the identification of gaps in order to inform priority-setting must be iterative and continue in the future.

As noted above, the Council's priority-setting process was informed by public input, and that input had a substantial influence on how the Council formulated its framework and priorities for CER. CER is an important mechanism to improve health and continued public input is vital for agenda setting.

Priority Recommendations

In developing its recommendations for how to invest the OS ARRA funding of $400 million, the Council sought to respond to patient and physician needs for CER, to balance achieving near-term results with building longer-term opportunities, and to capture the unique value that the Secretary's ARRA funds could play in filling gaps and building the foundation for future CER. The Council recommended that, among the four major activities and three cross-cutting themes in the CER

framework, the primary investment for this funding should be data infrastructure. Data infrastructure could include linking current data sources to enable answering CER questions, development of distributed electronic data networks and patient registries, and partnerships with the private sector.

Secondary areas of investment are dissemination and translation of CER findings, priority populations, and priority types of interventions. The priority populations identified that could be the focus of cross-cutting themes were racial and ethnic minorities, persons with disabilities, persons with multiple chronic conditions (including co-existing mental illness), the elderly, and children. CER will be an important tool to inform decisions for these populations and reduce health disparities. High-priority interventions for OS to consider supporting include medical and assistive devices, procedures/surgery, behavioral change, prevention, and delivery systems. For example, behavioral change and prevention have the potential to decrease obesity, decrease smoking rates, increase adherence to medical therapies, and improve many other factors that determine health. Delivery system interventions, such as comparing different discharge and transitions of care processes on hospital readmissions, community-based care models, or testing the effect of different medical home models on health have substantial potential to drive better health outcomes for patients.

The OS funds may also play a supporting role in research and human and scientific capital. Because the Council anticipates that AHRQ, NIH, and VA will likely continue to play a major role in these essential activities for the CER enterprise, OS funding would likely only fill gaps in these areas.

Longer-Term Outlook and Next Steps
This report and an Institute of Medicine report funded by the Department will inform the priority-setting process for CER-related funding. The most immediate next step will be the development of a specific plan, to be submitted by July 30, 2009, from the Secretary of Health and Human Services for the combined $1.1 billion of ARRA CER funding. In addition, an annual report from the Council is required under the ARRA legislation.

It will be important for this funding both to accomplish short-term successes and to build the foundation for future CER. The CER activity and investments should be coordinated across the Federal Government and avoid duplicative effort. In addition, the funding should complement and link to activities and funding in the private sector to maximize the benefits to the American people.

Clinicians, patients, and other stakeholders greatly need comparative effectiveness research to inform health care decisions. One private citizen unaffiliated with any health care group summarized, “It is more important than ever to engage in robust research on what treatments work and what do not. Doing so empowers doctors and patients, and helps make our practice of medicine more evidence-based.”

This is a unique opportunity to invest in the fundamental building blocks for transformation of health care in the United States to improve the quality and value of health care for all Americans. Physicians and patients deserve the best patient-centered evidence on what works, so Americans can have the highest quality care and achieve the best possible outcomes.

I. INTRODUCTION

The American Recovery and Reinvestment Act of 2009 (ARRA), Pub. L. 111-5, made available to the Department of Health and Human Services $1.1 billion for comparative effectiveness research (CER). Of this amount, $300 million was allocated to the Agency for Healthcare Research and Quality (AHRQ), $400 million to the National Institutes of Health (NIH), and $400 million was allocated to the Office of the Secretary (OS) for disbursement.

These and all Federal agencies distributing ARRA funds must do so in accordance with all nondiscrimination and equal opportunity statutes, regulations, and Executive Orders that apply to the distribution of funds under the Recovery Act. Agencies that grant funds also must ensure that their recipients comply with Title VI of the Civil Rights Act of 1964 (prohibiting race, color, and national origin discrimination), Section 504 of the Rehabilitation Act of 1973 (prohibiting disability discrimination), Title IX of the Education Amendments of 1972 (prohibiting sex discrimination in education and training programs), the Age Discrimination Act of 1975 (prohibiting age discrimination in the provision of services), and a variety of program-specific statues with nondiscrimination requirements.[3]

ARRA provides further guidance on how funds appropriated to the Office of the Secretary are to be allocated:

> … the funding appropriated in this paragraph shall be used to accelerate the development and dissemination of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that: (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions; and (2) encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data.

Section 804 of ARRA authorizes the establishment of the Federal Coordinating Council for Comparative Effectiveness Research (the Council). The Council is composed of senior Federal officials with responsibility for health-related programs. Most of the members are physicians and many have research expertise. The members represent not only the Department of Health and Human Services but also the Department of Veterans Affairs and the Department of Defense. Members of the Council come from a broad range of backgrounds, including the Office of Minority Health, the Office on Disability, community health centers, mental health, HIV and other infectious diseases, prevention, and others. The Council's purpose is to coordinate comparative effectiveness research and related health services research across the Federal Government with the intent of reducing duplication and encouraging the complementary use of resources. The Council is also charged with advising the President and Congress on strategies to address the infrastructure needs for CER within the Federal Government and organizational expenditures for CER by relevant Federal Departments and agencies.

[3] Memorandum from the Acting Assistant Attorney General for Civil Rights. 4 March 2009

The 15-member Council was announced by HHS via website on March 19, 2009, and has been meeting regularly since then.[4] One of the Council's responsibilities is to submit to the President and Congress an initial report describing current Federal activities on comparative effectiveness research and recommendations for CER conducted or otherwise supported from the $400 million made available for CER to be allocated by the Secretary. This report meets that requirement.

Rationale for Comparative Effectiveness Research

When patients ask clinicians about the evidence supporting one treatment choice, diagnostic plan, or prevention modality over another, the answer too often is that the evidence is unclear. Even when evidence exists, it is often from a trial that may not apply to the specific patient and/or situation under consideration, such as an elderly African-American woman with multiple comorbidities. When specific evidence is lacking, clinicians have to rely on their clinical experience to make the best treatment decisions possible. Nevertheless, these decisions can result in less than optimal, and sometimes inappropriate, treatment choices.

Due largely to government and scientific leadership accompanied by astonishing achievements in biomedical science, clinicians and patients often have a plethora of choices when making decisions about diagnosis, treatment, and prevention. Total investment in health services research, which includes CER, accounts for only 1.5 percent of medical research expenditures.[5] The Recovery Act greatly increased funding for CER and the prominence and important of such research. The purpose of CER is to provide information that helps clinicians and patients choose which option best fits an individual patient's needs and preferences. The amazing biomedical discoveries made in the United States to date can now support CER to routinely compare commonly used therapies or test which interventions work best for particular patients. This information is essential to translate new discoveries into better health outcomes for Americans.[6] We must generate this knowledge to be able to deliver the right treatment to the right patient at the right time. Patients increasingly and appropriately want to take responsibility for their care; therefore, we have an obligation to provide the comparative information that enables informed decisions.

No standardized Federal definition of comparative effectiveness research existed prior to the Council's definition. However, several government entities had developed individual definitions for CER. For example, the Congressional Budget Office has described comparative effectiveness research as "rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients." The Institute of Medicine refers to comparative effectiveness as "the extent to which a specific intervention, procedure, regimen, or service does what it is intended to do when it is used under real world circumstances." The Council's definition builds on these concepts and highlights key aspects of the ARRA CER provisions. The Council defined CER broadly, asserting that it is patient-centered, "real world" research that can help patients, clinicians, and other decision makers

[4] See Appendix D for Council membership.
[5] Moses III H, Dorsey EK, Matheson DHM, et al. Financial Anatomy of Biomedical Research. JAMA 2005; 294:1333-42
[6] Dougherty, D, Conway PH. The "3 T's" Roadmap to Transform U.S. Health Care: The "How" of High Quality Care. JAMA. 2008 May 21;299(19):2319-21

assess the relative benefits and harms of strategies to prevent, diagnose, treat, manage, or monitor health conditions and the systems in which they are made.[7] This definition will form the foundation of the common Federal definition.

The Department of Health and Human Services' ARRA appropriation for CER is a significant investment. CER and activities that support CER have been undertaken by a wide range of stakeholders both inside and outside the public sector. However, despite diverse activities across the Federal Government,[8] funds exclusively appropriated for CER have until now been funded under authorized by section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 for the Agency for Healthcare Research and Quality, which the Agency makes available for projects through its Effective Health Care Program. Since 2005, Congress has appropriated a total of $125 million for the program, including $50 million for comparative effectiveness in FY 2009.

The ARRA funding reflects the heightened interest in CER among the nation's clinicians, patients, policy makers and researchers and broader recognition of its potential to improve outcomes that matter to patients, including morbidity, mortality, and quality of life. CER has the ability to assess these very patient-centered outcomes in a comprehensive way. Furthermore, patients increasingly play an active role in their health care and expect to be active participants in decisions about their health care. These interests are rooted in the strong desire for better evidence upon which to make clinical and other health-related decisions at a time of heightened focus on the quality and variability of care delivered.

A health system guided by better information about "what works" would have benefits for all who have a stake in the nation's health system. Consumers and patients would develop more confidence that the increasingly complex array of treatments and interventions could be tailored to meet their individual needs; health professionals would have more certainty that their clinical decisions were evidence-based and serving patients well. Consequences of the lack of such information include wide geographic variations in treatments typically received for specific conditions and, with these variations, sizeable differences in related health care spending not accompanied by proportional differences in outcomes.

Noted medical author Dr. Atul Gawande recently summarized this issue, "In situations where the right thing to do is well established, physicians from high- and low-cost cities make the same decisions. But in cases where the science is more unclear, some physicians pursue the maximum possible amount of testing and procedures; some pursue the minimum. And what kind of doctor they are depends on where they came from. In case after uncertain case, more was not necessarily better… We will need to do in-depth research on what makes the best systems successful… and disseminate what we learn. Congress has provided vital funding for research that compares the effectiveness of different treatments, and this should help reduce uncertainty about which treatments are best. But we also need to fund research that compares the effectiveness of different systems of care—to reduce our uncertainty about which systems work best for communities. These are empirical, not ideological, questions."[9] This variation in care

[7] See Chapter 3 for the Council's definition of CER.
[8] See Chapter 6 for a comprehensive listing of CER activities across the Federal Government.
[9] Atul Gawande. "The Cost Conundrum." The New Yorker. June 1, 2009.

documented by Wennberg[10], Fisher[11] and others, means that Americans in one part of the country who are seeing particular clinicians may get vastly different care with potentially worse outcomes than Americans somewhere else. The health system can no longer produce highly variable results and tolerate low quality and inefficiency. The care delivered should be based on evidence and best practices, not on which physician a patient was referred to or where a patient lives. The Council believes that bringing to bear careful research across the continuum of care, from prevention, to diagnosis, to treatment, to delivery systems, will yield improved care for both individuals and for populations.

Current Comparative Effectiveness Research Landscape

In order to inform recommendations for comparative effectiveness research, the Council conducted an inventory of current CER activity. Section 6 summarizes CER activity in the Department of Health and Human Services, the Department of Veterans Affairs and the Department of Defense. Several examples of these activities are discussed below.

AHRQ has an established CER program as described above. As an example, an AHRQ Comparative Effectiveness Review in 2008 examined treatments for localized prostate cancer. There are a number of treatment options available for prostate cancer, each with its own potential for risks and benefits, so it is important that men understand what is known about the effectiveness of these treatments. Key findings from the report included:

- There is a lack of comparative studies across major modalities of treatment (e.g. surgery, radiation, watchful waiting).
- There were no randomized trials evaluating cryotherapy, laparascopic or robotic prostatectomy, primary androgen deprivation therapy, high-intensity focused ultrasound (HIFU), proton beam therapy, and intensity modulated radiation therapy (IMRT). While these therapies have become increasingly of interest for men considering treatments for prostate cancer, it is impossible to evaluate whether these therapies are more or less effective than other options.
- Of men who had surgery, those undergoing a radical prostatectomy were less likely to experience urinary incontinence and other complications if the operation was done by an experienced surgeon in a hospital that does many of the procedures.

NIH has funded numerous comparative trials with huge implications for the practice of medicine. For example, the Diabetes Prevention Program was a major multicenter trial to evaluate the comparative effectiveness of intensive lifestyle changes (diet and exercise), a pill for diabetes (Metformin), or a placebo in preventing the onset of type 2 diabetes in adults with pre-diabetes. This landmark trial found that while both lifestyle changes and Metformin reduced the risk of developing diabetes compared to a placebo, lifestyle changes were significantly more effective than Metformin. This effect was seen in men and women, and in all ethnic groups. With the increasing incidence of pre-diabetes in this country, the results of this trial were critical in informing patients and physicians about prevention strategies for diabetes. Similarly, the BARI

[10] Wennberg J, Gittelsohn A. Small area variations in health care delivery. Science. 1973; 182:1102-8.
[11] Fisher ES, Wennberg J. Health Care Quality, Geographic Variations, and the Challenge of Supply-Sensitive Care Perspectives in Biology and Medicine. 2003; 46(1): 69-79

2D trial compared optimal medical management with revascularization for preventing premature death in Type 2 diabetes and found medical management to deliver equivalent outcomes.[12]

VA also has a very strong history of conducting CER. For example, the COURAGE trial, published in 2007, compared the effectiveness of percutaneous coronary intervention (PCI, or angioplasty) plus optimal medical therapy with optimal medical therapy alone in the prevention of heart attack or death in veteran patients with stable heart disease. The results showed that patients treated with optimal medical therapy alone did just as well as patients who received PCI plus medical therapy. This trial can inform patients and clinicians about the most efficient use of PCI in patients with stable angina.

In addition to Federal activities, state level, private sector, and non-profit sector CER efforts are currently underway across the country.[13,14] For example, 14 states participate in the Drug Effectiveness Review Project (DERP), based at the Center for Evidence-Based Policy (EPC) at the Oregon Health & Science University. The project is a collaboration between the Oregon EPC and the Oregon Center for Evidence-Based Policy. Together, they produce evidence-based reviews of the comparative effectiveness and safety of drugs in many drug classes, and then make this information publicly available.

Large insurers and health organizations such as Aetna, CIGNA, UnitedHealthcare, and Humana have developed the capacity to conduct evidence reviews in-house. These payers may also commission external studies from entities such as the Blue Cross and Blue Shield Association Technology Evaluation Center, which has been conducting evidence-based technology assessments for more than thirty years. Pharmaceutical, biotechnology, and medical device companies may sponsor studies that share some of the attributes of CER. In the non-profit sector, organizations synthesize and publicize CER, rather than generating new evidence. For example, Consumers Union relies on DERP reports to provide information for its *Best Buy Drugs* Web site.

Although there are a number of institutions, both public and private, involved in CER, a number of challenges remain unaddressed. Much of the CER underway is fragmented, and not aligned with a common set of priorities or definition of what constitutes CER. Databases and patient registries that are invaluable for comparative effectiveness analysis are similarly fragmented and often limited in numbers of patients or of variable or unknown data quality. Some resources, such as privately maintained claims databases and Medicare claims data, are difficult for researchers to access due to licensing and cost issues. Furthermore, there are a number of gaps in the content of the research being conducted. Studies often do not include participants of sub-groups, such as racial minorities or people with disabilities, and generally focus on therapeutics at the expense of other types of interventions (e.g., devices or the delivery system). Many effective interventions for improving health are likely to involve prevention and community

[12] BARI 2D study group et al. N Engl J Med. 2009; 360(24):2570-2.

13 Academy Health. A First look at the Volume and Cost of Comparative Effectiveness Research in the United States. Available at: http://www.academyhealth.org/files/FileDownloads/AH_Monograph_09FINAL7.pdf. Accessed June 17, 2009.

[14] The following paragraphs draw on information contained in an environmental scan prepared by the Lewin Group for the Federal Coordinating Council on Comparative Effectiveness Research.

intervention, but these areas are currently understudied. CER should identify interventions that yield the most health improvement and represent the best value wherever and however the interventions are delivered.

The OS ARRA funds are a unique opportunity to address some of these gaps. The following box summarizes gaps in CER landscape:

Major Gaps in CER Landscape

- **Coordination across the CER framework**
  - Substantial CER assets exist across the Federal Government, but coordination is necessary to capture their full value
- **Research**
  - Many comparative, patient-centered research questions remain unanswered
- **Human and Scientific Capital**
  - CER methods development needed
  - Limited trained researchers for conducting CER
- **CER Data Infrastructure**
  - Fragmented data
  - Data sources limited in terms of clinical robustness of data and longitudinal data capture
  - Data capture and feedback loop at point of care often lacking
- **Dissemination and Translation of CER**
  - Suboptimal dissemination and translation of CER findings to patients and clinicians
  - Limited linkages between CER findings and directly improving patient outcomes
- **Priority populations**
  - Limited information on many priority populations and sub-groups
- **Priority Interventions**
  - Less information on certain comparative interventions such as behavioral change, procedures, devices, delivery system strategies, and prevention

Opportunity Provided by ARRA Funds

Within this context of national and international activity, the ARRA CER funds offer an extraordinary opportunity to complement ongoing research in the public and private sectors by establishing a solid infrastructure for future CER. Such investments could include development of data and methods, training of researchers who could accelerate the conduct of future studies, and rapid dissemination of results to patients and clinicians. For example, enhancing existing data resources and learning better how to maximize their utility could expand the types of questions addressed as well as identify high-impact opportunities for research. In addition, ARRA's investment in CER coincides with expected increases in the adoption of health information technology to improve health care quality and safety. That technology also offers the promise of including care delivery in the conduct of research (what some have termed a "learning health care system") and offering a platform for rapid dissemination of results to the

point of care to inform physician and patient decisions.[15] The field of CER is not entirely new, but increased availability of clinical electronic data resulting from diffusion of information technology demands improved methods and a cadre of researchers ready to take advantage of these expanding data resources.

As CER becomes a more integrated resource for health care decision-making, we must assure public trust by ensuring the privacy and security of health information and by maintaining access to appropriate care options. CER should not be used as a sole criterion for denying or awarding care or as justification for making care choices based on cost without consideration of effectiveness, safety, and convenience for an individual patient. CER has the potential to offer tremendous benefits to Americans so long as we apply its conclusions appropriately and protect the individual health information that informs it.

The Council believes that there is much to be learned about how research results can be incorporated into the everyday practice of medicine and inform consumer health care choices. The Council's hope is that ARRA funding has the potential to form a firm base for the Federal Government's future investments in CER and lay the foundation for a productive CER enterprise that improves care for all Americans.

II. VISION AND COUNCIL OBJECTIVES

Comparative effectiveness research has the potential to catalyze a patient-centered transformation of the U.S. health care system. By equipping patients and clinicians with the information needed to make joint medical decisions, and by optimizing the system in which the patient/clinician team makes these decisions, CER can improve the quality, safety, and value of care delivered while increasing patient satisfaction.[16] By passing ARRA, Congress recognized this vision and the need for CER, and also highlighted the need for an unbiased, cross-functional Council to "foster optimum coordination" of the Federal Government's CER efforts.

Given the Council's distinct role and the unprecedented resources available to the Secretary, the Council has a unique opportunity to begin working toward this vision for CER. The Council sees the following as potential accomplishments at the end of the ARRA funding period:

1. Establishment of a process for CER priority-setting that maximizes the value of Federal investments in CER through responsiveness to patient and other stakeholder needs, transparency, and effective coordination.

