Clinical research presents health care providers with information on the natural history and clinical presentations of disease as well as diagnostic and treatment options. In today's healthcare system, patients, physicians, clinicians and family caregivers often lack the sufficient scientific data and evidence they need to determine the best course of treatment for the patients' medical conditions. Initial National Priorities for Comparative Effectiveness Research (CER) is designed to fill this knowledge gap by assisting patients and healthcare providers across diverse settings in making more informed decisions. In this 2009 report, the Institute of Medicine's Committee on Comparative Effectiveness Research Prioritization establishes a working definition of CER, develops a priority list of research topics, and identifies the necessary requirements to support a robust and sustainable CER enterprise. As part of the 2009 American Recovery and Reinvestment Act, Congress appropriated $1.1 billion in federal support of CER, reflecting legislators' belief that better decisions about the use of health care could improve the public's health and reduce the cost of care. The Committee on Comparative Effectiveness Research Prioritization was successful in preparing a list 100 top priority CER topics and 10 recommendations for best practices in the field.
Summary

BACKGROUND

Today, when a patient and physician, perhaps with other clinicians and family caregivers, are discussing the best course of treatment for the patient’s medical condition, they often do not have the scientific evidence they need to make a determination. Although there may be studies that indicate that a treatment is efficacious relative to a placebo, there frequently are no studies that directly compare the different available alternatives or that have examined their impacts in populations of the same age, sex, and ethnicity or with the same comorbidities as the patient. Comparative effectiveness research (CER) is designed to fill this knowledge gap. CER focuses attention on the evidence base to assist patients and health care providers across diverse health settings in making more informed decisions. They will need useful, practical information concerning the most effective interventions and health care services for their particular situation.

To help identify which health care services work best, Congress, in the American Recovery and Reinvestment Act (ARRA) of 2009 (P.L. 111-5), appropriated $1.1 billion as a down-payment to provide strong federal support of CER. This provision in the law reflected the legislators’ belief that better decisions about the use of health care resources could improve the public’s health and reduce the costs of care. According to the legislation, CER covers “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.” The law appropriated $400 million to the National Institutes of Health
INITIAL NATIONAL PRIORITIES FOR CER

(NIH), $300 million to the Agency for Healthcare Research and Quality (AHRQ), and the remaining $400 million to the Secretary of Health and Human Services (HHS). According to the language of the law, the purposes of the appropriations were

- “to evaluate the relative effectiveness of different health care services and treatment options” and
- “to encourage the development and use of clinical registries, clinical data networks, and other forms of electronic data to generate outcomes data.”

The law also charged the Institute of Medicine (IOM) to form a consensus committee and solicit stakeholder input to recommend national priorities for spending the $400 million designated for the Secretary. The legislation imposed a short time frame on this study—the IOM report deadline of June 30, 2009, was 19 weeks after the president signed the legislation into law.

The National Academies President’s Fund generously supported the study process until the study’s sponsor, AHRQ, could contract with the IOM; IOM funds entirely paid for the public questionnaire and its analysis. The Robert Wood Johnson Foundation also contributed significantly to this study. This support permitted the IOM to rapidly establish a committee and to commence work. The committee encompassed a broad range of expertise, perspectives, and experience, including members who work with consumers and patients, in clinical care and research, or in health care and government administration.

The committee’s principal task was to prepare a list of priorities for CER funding; most of its time was spent developing a process for priority setting, eliciting a wide array of input from the public, and deliberating over a list of nominated research topics. Then, as the complexities of priority setting for CER became apparent, the committee began to outline the development of an infrastructure that would sustain a long-term, national CER effort. The committee provided recommendations to implement that infrastructure required for a sustained CER effort. The main justification for including economic considerations is that the overall value of a strategy can be understood best by considering costs and benefits together. In such a circumstance, value may be judged from the perspective of the patient, provider, or payer. Many stakeholders thought CER might persuade payers to support or improve reimbursement for particular services, but the committee did not discuss leveraging research findings to payment policy.

The committee presents its recommended list of 100 top priority CER topics in Table S-1. The individual topics are grouped into quartiles according to the number of votes each received during the committee’s voting
SUMMARY

process. Topics within the First Quartile were considered higher priority than those in the Fourth Quartile, but the order within quartiles does not signify rank. Following Table S-1 is a brief discussion of how the committee created the priority list, a section on what the committee learned from the process, and implications and recommendations for establishing a solid foundation for CER in the future.

LIST OF PRIORITY CER TOPICS

TABLE S-1 Final List of Priority Topics, by Quartile Ratings
*display within quartile does not indicate priority rank—topics are listed alphabetically by primary research area

<table>
<thead>
<tr>
<th>First Quartile</th>
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<tbody>
<tr>
<td>CAD</td>
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<tr>
<td>DIS</td>
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<tr>
<td>ENDO</td>
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<tr>
<td>GI</td>
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<tr>
<td>HCDS</td>
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<td>HCD</td>
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<td>IMUN</td>
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<td>INFD</td>
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<table>
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<tr>
<th>Initial National Priorities for Comparative Effectiveness Research</th>
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<tr>
<td><strong>TABLE S-1</strong> Continued</td>
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<tr>
<td><strong>INFD</strong></td>
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<td><strong>KUT</strong></td>
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<tr>
<td><strong>MS</strong></td>
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<td><strong>NEURO</strong></td>
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<td><strong>NEURO</strong></td>
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<td><strong>NUTR</strong></td>
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<td><strong>NUTR</strong></td>
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<td><strong>ONC</strong></td>
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<td><strong>ONC</strong></td>
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<td><strong>ONC</strong></td>
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<td><strong>ORAL</strong></td>
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</tbody>
</table>
SUMMARY