2. Development of a robust, foundational infrastructure for CER.

3. Implementation of a strategy to support rapid, systematic dissemination of CER results to empower patients, clinicians, and other stakeholders to make more informed decisions and increase the quality of care.

[15] Conway PH, Clancy C. Transformation of Health Care at the Front Line. JAMA. 2009 Feb 18;301(7):763-5.
[16] Naik AD, Peterson LA. The Neglected Purpose of Comparative Effectiveness Research. NEJM. 2009 May 7; 360(19):1929-31.

To accomplish this vision, the Council outlined three specific, near-term objectives that build on those established in ARRA:

1. Develop a definition, establish prioritization criteria, create a strategic framework, and identify priorities that lay the foundation for CER.

2. Foster optimum coordination of comparative effectiveness research conducted or supported by relevant Federal departments.

3. Formulate recommendations for investing the $400 million appropriated to the HHS Office of Secretary as part of this Report to Congress.

III. COMPARATIVE EFFECTIVENESS RESEARCH DEFINITION AND CRITERIA

One of the first activities of the Council was to build on previous definitions of comparative effectiveness research, including IOM, CBO, and others, to develop a definition of comparative effectiveness research for the Council. After much discussion and sharing with the public for feedback, the Council established the following definition.

Definition

Comparative effectiveness research is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in "real world" settings. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.

- *To provide this information, comparative effectiveness research must assess a comprehensive array of health-related outcomes for diverse patient populations and sub-groups.*
- *Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.*
- *This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness and actively disseminate the results.*

The definition above is not meant to exclude randomized trials; however, these trials would need comparator arms other than placebo and be representative of populations seen in "real world" practice.

Once a definition was established, the Council drafted threshold criteria for consideration and prioritization criteria for comparative effectiveness research and related investment. These criteria were posted on a public Web site, feedback was received, and modifications were made. The following are the current Council criteria.

Prioritization Criteria for Comparative Effectiveness Research Related Investments

Minimum Threshold Criteria (i.e. must meet these to be considered):

- Included within statutory limits of Recovery Act and FCC definition of CER
- Potential to inform decision-making by patients, clinicians, or other stakeholders
- Responsiveness to expressed needs of patients, clinicians, or other stakeholders
- Feasibility of research topic (including time necessary for research)

The prioritization criteria for scientifically meritorious research and investments are:

- Potential impact (based on prevalence of condition, burden of disease, variability in outcomes, costs, potential for increased patient benefit or decreased harm)
- Potential to evaluate comparative effectiveness in diverse populations and patient sub-groups and engage communities in research
- Uncertainty within the clinical and public health communities regarding management decisions and variability in practice
- Addresses need or gap unlikely to be addressed through other organizations
- Potential for multiplicative effect (e.g. lays foundation for future CER such as data infrastructure and methods development and training, or generates additional investment outside government)

This definition and criteria guided the Council as it considered potential priority recommendations for the OS funds and will guide AHRQ and NIH in allocating their CER funds.

IV. IMPORTANCE OF PRIORITY POPULATIONS AND SUB-GROUP ANALYSIS

As the United States has grown in its diversity, there has remained a persistent under-representation of women, the elderly, persons with disabilities, and racial and ethnic minorities in clinical and other research studies. While the NIH has a policy of inclusion of women and racial and ethnic minorities in all NIH-funded clinical trials,[17] the majority of research conducted in the U.S. does not require the inclusion of these and other priority populations. The lack of adequate representation of important patient populations in many research studies presents a major challenge in applying the results of these studies to important populations and sub-groups. In recognition of this fact, the ARRA legislation notes that "research conducted with funds appropriated shall be consistent with Departmental policies related to the inclusion of women and minorities." This criterion is critically important for ensuring that information gained from comparative effectiveness research improves the quality of care for all Americans.

[17] http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

Indeed, focused attention is needed on priority populations,[18] including racial and ethnic minorities, individuals with disabilities, children, persons with multiple chronic conditions, and the elderly, not only because of their under-representation in current research but also because of the increased disease burden and health disparities faced by these sub-groups.

The following sections highlight some of the challenges facing our health system as it relates to priority populations. Disparities in health care and health outcomes for these populations persist, affecting an ever-increasing proportion of residents of the United States. Also outlined are some of the research challenges that exist for priority populations, followed by recommendations to address these issues.

Growth in Priority Populations

Priority populations not only account for a large proportion of current health services utilization, but their numbers are growing; their need for health care services will likewise continue to grow. The most recent U.S. Census Bureau data reveal that over 100 million people living in the United States belong to a racial or ethnic minority group; this equates to 34 percent of the total U.S. population, and these minorities will likely become the majority of the U.S. population within 30 years.[19] Similarly, the number of elderly Americans is growing, with that segment of the population expected to increase from 35 million today to 71 million by 2030— or nearly 20 percent of the overall U.S. population. The population over the age of 85 is projected to grow from 5.3 million today to 21 million by 2050.

Health Disparities

A number of important reports have highlighted disparate disease prevalence, progression, and health outcomes for racial and ethnic minorities, elderly Americans, individuals with disabilities people of low socioeconomic status, people with mental illness, and others.[20,21] In this context, health disparities are defined as significant gaps or differences in the overall rate of disease incidence, prevalence, morbidity, mortality, or survival rates in the priority population as compared to the health status of the general population.[22] For example, African-American women are 34 percent more likely to die from breast cancer, even though they are diagnosed with the disease 10 percent less frequently than white women; Hispanics in the U.S. are 50 percent more likely than whites to suffer from diabetes; and the incidence of diabetes among

[18] Priority populations are defined in Sec. 901 of the Healthcare Research Act of 1999, S. 580.
[19] U.S. Census Bureau. Minority Population Tops 100 Million: Press Release. Available at: *http://www.census.gov/Press-Release/www/releases/archives/population/010048.html*. Accessed April 1, 2009.

[20] Report of the Secretary's Task Force on Black and Minority Health. U.S. Department of Health and Human Services. 1985.

[21] Brown ER et al. Racial and Ethnic Disparities in Access to Health Insurance and Health Care. UCLA Center for Health Policy Research and the Henry J Kaiser Family Foundation. 2000.

[22] Minority Health and Health Disparities Research and Education Act of 2000. Public Law 106-525. November 20, 2008.

Native Americans is more than twice that for whites. Elderly Americans also face particular health challenges, from greater susceptibility to multiple chronic conditions to a lower likelihood of obtaining preventive treatments, including mammograms and immunizations. In addition, approximately 42 percent of individuals over the age of 65 report a functional limitation.[23]

Persons with Disabilities

According to the 2007 Institute of Medicine report *The Future of Disability in America,* from 40 to 54 million people in the United States have disabilities. These numbers will grow considerably in coming decades as baby boomers age and as new medical interventions extend the lives of young persons with significant impairments who would once otherwise have died. Although rates are lower in children, disability prevalence is rising at younger ages. According to figures from the National Health Interview Survey, childhood disability has risen by 350 percent during the last 40 years, with the largest increase occurring during the past decade.

Across the lifespan, disabilities are clinically and functionally heterogeneous, encompassing diverse cognitive, sensory, physical, and mental health impairments. Traditionally patients with disabilities have been excluded from clinical trials, yet they have the same risk for diseases as non-disabled persons. Future clinical trials should exclude persons with disabilities only if there are clear and compelling reasons to do so.

Comparative effectiveness research relating to persons with disabilities is important in a number of areas.

First, research would be beneficial about the most effective interventions to prevent or mitigate disability and the disabling effects of chronic diseases. All research including comparative effectiveness research relating to disability should include outcome measures that address functional abilities, people's abilities to participate in daily activities, and quality of life. This is critical as the world's population is growing older at a very fast pace and this has serious implications due to expected increasing rates of chronic conditions. Moreover, with the advances in science and technology, lifespan has increased considerably; this is also true for persons with disabilities.

Second, future comparative effectiveness research should look into community-based models of care for persons with disabilities. Following the Supreme Court *Olmstead v. L.C. ex rel. Zimring, 527 U.S. 581 (1999) Decision,* traditionally institutionalized individuals with disabilities or those at risk of being placed in institutions are increasingly being cared for in their own homes and/or communities. Underscored by the *Olmstead Decision* states now have to consider civil rights when developing their programs. Effective care coordination/care management is critical to help persons with disabilities live independently in their communities with added years of quality life. Care coordination/care management is even more important for those individuals with multiple chronic conditions, which are often associated with certain levels of disability. While care

[23] Federal Interagency Forum on Aging-Related Statistics. Older Americans 2008: Key Indicators of Well Being. Federal Interagency Forum on Aging-Related Statistics. Washington, DC: U.S. Government Printing Office. March 2008

coordination/care management is the current state-of-the-art, it is still considered to be in its early stage. This represents a major opportunity for building the infrastructure to support future CER studies. In addition, because the definition of care coordination varies according to settings and models of care, its effectiveness has not been clearly established, particularly as it relates to the role support services play and how better integration of health and support services can lead to improved health outcomes for persons with disabilities and reduced health care costs for our nation.

Third, persons with disabilities are at increased risk for developing secondary conditions that are associated with their primary disabling condition. For example, without preventive measures, individuals with spinal cord injuries may acquire a number of adverse health conditions, including cardiovascular disease, genitourinary tract disorders, depression, obesity, and pressure sores. Comparative effectiveness studies should determine which interventions are most likely to prevent secondary conditions or ameliorate their consequences.

Fourth, studies should investigate the comparative effectiveness of rehabilitation interventions to restore or maintain functioning or minimize its loss. For example, much more research is needed to identify effective speech-language, physical, and occupational therapy interventions. This research could include a comparison of conventional treatments to newer interventions or a comparison of various systems of care. More research is also required about various assistive devices, medical equipment, and technologies, including technologies addressing sensory deficits, communication impairments, and physical and motor limitations.

Fifth, comparative effectiveness studies of therapeutic and preventive interventions need to address explicitly the needs of children with disabilities and be sensitive to the developmental stage of the child. For many children with disabilities and complex health care needs, the transitions through adolescence and into adulthood are complicated by the absence of comprehensive care programs that fully address their needs. Comparative effectiveness studies should examine different care models to determine which ones offer the best care coordination and generate the greatest patient and family satisfaction and health outcomes.

Other underrepresented populations

Children represent another group that can benefit tremendously from comparative effectiveness research. Evidence cannot simply be extrapolated from adults to the pediatric population. There is a dearth of information to inform decisions by children and their families, especially since outcomes, such as quality of life and functioning, are often more subtle. In addition, comparative preventive interventions (e.g. for obesity) will often have the most long-term effects if started in the pediatric population.

At the other end of the continuum, the elderly represent another group for which there exists little information about best care practices. As our population ages, knowledge about the best and most effective treatments for this group will become essential. Other important areas of focus for the elderly include home health care strategies and optimal approaches to delivery of care within nursing facilities.

Veterans and service members often have many conditions for which CER could be informative. They have a number of special considerations in deployment-related illness such as post traumatic stress disorder, traumatic brain injury, exposures, infectious diseases, disabilities and others. CER provides a vital opportunity to glean additional information necessary for clinicians to make informed decisions about particular veterans needs and information to assist veterans in their participation in care decisions.

Finally, research to compare the effectiveness of prevention strategies, treatments, diagnostics, and care delivery for patients with multiple chronic conditions is essential. Again, as our population ages, patients increasingly have several comorbidities which may impact their response to treatment. The majority of clinical research to date excludes such patients, so the applicability of "standard" treatments to this population is unclear. A physician advising a 45-year-old woman with asthma and HIV about treatment for breast cancer simply does not have the evidence necessary to factor her comorbidities into her patient's treatment decision. By utilizing varied and robust research methodologies, CER affords the opportunity to target treatments and other interventions to improve the quality of life and overall health of this important group of patients.

Personalized Medicine and Patient Sub-groups

The need to identify and address the needs of emerging patient sub-groups, and indeed the very concept of sub-categories of conditions to which medical products are applied, is expected to change and grow as our understanding of genomics and molecular medicine increases and becomes an integral part of health care. Better understanding of an individual's genomic and other individual biological characteristics will enable us to recognize and respond to human variability with a new degree of specificity. Understanding biological differences at the molecular level promises a significant leap in our ability to use and develop medical technologies more effectively, targeting interventions at more defined groups of individuals with greater precision. This potential, sometimes referred to as personalized medicine, has strong bearing on comparative effectiveness research.[24] Many drugs prescribed in the United States today are effective in fewer than 60 percent of treated patients. This is not a fault of the drugs, but reflects the variability of metabolism or other factors from person to person.[25]

Unfortunately, it remains common medical practice to follow a trial-and-error approach in selecting medical interventions for patients to achieve a satisfactory therapeutic outcome. In the case of breast cancer, for example, while chemotherapy can be an important positive treatment for some patients, we have few tools today to successfully predict which patients will benefit– and the result is that many women who are treated with chemotherapy today are receiving treatments that may not be effective for their condition.

Personalized medicine aims to make medical care more precise and effective. Increased understanding of our individual genomic profiles and other individual biological characteristics

[24] Willard HW: Organization, Variation and Expression of the Human Genome as a Foundation of Genomic and Personalized Medicine. In *Genomic and Personalized Medicine. Volume 1.* Edited by Willard HW and Ginsburg GS. London: Academic Press; 2009:4-21.
[25] Spear BB, Heath-Chiozzi M, Huff J. Trends Mol Med. 2001 May; 7(5):201-4.

will enable us both to use more effectively the therapies we have now and to identify significant areas where research and development of new products may be needed. Pharmacogenomics, the use of genetic information or other biomarkers to assist in accurate medical therapy decision-making, is expected to be a hallmark of this approach.

CER can be an important partner in helping to bring about this new level of medical effectiveness, personalization, and innovation. At the same time that CER is being used to identify which interventions and strategies work best on average, it can also help to identify different responses by different groups of patients. In some cases, different existing therapies may be identified as most effective for specific sub-groups. In other cases, CER may help to identify significant sub-groups for whom effective therapies do not yet exist. CER may also help steer research efforts toward the development of products and strategies for areas of significant need.

Research Challenges

Multiple research challenges exist for priority populations. Examples include a need for increased diversity in research populations, expanded data sources for evidence-based studies in diverse populations, enhanced collection of racial and ethnic health data, a better understanding of the effectiveness of interventions in the context of comorbidities, and a greater focus on implementation research.

Generalizations that result from comparative effectiveness research that fail to consider sub-groups and individual differences may have limited applicability. Currently there are gaps in knowledge about whether specific treatment strategies work across different sub-groups under a variety of circumstances. Recognizing that there might be variations in the effectiveness of specific interventions in the elderly, racial and ethnic minorities, individuals with disabilities, and other priority populations is key to designing evidence-based strategies to successfully improve the quality of care that is delivered. Infrastructure investments that capture priority populations and patient sub-groups will be critical to overcoming these challenges.

Strategies to Strengthen Comparative Effectiveness Research for Priority Populations

In light of the aforementioned challenges, comparative effectiveness research presents an opportunity to be more inclusive of minorities, the elderly, persons with disabilities, and other priority populations. This feature of CER is especially true in the context of conducting specific studies that take into account health conditions and linguistic and cultural attributes in order to develop the most appropriate and effective interventions.

Investments in CER can be used to address the needs of priority populations by doing the following:

Evaluating and identifying interventions that are tailored for priority populations. To explore which interventions are most effective for addressing the needs of priority populations, specific studies are needed to look at interventions that target diseases with a high prevalence in racial and ethnic minority communities, the elderly, and individuals with disabilities. These

studies may need to simultaneously address several diseases/conditions, or assess combinations of interventions (e.g., behavioral and physical treatments/interventions) that are most effective in promoting desired outcomes for these populations. Studies examining care delivery interventions tailored for priority populations are also needed in order to ensure that care is delivered to these individuals through effective approaches that are targeted to their needs. To ensure effective communication with the priority populations both in conducting the research and implementing its results, investigators should ensure that those language and communication services are available for those with limited English proficiency or disabilities.

Creating and enhancing potential databases looking at interventions in priority populations. Successfully examining and evaluating a range of interventions that are effective for priority populations will require a broad range of potential data sources and infrastructure investments. In addition to traditional patient registries and systematic reviews, the inclusion of distributed data networks that utilize community-based infrastructure, such as Federally Qualified Health Centers, will be an important asset in broadening the tools to evaluate effectiveness in various priority populations. CER studies should routinely perform and report sub-group analyses to examine possible differences in effectiveness for important racial and ethnic groups, and should over-sample such groups whenever there is existing evidence to suggest differences in effects or outcomes in any priority population. Standardized reporting and analysis of priority population sub-groups will also permit pooling of research results across studies to explore sub-group differences.

In addition, efforts should be made to build capacity and infrastructure within traditionally underserved racial/ethnic communities to allow for standardization of data collection and to enable the seamless integration of such data with larger databases/systems currently in use by the research community. This will allow for more accurate downstream comparisons to pre-existing and future majority data sets, producing more comprehensive and reliable CER study results.

Finally, this infrastructure for CER in priority populations is particularly important for developing and implementing Clinical Preventive Services Guidelines and recommendations for the U.S. Preventive Services Task Force. According to the IOM, CER data on priority populations is often unavailable for developing guidelines, and what information is available is often insufficient for making conclusions on how to treat priority populations.

Increasing the number of community-based studies, including community-based participatory research (CBPR) studies. CBPR is defined as a collaborative research approach in which communities and researchers are equally involved in the design and conduct of research that is conducted in their communities. Successful and effective CBPR studies result in the development of research tools, strategies, and interventions that are effective in creating sustainable and positive behavior changes and outcomes among priority populations within communities. Because CBPR studies are conducted with substantial input from the community, interventions are typically tailored to fit the needs and characteristics of the community. Furthermore, communities become “owners” of the research, which results in sustainable research outcomes.

Increasing cultural competency. Understanding the linguistic, cultural, social, and environmental attributes of priority populations is essential in designing interventions and promoting strategies that are effective in addressing the needs of these populations. Specifically, doing so allows for the development of culturally and linguistically appropriate interventions. For example, an obesity/diabetes intervention involving diet and/or physical activity would require an understanding and assessment of the populations' cultural attributes (e.g., food preferences), social attributes (e.g., competing family and work demands), and environmental attributes (e.g., access to 'healthy' foods and safe walkways) that support or inhibit adhering to a diet and/or physical activity intervention.

Building workforce capacity. Racial/ethnic minorities, individuals with disabilities, and women are underrepresented in the research and medical communities. The lack of a diverse and linguistically competent scientific workforce adds to disparities in research development, service delivery, and quality of care. Initial CER investments in workforce capacity could create opportunities to engage researchers and providers from diverse backgrounds. For example, 90 percent of minority physicians educated at Historically Black Medical Colleges live and serve in minority communities. Hispanic-Serving Institutions (HSIs) also play a major role in educating Hispanics researchers. Approximately 49 percent of all Hispanic students attend an HSI. A special focus on priority populations could provide an avenue for engaging Historically Black Colleges and Universities and HSIs in the conduct of CER among priority populations.

Developing and implementing outreach strategies to various racial, ethnic, and health disparity populations for participation in research protocols. In order to strengthen CER, effective outreach strategies must be developed and implemented that will increase the participation of priority populations in clinical research protocols. Developing appropriate strategies to reach out to various priority communities requires an understanding of the history of these populations in research and the identification and recruitment of trusted community members who can champion the research benefits and inform communities about risks. Community health workers can be important partners in addressing and advocating for the needs and concerns of priority populations. In addition, clinicians and providers will need to be educated on the benefits and implications of CER and the utilization of evidence-based interventions.