TABLE S-1 Continued

| PEDS  | Compare the effectiveness of various primary care treatment strategies (e.g., symptom management, cognitive behavior therapy, biofeedback, social skills, educator/teacher training, parent training, pharmacologic treatment) for attention deficit hyperactivity disorder (ADHD) in children. |
| PSYCH | Compare the effectiveness of wraparound home and community-based services and residential treatment in managing serious emotional disorders in children and adults. |
| RED   | Compare the effectiveness of interventions (e.g., community-based multi-level interventions, simple health education, usual care) to reduce health disparities in cardiovascular disease, diabetes, cancer, musculoskeletal diseases, and birth outcomes. |
| RED   | Compare the effectiveness of literacy-sensitive disease management programs and usual care in reducing disparities in children and adults with low literacy and chronic disease (e.g., heart disease). |
| WH    | Compare the effectiveness of clinical interventions (e.g., prenatal care, nutritional counseling, smoking cessation, substance abuse treatment, combinations of these interventions) to reduce incidences of infant mortality, pre-term births, and low birth weights, especially among African American women. |
| WH    | Compare the effectiveness of innovative strategies for preventing unintended pregnancies (e.g., over-the-counter access to oral contraceptives or other hormonal methods, expanding access to long-acting methods for young women, providing free contraceptive methods at public clinics, pharmacies, or other locations). |

Second Quartile
(listed alphabetically by primary research area)

| BDEV  | Compare the effectiveness of therapeutic strategies (e.g., behavioral or pharmacologic interventions, the combination of the two) for different autism spectrum disorders (ASD) at different levels of severity and stages of intervention. |
| BDEV  | Compare the effectiveness of the co-location model (psychological and primary care practitioners practicing together) and usual care (identification by primary care practitioner and referral to community-based mental health services) in identifying and treating social-emotional and developmental disorders in children ages 0-3. |
| BDEV  | Compare the effectiveness of diverse models of comprehensive support services for infants and their families following discharge from a neonatal intensive care unit. |

*continued*
TABLE S-1 Continued

| CAD | Compare the effectiveness of treatment strategies for vascular claudication (e.g., medical optimization, smoking cessation, exercise, catheter-based treatment, open surgical bypass). |
| CAM | Compare the effectiveness of mindfulness-based interventions (e.g., yoga, meditation, deep breathing training) and usual care in treating anxiety and depression, pain, cardiovascular risk factors, and chronic diseases. |
| ENDO | Compare the long-term effectiveness of weight-bearing exercise and bisphosphonates in preventing hip and vertebral fractures in older women with osteopenia and/or osteoporosis. |
| HCDS | Compare the effectiveness of shared decision making and usual care on decision outcomes (treatment choice, knowledge, treatment-preference concordance, and decisional conflict) in children and adults with chronic disease such as stable angina and asthma. |
| HCDS | Compare the effectiveness of strategies for enhancing patients’ adherence to medication regimens. |
| HCDS | Compare the effectiveness of patient decision support tools on informing diagnostic and treatment decisions (e.g., treatment choice, knowledge acquisition, treatment-preference concordance, decisional conflict) for elective surgical and nonsurgical procedures—especially in patients with limited English-language proficiency, limited education, hearing or visual impairments, or mental health problems. |
| HCDS | Compare the effectiveness of robotic assistance surgery and conventional surgery for common operations, such as prostatectomies. |
| HCDS | Compare the effectiveness (including resource utilization, workforce needs, net health care expenditures, and requirements for large-scale deployment) of new remote patient monitoring and management technologies (e.g., telemedicine, Internet, remote sensing) and usual care in managing chronic disease, especially in rural settings. |
| HCDS | Compare the effectiveness of diverse models of transition support services for adults with complex health care needs (e.g., the elderly, homeless, mentally challenged) after hospital discharge. |
| HCDS | Compare the effectiveness of accountable care systems and usual care on costs, processes of care, and outcomes for geographically defined populations of patients with one or more chronic diseases. |
| HCDS | Compare the effectiveness of different residential settings (e.g., home care, nursing home, group home) in caring for elderly patients with functional impairments. |
### SUMMARY

**KUT**
Compare the effectiveness (including survival, hospitalization, quality of life, and costs) of renal replacement therapies (e.g., daily home hemodialysis, intermittent home hemodialysis, conventional in-center dialysis, continuous ambulatory peritoneal dialysis, renal transplantation) for patients of different ages, races, and ethnicities.

**MS**
Compare the effectiveness of treatment strategies (e.g., artificial cervical discs, spinal fusion, pharmacologic treatment with physical therapy) for cervical disc and neck pain.

**ONC**
Compare the effectiveness of film-screen or digital mammography alone and mammography plus magnetic resonance imaging (MRI) in community practice-based screening for breast cancer in high-risk women of different ages, risk factors, and race or ethnicity.

**ONC**
Compare the effectiveness of new screening technologies (such as fecal immunochemical tests and computed tomography [CT] colonography) and usual care (fecal occult blood tests and colonoscopy) in preventing colorectal cancer.

**PELC**
Compare the effectiveness of coordinated care (supported by reimbursement innovations) and usual care in long-term and end-of-life care of the elderly.

**PSYCH**
Compare the effectiveness of pharmacologic treatment and behavioral interventions in managing major depressive disorders in adolescents and adults in diverse treatment settings.

**RD**
Compare the effectiveness of an integrated approach (combining counseling, environmental mitigation, chronic disease management, and legal assistance) with a non-integrated episodic care model in managing asthma in children.

**SKIN**
Compare the effectiveness (including effects on quality of life) of treatment strategies (e.g., topical steroids, ultraviolet light, methotrexate, biologic response modifiers) for psoriasis.

**TEMC**
Compare the effectiveness of treatment strategies (e.g., cognitive behavioral individual therapy, generic individual therapy, comprehensive and intensive treatment) for Post-traumatic Stress Disorder stemming from diverse sources of trauma.

**WH**
Compare the effectiveness and outcomes of care with obstetric ultrasound studies and care without the use of ultrasound in normal pregnancies.

**WH**
Compare the effectiveness of birthing care in freestanding birth centers and usual care of childbearing women at low and moderate risk.

*continued*
TABLE S-1 Continued

Third Quartile
(listed alphabetically by primary research area)

| ADDO | Compare the effectiveness of different opioid and non-opioid pain relievers, in different doses and durations, in avoiding unintentional overdose and substance dependence among subjects with acute and non-cancer chronic pain. |
| CAD  | Compare the effectiveness of aggressive medical management and percutaneous coronary interventions in treating stable coronary disease for patients of different ages and with different comorbidities. |
| CAD  | Compare the effectiveness of innovative treatment strategies (e.g., cardiac resynchronization, remote physiologic monitoring, pharmacologic treatment, novel agents such as CRF-2 receptors) for congestive heart failure. |
| CAD  | Compare the effectiveness of traditional risk stratification for coronary heart disease (CHD) and noninvasive imaging (using coronary artery calcium, carotid intima media thickness, and other approaches) on CHD outcomes. |
| CAD  | Compare the effectiveness of different treatment strategies (e.g., modifying target levels for glucose, lipid, or blood pressure) in reducing cardiovascular complications in newly diagnosed adolescents and adults with type 2 diabetes. |
| CAM  | Compare the effectiveness of acupuncture for various indications using a cluster randomized trial. |
| CAM  | Compare the effectiveness of dietary supplements (nutriceuticals) and usual care in the treatment of selected high-prevalence conditions. |
| EENT | Compare the effectiveness of different treatment options (e.g., laser therapy, intravitreal steroids, anti-vascular endothelial growth factor [anti-VEGF]) for diabetic retinopathy, macular degeneration, and retinal vein occlusion. |
| EENT | Compare the effectiveness of treatment strategies for primary open-angle glaucoma (e.g., initial laser surgery, new surgical techniques, new medical treatments) particularly in minority populations to assess clinical and patient-reported outcomes. |
| ENDO | Compare the effectiveness and cost-effectiveness of conventional medical management of type 2 diabetes in adolescents and adults, versus conventional therapy plus intensive educational programs or programs incorporating support groups and educational resources. |
| HCDS | Compare the effectiveness of alternative redesign strategies—using decision support capabilities, electronic health records, and personal health records—for increasing health professionals’ compliance with evidence-based guidelines and patients’ adherence to guideline-based regimens for chronic disease care. |
SUMMARY

TABLE S-1 Continued

HCDS  Compare the effectiveness of adding information about new biomarkers (including genetic information) with standard care in motivating behavior change and improving clinical outcomes.

HCDS  Compare the effectiveness of different quality improvement strategies in disease prevention, acute care, chronic disease care, and rehabilitation services for diverse populations of children and adults.

HCDS  Compare the effectiveness of formulary management practices and usual practices in controlling hospital expenditures for products other than drugs including medical devices (surgical hemostatic products, radiocontrast, interventional cardiology devices, and others).

HCDS  Compare the effectiveness of different benefit design, utilization management, and cost-sharing strategies in improving health care access and quality in patients with chronic diseases (e.g., cancer, diabetes, heart disease).

INFD  Compare the effectiveness of HIV screening strategies based on recent Centers for Disease Control and Prevention recommendations and traditional screening in primary care settings with significant prevention counseling.

MS  Establish a prospective registry to compare the effectiveness of surgical and nonsurgical strategies for treating cervical spondylotic myelopathy (CSM) in patients with different characteristics to delineate predictors of improved outcomes.

NEURO  Compare the effectiveness of traditional and newer imaging modalities (e.g., routine imaging, magnetic resonance imaging [MRI], computed tomography [CT], positron emission tomography [PET]) when ordered for neurological and orthopedic indications by primary care practitioners, emergency department physicians, and specialists.

NEURO  Compare the effectiveness of comprehensive, coordinated care and usual care on objective measures of clinical status, patient-reported outcomes, and costs of care for people with multiple sclerosis.