Dissemination, translation and adoption of research results is one of the biggest challenges within comparative effectiveness research, particularly as applied to priority populations, but also as applied to the population as a whole. The young science of implementation research focuses on the acceleration of translation of evidence into everyday care, and affords an opportunity to build a more coordinated approach to improving the quality of health care of priority populations. This is not a one-way transfer of knowledge. Racial and ethnic minorities, persons with disabilities, children, and the elderly, can offer insights into how best to engage their communities. Active listening and thoughtful planning of the dissemination process can create better health outcomes for all Americans.

Making CER investments that are responsive to the needs of priority populations and sub-groups is critical to ensuring that the benefits of CER reach those with the greatest needs. Such

investments, however, can also benefit the population as a whole by validating new strategies and approaches for comparative research and implementation.

V. STRATEGIC FRAMEWORK FOR CER

There are countless opportunities for action and investment in CER. Many Federal, state, and private institutions are already involved in CER and have made choices about which of these activities and investments to pursue. After completing the draft definition and criteria for prioritization of potential CER investments, the Council recognized the need to develop a strategic framework for CER activity and investments to categorize current activity, identify gaps, and inform decisions on high-priority recommendations.

This framework represents a comprehensive, coordinated approach to CER priorities. It is intended to support immediate decisions for investment in CER priorities and to provide a comprehensive foundation for longer-term strategic decisions on CER priorities and the related infrastructure. At the framework's core is responsiveness to expressed needs for comparative effectiveness research to inform health care decision-making by patients, clinicians, and others in the clinical and public health communities. The framework will be supported by detailed inventories of Federal CER activities and research/data infrastructure, and a priority-setting approach. This organizing framework fosters consideration of the balance of activities and priority themes, focuses on the most pressing needs expressed by patients and clinicians, and allows for identifying and addressing gaps in the current landscape of CER.

CER activities and investments made by the government or other institutions can be grouped into four major Core Categories:

- **Research** includes activities or investments in primary research or meta-analysis. Organizations involved in this group of activities may be funding research, conducting research themselves, or helping to establish a common set of research priorities to create momentum around the most critical research topics.

- **Human and Scientific Capital** includes activities or investments that enhance the United States' capacity for CER by expanding and strengthening relevant research skills or by advancing CER approaches and methodologies. Organizations involved in this group of activities may be directly involved in training and workforce development, developing new CER methods, validating results of CER, or driving consensus on valid approaches to CER.

- **CER Data Infrastructure** includes activities or investments that develop, build, or maintain data infrastructure, systems, or tools. These investments could include the creation of new research data sets and repositories, aggregation of existing data sources, development of new tools to query and analyze existing data sets, or creation of standards for new data collection.

• **Dissemination and Translation of CER** includes activities or investments that disseminate CER findings and put them into practice. Activities and investments range from dissemination and distribution of CER information to improving processes and outcomes in health care and public health delivery systems through CER translation and adoption.

Table 1
Example Activities in Each Major Category

Activity	Examples
Research	Comparing outcomes of treatments or care delivery for a specific condition
Human & Scientific Capital	Training new researchers to conduct CER or developing CER methodology and standards
CER Data Infrastructure	Developing a distributed practice-based data network, linked administrative or EHR databases, or patient registries
Dissemination and Translation of CER	Building tools and methods to disseminate findings and translate CER into practice to improve health outcomes for patients

Furthermore, investments or activities focused on a specific priority theme can cut across these categories. The potential themes include:

•**Conditions.** Organizing investments and activities around a condition or disease state is common in research and reflects the organization of medical practice. Focusing on a single disease state across all four major categories of activity (e.g., funding primary CER in oncology, developing new methodologies for CER in palliative care settings, expanding the Surveillance, Epidemiology, and End Result database (SEER), and partnering with an academic cancer center to pilot CER implementation strategies) could result in significantly improved patient-centered outcomes in that disease area.

•**Patient populations.** While clinical research is relevant to the patient population it is designed to address, it often provides little information relevant to patient groups not typically enrolled in clinical studies. In private-sector-funded trials, this often includes the elderly, racial and ethnic minorities, children, and persons with disabilities. The NIH, however, already requires that all publicly funded trials include appropriate numbers of women and racial and ethnic minorities. Cross-cutting activities and investments that facilitate studies responsive to the needs of these populations can ensure that all Americans benefit from CER.

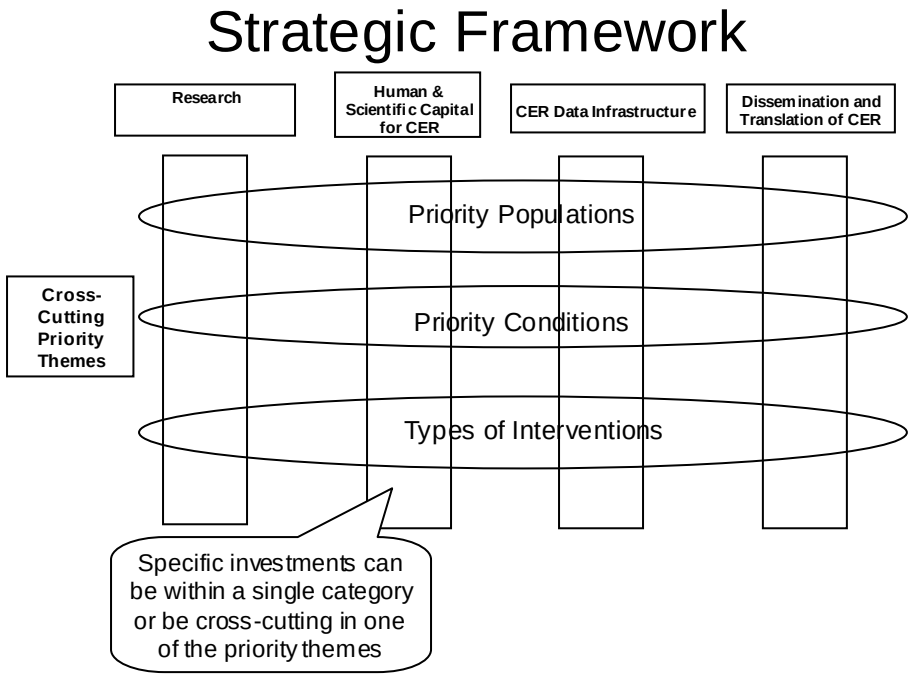
•**Type of intervention.** Several potential areas of focus emerge from studying interventions by type. In defining CER, the Council specifically included the following types of interventions: medications, medical and assistive devices, procedures, behavioral change, diagnostic testing, and delivery system strategies. Each of these has unique opportunities for coordinated investment in data infrastructure, research, building

research capacity, and translation. In addition, one could focus on interventions at a stage of the disease (i.e., prevention, diagnosis, treatment, and management).

Together, these activities and themes make up the CER strategic framework (Figure 1).

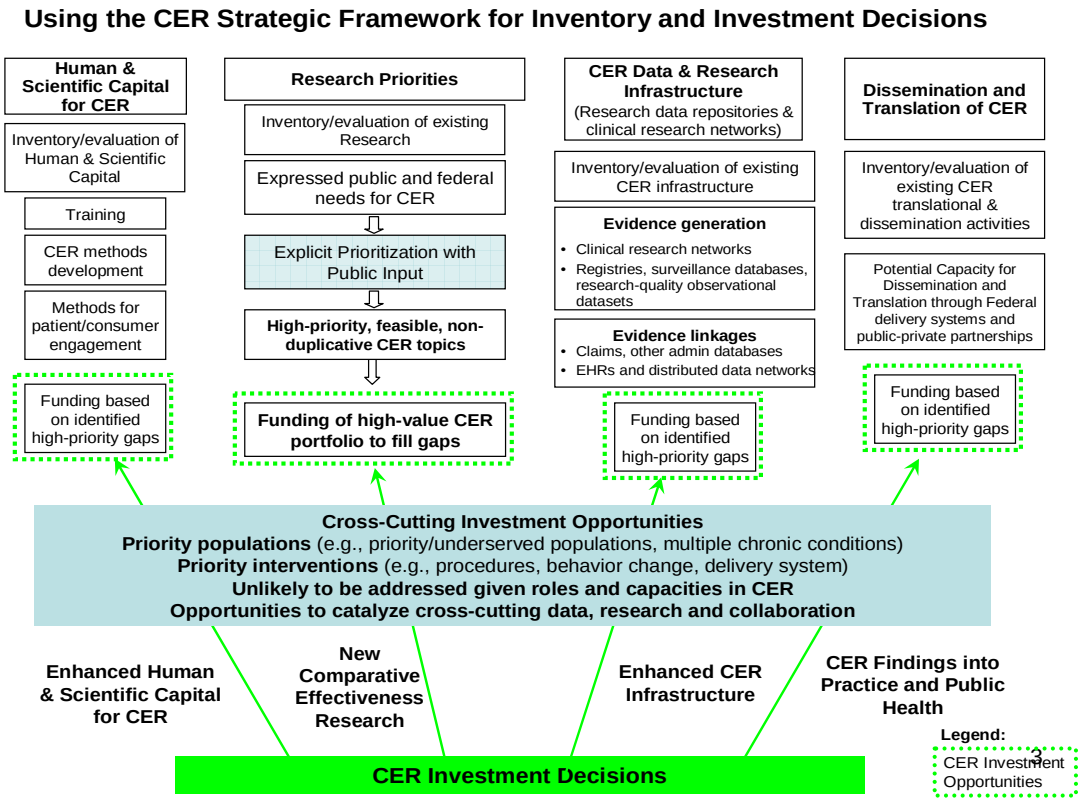
Agencies or organizations that are engaged in CER will often make investments in one group of activities or across multiple groups within a cross-cutting theme. The pattern of activity and investment for a single organization highlights its strategy. For example, a medical information database company may concentrate its CER activities in data infrastructure, whereas the National Cancer Institute is involved in multiple types of activities with a focus on cancer. When patterns of activity for the most critical agencies and organizations involved in CER are viewed in aggregate, the CER framework reveals gaps in CER activities and investments. These gaps are potential areas of opportunity and impact for the Secretary's ARRA funds. As such, the framework is useful for determining what investments are appropriate for ARRA funds and for future Federal investments in CER, as well as for codifying the ongoing activities of Federal agencies involved in comparative effectiveness research.

Figure 1



Creating and maintaining an inventory summarizing current and past Federal efforts across the CER framework is critical to its value in decision-making. This inventory of Federally-sponsored CER activities will also be a critical component of future Council annual reports. This process of inventory-taking, gap analysis, and establishing priorities for investment should be iterative. The process for developing the inventory and aligning findings from that process with CER investment decisions is outlined in Figure 2.

Figure 2



Overall, the CER framework is a useful strategic and analytic tool to help organize ongoing CER activities of Federal agencies, to facilitate development of a strategy for the Secretary's ARRA investments, and to continually monitor progress in CER across the different dimensions of the framework.

VI. CURRENT CER INVENTORY AND CER DATA INFRASTRUCTURE

The following CER inventory and data infrastructure was collected for the first time and on a very short timeline. The counts of CER studies are based primarily on electronically accessible sources, informed in part by interviews of senior agency staff. Attributes of the research reported here (study designs, types of interventions studied, etc.) were determined from study summaries or abstracts rather than inspection of full-text reports of these studies.

As described below, providing a high-confidence estimate of the number of Federally-funded CER studies underway for a given fiscal year is not currently feasible. Prospective identification of CER studies using keywords or other "tagging" in one or more readily searchable electronic databases would enable tracking of completed and ongoing CER. Therefore, this preliminary inventory is informed by a convenience sample and should be viewed as a rough estimate of what will be an iterative process going forward.

Although ARRA is the first coordinated Federal CER effort, several Federal agencies have been conducting comparative effectiveness research and maintaining data and infrastructure for CER. Most of this activity has been conducted independently within the given agency. The agencies most active in CER include AHRQ, NIH, and the Veterans Health Administration (VHA). But many other agencies conduct or have resources related to CER to a lesser degree, such as comparative effectiveness research studies, related data infrastructure, or the potential to be effector arms for research dissemination and translation. Finally, it is important to note that this inventory does not include CER conducted by private or not-for-profit organizations.

CER Inventory

Table 2 provides information about the numbers of studies for these agencies. There is no standard, systematic means of reporting on CER studies and funding across Federal agencies. It is not possible at this time to estimate the total number of primary or secondary CER studies conducted by the Federal Government. Other than AHRQ, by virtue of its dedicated Effective Health Care Program, agencies have limited ability to track CER studies and spending, reflecting that CER is a relatively new field of inquiry, has no standard definition, and is not "tagged" or readily searchable in biomedical or health services research databases. AHRQ tracks its funding and number of studies by fiscal year. Funding for CER studies for AHRQ ranges from 12 million to 35 million per fiscal year since FY 2006, with 12-18 studies funded per year. Estimates for the number of CER studies and funding for DoD and VHA are approximations per year rather than specific numbers for particular years. For example, DoD estimates its funding to be approximately $125,000 to $500,000 per year for 5-10 studies per year; the VHA estimates are 50 million to 70 million per year for 40-50 studies per year.

As part of its large portfolio of biomedical research, the CER funded by NIH makes that agency the single largest sponsor of primary comparative effectiveness research. These studies are difficult to identify, however, as they are not "tagged" or otherwise readily searchable as CER in such databases as ClinicalTrials.gov or CRISP (Computer Retrieval of Information on Scientific Projects, a database of biomedical research funded by NIH).

For purposes of this pilot inventory, a keyword search of ClinicalTrials.gov yielded an initial set of 1,800 NIH-funded trials during the years 2006-2009 that were candidates for CER. Subsequently, in cooperation with NIH, a sample set of 463 NIH CER studies for 2008 was identified, starting with a new searching process under development by NIH to track CER studies and spending.[26]

[26] NIH recently developed an initial process involving a keyword searching software algorithm based on consensus among several experts regarding which studies from among those funded by NIH qualify as CER. NIH applied this algorithm to all studies funded by NIH in 2008, which yielded more than 800 studies with a score above a certain threshold—tagging them as potential CER. Inspection of all of the records of all of these studies in CRISP by staff supporting the Coordinating Council identified the set of 443 that appeared to qualify as CER. This set of 443 does not necessarily represent the full set of CER studies funded by NIH in 2008.

Table 2: Estimated CER Grant/Study Counts FY 2006 – FY 2009[1]

Agency	CER Grants/Studies FY2006-FY 2009 (YTD)
AHRQ	144
DoD	25
VHA	96
NIH[2]	463

[1]As of June 2009, based on review of agency/department websites and agency/department generated lists

[2]NIH is in process of cataloging CER. This primarily represents FY 2008.

CER studies conducted or sponsored by VHA and DoD often focus on the particular populations they serve. These include CER studies involving patient groups that fall within designated U.S. priority populations (e.g., the elderly, racial and ethnic minorities, patients with multiple chronic conditions, persons with disabilities).

The main findings from analyses of Federal CER for fiscal years 2006-2009 include the following:

- In this initial compilation, the inventory of CER that could be confirmed independently for those agencies that perform or sponsor it was generally comparable to the inventory as described in interviews with agency staff. The main exception was NIH, where the volume of CER is acknowledged to be large yet remains to be quantified.
- Other than that for AHRQ, agency budgets for CER are not well defined. Agency staff typically described rough percentages of total research budgets or approximate ranges of annual expenditures on CER, but generally could not cite budget amounts allocated to CER (e.g., by Federal fiscal year).
- Excluding AHRQ, which could cite studies in its Effective Health Care program as at least a core set of CER, agency staff could not specify the number of CER studies conducted per year or other period. Three main factors account for this. First, there has not been a standard definition of CER. Second, while agencies may have a sense of expenditures or relative emphasis of CER, individual studies are typically not titled, given keywords, or otherwise "tagged" in a manner for identification as CER. Third, the time frame for CER study counts is not standardized; some agencies provided counts in terms of studies underway during a given year, others provided counts of studies initiated in a given year. Thus, providing a high-confidence estimate of the number of Federally-funded CER studies underway for a given fiscal year is currently not feasible. Clear identification of CER studies, particularly prospectively, would better enable tracking of completed and ongoing CER.
- Combined Federal CER is broadly distributed across study types (i.e., primary versus secondary studies). The volume of primary CER sponsored by NIH, particularly Randomized Controlled Trials (RCTs) and other trials, accounts for the largest general type of CER.
- The greatest concentrations of Federal CER are systematic reviews by AHRQ, RCTs by NIH, and RCTs by VHA (Table 3).

- Most AHRQ CER comprises secondary research (i.e., systematic reviews and other syntheses) and VHA supports secondary research through its Evidence-based Synthesis Program. Otherwise there is little emphasis on secondary research. Moreover, mathematical modeling is infrequently used in Federal CER (Table 3).
- Most primary research is done through RCTs (Table 3).
- Without careful inspection on a trial-by-trial basis, reliable detection of "practical" (or "pragmatic") trials among the primary CER studies is not possible. As a group, the VHA trials appear to have more such "practical" characteristics than trials sponsored by other agencies.
- Relative to the RCT volume from NIH and VHA, the use of observational analyses, including those involving large patient-level databases, is relatively infrequent.
- The locus of research varies by agency. All CER funded by VHA and most by DoD is intramural. Most CER funded by AHRQ is extramural. Although NIH conducts some intramural primary research, most CER is done extramurally.
- The interventions studied most often in Federal CER are pharmacologic, which account for the majority of the interventions studied by AHRQ and NIH. These are followed by studies of the health care delivery system, led by VHA, and behavioral interventions (which are often compared to pharmacologic interventions), led by NIH and VHA (Table 4).
- Roughly 86 percent of the CER studies in this sample across agencies focus on at least one priority disease/condition. The leading categories among these are depression and other mental health disorders, substance abuse, cardiovascular disease, and diabetes (Appendix C).
- The distribution of priority diseases/conditions studied by DoD and VHA largely reflects the respective populations they serve. For DoD, they are cancer, functional limitations and disability, and depression and other mental health disorders. For VHA, they are cardiovascular disease, and depression and other mental health disorders (Appendix C).

Table 3: Estimated Types of CER by Agency/Department

Study Type[1]	AHRQ	NIH[2]	DoD	VHA	Total
Primary Research					
Randomized Controlled Trial	11%	79%	0%	77%	60%
Practical/Pragmatic Controlled Trial[3]	3%	1%	16%	1%	2%
Other Non-Randomized Controlled Trial	2%	2%	32%	0%	3%
Observational Study (natural experiment)	1%	2%	0%	4%	2%
Observational Study (Prospective/Registry)	4%	3%	16%	6%	4%
Observational Study (Retrospective)	9%	5%	6%	4%	6%
Secondary Research					
Systematic Review	58%	0%	13%	0%	14%
Meta-Analysis	3%	0%	0%	0%	1%
Mathematical Model	4%	3%	3%	3%	3%
Research Training	n/a[4]	0%	13%	0%	1%
Other Capacity Building	n/a[4]	0%	0%	1%	0%
Other	2%	2%	0%	3%	2%

[1] Some studies include more than one study design, totals may not equal 100% due to rounding.
[2] NIH 2008 (based on sample of 443 studies) plus NIH multi-year (based on 30 studies across years).
[3] Rough estimate given no standard definition for pragmatic trial.
[4]AHRQ has been heavily involved in development of human and scientific capital for CER. It provides career development (K) grants for CER as well as a T and R grant for CER capability building. It also has funded numerous methodology studies for CER. These will be more fully quantified in the completed inventory.