NUTR  Compare the effectiveness of treatment strategies for obesity (e.g., bariatric surgery, behavioral interventions, pharmacologic treatment) on the resolution of obesity-related outcomes such as diabetes, hypertension, and musculoskeletal disorders.

ORAL  Compare the clinical and cost-effectiveness of surgical care and a medical model of prevention and care in managing periodontal disease to increase tooth longevity and reduce systemic secondary effects in other organ systems.

continued
### TABLE S-1 Continued

<table>
<thead>
<tr>
<th>Primary Research Area</th>
<th>Comparative Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSYCH</td>
<td>Compare the effectiveness of atypical antipsychotic drug therapy and conventional pharmacologic treatment for Food and Drug Administration-approved indications and compendia-referenced off-label indications using large datasets.</td>
</tr>
<tr>
<td>PSYCH</td>
<td>Compare the effectiveness of management strategies (e.g., inpatient psychiatric hospitalization, extended observation, partial hospitalization, intensive outpatient care) for adolescents and adults following a suicide attempt.</td>
</tr>
<tr>
<td>RED</td>
<td>Compare the effectiveness of different strategies to engage and retain patients in care and to delineate barriers to care, especially for members of populations that experience health disparities.</td>
</tr>
<tr>
<td>SKIN</td>
<td>Compare the effectiveness of topical treatments (e.g., antibiotics, platelet-derived growth factor) and systemic therapies (e.g., negative pressure wound therapy, hyperbaric oxygen) in managing chronic lower extremity wounds.</td>
</tr>
</tbody>
</table>

### Fourth Quartile

(listed alphabetically by primary research area)

<table>
<thead>
<tr>
<th>Primary Research Area</th>
<th>Comparative Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADDO</td>
<td>Compare the effectiveness of smoking cessation strategies (e.g., medication, individual or quitline counseling, combinations of these) in smokers from understudied populations such as minorities, individuals with mental illness, and adolescents.</td>
</tr>
<tr>
<td>CAD</td>
<td>Compare the effectiveness of computed tomography (CT) angiography and conventional angiography in assessing coronary stenosis in patients at moderate pretest risk of coronary artery disease.</td>
</tr>
<tr>
<td>CAD</td>
<td>Compare the effectiveness of anticoagulant therapies (e.g., low-intensity warfarin, aspirin, injectable anticoagulants) for patients undergoing hip or knee arthroplasty surgery.</td>
</tr>
<tr>
<td>DIS</td>
<td>Compare the effectiveness of focused intense periodic therapy and usual weekly therapy in managing cerebral palsy in children.</td>
</tr>
<tr>
<td>ENDO</td>
<td>Compare the effectiveness of different disease management strategies in improving the adherence to and value of pharmacologic treatments for the elderly.</td>
</tr>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of care coordination with and without clinical decision supports (e.g., electronic health records) in producing good health outcomes in chronically ill patients, including children with special health care needs.</td>
</tr>
</tbody>
</table>
SUMMARY

TABLE S-1 Continued

<table>
<thead>
<tr>
<th>HCDS</th>
<th>Compare the effectiveness of coordinated, physician-led, interdisciplinary care provided in the patient’s residence and usual care in managing advanced chronic disease in community-dwelling patients with significant functional impairments.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of minimally invasive abdominal surgery and open surgical procedures on post-operative infections, pain management, and recuperative requirements.</td>
</tr>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of traditional behavioral interventions versus economic incentives in motivating behavior changes (e.g., weight loss, smoking cessation, avoiding alcohol and substance abuse) in children and adults.</td>
</tr>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of diagnostic imaging performed by non-radiologists and radiologists.</td>
</tr>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of different techniques (e.g., audio, visual, written) for informing patients about proposed treatments during the process of informed consent.</td>
</tr>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of different disease management strategies for activating patients with chronic disease.</td>
</tr>
<tr>
<td>HCDS</td>
<td>Compare the effectiveness of different delivery models (e.g., home blood pressure monitors, utilization of pharmacists or other allied health providers) for controlling hypertension, especially in racial minorities.</td>
</tr>
<tr>
<td>INFD</td>
<td>Compare the effectiveness of alternative clinical management strategies for hepatitis C, including alternative duration of therapy for patients based on viral genomic profile and patient risk factors (e.g., behavior-related risk factors).</td>
</tr>
<tr>
<td>MS</td>
<td>Compare the effectiveness of different treatment strategies in the prevention of progression and disability from osteoarthritis.</td>
</tr>
<tr>
<td>MS</td>
<td>Compare the effectiveness (e.g., pain relief, functional outcomes) of different surgical strategies for symptomatic cervical disc herniation in patients for whom appropriate nonsurgical care has failed.</td>
</tr>
<tr>
<td>NEURO</td>
<td>Compare the effectiveness of different treatment strategies on the frequency and lost productivity in people with chronic, frequent migraine headaches.</td>
</tr>
<tr>
<td>NEURO</td>
<td>Compare the effectiveness of monotherapy and polytherapy (i.e., use of two or more drugs) on seizure frequency, adverse events, quality of life, and cost in patients with intractable epilepsy.</td>
</tr>
<tr>
<td>ONC</td>
<td>Compare the effectiveness of surgical resection, observation, or ablative techniques on disease-free and overall survival, tumor recurrence, quality of life, and toxicity in patients with liver metastases.</td>
</tr>
</tbody>
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continued
### TABLE S-1 Continued

<table>
<thead>
<tr>
<th>PELC</th>
<th>Compare the effectiveness of hospital-based palliative care and usual care on patient-reported outcomes and cost.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSYCH</td>
<td>Compare the effectiveness of different treatment approaches (e.g., integrating mental health care and primary care, improving consumer self-care, a combination of integration and self-care) in avoiding early mortality and comorbidity among people with serious and persistent mental illness.</td>
</tr>
<tr>
<td>PSYCH</td>
<td>Compare the effectiveness of traditional training of primary care physicians in primary care mental health and co-location systems of primary care and mental health care on outcomes including depression, anxiety, physical symptoms, physical disability, prescription substance use, mental and physical function, satisfaction with the provider, and cost.</td>
</tr>
<tr>
<td>PSYCH</td>
<td>Compare the effectiveness of different treatment strategies (e.g., psychotherapy, antidepressants, combination treatment with case management) for depression after myocardial infarction on medication adherence, cardiovascular events, hospitalization, and death.</td>
</tr>
<tr>
<td>SKIN</td>
<td>Compare the effectiveness of different long-term treatments for acne.</td>
</tr>
<tr>
<td>WH</td>
<td>Compare the effectiveness of different strategies for promoting breastfeeding among low-income African American women.</td>
</tr>
</tbody>
</table>

**NOTE:** ADDO = Alcoholism, Drug Dependency, and Overdose; BDEV = Birth and Developmental Disorders; CAD = Cardiovascular and Peripheral Vascular Disease; CAM = Complementary and Alternative Medicine; DIS = Functional Limitations and Disabilities; EENT = Eyes, Ears, Nose, and Throat Disorders; ENDO = Endocrinology and Metabolism Disorders and Geriatrics; GI = Gastrointestinal System Disorders; HCDS = Health Care Delivery Systems; IMM = Immune System, Connective Tissue, and Joint Disorders; INFD = Infectious Diseases Liver and Biliary Tract Disorders; KUT = Kidney and Urinary Tract Disorders; MS = Musculoskeletal Disorders; NEURO = Neurologic Disorders; NUTR = Nutrition (including obesity); ONC = Oncology and Hematology; ORAL = Oral Health; PEDS = Pediatrics; PELC = Palliative and End-of-Life Care; PSYCH = Psychiatric Disorders; RD = Respiratory Disease; RED = Racial and Ethnic Disparities; SKIN = Skin Disorders; TEMC = Trauma, Emergency Medicine, and Critical Care Medicine; WH = Women’s Health.
DEFINING COMPARATIVE EFFECTIVENESS RESEARCH

An agreed-upon definition of CER is an essential first step for setting priorities and developing a sustainable national CER Program. It informs the public of the focus of this research and its importance in their lives, and it informs investigators of the characteristics of the research to be supported by CER funds. It provides a basis for judging research proposals to perform CER and for evaluating the impact of that research and the success of a national CER Program. In formulating its definition, this committee drew upon definitions by several government agencies and other IOM committees (see Chapter 2):

Comparative effectiveness research (CER) is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.

CREATING THE PRIORITY LIST OF CER STUDIES

The committee received several broad directives. The legislative language directed the IOM to solicit the opinions of stakeholders. The IOM’s charge from the contracting agency, AHRQ, stipulated that the committee provide a well-balanced portfolio of research topics for the list of priorities. The committee’s approach to priority setting included the following:

- **Extensive consultation with and input from stakeholders.** The committee widely solicited input through three mechanisms: (1) an invitation to the public and key stakeholders to testify at a 1-day public meeting in Washington, DC, at which the committee heard 54 speakers and received additional written testimony (available on the report’s website at www.iom.edu/cerpriorities); (2) a web-based nomination process through which 1,758 respondents, mostly physicians and representatives of professional organizations, but also members of the general public nominated a total of 1,268 unique research topics (see questionnaire in Appendix B); and (3) the project’s website, which received emails and letters (see Chapter 3).

- **Development and consideration of written priority-setting criteria.** To guide judgments about each nominated topic, the committee formulated priority-setting criteria to identify high priority target conditions, such as their prevalence, mortality, aggregate costs,
gaps in knowledge, and small area variation in rates of tests and
treatments of top conditions as well as criteria focused on specific
research topics (see Chapter 4).

• **Commitment to developing a broad-based portfolio of high priority
topics.** The committee’s criteria for creating a balanced portfolio
considered four dimensions: (1) clinical category (e.g., cardio-
vascular and peripheral vascular disease), (2) study population,
(3) categories of interventions, and (4) research methodology (e.g.,
randomized trial, cohort study) suggested by the nominator (see
Chapter 5).

• **A three-round voting process to narrow the nominated CER topics
to a final list of 100.** Members voted independently based on the
committee-specified criteria and their own values; votes were tallied
to rank each nominated topic (see Chapter 4).

• **Committee discussion of the highest-scored topics.** After the second
round of voting, the committee had a detailed discussion of the
highest-scored topics. The objective of this discussion was to see if
the committee agreed on the nominator’s intent and also to reframe
some of the nominations to adhere to a common format. The com-
mittee also reached consensus on topics to fill or eliminate gaps in
the portfolio representation. A total of 26 topics were nominated
by the committee. These topics were incorporated into the 129
remaining submitted topics without distinguishing them, providing
a total of 155 unique nominated research topics for consideration
in the third round of voting.