Table 4: Estimated Types of Interventions Included in Studies

Study Intervention Type[1]	AHRQ	NIH[2]	DoD	VHA	Total
Pharmacologic Treatment	35%	68%	24%	10%	34%
Biologic Treatment	1%	1%	10%	4%	4%
Alternative Medicine	2%		8%	1%	2%
Medical Device/Equipment	17%	6%	0%	7%	11%
Surgical Procedure	11%		3%	9%	9%
Behavioral Intervention	11%	24%	11%	24%	16%
Public Health Intervention	2%	1%	17%	3%	3%
Delivery System	11%		19%	41%	20%
Other	10%		8%	1%	2%

[1] Some studies include multiple types of interventions and may not total 100% due to rounding
[2] NIH multi-year. Will need to be updated once inventory based on types of NIH interventions is complete.

The involvement of priority populations in CER sponsored by Federal agencies is varied. While several studies do not explicitly focus on a priority population, investigators sometimes report on analyses of one or more specific sub-groups:

- About half of CER studies across these Federal agencies involve a priority population, with nearly 60 percent of VHA studies doing so. Many studies focus on more than one population group. In part consistent with their respective missions, the agencies exhibit different distributions of emphasis on priority populations.
- Among those studies that do involve priority populations, those involving patients requiring chronic care, and those who are elderly are the most common. While no studies specifically indicate a focus on low-income groups, such individuals often comprise some of the patients studied, including the elderly, those with multiple chronic conditions, and minority groups.
- Studies vary as to whether there is sufficient representation of one or more priority groups in the study population to enable sub-group analysis, even if the study does not focus on a priority population as a principal objective. Particularly at AHRQ, in cases where studies do not have as their primary focus a priority population, sufficient numbers of members of priority groups may not be present for sub-group analyses, especially in the case of systematic reviews.
- Future iterations of the inventory will need to drill down on the representation of priority populations in studies.

CER Data Infrastructure

Substantial Federal and private sector infrastructures exist that could be used to identify potential CER priorities, to support the conduct and improve the productivity of CER, and to enable the translation of research findings into actionable information. However, the current infrastructure for CER is fragmented, and it is not coordinated or mobilized in a way that would enable providing coherent and targeted support for CER.

Patient-level Databases and Databases to Support Researchers

Federal agencies support or have access to substantial patient- and person-level databases that could support CER. Additional databases in the private sector can also deliver specialized content for CER. For example, these Federal and private sector databases can support or enable:

- Analyses preparatory to CER, such as.:
    - Disease prevalence and burden to help determine priority areas for comparative effectiveness research.
    - Utilization and distribution (e.g., geographic) of alternative interventions to help identify variations in practice and candidate interventions for CER.

    - Patient characteristics, socioeconomic attributes, comorbidities, and so forth, to determine the availability of certain patient populations for clinical trials, registries, and other person-level studies.
- Observational studies and retrospective data analysis (e.g., mining data from natural experiments).
- Support for prospective studies, including efficient development of registries and objective collection of treatment detail.

Important considerations for investing in and applying patient/person level databases to CER include:

- Potential to link to other databases that enrich the person/patient view, such as databases containing socioeconomic characteristics of individuals and mortality information (e.g., the Social Security Deathmaster or the CDC National Death Index).
- Potential to link databases that contain clinical information to those with transactional information (e.g., linking claims databases that have chemotherapy detail on cancer patients to electronic health records or registries for the same patients that have clinical data such as cancer stage, histology, and patient status).
- Research readiness of the databases (e.g., requiring minimal time on the part of the researcher to learn database attributes and develop special programs for data clean-up and access).
- Requirement to maintain security and privacy for any personally identifiable health information.

Appendix C lists some key patient-level databases with potential applications for CER. Among the ones available through Federal agencies are the major administrative databases maintained by CMS, the medical records databases at VHA, targeted databases maintained by AHRQ and NIH focused on service areas (e.g., HCUP on hospital-based care), and the NIH's SEER cancer registry.

Key private sector databases for CER include large administrative databases with longitudinal health care detail on millions of patients, and consolidated databases on EHRs. To the extent that these repositories can be linked (for which many have the potential), they can be highly valuable assets for CER, particularly because they account for commercially insured populations that are not captured in Federal and state databases.

In supporting research activities, the following Federal data infrastructure assets can speed communication among researchers and expedite identification of researchers with special skills:

- AHRQ: the DEcIDE Network, the CERTs (Centers for Education & Research on Therapeutics), and group of EPCs (Evidence-Based Practice Centers).
- NIH Clinical Translational Research Awards (CTSAs) recipients.
- CDC: Evaluation of Genomic Applications in Practice and Prevention (EGAPP) workgroup.
- HRSA research networks: Pediatric Research in Office Settings (PROS) and Emergency Medical Services for Children (EMSC) groups, among others

- SAMHSA: National Child Traumatic Stress Network
- VA Research Center of Excellence

Other databases for supporting researchers include:

- ClinicalTrials.gov (Federally and privately supported clinical trials).
- MEDLINE/PubMed (biomedical journal literature), HSRProj (Health Services Research Projects in Progress).
- CRISP (biomedical research funded by NIH, including clinical trials and other studies).
- Disease-oriented databases, surveys and Web sites, including the Longitudinal Studies on Aging (NCHS and NIA) and the Cardiovascular Health Study (NHLBI).
- Survey of Mental Health Organizations, General Hospitals Mental Health Services, and Managed Care Organizations (SAMHSA).
- Numerous CDC disease and research data assets and sites, including the NCHS surveillance systems, cancer registries, and vaccine registries.

None of these databases with actual or potential applications in CER were developed for the explicit purpose of comparative effectiveness research. Furthermore, they generally have not been organized or indexed to enable searching for CER. For example, careful record-by-record inspection of such research study databases as ClinicalTrials.gov and CRISP is required to identify CER. In order to assess current gaps and support translation and adoption of CER findings efficiently, these databases would require "tagging" of records or related searching functions that would enable accurate identification of CER.[27]

Dissemination and Translation Infrastructure

A few agencies, notably AHRQ, VHA, NIH, and SAMHSA, have capacities to translate CER into actionable information for practitioners, patients, and other target audiences. The VHA's capabilities for translation and adoption are inherent in its integration of research and patient care at VHA treatment centers. Additional agencies also have capabilities for disseminating information to segments of consumers and practitioners. All of these agencies have the potential to influence adoption of CER findings.

There are, however, minimal formal mechanisms to disseminate and translate CER from research agencies such as AHRQ and NIH into the delivery system side of HHS (e.g., HRSA, IHS, SAMHSA, CMS QIO's). In addition, given the current expansion of CER and the increased emphasis on achieving impact from its findings, the current dissemination and translation capacity of the relevant agencies involved in CER is likely to be insufficient for achieving CER's potential.

Some of the key elements that can be leveraged in a comprehensive and articulated CER dissemination and translation strategy are outlined below.

[27] In MEDLINE, for example, indexing tags for particular "publication types," such as Randomized Controlled Trial, Clinical Trial, Phase III, Meta-Analysis, and Review, would readily enable searching for journal articles that report such studies.

- AHRQ
  - CER methods guides, tools, and resources made available via the AHRQ Web site, Web conferences, public service announcements, advertising campaigns, online audio guides available to public, and other means for informing consumers, clinicians, and policymakers.
  - The John M. Eisenberg Clinical Decisions and Communications Science Center, which focuses on translation of research to various target audiences.
  - AHRQ Publications Clearinghouse.
  - AHRQ dissemination partnerships, including with health professional societies, patient advocate groups, and non-profit organizations focused on particular diseases/conditions.
  - Effective Health Care Program Stakeholder Group, which helps to identify important information gaps, ensure transparency, and provide feedback on reports.

- CDC
  - Information to monitor the adoption of CER recommendations and to track the effects from changes in clinical practices and policies on the following process and outcomes measures: clinical management of specific conditions, including the use of medications and other specific services, and intermediate health-related outcomes, such as test results; incidence and prevalence of specific conditions; personal behaviors, health status, and functioning; and births and deaths.
  - Public use data from NCHS surveys available through the CDC/NCHS Web site and internal confidential data available for researchers through the NCHS Research Data Centers.
  - NCHS/CDC reports, including Data Briefs and E-Stats, and other analyses available through the Web site, and articles in the peer-reviewed literature.
  - Dissemination by and with collaborators, including sponsors of specific data collection and analysis.

- DoD
  - Searchable publication libraries, including the Military Health System Publication Search.
  - DeployMed Research Link, which informs Service members, researchers, health care providers, military leaders, and others about DoD and other Federally funded medical research related to deployments since 1990.

- NIH
  - Clinical and Translational Science Awards (CTSAs), which are NIH-funded academic centers that translate research into practice.
  - Nation Cancer Institute's Physician Data Query, an online database that summarizes study results in prevention, screening and management of cancer in versions appropriate for physicians and for patients.
  - Research databases, including MEDLINE/PubMed, HSRProj, CRISP, and ClinicalTrials.gov.

- Public health campaigns, such as Red Dress (women's heart health) and Small Steps Big Rewards (weight loss).
- NIH Consensus Development Conference program, which summarizes knowledge about a variety of clinical and public health interventions.

- VHA
  - QUERI (Quality Enhancement Research Initiative) program for enhancing the uptake of evidence within VHA.
  - Periodic research summaries and issues briefs for senior VHA clinical and policy leaders, and related research results disseminated to researchers.
  - CME programs for nurses and other health professionals that incorporate recent research findings.
  - Print and online patient education tools, including the MyHealthE Vet Web site, for dissemination to patients.
  - Point-of-service decision-support tools and reminders to clinicians within the VHA EHR system guiding practice toward the most effective treatment, including a Web portal for clinicians to access clinical practice guidelines.

- SAMHSA
  - National Registry of Evidence-based Programs and Practices (NREPP) and the Technical Assistance Centers can serve as translation vehicles. NREPP is a searchable online registry of approximately 140 mental health and substance abuse interventions and targeted outcomes; it provides quality of research and "readiness for dissemination" ratings.
  - The Addiction Technology Transfer Center (ATTC) Network is comprised of 14 Regional Centers and a national office which facilitates alliances among providers, administrators, and recovery and treatment communities, and connects them to the latest research and information through activities such as skills training, academic education, online and distance education, conferences, workshops, and publications.
  - The National Centers for the Application of Prevention Technologies (CAPT) work to bring research to practice by assisting States/Jurisdictions and community-based organizations in the application of the latest evidence-based knowledge to their substance abuse prevention programs, practices, and policies.
  - The SAMHSA Health Information Network (SHIN) provides a one-stop, quick access point that connects the behavioral health workforce and the general public with the latest information on the prevention and treatment of mental and substance abuse disorders.

- FDA
  - Web site provides news and other information to physicians and consumers on drugs, biologics, and devices.

- Office of Public Health and Science (OPHS)
  - Comprises 12 core public health offices and the Commissioned Corps, some of whom work with population and community-based networks to disseminate health information (e.g., Office of Disease Prevention and Health Promotion, Office of

- Office of the National Coordinator for Health Information Technology (ONC)
  - Efforts to develop and implement a nationwide, interoperable health information technology infrastructure could provide a means for incorporating CER into decision-support systems for clinicians and other applications in health care.

- HRSA
  - Among multiple dissemination vehicles, the AIDS Education and Training Centers Program and the Ryan White HIV/AIDS Program support a network of 11 regional centers and more than 130 associated sites that conduct targeted, multidisciplinary education and training programs for health care providers treating people living with HIV/AIDS.
  - HRSA's Maternal and Child Health Bureau disseminates information using cooperative agreements with professional organizations and academic institutions, and funds grants for continuing education to academic centers across the country, specifically for the purpose of translating research into practice.

There is virtually no capacity to track the impact of CER dissemination, translation, and adoption activities. As a result, this limits the ability to measure the impact of CER and to conduct research on effective approaches. Claims databases could be one resource for tracking changes in practice over time and their impact.

Human and Scientific Capital

The future workforce engaged in CER should include experts from a wide array of disciplines, including biostatistics, epidemiology, mathematics, economics, and ethics. To date, however, there has been little focus on human and scientific capital infrastructure for CER. The principal exception is the close affiliation of certain AHRQ activities involving academic centers and other organizations, including the DEcIDE network, CERTs, EPCs, the Eisenberg Center, and various awards to researchers. AHRQ funding of DEcIDE network members and EPCs supports research trainees at those organizations. AHRQ also provides career development (K) grants focusing on generation of new scientific evidence and analytic tools that enable the prioritization of evidence-based services and goals for patients with multiple comorbidities.[28] In addition, AHRQ has sponsored other scientific and methodological activities, including development of methods guides, training seminars, and related events (e.g., at AcademyHealth and other professional conferences), and various workshops and support materials on MEPS, HCUP, and other data sets.

NIH provides significant training opportunities that could incorporate CER, including support for medical students interested in research, clinical fellowships, workshops for researchers, training grants, and consensus conferences. The CTSA program at NIH provides translational development support at academic and other research centers, some of which addresses evidence-

[28] http://grants.nih.gov/grants/guide/notice-files/NOT-HS-08-004.html.

based medicine approaches, if not CER in particular. The NIH K30 Clinical Research Curriculum Awards support training in design of clinical research projects, hypothesis development, biostatistics, epidemiology, disease mechanisms, medical technology, human genetics, and the legal, ethical, and regulatory issues related to clinical research.[29]

Although DoD has an extensive training and professional education infrastructure, it does not focus on CER.

A small number of training programs at academic centers focus on areas that address methodologies and study designs related to CER. Among these are the Clinical Research Training (CREST) program at Boston University, which provides training in clinical research that includes epidemiology, clinical epidemiology, health services research, biobehavioral research, and translational research,[30] and the Duke Clinical Research Training Program, which provides training in quantitative and methodological principles of clinical research, including research design, research management, medical genomics, and statistical analysis.[31]

Several agencies draw on the considerable scientific and methodological expertise resident in the FDA, but there is little emphasis on comparative effectiveness research at that agency. These informal links to scientific expertise could be formalized; also, specific CER expertise could be housed in selected agencies with an expectation of a cross-agency role. FDA expertise would be of exceptional value in, for example, understanding the respective merits of alternative study designs for assessing efficacy vs. effectiveness and for collecting and assessing adverse event data, strengths and limitations of using surrogate endpoints and other biomarkers in CER, incorporation of genomics and other aspects of personalized medicine into CER. Phase III and phase IV studies could also generate evidence on comparative effectiveness, as well as on other scientific and methodological aspects of CER.

Despite the promise of "practical" or "pragmatic" trials for CER, methodological gaps and threats to internal and external validity remain. Real world trials must deal with confounders, including confounding by indication and presence of comorbidities, selection bias, and other factors that impede the assessment of cause and effect. Focused research to improve the validity of practical trials and interpretation of their findings could enhance the use of these study designs.

Further development of mathematical modeling approaches and retrospective data analysis capabilities would also provide alternative means of analyzing comparative effectiveness, as well as generating viable research hypotheses and providing input for designing primary and secondary CER.

Gaps in the Current CER Landscape and Investment Opportunities

The inventories of CER and CER data and research infrastructure reveal gaps and other challenges for achieving the potential of comparative effectiveness research.

[29] http://grants.nih.gov/training/K30.htm.
[30] http://www.bumc.bu.edu/clinepi/crest/general-info/
[31] http://crtp.mc.duke.edu/content.asp?page=about

Coordination across the CER framework: Substantial CER assets exist across the Federal Government, but coordination is necessary to capture their full value. Several challenges exist in achieving this:

- Prior to this report, there was no standardized Federal definition for CER; aligning organizations around this definition will be necessary for identifying, cataloging, and disseminating CER in a coordinated manner
- Difficulty in setting national CER priorities.
- Structural barriers that limit collaborations among agencies.
- Limited coordination with private sector CER efforts. This includes lack of integration of existing data sets across payers, suboptimal development of CER data infrastructure, an inability to track populations and treatments across payers, and suboptimal translation and adoption of CER findings.
- Unrealized benefits of stakeholder involvement. Greater involvement of stakeholders (e.g., patient advocates, health professionals, researchers, technology manufacturers, payers) in CER processes can help to achieve the goals of CER, including more informed priority setting, input on certain aspects of study design (e.g., identification of important subgroups and patient-centered outcomes), and identification of target audiences for CER and strategies to reach them.

Research: Despite the comparative effectiveness research to date, there are many unanswered questions.

- Those who sponsor and design clinical trials continue to face challenges in tradeoffs between internal validity of CER for causal effects of interventions on outcomes and external validity of CER to heterogeneous patient groups and routine health care settings.
- Increased emphasis on well-conducted pragmatic trials could increase acceptance of CER findings.
- May research questions for important clinical health care decisions remain unanswered

Human and scientific capital: Due in part to the increasing interest in comparative effectiveness research, continued investment in human and scientific capital for the field is needed.

- Greater investment is needed in developing education and training programs to support the development of professional talent, the development of methods for linking and using databases for CER, the development of new methodologies for pragmatic trials, effective translation and adoption of CER findings into practice, modeling approaches for CER, and evaluation of the impact of CER
- More methods work is needed to advance the state-of-the-art for pragmatic trials and to provide training for using these study designs.
- Recent growth in training for the related fields of health technology assessment, outcomes research, and health economics, among others, has helped to yield a cohort of researchers who are well-positioned to become more expert in CER, along with

CER Data Infrastructure: The scope and scale of CER requires data infrastructure that may outstrip current capabilities.

- Current data sources are fragmented and limited in terms of clinical robustness and longitudinal data capture.
- An evolving inventory of CER data infrastructure is needed to track the capacity of this infrastructure and provide a basis for its further development; this inventory should include observational databases, registries, claims and other administrative data, pharmacy and laboratory data, adverse events registries, EHR networks, and other health information technology.
- In addition to one or more inventories, greater understanding is needed regarding the strengths and limitations of these data sources, and areas for their further development. An example of a relevant resource is the 2007 *Registries for Evaluating Patient Outcomes: A User's Guide*, produced by the AHRQ's DEcIDE Research Center.
- Investment in linking such data sources is more likely to be realized by establishing clear information policies and technical standards, standardized terminology, improved platform capability, novel search algorithms, mechanisms to maintain patient privacy, and controls to access data, and by reducing and coordinating data processing times.[32]
- There are few searchable electronic inventories or related databases of CER and CER infrastructure. While sources like ClinicalTrials.gov, CRISP, MEDLINE, and HSRProj contain information about completed and ongoing CER, but they are not presently configured or linked to serve the needs of CER.
- Absence of an inventory of CER limits the ability to assess the magnitude and nature of the current portfolio of completed and ongoing CER, to identify CER on particular topics, and to inform priority-setting for CER.
- A comprehensive inventory of CER infrastructure would improve the ability to conduct CER and to allocate resources to develop the national capacity to conduct CER.

CER Dissemination and Translation: Many findings to date from CER have not yet been fully integrated into clinical practice or made accessible to patients in easy-to-understand language.

- Certain effective dissemination avenues are in place, including among some of the agencies engaged in CER. Except for AHRQ, however, these agencies are not yet oriented to CER and do not adequately extend beyond dissemination alone to translation and adoption of CER into practice.
- Tools and mechanisms to support clinicians and patients in incorporating available CER information are lacking. This information needs to be delivered to the front line of care where health decisions are made and results measured.