**PORTFOLIO DISTRIBUTION OF THE PRIORITY TOPICS**

The committee’s goal in examining the list of priority research topics
as a portfolio was to include balance across the four dimensions previously
mentioned. A balanced CER portfolio not only studies those diseases and
conditions with the greatest effects on the health of the U.S. population,
but also includes rare diseases and conditions that disproportionately and
seriously affect subgroups of the population (such as women, minorities,
and different groups across the age continuum). The committee sees great
value in extending the concept of drug-to-drug comparisons to a variety of
interventions including tests to screen for or monitor disease (e.g., imaging
for cancer or during normal pregnancy), surgical techniques (e.g., closed
vs. open procedures), and therapeutic alternatives (e.g., medical therapy
vs. surgery vs. radiotherapy for prostate cancer). Additionally, CER that
examines different means of delivering health care was considered to be an important determinant of quality and was incorporated into the options for intervention.

Finally, CER priorities should be balanced in the primary methodologies employed to conduct them: systematic reviews, database research, observational studies, and randomized trials. There are some studies that can be completed in the short term with relatively minimal resources, but other studies will require a longer time frame and a substantial investment of resources. The committee was charged with developing a portfolio of topics that would lead to an appropriate expenditure of the $400 million for CER under the ARRA time frame. Determination of the specific design, questions to be answered by each individual research project, and methodology, as defined by the potential researcher, will determine the research costs; however, this task is well beyond the scope of this committee. The committee sought balance in the methodologies proposed by the nominators for all 100 priority topics and determined that they were reasonably well balanced across the four major study methodologies.

Systematic review of existing literature is a relatively inexpensive and rapidly performed methodology when compared with other methods. It can identify both information gaps requiring new data generation as well as areas in which sufficient data exist to establish best practices. Research using established databases and registries can be undertaken in a reasonable time frame, inexpensively, and can generate new hypotheses and identify major health care gaps. The generation of new information, either through initiation of new databases or prospective observational studies or through prospective, randomized controlled trials is far more expensive and time consuming, but is often necessary to provide sufficient evidence of what works best and for whom. Thus, the committee balanced the types of study designs so that many studies could be conducted within the time period identified in ARRA.

An interactive file of the list of priority topics is available on the report website at www.iom.edu/cerpriorities. Using this file, readers can sort the list of topics by various portfolio characteristics such as research area, study population, or type of intervention.

RECOMMENDATIONS FOR A ROBUST NATIONAL CER ENTERPRISE

Based on stakeholder input and its own deliberations, the committee concluded that the country needs a robust CER infrastructure—referred to throughout as the “CER Program”—to sustain CER well into the future, including carrying out the research recommended in this report and studying new topics identified by future priority setting. The committee’s list of
100 priority topics responds to the requirements of ARRA to advise the Secretary on how to distribute CER funds from the bill. In addition, the list could be useful beyond the $400 million appropriated to the Secretary by influencing the distribution of funds by NIH, AHRQ, and other agencies that fund CER. The list is not sufficient, however, to ensure the needs of a future in which new interventions and new diseases will mandate new priorities for CER. The committee’s examination of previous priority-setting efforts and its study of the nominated research topics conveyed through its questionnaire led it to conclude that CER must be an ongoing process. Health care is dynamic; new diseases and health needs can arise suddenly and other health problems might become insignificant when a treatment is found. As new CER produces new evidence and closes gaps in evidence, CER might need to take new directions. A continuous process is necessary to update funding priorities as conditions change and the impact of previous CER becomes evident (see Chapter 4 for discussion of Recommendations 1 through 4).

Recommendation 1: Prioritization of CER topics should be a sustained and continuous process, recognizing the dynamic state of disease, interventions, and public concern.

The committee acknowledges the critical role that the general public and other stakeholders played in this current report and their potential to enhance CER in the future. CER generates results that bear directly on decisions in which individual patients play an active role. Active involvement of consumers, patients, and caregivers is essential to identifying CER topics of real concern to them as well as for suggesting criteria for the prioritization process that reflect public goals and values.

Recommendation 2: Public (including consumers, patients, and caregivers) participation in the priority-setting process is imperative to provide transparency in the process and input to delineating research questions.

The committee noted that more complete background information about the suggested research topics would have substantially enhanced its prioritization process. A national CER enterprise should, on an ongoing basis, collate national data concerning the significance of diseases and conditions as well as information about current research gaps and redundancies related to the specific research topics under consideration. The committee found that the descriptions of research topics were often difficult to understand; an opportunity for a priority-setting body to interrogate CER topic nominators would help to clarify the nominator’s intent.
SUMMARY

Recommendation 3: Consideration of CER topics requires the development of robust, consistent topic briefs providing background information, current practice, and research status of the condition and its interventions.

The committee concluded that a high level of transparency is essential for setting priorities for expending public funds on research from which the public expects so much. Given the magnitude of public investment in CER, a rolling evaluation of the selection and prioritization processes, as well as the return on investment of prior CER research by application throughout the health system should be incorporated in the prioritization process to ensure quality improvement.

Recommendation 4: Regular reporting of the activities and recommendations of the prioritizing body is necessary to evaluate the portfolio’s distribution, its impact for discovery, and its translation into clinical care in order to provide a process for continuous quality improvement.

The committee’s work, including stakeholder input, revealed the scope of research infrastructure needed to support CER in its goal of improving health care decisions and their implementation. The committee does not attempt to fill in all the details, but it concludes that the country must have a federal organizational infrastructure with appropriate responsibility and authority to coordinate the prioritization process, support the development of necessary databases and registries, fund the training of needed researchers, conduct the research, and support a vigorous translational effort to help bring research findings into everyday clinical practice. Without federal support for an infrastructure to coordinate the national CER effort, all the CER that the committee identified as high priority is unlikely to occur (see Chapter 6 for a discussion of infrastructure issues).

Objectivity will be central to the public’s trust and confidence in the integrity of the CER Program. CER is as vulnerable to bias and conflict of interest as any other area of medical research. A 2009 IOM report, Conflict of Interest in Medical Research, Education, and Practice, recommends principles to inform the design of policies to identify, limit, and manage conflicts of interest in health care research. The committee urges that the CER Program be constituted and managed in accordance with the recommendations of this report.

Recommendation 5: The HHS Secretary should establish a mechanism—such as a coordinating advisory body—with the mandate to strategize, organize, monitor, evaluate, and report on the implementation and impact of the CER Program.
A central focus on the patient is fundamental to high-quality health care. To meet the requirement of patient-centeredness, respect for individual patients’ unique needs, beliefs, and values must drive the development of the field of CER and the application of its findings to patient care. Consumers, patients, and caregivers have a key role to play in informing and framing CER. They typically have different perspectives from researchers, and there is strong evidence that many consumers—but not all—want to be involved in decision making about their care. Involving them in CER will help to keep the research relevant and applicable to real-world settings. Also, if consumers, patients, and caregivers are engaged and informed about CER activities, they are more likely to trust the research findings and insist that their own care take account of the results.

Recommendation 6: The CER Program should fully involve consumers, patients, and caregivers in key aspects of CER, including strategic planning, priority setting, research proposal development, peer review, and dissemination.

- The CER Program should develop strategies to reach out to, engage, support, educate, and, as necessary, prepare consumers, patients, and caregivers for leadership roles in these activities.
- The CER Program should also encourage broad participation in CER in order to create a representative evidence base that could help identify health disparities and inform decisions by patients in special population groups.

CER comprises a broad spectrum of established and emerging research methods including clinical trials, observational studies, and systematic reviews of existing evidence. There is a significant need for better research methods. Current study designs—experimental and nonexperimental—must be refined to ensure scientific rigor. Clinical trials will always be essential to CER, but more efficient, larger, simpler, and pragmatic designs are needed. In systematic reviews, for example, research is needed on how to identify and use evidence from observational studies on intervention effectiveness, and also on how to assess a heterogeneous body of evidence. New analytic techniques are needed to evaluate the effects of bias due to confounding when assessing comparative effectiveness using large observational datasets.

Recommendation 7: The CER Program should devote sufficient resources to research and innovation in the methods of CER, including the development of methodological guidance for CER study design such as the appropriate use of observational data and more informative, practical, and efficient clinical trials.
SUMMARY

CER should also draw from analyses of existing data, such as that held by payers, health care delivery systems, and electronic health records. However, if the CER enterprise is to harness the rich potential of these data, it must protect the privacy and maintain the security of patient data, develop efficient means for linking data from multiple databases, and engage holders of large datasets such as health insurers, health care delivery systems, and health care providers.

Recommendation 8: The CER Program should help to develop large-scale, clinical and administrative data networks to facilitate better use of data and more efficient ways to collect new data to inform CER.

- The CER Program should ensure that CER researchers and institutions consistently adhere to best practices to protect privacy and maintain security.
- The CER Program should support the development of methodologies for linking patient-level data from multiple sources.
- The CER Program should encourage data holders to participate in CER and provide incentives for cooperation and maintaining data quality.

ARRA’s infusion of federal funds into CER will stress the limited capacity of the current CER workforce. AHRQ’s CER appropriation alone increased tenfold. Whether the current research workforce can meet the human resource demands of the $1.1 billion ARRA appropriation for CER is uncertain. A significant increase in CER activity will certainly create a substantial need for experts in biostatistics, epidemiology, systematic reviews (including meta-analysis), clinical trials (including head-to-head effectiveness trials), statistical modeling, observational analytic methods, use of analysis of large datasets, cost-effectiveness analysis, clinical outcomes research, and communication of research findings. The methods of CER must advance, which will require training and career support for methodologists.

Recommendation 9: The CER Program should develop and support the workforce for CER to ensure the nation’s capacity to carry out the CER mission. Important next steps include the following:

- Development of a strategic plan for research workforce development.
- Long-term, sufficient funding for early career development including expanding grants for graduate and postgraduate training opportunities in comparative effectiveness methods as well as career development grants and mid-career merit awards.
The substantial geographic variability in health care delivery suggests that physicians differ in what they consider to be “best practice.” By discovering what works best, for whom, and under what circumstances, CER has the potential to narrow the spectrum of what health professionals consider to be best practice. Health care professionals and patients should be able to use CER results to make informed decisions based on the best available evidence, the patients’ preferences, and the patient’s unique characteristics.