[32] See, for example: Diamond CC, Mostashari F, Shirky C. Collecting and sharing data for population health: a new paradigm. Health Aff (Millwood) 2009;28(2):454-66.

Priority populations and other sub-groups: At present, the agencies have largely separate approaches to addressing these groups. A better-coordinated Federal approach is needed to address priority populations and priority conditions, including sub-groups with multiple chronic conditions.

- Greater attention on designing studies with sufficient power to discern treatment effects and other impacts of interventions among patient sub-groups (e.g. accounting for heterogeneity of treatment effects) will better serve clinical decision-making, enabling more individualized, patient-specific care.
- Improved partnerships with Federal grantees serving priority populations, such as Community Health Centers, will enhance their engagement with CER.
- Improved access to and utilization of Federally sponsored databases that include priority populations can significantly enhance the inclusion of sub-groups into CER.

Types of interventions: To date, CER has been disproportionately focused on pharmacologic treatments rather than the full spectrum of intervention types. This likely derives in part because of the relative emphases of the research agendas of agencies that sponsor CER and the focus of the private sector is primarily on new drugs and biologics. The emphasis on pharmacologic treatments has meant fewer resources for other interventions, including behavioral, procedures, prevention, and delivery system interventions, that can have major impacts on health outcomes.

VII. PRIORITY-SETTING PROCESS

The Council actively sought public input throughout this process, and this input significantly influenced all Council decisions. To help guide the Council's deliberations on the definition, framework, and priorities for comparative effectiveness research, the Council held three listening sessions and solicited additional public comments online. The Council heard from over 300 stakeholders representing health care associations; consumer, community, and advocacy organizations; academia and think tanks; patients; providers; hospitals and hospital systems; payers; pharmaceutical companies; foundations, public health entities; and private sector companies engaged in the health care field. One U.S. Senator also submitted comments.

Several respondents honed in directly on the reason why investments in CER are important. One person, for example, said that CER is crucial to reforming the practice of medicine to increase the quality, safety, value, and effectiveness of what providers bring to patients on a daily basis. Other respondents addressed a wide range of interrelated issues, including priorities for the research agenda, collaboration, infrastructure development, research methodology, transparency, care delivery, cost, and knowledge transfer. Many patients expressed their need for this type of research; one of the most emotional and moving testimonies came from the mother of a child with a seizure disorder in Chicago who had struggled to find the best treatment for her child. A physician from the American Board of Orthopedics summarized many physicians' testimony by saying, "developing high quality, objective information will improve informed patient choice, shared decision-making, and the clinical effectiveness of physician treatment recommendations."

The public input has been extremely valuable in informing the Council's deliberations, and many of the major thematic threads that run thought the public comments are reflected in the strategic framework, focus, and recommendations for priorities for OS CER funds. Details about what the public had to say are contained in Appendix A.

The Council also conducted a first draft inventory of CER and data infrastructure (outlined above) to help identify gaps in the current CER landscape. For the Office of Secretary funding recommendations, the Council proceeded through structured deliberations informed by public input, developed an inventory of current activities, established prioritization criteria and a strategic framework, and discussed the unique role for OS funds to fill gaps and build the foundation for future CER. In the future, the Council should continually and actively engage stakeholders inside and outside the government, including patients, providers, payers, employers, industry, academia, and others. This critical component of the priority-setting process could take the form of even more active participation by external stakeholders in the future.

VIII. PRIORITY RECOMMENDATIONS FOR OFFICE OF SECRETARY CER FUNDS

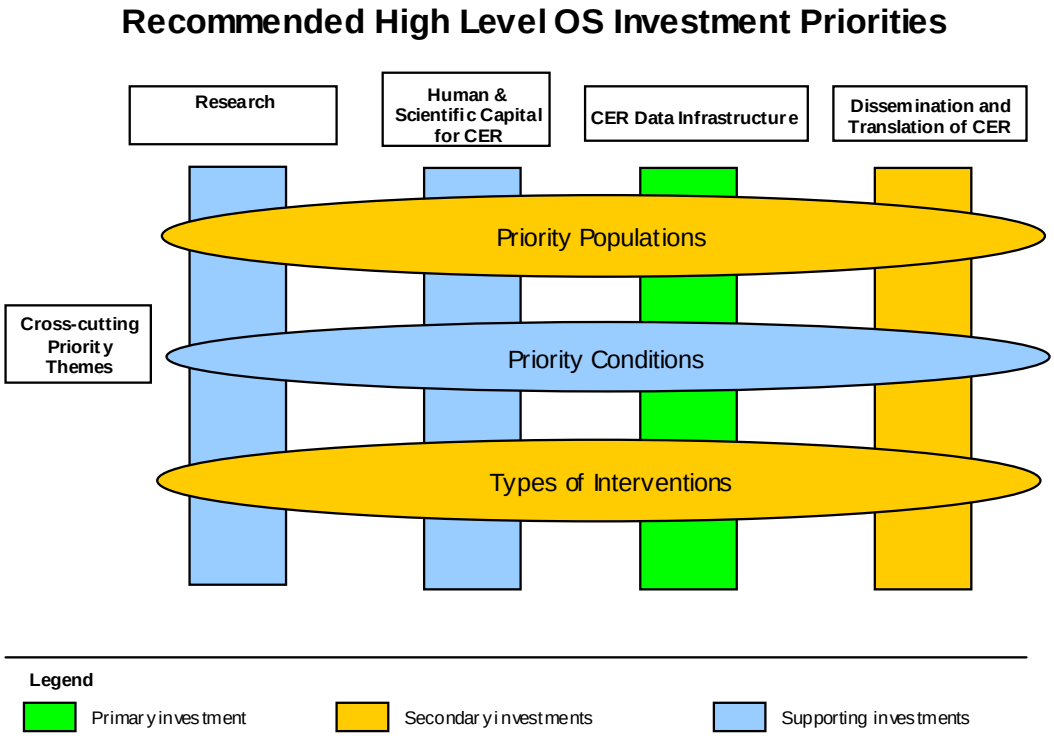
Using the strategic framework for CER discussed in Section V, and taking into consideration the unique role that OS funds can play in addressing high priority gaps, the Council developed a recommended high-level investment strategy for the use of the OS ARRA funds. The strategy has three different levels of priority recommendations for OS fund investments in the Core Activities and Cross-cutting Priority Themes in the CER framework (Figure 3).

- **Primary investment.** This area of investment should represent a large portion of the OS funds. It best fulfills the full range of prioritization criteria and requires scaled investment in order to be successful. The Council recommends that CER Data Infrastructure be the primary investment.

- **Secondary investments.** These areas should also receive significant investment. They are as critical to success in CER as the primary focus, but individually may require a smaller amount of funding to be successful. The Council recommends that Dissemination and Translation of CER, Priority Populations, and Priority Types of Intervention be secondary investments.

- **Supporting investments.** These areas should not be the major focus of OS funding as they do not fulfill the prioritization criteria as well as primary and secondary investments, but some funding may be necessary to support and enable investments in higher priority areas and fill identified gaps. The Council recommends that Human and Scientific Capital, Research, and Conditions receive supporting investments. It is important to note that these recommendations pertain only to OS funds; AHRQ, NIH, and VA have a history of significant investments in Research, Human and Scientific Capital, and Conditions.

Figure 3



The Council believes that this strategy and distribution of investments will best position the Secretary to:

- Respond to patient and physician demand for CER.
- Balance achieving near-term results with building longer-term opportunities.
- Capture the distinctive value of the Secretary's ARRA funds.

While it is the responsibility of the Office of the Secretary to operationalize this strategy, the Council's rationale for these recommendations is designed to help guide the Secretary in making specific investment decisions. The Council based its rationale for each level of investment in the strategy on the prioritization criteria described above, as well as representative examples of investment in each area proposed through the public comment process and by Federal agencies.

Primary investment

CER data infrastructure development is the most distinctive opportunity for OS ARRA funding. It requires a large, up-front infusion of capital to be successful that is unlikely to come from any source other than OS ARRA funds, making it ideal for this funding mechanism. It has broad potential impact, with the ability for resulting research to address conditions and populations captured in the primary data. Given the absence of comprehensive databases and data evaluation

tools (See Section VI), there is significant demand from the patient, clinical, and public health communities for new, expanded data infrastructure and data access to support decision-making. Finally, investments in data infrastructure have the potential to generate significant additional investments in two ways. First, some of these investments could take the form of public-private partnerships. Second, data infrastructure is a tool that, once developed, will result in new research conducted and/or funded by entities such as biomedical research organizations, payers, foundations, and health care providers.

The Council received proposals on a number of potentially promising initiatives related to data infrastructure, including but not limited to:

- Building, expanding, and linking longitudinal administrative claims databases.
- Linking administrative data with EHR-based or registry data.
- Expanding high-impact patient registries, (e.g., collaborations with specialty organizations, SEER).
- Distributed data networks populated by EHRs in practice and provider settings.
- Expanding analysis of FDA and private sector data on drug and device trials and safety.

As the Office of the Secretary identifies specific opportunities in data infrastructure, the Council recommends that it consider most carefully those that:

- Expand access to existing resources, especially those currently managed by Federal agencies.
- Create scaled platforms by leveraging existing data and capabilities in the private sector.
- Capitalize on linkages between health IT investments and the potential for CER infrastructure to develop evidence to inform decision-making.
- Ensure that infrastructure is responsive to needs of patients, providers, and other decision-makers—and not driven by what is most feasible.

The Council appreciates the relationship and need for coordination between CER and health IT (e.g. through a distributed network of EHRs) investments. As the Secretary develops HHS's full portfolio of ARRA investments, it will be critical to consider both CER and health IT holistically, not as policy silos, recognizing that success in CER is largely dependent on success in health IT and vice versa.

With all data infrastructure investments, the government will need to ensure data security and privacy. Protecting security and privacy is key to maintaining the public's trust.

Secondary investments
Secondary investments include a core area of investment—Dissemination and Translation of CER—and two cross-cutting themes—Priority Populations and Types of Intervention.

Dissemination, translation and adoption of CER is about realizing the benefits that comparative effectiveness research has to offer both patients and providers. While the breadth and depth of the near-term impact depends on what types of pilot programs the OS supports, the lessons and tools for translation developed by those pilots will be relevant to all.

The lack of reliable success in disseminating findings from CER in ways that translate into better health outcomes highlights the uncertainty and difficulty of this enterprise. However, dissemination and translation is essential to improving outcomes for patients and the link between evidence production and how best to get this information to physicians and patients in a way they understand is critical to capitalizing on the CER investment. Despite important efforts by the Federal Government, especially AHRQ, NIH, VA and DoD, the majority of current funding goes to building evidence as opposed to ensuring that the existing evidence base is utilized in patient care and health systems management. This creates a unique role for OS ARRA funding. Investments in dissemination and translation programs also have the potential to generate additional investments, especially from providers, if private institutions elect to implement similar efforts or partner with the Federal Government on translation efforts.

There are a wide range of potential dissemination, translation and adoption programs that the OS could support, including:

- Investing in dissemination and translation of CER findings throughout the Federal delivery system.
- Dissemination and translation through partnerships with provider and/or patient organizations.
- Decision support and shared decision-making tools to provide information to clinicians and patients at the point of care.
- Developing standards for communication tools for patients and providers, (e.g., a patient-friendly simple scoring system).
- Partnering with an existing consumer media channel (e.g., Internet search engine or health information site) to expand patient access to existing CER data.
- Creating a National Patient Library with a primary focus on providing evidence to patients in easy-to-use and understandable formats.

The Council recommends that the Office of the Secretary consider the following in making investments in dissemination and translation:

- Investing in better understanding the most effective methods to disseminate and translate research findings to improve patient outcomes.
- Identifying opportunities both to develop tools for translation and to pilot implementation of these tools.
- Partnering with provider organizations in Federal agencies, as well as in states and the private sector.
- Accounting for potential surrogate decision-makers (e.g., families) and the context for decisions in patient-focused tools.
- Ensuring that programs address a specific need articulated by the implementing organization or the partner to ensure success and the sustainability of dissemination activities.
- Focusing on developing standards for communication.
- Increasing understanding of the most effective methods to disseminate findings to clinicians and patients to inform decision-making

From an operational perspective, investments in the cross-cutting themes are somewhat distinct from investments in the core areas. Whereas funding for a core area might go to a project or organization focused on a specific activity, funding for a cross-cutting theme requires multiple coordinated investments and activities to be successful. Investments in these themes could cover some or all of the four core activities: research, data infrastructure, human and scientific capital, and dissemination and translation. These investments could involve a coordinated investment across HHS or the Federal Government, or they could be focused in academic centers, integrated delivery system organizations, private industry, or other non-governmental entities. Collaborative efforts to inform and transform care will be essential to achieving meaningful impact across these cross-cutting themes.

Investments in specific populations, meanwhile, will help ensure that the benefits of CER are available to all. It can also focus CER efforts on populations with existing health disparities and worse outcomes. CER has the potential in some populations, such as racial and ethnic minorities, to fill critical gaps that, historically, efficacy research has left unaddressed.

The Council identified several populations for whom the Secretary should consider allocating CER funds:

- Racial and ethnic minorities
- Persons with disabilities
- Elderly
- Children
- Patients with multiple chronic conditions

Investment in specific types of interventions in a cross-cutting manner also presents a unique opportunity for the nation's health system. The Council has identified six specific interventions for the Secretary to consider that address large and varied populations, resulting in high potential impact, are areas of high clinical uncertainty, and are not being adequately addressed by other entities. They are:

- Medical and assistive devices (e.g., comparing rehabilitative devices).
- Procedures and surgery (e.g., evaluating surgical options or surgery versus medical management).
- Diagnostic Testing (e.g. comparing imaging modalities for evaluating certain types of cancer)
- Behavioral change (e.g., developing and assessing smoking cessation programs).
- Delivery system strategies (e.g., testing two different discharge process care models on readmission rates or testing two different medical home models on preventing hospital admissions and improving quality of life).
- Prevention (e.g., comparing two interventions to prevent or decrease obesity, comparing strategies for reaching populations that do not access the health care system with prevention efforts).

Furthermore, the Council recommends that the Office of the Secretary consider the following in making investments in the cross-cutting themes of priority populations and types of interventions:

- Focusing on immediate, specific patient needs that can generate results.
- Concentrating on areas with cross-cutting gaps in research, data infrastructure, scientific capital, and/or translation.
- Building on promising systems and practices already in place, both within the government and in the private sector, and measuring results when scaled up and disseminated.
- Strongly encouraging coordination across the government and with entities outside of the government.

Supporting investments

The Council recommends that the OS reserve some ARRA funding for Research, Human & Scientific Capital, and the Conditions cross-cutting theme. Because these investments and topics are the major foci of CER activities at NIH and AHRQ, both of which will likely utilize ARRA funds administered by those organizations for these purposes, they do not represent distinctive investment for OS funds. However, there will likely be targeted investments in these areas that could support other OS ARRA efforts, such as training new researchers in CER methods or addressing gaps not addressed elsewhere in the Federal Government.

In making these targeted investments, the Council recommends the Office of the Secretary consider:

- Focusing on areas that maximize the value of the Secretary's investments in other areas.
- Avoiding duplication of efforts with other agencies.

For all of the above investments, the Council recommends that the Office of the Secretary consider the portfolio of investments and where synergies exist to leverage one investment into multiple areas. For example, a data infrastructure investment that can also be used for a cross-cutting priority theme would be of higher value than an investment that has more limited applications. Doing so will help to ensure that the funds allocated to the Office of the Secretary for CER will have a significant positive impact on the quality of patient care in the near term, and lay the foundations for continued improvements going forward.

IX. LONGER-TERM OUTLOOK AND NEXT STEPS

Outlook

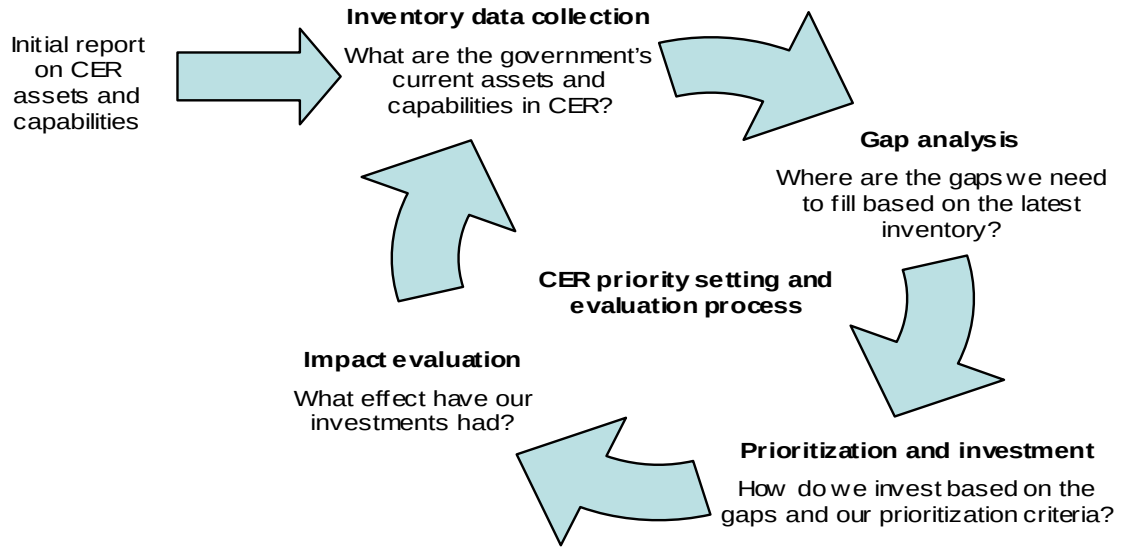
The CER investment strategy recommended in the previous section, if implemented successfully, has the potential to further a number of elements of the Council's vision for improved patient care. In the near term:

- CER dissemination and translation pilots in Federal health care delivery systems could help empower patients and their physicians to make better decisions now about their care and serve as models for expansion to private delivery systems. Moreover, a time limited investment can support establishment of a systematic strategy for translating the products of all relevant research to benefit patients served by Federal programs.
- An increased emphasis on CER for priority populations could ensure that all will benefit from comparative effectiveness research.
- Improved access for researchers to existing Federal data sources, and development and enhancement of distributed data networks and patient registries outside of the Federal Government, could jump-start a new wave of CER in the areas that matter most to patients.
- The inventory of Federal activities in CER will help reduce duplicative or uncoordinated investments among Federal agencies and help create transparency for patients.

It will be essential that a continuous cycle of CER priority-setting and evaluation of impact take place. The four critical steps in this cycle are inventory of CER and infrastructure; gap analysis; priority setting; and evaluation of impact. Figure 4 below depicts this process.

Figure 4

Continuous Evaluation of CER Inventory, Gaps, Priority Setting, and Impact



The strategic framework for comparative effectiveness research is intended to lay the groundwork for longer-term initiatives, such as innovative public-private partnerships to build data infrastructure and conduct CER. The goal of this investment is to generate some near-term results and momentum for the future. This strategy allows the government to facilitate the building of needed infrastructure, to expand access to existing infrastructure, and to demonstrate proof of concept for implementation efforts. These efforts are only a first step, however, to

achieving the vision of improved quality, safety, efficiency, equity, and patient satisfaction through improved medical decision-making and an optimized health care delivery system.

Indeed, a number of clear issues and challenges will remain for Federal CER efforts in the near term:

- **Listening and Engaging External Stakeholders.** While the Council has worked to create transparency and responsiveness in this process to date, it is critical that it continue to have a patient-centered focus going forward. In the future, the Federal Government may want to consider the options of listening and engaging stakeholders with representatives including, at minimum, patients, providers, payers, employers, and industry representatives, to guide CER or broader patient-centered outcome efforts.
- **Continued Coordination.** The Council laid the groundwork for coordination, but coordination will need to become embedded across the Federal Government. As the government makes investments in CER, there must be a mechanism in place to track and coordinate these investments and avoid duplication of efforts.
- **Building Scientific and Human Capital.** To maximize the potential benefit of investments in CER, the nation needs more researchers trained in the applicable research methods and further development of these methodologies. This presents both a short-term and a long-term challenge.
- **Maintaining Gains.** These investments represent only the beginning of CER efforts. New research findings will need to be disseminated and successful translation of evidence efforts should be expanded. New databases and data sets need to be maintained and kept current, and the catalog of Federal activities and data infrastructure in CER needs to become a living document.
- **Building Leverage.** The Federal Government is now a major funding source of CER, but the private sector still represents a majority of the investment in biomedical research. The government needs to find innovative ways of partnering with the private sector to leverage government investments and help private-sector investment better serve patients.
- **Keeping it Current.** There are no widely accepted and applied common standards or approaches for periodically re-evaluating CER to ensure that previous conclusions still hold. A system must be developed to ensure that the conclusions from CER remain valid over time.

These issues reflect both the fact that comparative effectiveness research remains in its infancy and that it must be seen as a continuous and iterative process that needs to constantly evolve based on the changing needs of the patient.

Next steps

There are a number of next steps leading to the Secretary's integrated strategy and spend plan for CER on July 30, 2009, and several requirements for the success in implementation of that strategy. Most importantly, it is critical to the success of CER and health care transformation that the plan is coordinated across the ARRA CER funding allocated to the Secretary, AHRQ, and NIH. Furthermore, the Secretary should develop the plan as part of HHS's broader portfolio of ARRA investments, not as a stand-alone program.

The following steps are needed to finalize the CER operational strategy prior to the July 30 deadline mandated by Congress:

- Integrate IOM and Council strategic recommendations and leverage the investments, resources, and capacity identified through the initial inventory effort.
- Provide more specific recommendations for a portfolio of initiatives for all of HHS' ARRA funds within the framework outlined in the report.
- Define metrics for evaluating success.
- Coordinate the submission of the CER ARRA spend plans to ensure that they cover the gaps in CER outlined in this report, and that the agencies' investments leverage the strengths of each agency and are complementary, not duplicative.
- Maintain transparency and engagement with the public.

The Federal Government will need to continue its work to coordinate CER investments and assure Americans that these resources are being invested wisely. ARRA required that the Council submit an annual report regarding its activities and recommendations concerning the infrastructure needs, organizational expenditures, and opportunities for better coordination of comparative effectiveness research by relevant Federal departments and agencies. The first annual report will likely be in June 2010.

Comparative effectiveness research is being considered as a key piece of health reform, and the Federal Government must demonstrate its capability to coordinate that investment, achieve impact, and measure the results. This report outlines the priorities and path forward. Now the Federal Government must make progress and deliver results for the American people.

APPENDICES

Appendix A. LISTENING SESSIONS AND PUBLIC COMMENT SUMMARY

Overview

In order to help guide the Council's thinking on the definition, framework, and priorities for comparative effectiveness research (CER), the Council held three listening sessions (April 14 in Washington, D.C.; May 13 in Chicago; and June 10 in Washington, D.C.) and solicited public comments through the hhs.gov/recovery Web site. The response was strong:

- 92 panelists testified
- Greater than 300 individuals and organizations submitted comments

A breakdown of the responses by stakeholder type reveals that over half of the comments came from three groups: health care associations; academia and think tanks; and consumer, community-based, and advocacy organizations. Additional comments were received from patients, providers, payers, hospital and health systems, pharmaceutical companies, foundations, public health entities, and private sector companies in the health care field. One U.S. Senator also submitted comments.

More important than the diversity of respondents is what individuals and organizations had to say. Respondents provided a wide range of opinions and offered recommendations on everything from stakeholder participation to how to prioritize investments in CER to specific areas of focus to knowledge transfer and dissemination.

Without question, the public input has been extremely valuable in informing the Council's deliberations; many of the major thematic threads that run through the public comments are reflected in the Council's strategic framework, focus, and recommendations for priorities for OS CER funds. Of particular value to the Council was the opportunity to engage with panelists at the listening sessions. This back-and-forth discussion enabled Council members to refine their ideas and solicit further feedback.

Before summarizing the key themes, it is useful to note that several respondents honed in directly on the reason why investments in comparative effectiveness research are important—CER matters. For example, one respondent talked about the value of and application of CER for everyone's health and health care. Another talked about how funding is crucial to reforming the practice of medicine to increase the quality, safety, cost benefits, and real world effectiveness of what providers bring to patients on a daily basis.

One theme that wove through many of the comments was the need for greater collaboration among Federal agencies, among organizations at the Federal, state and local levels, and between the public and private sectors. One respondent stated that because expertise on comparative effectiveness research resides in both public and private entities, every effort should be made to encourage public-private collaboration in the design, conduct, analysis, and reporting of CER. This discussion about collaboration dovetailed with the question of stakeholder input, including the need to ensure that patients have a defined and central role in the CER process.

Key Themes

Some respondents recommended targeted research topics; these ranged from testing the total effects of medication on the frail elderly, to testing the efficacy of a diet to treat children with seizures, to informing prescribing physicians on a wide range of what does and doesn't work well for patients with various complex conditions.

Most of the comments, however, fell into several broad categories—prioritizing the agenda, infrastructure development, research methodology and conduct, care delivery, knowledge transfer, cost, and health disparities and personalized medicine. A number of key themes and specific comments are summarized below.

Prioritizing the Agenda

A number of respondents tried to step back and look broadly at the question of how to prioritize the agenda for comparative effectiveness research and what criteria should guide decision-making in this arena. An overarching theme that echoed through many of these comments was the need to think big and look system-wide. One respondent stated that CER that is localized to a single disease may be less of a priority than questions that cross over diseases. Another talked about the need for CER to be undertaken for quality, efficiency, effectiveness, and other appropriate dimensions for health care delivery systems along the entire spectrum of systems integration, adding that the spectrum should include integrated delivery systems, multi-specialty group practices, single-specialty groups, "virtual" groups, and small medical practices.

A number of recommended areas of focus emerged. Many respondents talked about focusing on areas of major clinical significance and the greatest impact on health care delivery, including chronic conditions. One respondent specifically noted that CER on chronic diseases should focus on all relevant health care services, including medical and surgical procedures, diagnostics, and medical devices. Another respondent said that more attention is needed in the areas of post-acute and long-term care. Still others talked about the need for comparative effectiveness research on emergency care processes, and CER to evaluate regional differences in trauma care. A few people talked about studying the role of alternative treatments, including homeopathic treatments for chronic and acute disease states. Several respondents also talked about looking at conditions with the greatest impact on morbidity, and a few about doing research on conditions with the greatest impact on cost.

A few respondents discussed the need to ensure that the priorities of state and local jurisdictions be given consideration in evaluating various CER strategies. For example, one participant noted that many jurisdictions have on-going investigative agendas designed to improve program effectiveness that can be considerably amplified by Federal support, adding that such efforts would extend beyond purely clinical protocols to include the evaluation of public health, community-based, and behavioral strategies that may enhance the effectiveness of public programs.

One respondent suggested that significant resources be devoted to population-level interventions as well as patient-level effectiveness. Another respondent talked about the need for comparative effectiveness priority research areas to include critical cross-cutting research questions and cited

several examples (clinical decision-making, human-technology partnership, team coordination and continuity of care).

In addition, respondents talked about the need for Federal investments in CER to focus on health disparities and understudied sub-groups. Many of the respondents who addressed this topic talked about under-sampling of minorities in clinical trials and stressed the need for research that looks at the impact of various treatments on specific sub-groups, including women, minorities, people in rural communities, persons with disabilities, and children.

Infrastructure Development

A number of respondents honed in on the need to scale up the capacity to do comparative effectiveness research. As one respondent put it: "All healthcare reform proposals are predicated on the presumption that a robust and well-developed quality infrastructure exists. However, this is not uniformly the case."

Infrastructure capacity, as framed by the public comments, incorporates three components: human and scientific capital, organizational capacity, and data capacity.

Regarding human and scientific capital, respondents said that investments are greatly needed to enhance the skills, supply, and diversity of the research work force. One respondent pointed specifically to a dearth of researchers focused on mental health and substance abuse and treatment. Another respondent talked specifically about the need to increase the number of Hispanic health professional researchers, and suggested that HHS target Hispanic health professional, students, residents, and graduate students interested in serving in their communities.

Regarding organizational capacity, many of the comments focused on building capacity at the regional and local level. For example, one respondent talked about the role that health improvement collaboratives and chartered value exchanges can play in maintaining patient registries and other databases, and about using the information for performance reporting. A second respondent talked about the role that more community organizations could play in helping to address racial and ethnic health disparities were they to have the appropriate infrastructure and capacity.

The third critical subset of infrastructure development is data. A number of respondents talked about the need for both better data and access to data for comparative effectiveness research and decision-making. They urged the Council to access as much available data as possible, including clinical trials data, electronic health record systems, health care claims systems, administrative data, and Federal health data (including data from Medicare and Medicaid and that collected by the Veterans Health Administration). Respondents also talked about the need to invest in a coordinated effort to link public and private sector databases, as well as the need for standardized data available from the point of patient care.

Several respondents also talked about the value of registries, and the need to link data sets in order to provide valuable sources of data to examine appropriate use, effectiveness of care, cost of care, value-based health care, and other criteria. Another respondent stressed the need for

research that involves collaboration in different data environments and research that explores the use of different types of electronic health care data.

Research Methodology and Conduct

How should CER be undertaken? This is another theme that ran through many of the comments. Those who tackled this question addressed key issues that ranged from the enterprise level to guidance on study design. At the broader level, one respondent talked about the need for a broad Federal CER enterprise that spans treatment, prevention, promotion, and health-determinant interventions designed for both people and populations. Another respondent recommended adopting value of information principles and tools to prioritize CER investments on those studies where there is a greater likelihood that the research will lead to changes in practice. A third person spoke about the opportunity to fund research into "the science of CER" to build a foundation for this work.

Others talked about the scope of CER, noting that much of the research is conducted in single settings of care. One respondent, for example, noted that this poses a challenge for "generalizability," and suggested that many of the questions that remain unanswered relate to uncommon conditions or outcomes that have proven challenging to study. He recommended the use of multi-center research networks to address this issue.

Looking more closely at study design, one respondent noted that CER should continue to use a variety of study designs to generate evidence about the comparative effectiveness, comparative safety, and cost effectiveness of medical interventions. A second respondent talked about the limitations of randomized clinical trials, suggesting that the Council should also consider designs that are more common for evaluating comprehensive population-focused interventions, such as observational cross-sectional studies, quasi-experimental designs, and time series analyses. Another respondent stressed that clinical trial design and CER infrastructures must accommodate the goal of addressing health disparities. Another respondent pointed out that comparative effectiveness can at times be determined by assessing technology and using quantitative metrics rather than via an expensive and sometimes-lengthy clinical trial. A fourth respondent talked about the need to include utilization of laboratory services in order to effectively compare treatments and outcomes for major chronic disease cost drivers.

Several respondents also addressed the need for greater transparency throughout the process. They talked about the critical importance of transparency for reducing bias and rebuilding trust, and they recommended that researchers show results prior to adjustments as well as adjusted results. Respondents who tackled the issue of transparency also talked about the need to disclose in detail the methods and metrics used in any research. One respondent stressed that patients and providers need to know all the inputs that go into a research analysis so that they can weigh the costs, safety, and quality issues appropriately in each instance.

A corollary to transparency is addressing potential conflicts of interest. Respondents talked about the need to develop a strong and clear policy for conflicts of interest in both research and publishing, and suggested that funding decisions for CER should favor researchers and institutions that are focused on the public interest and do not have current conflicts. They also talked about the need for 100-percent disclosure and transparency at the outset of all conflicts by

individual researchers and institutions. One respondent specifically said that the ARRA expenditures on CER offer an opportunity to move to a platform where research funding is completely independent of other sources of funds in order to get to research that is independent, unbiased, untainted, and neither methodologically flawed nor influenced by industry.

Care Delivery

Several respondents pointed out that care delivery is critical, and that investments in CER are needed to look at how the health care delivery system should be organized and the best models for delivering care to patients. One respondent recommended that the Council invest in research that looks at optimal practice models for delivering patient care along with strategies for using information technology and clinical decision support tools to implement research findings into clinical practice. Another respondent suggested that CER is needed to look at the organization, design, and management of patient care. A third said that CER should focus on medical delivery systems and operations, resulting in information that can be leveraged to foster better clinical and cost outcomes.

Much of the discussion on care delivery was focused on people with one or more chronic conditions (e.g., diabetes). One respondent, for example, talked about the need for CER studies that compare current, more traditional models of chronic care delivery with team-based, patient-centers models that include patient education and self-care. Another respondent emphasized the need to focus research on the impact of non-medical services (e.g., providing housing) on cost-effective and clinical outcomes for chronically medically ill populations. A third person talked about CER around the role of support services (e.g., case management) in the health outcomes of people with HIV/AIDS; a fourth, about the need for CER on crisis residential services as an alternative to psychiatric hospitalization. Yet another respondent talked about the need to study the cost-effectiveness of community health worker interventions.

One respondent talked about the need to study care models that integrate primary and tertiary care. Another respondent suggested that there was a need for research into how to deliver care in a way that helps patients get the care they need, adhere to proposed treatment regimes, and prevent subsequent untoward effects of chronic diseases. Regarding adherence to treatment regimes, one respondent specifically noted that patient compliance is a seldom-accounted-for variable in CER, and he talked about the value of electronic verification devices to track compliance. Another respondent talked about the need to compare palliative care models to understand which processes of care and specific program interventions and models are the most effective.

One respondent noted that much of the literature on the impact of electronic medical records is anecdotal, and he expressed concern that people are considering the value of electronic health records without understanding the totality of what an effective system does for health care delivery. As a result, he urged that research be done to evaluate the comparative effectiveness of different types of EHR-mediated interventions. A second respondent likewise talked about the needs for research on how health information technology and EHR exchanges can be used to create more robust data sources and to help evaluate comparative effectiveness issues across a broader range of settings.

Knowledge Transfer

A number of respondents pointed out that all the data is meaningless if the information is not disseminated effectively. One respondent, for example, stressed that knowledge translation research must not be overlooked, while another respondent pointed out that both research and dissemination of research findings are essential to realizing the quality improvements and returns-on-investment that are integral to the success of comparative effectiveness research.

While respondents had different recommendations for how to approach knowledge transfer, there was a consensus that this work is critical. One respondent noted that the evidence base that is developed around clinical comparative effectiveness offers a substantial opportunity to improve value in health care if the information is disseminated and applied by physicians and patients. Others talked about the need to identify what approaches and incentives to dissemination and adoption are most effective (and under what circumstances), and when dissemination should target change at the organizational level, the community level, or the individual level. One respondent talked about cultural competence and health literacy research, and the need for both in order to change behaviors and improve lifestyles.

One respondent noted that while technology (including electronic health records) is one avenue for dissemination, other effective dissemination and translation techniques are also needed. She noted that while many strategies have been used to enhance the rate and extent of adoption of evidence-based best practices (including clinical guidelines, continuing education for health care professionals, patient education tools, and academic detailing), the approaches have not been well studied and the results are variable.

One respondent suggested that an independent body be established to disseminate comparative effectiveness research findings; others took the approach that everyone—including providers, payers, consumers, and employers—has a role to play in disseminating research results. Another respondent suggested creating a national citizens' advisory board to help HHS better understand the perspectives and values of the general public when designing and disseminating CER. Another respondent talked about the need not only to provide the evidence base for best disease prevention, health promotion, and/or clinical interventions, but also to look at how these findings can be implemented in "real-world, complex organizational settings."

Cost

Two distinct opinions about cost emerged: (1) that it should be a factor in comparative effectiveness research or (2) that it has no place in the discussion.

Those opposed to factoring cost into CER expressed concern that too often people put cost into a separate silo and make decisions without regard to efficacy, and they suggested that a focus on costs could lead to limiting access and benefits. For example, one respondent said that comparative effectiveness research should not be focused on looking for cheaper treatments, and it should not be the basis for coverage decisions. Another talked about the fear that CER results might impact physician reimbursement rates. Several respondents also expressed concern that CER could be used to restrict access to care, to deny coverage, or to reduce payments for interventions, thus undermining physician/patient decision-making and limiting patient access to treatment options.

On the flip side, other respondents felt equally strongly that cost was an integral component of informed decision-making. For example, one respondent said that information about costs enables understanding not only of the direct differences in terms of clinical outcomes but also of the value of interventions and whether they represent an efficient use of resources. Another respondent suggested that, if costs are not considered, the tradeoff in terms of lost health benefits would be too steep. Others stressed that a wide range of stakeholders—including employers, policymakers, and state and local public health departments—have said that they need cost information to make decisions.

Health Disparities and Personalized Medicine

Several respondents spoke about the related topics of the need to address health disparities within CER and support for the growth of personalized medicine. Inclusion of and attention to underrepresented sub-groups was spoken of as a means to address the problem of disparities in care. Others spoke of the importance of fostering the application of personalized medicine.

Respondents cited the need for more CER in the areas of preventive care, pediatric care and children's health, behavioral health interventions, addiction, mental disorders, and suicide prevention. One respondent pointed out that CER is needed to understand the cost and quality implications to the overall health system of continuing to under-treat conditions in systems that are siloed and distinct from mainstream health and health care. Another respondent specifically noted that the aim of personalized medicine and the mapping of the human genome is to achieve disease interventions much earlier (ideally at the point of preventing the disease from ever taking hold, he said).

One respondent stressed that CER must be mobilized to improve the health outcomes of various racial and ethnic minorities in order to close the gap that exists between the health status of some minority populations and other Americans. Others warned about relying on small, narrowly focused studies, suggesting that understanding and addressing health disparities requires a broader approach; conversely, respondents also cautioned against "one-size-fits-all" approaches that could decrease access to treatments. One respondent specifically talked about the need for research that examines health intervention outcomes across the lifespan, and for different minority and gender groups, in order to understand the effectiveness of interventions within and between population groups.

Several people talked about the need to design studies that appropriately include minority populations (see also *Prioritizing the Agenda*, above). For example, one respondent said that the design of studies must reflect the diversity of patient populations, including racial and ethnic diversity, and must communicate results in ways that reflect the differences in individual patient needs. Another respondent stressed that clinical trial design and CER infrastructures must accommodate the goal of addressing health disparities. There was also discussion more broadly about the need to build the infrastructure to address health disparities relating to people of color.

One respondent pointed to the dichotomy between studying populations and the promise of personalized medicine, asking: How can CER at a broad population level be balanced with the

goals and rapid scientific advancements in the area of personalized and stratified medicine in order to encourage the development of targeted therapies for sub-groups?

One respondent talking about personalized medicine recommended that CER studies include the evaluation of approaches to health care delivery and care management that foster the effective application of personalized medicine.