However, an ambitious research enterprise alone will not improve health care in the United States without significant attention to high fidelity translation of knowledge into practice. At present, the translation of research findings into practice is slow and incomplete. Many barriers exist: perverse reimbursement incentives, physician perceptions about patients’ expectations, and patients’ concerns about denials of care or their reluctance to question clinicians. The CER Program should require researchers to publish all federally funded CER studies and make the research available to the public. Moreover, research into knowledge translation must be a high priority.

Recommendation 10: The CER Program should promote rapid adoption of CER findings and conduct research to identify the most effective strategies for disseminating new and existing CER findings to health care professionals, consumers, patients, and caregivers and for helping them to implement these results in daily clinical practice.
“Knowing is not enough; we must apply. Willing is not enough; we must do.”

—Goethe
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IN MEMORIAM

This report is dedicated to Maria Carolina Hinestrosa, a hard-working and devoted committee member who, while stricken with cancer, continued to work tirelessly on this report until its completion.
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This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by PAUL D. CLEARY, School of Public Health and School of Medicine, Yale University and GILBERT S. OMENN, Center for Computational Medicine and Biology, University of Michigan Medical School. Appointed by the National Research Council and the Institute of Medicine, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.
Foreword

A patient has a right to expect the best possible care, and a health professional has a duty to provide it. But how can one know what is best? Scientific understanding of normal biology and pathological processes can provide a foundation, but scientific principles alone can go only so far. Studies that measure results in practice are the only way to learn what works, how well, for what groups of patients, and in what specific circumstances. Yet, for want of appropriate studies, innumerable practical decisions facing patients and doctors every day do not rest on a solid foundation of knowledge about what constitutes the best choice of care. One consequence of this uncertainty is that highly similar patients experience widely varying treatment in different settings, and these patients cannot all be receiving the best care.

Comparative effectiveness research is a strategy that focuses on the practical comparison of two or more health interventions to discern what works best for which patients and populations. Because there is so much uncertainty about the effects of health care, the number of possible studies vastly exceeds the reach of available resources. Logically, the research agenda should focus on those disorders that are the most common among us, those with the greatest morbidity and mortality, those with the greatest degree of variation in their care, and those that are most costly to society. The U.S. Congress asked the Institute of Medicine (IOM) to help identify priorities from among the huge array of possible studies of comparative effectiveness. The IOM convened a highly qualified committee with diverse backgrounds who, working as volunteers and supported by a very able staff, undertook their task with energy and intensity.
FOREWORD

This report is the product of the committee's effort. Drawing on an extensive body of evidence, including input from lay and professional bodies, stakeholders, researchers, and policy makers, the committee has produced a well-grounded report. More than a list of priority topics, this report clarifies the meaning of comparative effectiveness and sets forth criteria for choosing both individual topics and the portfolio of topics for comparative effectiveness research. It is our hope that this document will prove valuable both as an immediate indicator of priorities and as an ongoing guide to the future selection of new subjects for assessment.

Harvey V. Fineberg, M.D., Ph.D.
President, Institute of Medicine
June 2009
Preface

The U.S. Congress mandated this study in the American Recovery and Reinvestment Act of 2009, which the President signed into law on February 17, 2009. The legislation required the Institute of Medicine (IOM) to convene a committee to establish a list of research questions that would have the highest priority for study with comparative effectiveness research (CER) funds that the law placed at the discretion of the Secretary of Health and Human Services. Moreover, the law required the committee to seek advice from stakeholders who might benefit from the research: researchers, physicians, professional organizations, and the general public. Basing its approach on methods developed by the Agency for Healthcare Research and Quality, the committee held a public meeting to get advice from professional and consumer groups and from the general public and solicited nominations for research questions through a web-based questionnaire. The committee developed a process for deciding which conditions to place on its list of the highest priority research questions, and, over a 10-day period, winnowed over a thousand nominations to a list of 100 high priority topics.

The principal products of the committee’s work are a definition of CER, a list of 100 priority topics, and 10 recommendations. To guide its work, the committee developed a working definition of CER, using features of definitions offered by other organizations. The priority list contains 100 research questions divided into four quartiles. The committee discussed each question and refined the wording of most of them, while still striving to preserve the spirit of the original nomination. Finally, the committee
developed 10 recommendations for an infrastructure to support a national system for conducting CER. We believe that these elements of our report will help to establish the groundwork for a research program that will serve the nation well.

Producing a full IOM report in just over 4 months required an intense, sustained effort. On very short notice, nominees to serve on the committee found time in their schedules to attend 5 days of meetings and spend many hours reading the dossiers of hundreds of research questions and deciding which were the most important. The IOM assembled an experienced, outstanding study staff who simply worked miracles day after day. Collectively, we had the pleasure of working together on a task whose importance was self-evident and the honor of serving our country.

Harold C. Sox, Co-Chair
Sheldon Greenfield, Co-Chair
Committee on Comparative Effectiveness Research Prioritization
Acknowledgments

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The individuals who testified before the committee during the public meeting are all listed in Appendix A and their written testimony is available at www.iom.edu/cerpriorities. The committee appreciates all 1,758 individuals who responded to its questionnaire, either for themselves or their organization.

We especially thank Joshua Benner and Steven Pearson for their valuable contribution to Chapter 2 of the report.

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