Appendix B: SUMMARY OF THE COUNCIL'S MEETINGS AND DELIBERATIONS

The following contains a summary of the Council's deliberations as they unfolded once the Council was officially convened.

April 10, 2009

The Council was presented with background information on comparative effectiveness research and briefed on CER activity at AHRQ, NIH, and VA. The Council also discussed the scope of their work and objectives.

Next, the Council began discussion of the components of the definition of CER and potential criteria for prioritization. The Council also discussed how CER and data infrastructure for CER might be categorized. Finally, the Council reviewed the timeline and discussed plan for listening sessions, including the first listening session on April 14, 2009.

April 22, 2009

The Council met to discuss what they had heard at the April 14 listening session. Members identified several key themes, including the need to outline a clear, well-delineated definition of comparative effectiveness research. They noted that participants had also talked about the need to prioritize methodology, and the fact that CER should be inclusive of all components of medical care.

Council members also noted that they had heard, loud and clear, that the Council's governance and processes must be transparent, and that the Council must incorporate input from all stakeholders to gain credibility and build trust.

Other themes that emerged from the listening session include the need to focus on patients and outcomes; the importance of incorporating diverse populations and multiple research methods; and the need for investments in infrastructure. Regarding the focus on patients and outcomes, Council members noted that participants had talked about the importance of considering patient input from the start and the fact that the results must be framed and disseminated in ways that are relevant to patients and providers. Regarding diverse populations, Council members observed that there was discussion about the need to include sub-groups with multiple chronic conditions, and the need more broadly to make CER relevant to sub-groups. Members also noted that participants had talked about the need to use a multitude of different research methodologies (not just randomized clinical trials), and to look at the Department of Veterans Affairs' experience using registries.

Regarding infrastructure, Council members observed that participants had stressed there was a need to expand, improve, and build on existing information and registries, and that perhaps this investment could lay the foundation for distributed data networks with the capability to answer many future CER questions. Members also noted that there had been discussion about the need to make data monitoring easier and more routine.

Finally, Council members talked about how they could tweak the listening session format to allow for a more robust conversation with participants.

May 1, 2009

The Council looked at the timetable for its work and the due dates for its key deliverable. The Report to Congress is due June 30, and the preliminary timetable builds in time for HHS and OMB clearance, comments, and suggested edits. The Council also briefly discussed the upcoming second listening session, slated for May 13 in Chicago.

Next, the Council briefly discussed the process for compiling the CER and data infrastructure inventories, and agreed that members would identify primary contacts in their division or agency who can work with the contractor to drive that process.

The Council's next goal was to arrive at consensus on a draft definition of comparative effectiveness research, prioritization criteria, and a categorization framework for CER. Once complete, the Council agreed to post the draft language on the hhs.gov/recovery Web site and to solicit public feedback.

To begin that work, the Council tackled the draft definition. There was considerable discussion about what the definition of CER should be. Members expressed the belief that the definition needed to be inclusive of the multiple stakeholders in the health care arena, including communities, and they also looked at what types of interventions should be called out. The Council ultimately came to consensus that they wanted a definition that was broad-based and inclusive, but that was not so detailed as to inadvertently narrow the scope of comparative effectiveness research.

The Council next turned its attention to the prioritization criteria. Before doing so, however, the Council first wrestled with the question of whether the criteria should be focused broadly or more narrowly targeted to provide guidance to the Office of the Secretary in allocating its Recovery Act funds. The Council generally felt that the criteria should be broad enough to allow the Council to make recommendations on overall funding and funding criteria.

Next, Council members discussed how to prioritize the CER criteria, including whether impact should be listed first, with feasibility and scientific merit second. One person spoke out about the need to keep the criterion on diverse populations and patient sub-groups within the top five. There was also discussion about whether knowledge gap was a criterion, or whether it should perhaps be wrapped into the criterion on impact.

The Council also looked at several potential frameworks for comparative effectiveness research, including categorization by type of CER investment, by patient sub-groups, by condition, and by type of intervention. The aim of developing a framework was to help categorize current CER activity and to identify gaps for potential future investments in CER. Council members also discussed CER centers, and agreed that Recovery Act funding could be used to support this work. One member suggested that the Council, at a future date, should discuss how to coordinate interest in CER centers across agencies.

Finally, the Council received a presentation on enhancing the inclusion of minority and other underserved populations in comparative effectiveness research. As a result, the Council agreed to establish a small workgroup co-led by NIH, AHRQ, the HHS Office of Minority Health, and the HHS Office on Disability. The workgroup will have two key tasks: (1) to develop recommendations for the inclusion of minority and other underrepresented populations in the expanded comparative effectiveness research agenda, and (2) to receive input from non-Federal groups on targeted actions.

May 8, 2009

The Council reviewed a revised definition of comparative effectiveness research and agreed to post the definition on the hhs.gov/recovery Web site on or about May 15.

Next, the Council resumed its discussion of the prioritization criteria. There was considerable discussion about whether "scientific rigor and validity" needed to be included in the threshold minimal criteria, with some members saying that it was implicit (and something already being done) and others expressing concerned about including a yes/no component to the threshold minimal criteria. The consensus of the Council was that scientific rigor and validity be included as part of a concept statement.

The Council then looked at a first draft outline of the Report to Congress. It included (1) Introduction, (2) Objectives, (3) Definition and Criteria, (4) Framework for CER, (5) Current CER and CER data infrastructure, (6) Recommendations for Priorities for OS CER Funds, and (7) Longer-term Vision and Opportunities.

Council members discussed a number of items that they believed needed to either be included or called out in the report, including concrete examples of what CER is and why it matters as well as a discussion about the full range of CER activities (and not just randomized clinical trials). There was also discussion about having a stand-alone section on high level priorities; the need to call out the roll of public/private partnerships; including a sub-section on the need for CER data to be synthesized and operationalized, along with some mechanisms for achieving this outcome; and the need to add language on sub-groups. Members also agreed to add a new section, Summary of the Listening Sessions, and to include a high-level Executive Summary.

Next, the Council began its discussion of CER priorities. To frame their discussion, members looked at four categories: primary research, dissemination of results, data infrastructure, and cross-cutting coordinated investments. One member asked, "What are the gaps that no one else can fill?" The Council agreed to continue its discussion at its next meeting.

May 22, 2009

The Council opened its meeting with a debrief from the May 13 listening session in Chicago. Members said they found the meeting both useful and exciting, and cited some themes they had heard that particularly struck them. These included the need to study chronic diseases (and to include sex, ethnicity, and race in the analysis); the idea of using theoretical models to assess how to approach a study (and to ensure the information is useable); the inclusion of mental health as a priority area; the importance of CER on pediatric populations; the importance of CER on prevention; and the need for training, and for starting to build the pipeline early.

The Council then briefly addressed next steps on the Report to Congress, including the fact that certain members would be assigned to draft specific sections of the report.

Next, the Council resumed its discussion of CER priorities where it had left off: looking at research, dissemination, data infrastructure, and cross-cutting investments. There was general consensus that OS funds should focus primarily on the latter three areas (as AHRQ and NIH are likely to make CER investments in research); there was also discussion about how to frame the priorities, including whether they should be framed around the type of CER investment or around types of diseases (e.g., people with multiple chronic illnesses, or people with disabilities and chronic illnesses). There was also specific discussion about the need to improve dissemination of research results—and a related topic, impacting practice. "If we just talk about dissemination," said one Council member, "we won't get anywhere. We need to look at the best methods for impacting practice."

There was also discussion around the question of how the Council should think about structuring its Report to Congress. At issue was whether the report should focus primarily on guidance to the HHS Secretary on how to allocate the $400 million in OS funds. In addition, the Council discussed the research time horizon, and whether ARRA monies could be used to fund projects that will have a time horizon longer than two years. One member suggested that one way to think about the question was to reframe it and ask, "Can we think about creating research centers that will be great resources into the future?"

Council members also stressed the need for the Council to address in its report the *process* for its deliberations and its recommendations, including making clear that CER investments are weighted to public health needs and responsive to the needs of decision makers. Council members suggested that some of the discussion about impacting practice might be linked to the discussion about data infrastructure investments.

May 29, 2009

The Council honed in on the details of the strategic framework for comparative effectiveness research, and the fact that it represents a comprehensive, coordinated approach to Federal investment in CER priorities that is intended to support immediate decisions for investments in CER priorities and to provide a comprehensive basis for longer-term CER investment decisions.

The Council discussed a framework that includes four major categories of activity (research, human and scientific capital, data and research infrastructure, and translation and adoption). The framework is designed to allow for investments within a single category or to cross-cut priority

themes. The Council agreed upon the categories. The Council's next step will be to determine the recommended mix among the major activities for OS funds.

The Council agreed to post on the hhs.gov/recovery Web site a copy of the broad framework diagram as well as a more detailed version to inform the public and to seek feedback on the strategic framework.

Next, the Council looked at some examples of the types of investments that might be made in the areas of infrastructure and translation and adoption. The idea of the discussion was to enable members to think about what types of projects might address gaps and further the CER enterprise.

The Council also looked briefly at an updated draft outline for the Report to Congress, and then members heard a presentation on three possible categories for investments in disability comparative effectiveness research.

June 5, 2009

The Council discussed the first draft of the Report to Congress. There was consensus that the Executive Summary needed to better frame the conversation around the value of CER to inform patients, clinicians, and other stakeholders. There was also discussion about setting out, early in the body of the report, why CER matters and how it matters to each stakeholder group. In addition, the Council agreed to add an additional appendix that contains a summary of its meetings and deliberations.

Next, the Council took up its recommendations for priorities. The discussion revolved around four key issues: the balance in spending priorities among the major activities versus cross-cutting themes; the distribution of spend priorities across the four major activities; what themes should be prioritized (and what the distribution of spend priorities should be across those themes); and whether the overall distribution makes sense vis-à-vis the prioritization criteria.

Regarding the distribution of spend priorities across the four major activities, Council members generally agreed that the majority of funding (e.g. 60 percent) should be spent on activities rather than themes. At the same time, there were lingering questions about the need to identify research gaps, implementation gaps, or both.

Regarding the distribution of spend priorities across the four major activities, the Council supported a breakdown that focuses the bulk of the funding in the areas of infrastructure (e.g. 60 percent) and translation (e.g. 20 percent). Members noted that there is a unique opportunity with ARRA funds to make significant investments in infrastructure.

Regarding potential priorities, members looked at draft lists of both priority populations and types of interventions. On the populations side, one Council member said that all of the proposed priority populations share in common that they have not traditionally been enrolled in clinical trials. There was also discussion about the need to include veterans as well as people with co-occurrence of mental health disorders along with physical comorbidities. On the interventions side, there was some discussion about the inclusion of delivery systems, and that

CER on delivery systems offers an opportunity to look at promising practices and how they might be scaled up and disseminated.

Finally, the Council was divided as to whether the bulk of OS funds should be used primarily for investments in populations or in interventions—or whether they should be equally important priorities.

June 12, 2009

The Council debriefed on what was heard in the third listening session. This generated enhancement to the common themes and some new information to be incorporated. The Council then revised the definition, threshold and prioritization criteria, and strategic framework based on the feedback from the session and the feedback received online. The Council then further discussed priority recommendations and the Report to Congress. The Council suggested edits for the Report prior to it going into clearance the next week.

Appendix C. PRELIMINARY DATA INFRASTRUCTURE AND CER BY CONDITION

The following is a preliminary inventory of examples of CER data infrastructure and CER by condition.

Person-Level Health Care Research Databases from First Inventory

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
US Federal							
Healthcare Cost and Utilization Project (HCUP)	AHRQ	Hospital information system	—	All	Y	N	Y
HIV Cost and Services Utilization Study (HCSUS)	AHRQ	Surevy & records abatsraction	2,864	HIV	Y	N	Y
AIDS Cost and Services Utilization Study (ACSUS)	AHRQ	Hospital information system	1,900	AIDS	Y	N	Y
National Vital Statistics	CDC	Surveillance program/registry data	—	All	n/a	N	N

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
National Vital Statistics—Natality	CDC	Surveillance program/registry data	4 million	All	n/a	N	Y
National Health Interview Survey	CDC	Survey	87,000	All	n/a	Y	Y
National Health and Nutrition Examination Survey	CDC	Survey	5,000	All	n/a	Y	Y
National Ambulatory Medical Care Survey	CDC	Survey and records abstraction	n/a	All	N	Y	Y
National Hospital Ambulatory Medical Care Survey	CDC	Survey and records abstraction	n/a	All	N	Y	Y
National Hospital Discharge Survey	CDC	Survey and records abstraction	n/a	All	N	Y	Y
National Nursing Home Survey	CDC	Survey and records abstraction	13,507	All	N	Y	Y
National Home and Hospice Care Survey	CDC	Survey and records abstraction	9,416	All	N	Y	Y
Chronic Condition Data Warehouse	CMS	Administrative claims database, enrollment data, health assessment data, prescription drug event data	45 million	All	Y	Y	Y
Hospice Standard Analytical File (Hospice SAF)	CMS	Administrative claims database	—	All	Y	Y	?

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
Medicaid Statistical Information System Personal Summary File (MSIS Personal Summary File)	CMS	Administrative claims database, EMR/EHR system	—	All	Y	Y	Y
National Claims History (NCH) 100% Nearline Fil	CMS	Administrative claims database	—	All	Y	Y	?
MEDPAR Claims Data	CMS	Administrative claims database	—	All	Y	Y	Y
MMA Part D Claims Data	CMS	Pharmacy claims database	25 million	All	Y	Y	Y
Sentinel System	FDA	Surveillance program/registry data	N/A	n/a	N	Y	N
SEER (Surveillance Epidemiology and End Results)	NCI	Surveillance program/registry data	11.4 million	Cancer	Y	N	Y
SEER-Medicare database	NCI, CMS	Administrative claims database, Surveillance program/registry data	3.3 million	Cancer	Y	Y	N
Cancer Research Network (CRN)	NCI, AHRQ	Administrative claims database, EMR/EHR system	—	Cancer	Y	Y	N
Computerized Patient Record System (CPRS)	VA	EMR/EHR system	4.2 million	All	Y	N	N
Diabetes Epidemi-ology Cohort	VA	Surveillance program/registry data	> 4,800	Diabetes	Y	Y	Y

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
Hepatitis C Registry	VA	Surveillance program/registry data	>60 K	Hepatitis C	Y	N	Y
Immunological Case Registry	VA	Surveillance program/registry data	>15 K	HIV	Y	N	Y
Dementia Registry	VA	Surveillance program/registry data	>150 K	Dementia	Y	N	N
National Surgery Quality Improvement Program	VA	Surveillance program/registry data	>1 Million	All major surgery	Y	Y	Y
Scientific Registry of Transplant Recipients (SRTR)	HRSA	Transplant registry and outcomes data		Organ specific	Y	Y	Y
Pediatric Emergency Care Applied Research Network (PECARN) CDMCC*	HRSA	Emergency medical services for children	800,000 + patients	Emergency Services to Children	Y	Y	Y
AIDS Drug Assistance Program (ADAP)	HRSA	Care Program Registry Data	—	HIV/AIDS	Y	Y	N
US Private Sector							
National Oncologic PET Registry (NOPR)	Academy of Molecular Imaging	Intervention program data	>100,000	Cancer	Y	Y	?
Cerner Health Facts Database	Cerner	EMR/EHR system	—	All	Y	Y	Y
GE Centricity	GE	EMR/EHR system	10 million	All	Y	N	Y

* Central Data Management and Coordinating Center

Database	Owner	Data Type	No. Lives	Disease Area	Data Linkable at Patient Level	Data Linkable to External Data	Researcher Ready
Ingenix Research Data Mart (RDM) Database	Ingenix	Administrative claims database	>39 million	All	Y	Y	Y
Premier Perspective Data Warehouse	Premier	Administrative claims database	—	All	Y	Y	Y
MarketScan Data Warehouse	Thomson-Reuters	EMR/EHR system	—	All	Y	N	N
International Databases							
General Practice Research Database (GPRD)	NHS (UK)	EMR/EHR system	> 3.6 million	All	Y	Y	Y
NHS Care Records Service (CRS)	NHS (UK)	EMR/EHR system	2 million	All	Y	N	Y
The Health Improvement Network (THIN)	INPS and EPIC (UK)	EMR/EHR system	—	All	Y	Y	Y

Priority Diseases/Conditions in CER

Priority Diseases/Conditions	AHRQ (n=178)	NIH (n=513)	DoD (n=26)	VHA (n=106)	Total (n=823)
Arthritis and non-traumatic joint disorders	6%	1%	0%	3%	**2%**
Cancer	10%	7%	23%	7%	**8%**
Cardiovascular disease, including stroke and hypertension	20%	10%	4%	23%	**13%**
Dementia, including Alzheimer's Disease	1%	1%	0%	3%	**1%**
Depression and other mental health disorders	8%	16%	8%	18%	**14%**
Developmental delays, attention-deficit hyperactivity disorder, and autism	4%	1%	0%	0%	**1%**
Diabetes mellitus	11%	11%	0%	8%	**10%**

Functional limitations and disability	8%	4%	15%	7%	**5%**
Infectious diseases including HIV/AIDS	3%	11%	0%	6%	**8%**
Obesity	1%	3%	0%	2%	**3%**
Peptic ulcer disease and dyspepsia	0%	0%	0%	0%	**0%**
Pregnancy, including preterm birth	1%	4%	0%	0%	**2%**
Pulmonary disease/asthma	5%	3%	0%	4%	**3%**
Substance abuse	2%	19%	0%	9%	**14%**
Other	20%	11%	50%	12%	**14%**

*Studies focusing on patients with more than one priority disease or condition are counted in applicable rows..
**NIH 2008 plus NIH multi-year sample.

Appendix D. COUNCIL LIST AND STAFF SUPPORT

1. Carolyn Clancy, MD	AHRQ
2. Peter Delaney, PhD, LCSW-C	SAMHSA
3. Ezekiel Emanuel, MD, PhD	OMB
4. Jesse Goodman, MD, MPH	FDA
5. Garth Graham, MD, MPH	Office of Minority Health
6. Anne Haddix, PhD	CDC
7. Deborah Hopson, PhD, RN	HRSA
8. David Hunt, MD	ONC
9. Michael Kilpatrick, MD	Dept of Defense
10. Joel Kupersmith, MD	Dept of VA
11. Michael Marge, Ed.D.	Office of Disability
12. Elizabeth Nabel, MD	NIH
13. James Scanlon, PhD	ASPE
14. Neera Tanden, JD	Office of the Secretary
15. Tom Valuck, MD, MHSA, JD	CMS

Executive Director: Patrick Conway, MD, MSc
Deputy Executive Director: Cecilia Rivera Casale, PhD

Alternates to the Council participating: Kelley Brix, Margaret Cary, Rosaly Correa-de-Araujo (replaced Michael Marge on Council June 12th), Elisabeth Handley, Lynn Hudson, Michael Millman

Contributors to Council and Report: Kate Goodrich, Lauren Hunt, John Poelman, Daria Steigman, Caroline Taplin, Jordan VanLare.

Appendix E. THE AMERICAN RECOVERY AND REINVESTMENT ACT STATUTE RELATED TO CER AND COUNCIL

Appropriations

For an additional amount for 'Healthcare Research and Quality' to carry out titles III and IX of the Public Health Service Act, part A of title XI of the Social Security Act, and section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, $700,000,000 for comparative effectiveness research: *Provided,* That of the amount appropriated in this paragraph, $400,000,000 shall be transferred to the Office of the Director of the National Institutes of Health ('Office of the Director') to conduct or support comparative effectiveness research under section 301 and title IV of the Public Health Service Act: *Provided further,* That funds transferred to the Office of the Director may be transferred to the Institutes and Centers of the National Institutes of Health and to the Common Fund established under section 402A(c)(1) of the Public Health Service Act: *Provided further,* That this transfer authority is in addition to any other transfer authority available to the National Institutes of Health: *Provided further,* That within the amount available in this paragraph for the Agency for Healthcare Research and Quality, not more than 1 percent shall be made available for additional full-time equivalents.

In addition, $400,000,000 shall be available for comparative effectiveness research to be allocated at the discretion of the Secretary of Health and Human Services ('Secretary'): *Provided,* That the funding appropriated in this paragraph shall be used to accelerate the development and dissemination of research assessing the comparative effectiveness of health care treatments and strategies, through efforts that: (1) conduct, support, or synthesize research that compares the clinical outcomes, effectiveness, and appropriateness of items, services, and procedures that are used to prevent, diagnose, or treat diseases, disorders, and other health conditions; and (2) encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data: *Provided further,* That the Secretary shall enter into a contract with the Institute of Medicine, for which no more than $1,500,000 shall be made available from funds provided in this paragraph, to produce and submit a report to the Congress and the Secretary by not later than June 30, 2009, that includes recommendations on the national priorities for comparative effectiveness research to be conducted or supported with the funds provided in this paragraph and that considers input from stakeholders: *Provided further,* That the Secretary shall consider any recommendations of the Federal Coordinating Council for Comparative Effectiveness Research established by section 804 of this Act and any recommendations included in the Institute of Medicine report pursuant to the preceding proviso in designating activities to receive funds provided in this paragraph and may make grants and contracts with appropriate entities, which may include agencies within the Department of Health and Human Services and other governmental agencies, as well as private sector entities, that have demonstrated experience and capacity to achieve the goals of comparative effectiveness research: *Provided further,* That the Secretary shall publish information on grants and contracts awarded with the funds provided under this heading within a reasonable time of the obligation of funds for such grants and contracts and shall disseminate research findings from such grants and contracts to clinicians, patients, and the general public, as appropriate: *Provided further,* That, to the extent feasible, the Secretary shall ensure that the recipients of the funds provided by this paragraph offer an opportunity for public comment on

the research: *Provided further,* That research conducted with funds appropriated under this paragraph shall be consistent with Departmental policies relating to the inclusion of women and minorities in research: *Provided further,* That the Secretary shall provide the Committees on Appropriations of the House of Representatives and the Senate, the Committee on Energy and Commerce and the Committee on Ways and Means of the House of Representatives, and the Committee on Health, Education, Labor, and Pensions and the Committee on Finance of the Senate with an annual report on the research conducted or supported through the funds provided under this heading: *Provided further,* That the Secretary, jointly with the Directors of the Agency for Healthcare Research and Quality and the National Institutes of Health, shall provide the Committees on Appropriations of the House of Representatives and the Senate a fiscal year 2009 operating plan for the funds appropriated under this heading prior to making any Federal obligations of such funds in fiscal year 2009, but not later than July 30, 2009, and a fiscal year 2010 operating plan for such funds prior to making any Federal obligations of such funds in fiscal year 2010, but not later than November 1, 2009, that detail the type of research being conducted or supported, including the priority conditions addressed; and specify the allocation of resources within the Department of Health and Human Services: *Provided further,* That the Secretary, jointly with the Directors of the Agency for Healthcare Research and Quality and the National Institutes of Health, shall provide to the Committees on Appropriations of the House of Representatives and the Senate a report on the actual obligations, expenditures, and unobligated balances for each activity funded under this heading not later than November 1, 2009, and every 6 months thereafter as long as funding provided under this heading is available for obligation or expenditure.

Sec. 804. Federal Coordinating Council for Comparative Effectiveness Research

(a) ESTABLISHMENT— There is hereby established a Federal Coordinating Council for Comparative Effectiveness Research (in this section referred to as the 'Council').

(b) PURPOSE— The Council shall foster optimum coordination of comparative effectiveness and related health services research conducted or supported by relevant Federal departments and agencies, with the goal of reducing duplicative efforts and encouraging coordinated and complementary use of resources.

(c) DUTIES— The Council shall—

(1) assist the offices and agencies of the Federal Government, including the Departments of Health and Human Services, Veterans Affairs, and Defense, and other Federal departments or agencies, to coordinate the conduct or support of comparative effectiveness and related health services research; and

(2) advise the President and Congress on—
(A) strategies with respect to the infrastructure needs of comparative effectiveness research within the Federal Government; and
(B) organizational expenditures for comparative effectiveness research by relevant Federal departments and agencies.

(d) MEMBERSHIP—

(1) NUMBER AND APPOINTMENT— The Council shall be composed of not more than 15 members, all of whom are senior Federal officers or employees with responsibility for health-related programs, appointed by the President, acting through the Secretary of Health and Human Services (in this section referred to as the 'Secretary'). Members shall first be appointed to the Council not later than 30 days after the date of the enactment of this Act.

(2) MEMBERS—
(A) IN GENERAL— The members of the Council shall include one senior officer or employee from each of the following agencies:
(i) The Agency for Healthcare Research and Quality.
(ii) The Centers for Medicare and Medicaid Services.
(iii) The National Institutes of Health.
(iv) The Office of the National Coordinator for Health Information Technology.
(v) The Food and Drug Administration.
(vi) The Veterans Health Administration within the Department of Veterans Affairs.
(vii) The office within the Department of Defense responsible for management of the Department of Defense Military Health Care System.
(B) QUALIFICATIONS— At least half of the members of the Council shall be physicians or other experts with clinical expertise.
(3) CHAIRMAN; VICE CHAIRMAN— The Secretary shall serve as Chairman of the Council and shall designate a member to serve as Vice Chairman.

(e) REPORTS—

(1) INITIAL REPORT— Not later than June 30, 2009, the Council shall submit to the President and the Congress a report containing information describing current Federal activities on comparative effectiveness research and recommendations for such research conducted or supported from funds made available for allotment by the Secretary for comparative effectiveness research in this Act.

(2) ANNUAL REPORT— The Council shall submit to the President and Congress an annual report regarding its activities and recommendations concerning the infrastructure needs, organizational expenditures and opportunities for better coordination of comparative effectiveness research by relevant Federal departments and agencies.

(f) STAFFING; SUPPORT— From funds made available for allotment by the Secretary for comparative effectiveness research in this Act, the Secretary shall make available not more than 1 percent to the Council for staff and administrative support.

(g) RULES OF CONSTRUCTION—

(1) COVERAGE— Nothing in this section shall be construed to permit the Council to mandate coverage, reimbursement, or other policies for any public or private payer.

(2) REPORTS AND RECOMMENDATIONS— None of the reports submitted under this section or recommendations made by the Council shall be construed as mandates or clinical guidelines for payment, coverage, or treatment.

Title VIII—Departments of Labor, Health And Human Services, and Education, and Related Agencies

VA Comparative Effectiveness Research

Veterans Health Administration
R&D
www.research.va.gov

Joel Kupersmith, MD
Chief Research & Development Officer

VA Mission

Veterans Health Administration
R&D
www.research.va.gov

- **VA Mission**

"…to care for him who shall have borne the battle and for his widow, and his orphan"

A. Lincoln, 2nd Inaugural

- **VA Research Mission:**

"To discover knowledge and create innovations that advance the health and care of veterans and the nation."

- Veterans first and always in all we do

Attributes for Comparative Effectiveness Research

Veterans Health Administration
R&D
www.research.va.gov

- **VA attributes for Comparative Effectiveness Research for the benefit of veterans**
  - Large healthcare system
  - Outstanding research program embedded in healthcare system - "Intramural"
  - Infrastructure for clinical trials
  - Vehicles for translation and implementation of research into the health care system

Large Healthcare System

Veterans Health Administration
R&D
www.research.va.gov

- **Large system**
  - 5.5 million patients/yr, 7.8 million enrollees
  - >1200 Sites of Care
    - 153 Medical Centers
    - 737 Community-based Outpatient Clinics
    - 225 Readjustment Counseling Centers
- **Intramural research system - a unique strength**
- **Electronic Health Record**
- **117 VAMCs have Federal Wide Assurances for research**
- **Community of ≈3000 VA researchers**
  - Published 46,149 articles in past 7 years in the best journals
- **≈2100 VA funded projects**

Rich 60 Year History

Veterans Health Administration
R&D
www.research.va.gov

- **3 Nobel Laureates, 6 Lasker Award Winners**
- **Many important discoveries and inventions**
  - Cardiac Pacemaker, First liver transplant, Radioimmunoassay, CT Scanner
- ***Clinical Trials***
  - First large scale clinical trial – TB
  - Cooperative Studies Program

1848

VA Programs in Comparative Effectiveness Research

Comparative Effectiveness Research

Veterans Health Administration
R&D
www.research.va.gov

- **Definition**
  - CBO: "…a rigorous evaluation of the impact of different options that are available for treating a given medical treatment for a given set of patients."

- **Speaker's previous interest in the topic**
  - Kupersmith at al, Journal of Investigative Medicine, 2005

VA Comparative Effectiveness Research

Veterans Health Administration
R&D
www.research.va.gov

- **Research**
  - Cooperative Studies Program
    - Clinical trials
  - Health Services Research – health system oriented research
  - Rehabilitation
- **Implementation**
  - Quality Enhancement Research Initiative program
  - Evidence Based Synthesis program

VA Cooperative Studies Program

Veterans Health Administration
R&D
www.research.va.gov

- **Large VA clinical trials program**
  - **Major vehicle for Comparative Effectiveness Research**
- **Method of funding projects**
  - Letter of intent submitted
    - Ideas based on clinical practice observations, gaps in literature, etc
  - *Project review by experts who collaborate with the proposer*
    - Include clinicians, clinical researchers, trialists, biostaticians, pharmacists, others

VA Cooperative Studies Program

Veterans Health Administration
R&D
www.research.va.gov

- **Review considerations include clinical and policy considerations**
  - Clinical relevance and importance to VHA population, methodology, feasibility (testable hypothesis, sample size), ethics, resources needed, investigator qualifications
- **After approval, steps in a procedure to**
  - *Central IRB approval*
  - Form study Committees, Coordinating Center, etc
  - Local Medical Center approvals
  - Other
- **Collaboration with NIH and others in many trials**

VA Cooperative Studies Program -- Examples

Veterans Health Administration
R&D
www.research.va.gov

- **Computerized Tomography vs Positron Emission Tomography in solitary pulmonary nodule (PET better)**
  - Journal of Nuclear Medicine, 2008
- **Sotolol vs Amiodarone in atrial fibrillation (similar)**
  - New England Journal of Medicine, May 5, 2005
- **Standard care with & without Phlebotomy in stable peripheral artery disease (no sign difference)**
  - Journal of the American Medical Association, February 14, 2007
- **Medical therapy vs Coronary revascularization prophylaxis prior to elective vascular surgery (no sign difference)**
  - New England Journal of Medicine, December 30, 2004

VA Cooperative Studies Program -- Examples

Veterans Health Administration
R&D
www.research.va.gov

- **Percutaneous coronary intervention/optimal medical therapy *vs* Optimal medical therapy alone (COURAGE) (no sign difference)**
  - New England Journal of Medicine, March 27, 2007
- **Open mesh *vs* Laparoscopic mesh repair for inguinal hernia (open mesh better)**
  - New England Journal of Medicine, April 29, 2004
- **Care model (patient's self-management, continuity of care, information via nurse care coordinator) *vs* Standard care in Bipolar Disorder (care model better for most end points)**
  - Psychiatric Services, July 2006
- **Intensive *vs* Less Intensive Renal Support in Critically Ill Patients with Acute Kidney Injury (no sign difference)**
  - New England Journal of Medicine, July 8, 2008
- **Prolonged Exposure Therapy *vs* Patient-Centered therapy in PTSD (PET better)**
  - Journal of the American Medical Association, Feb 28, 2007

VA Cooperative Studies Program - Ongoing

Veterans Health Administration
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- **Radical Prostatectomy vs Palliative Expectant Management for localized Prostate Cancer**
- **Intensive vs Standard glycemic control in diabetes**
- **Home monitoring vs "High quality" anti-coagulation clinic in atrial fibrillation and/or mechanical heart valve**
- **CABG vs Percutaneous coronary intervention with stents in diabetes**
- **Robotic assisted training in upper extremity movement *vs* Intensive stretching and range of motion exercise via trained therapist *vs* Usual care in stroke**
- **Self-management (education, action plan & case management) *vs* Standardized care in severe Chronic Obstructive Lung Disease**

Health Services Research - Ongoing

Veterans Health Administration
R&D
www.research.va.gov

- **Health systems oriented projects**
- **Laboratory based *vs* Home evaluation of sleep apnea**
- **Examples of studies *vs* "usual care" control**
  - Collaborative care model for depression
    - Site randomization of Outpatient Clinics (CBOCs)
  - Plain language decision aid for patient decision making in prostate cancer
  - Collaborative care using primary care physician, RN and PharmD for hypertension/diabetes to implement strike risk management
  - Patient preference tailored information concerning colon cancer screening
  - Training caregivers with a Home Safety Toolkit in Alzheimer's

Analysis of Electronic Health Record

Veterans Health Administration
R&D
www.research.va.gov

- **Besides clinical trials, analysis of EHR represents an approach to Comparative Effectiveness Research**
  - Compare treatments and approaches to care in *clinically rich* data in EHR
- **Using EHR data provides**
  - Immediacy of results
  - Less costly studies
  - However, there are methodologic issues
    - E.g. are groups comparable?
    - Text recognition

Analysis of Electronic Health Record

Veterans Health Administration
R&D
www.research.va.gov

- **VA examples**
  - EHR diabetes cohort database shows no difference in mortality among oral antidiabetic drugs
    - Diabetes Care, July 2007
  - Blood trasfusion in surgical cases
    - NSQIP database in VA Patients (National Surgery Quality Improvement Program)
  - Comparison of obesity care practices
  - NSAID prescription strategies
  - Carvedilol *vs* Controlled-release Metropolol in heart failure

Implementation/Translation

Quality Enhancement Research Initiative

Evidence Synthesis Program

Veterans Health Administration
Research Development
Improving Veterans' Lives — www.research.va.gov

Quality Enhancement Research Initiative

QUERI Program

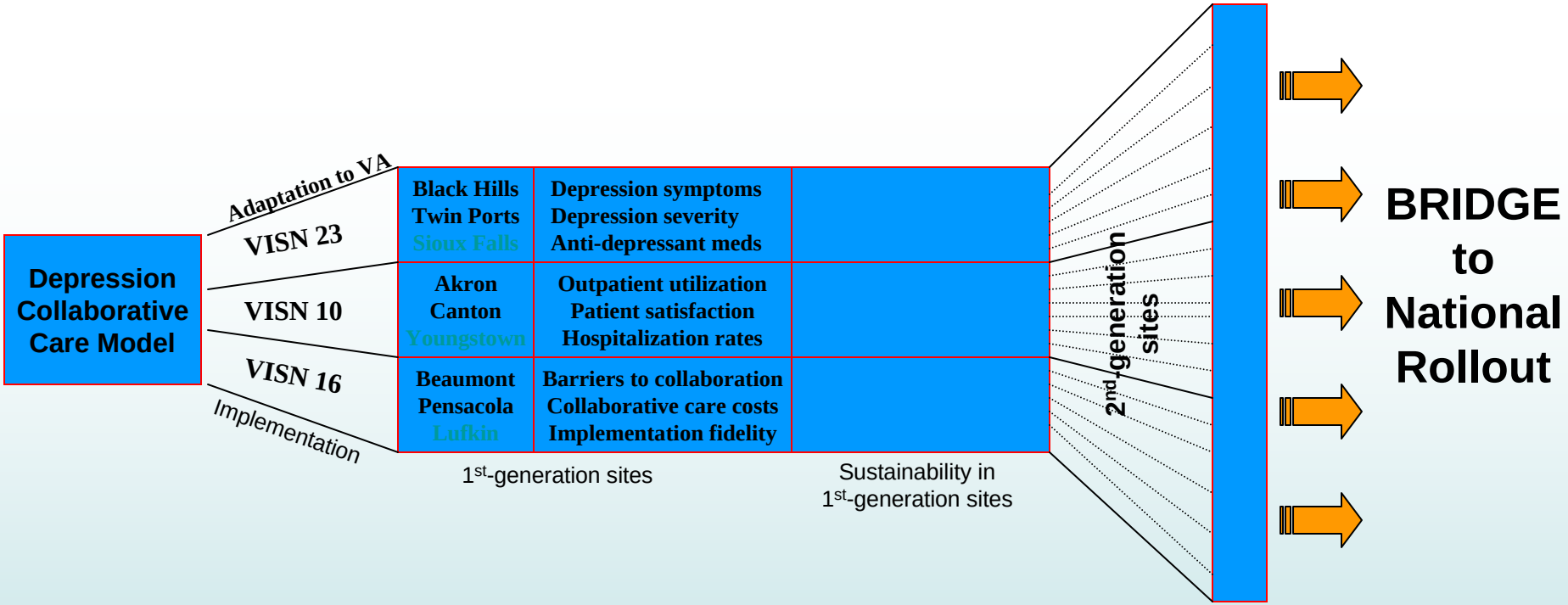
QUERI Program

Veterans Health Administration
R&D
www.research.va.gov

- ***Mission*** **-** Systematically implement/ translate evidence-based clinical practices & research findings into routine clinical practice

- **Steps in QUERI process**
  - Identify gap in Evidence Based Practice
  - Develop and implement a strategy for change
  - Test strategy
    - Single site pilot
    - Small scale implementation pilot
    - Large scale, multi-region implementation trial
    - System-wide roll-out
  - Document system improvements
  - Document outcomes & QOL improvements

Implementation of System Change Collaborative Care of Depression



Single site

3 VISNs 9 sites

18-30 sites 4 VISNs

National Rollout

Spinal Court Injury
National Vaccination Project

	VA performance measures: SCI		Veterans w/SCI Survey	
	Flu	PPV	Flu	PPV
1997	25%	20%	NA	NA
1998	26%	25%	NA	NA
2000	28%	40%	NA	NA
2001	33%	50%	57%	NA
2002	62%	78%	62%	60%
2003	61%	79%	68%	75%
2004	68%	88%	79%	82%
2005	65%	82%	72%	NA

VA Evidence Based Synthesis Program

VA Evidence Based Synthesis Program

Veterans Health Administration
R&D
www.research.va.gov

- **Reviewing the evidence on a topic**
- ***Policy oriented* synthesis of evidence to inform medical practice and health systems planning**
  - *Informed by policy considerations* with input by Patient Care Services
- **Recent topics**
  - Drug management of BPH – Led to Formulary change
  - Osteoporosis – Incorporated into Guideline on screening male veterans
  - Pain in Polytrauma – Need more research

Conclusions

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- **VA has many attributes to *undertake* and *implement* Comparative Effectiveness Research**
  - Intramural research program in a large healthcare system
  - Infrastructure for clinical studies
- **VA has a strong ongoing program and many accomplishments *in the service of veterans* in Comparative Effectiveness Research**
- **Besides clinical trials, analysis of the Electronic Health Record will be an approach to Comparative Effectiveness Research**

VA Research:
Improving Veterans' Lives

Thank You