



Initial National Priorities for Comparative Effectiveness Research

DETAILS

252 pages | 6 x 9 | HARDBACK
ISBN 978-0-309-38808-5 | DOI 10.17226/12648

AUTHORS

Committee on Comparative Effectiveness Research Prioritization, Institute of Medicine

BUY THIS BOOK

FIND RELATED TITLES

Visit the National Academies Press at NAP.edu and login or register to get:

- Access to free PDF downloads of thousands of scientific reports
- 10% off the price of print titles
- Email or social media notifications of new titles related to your interests
- Special offers and discounts



Distribution, posting, or copying of this PDF is strictly prohibited without written permission of the National Academies Press. (Request Permission) Unless otherwise indicated, all materials in this PDF are copyrighted by the National Academy of Sciences.

INITIAL NATIONAL PRIORITIES FOR
**COMPARATIVE
EFFECTIVENESS
RESEARCH**

Committee on Comparative Effectiveness Research Prioritization

Board on Health Care Services

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS 500 Fifth Street, N.W. Washington, DC 20001

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This study was supported by Task Order number HHSP 23337002T and Contract number HHSP 23320042509XI between the National Academy of Sciences and the Agency for Healthcare Research and Quality, by the National Academies President's Fund, and by the Robert Wood Johnson Foundation's Health Policy Fellowships. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the view of the organizations or agencies that provided support for this project.

International Standard Book Number-13: 978-0-309-13836-9

International Standard Book Number-10: 0-309-13836-1

Library of Congress Control Number: 2009934993

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, <http://www.nap.edu>.

For more information about the Institute of Medicine, visit the IOM home page at: www.iom.edu.

Copyright 2009 by the National Academy of Sciences. All rights reserved.

Printed in the United States of America

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

Suggested citation: IOM (Institute of Medicine). 2009. *Initial National Priorities for Comparative Effectiveness Research*. Washington, DC: The National Academies Press.

*“Knowing is not enough; we must apply.
Willing is not enough; we must do.”*

—Goethe



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the Nation. Improving Health.

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Charles M. Vest is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Charles M. Vest are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

IN MEMORIAM

This report is dedicated to Maria Carolina Hinstrosa, a hard-working and devoted committee member who, while stricken with cancer, continued to work tirelessly on this report until its completion.

COMMITTEE ON COMPARATIVE EFFECTIVENESS
RESEARCH PRIORITIZATION

- HAROLD C. SOX** (*Co-Chair*), Editor, *Annals of Internal Medicine*, American College of Physicians of Internal Medicine, Philadelphia, PA
- SHELDON GREENFIELD** (*Co-Chair*), Donald Bren Professor of Medicine and Executive Director, Center for Health Policy Research, University of California, Irvine
- CHRISTINE K. CASSEL**, President and CEO, American Board of Internal Medicine, Philadelphia, PA
- KAY DICKERSIN**, Professor of Epidemiology, Director, Center for Clinical Trials and Director, United States Cochrane Center, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
- ALAN M. GARBER**, Henry J. Kaiser, Jr. Professor and Professor of Medicine, Director, Center for Health Policy and Center for Primary Care and Outcomes Research, Stanford University, Stanford, CA
- CONSTANTINE GATSONIS**, Professor of Medical Science (Biostatistics) and Director, Center for Statistical Sciences, Brown University, Providence, RI
- GARY L. GOTTLIEB**, President, Brigham and Women's Hospital, Professor of Psychiatry, Harvard Medical School, Boston, MA
- JAMES A. GUEST**, President and CEO, Consumers Union, Yonkers, NY
- MARK HELFAND**, Professor of Medicine and Director, Oregon Evidence-based Practice Center, Oregon Health and Science University, and Staff Physician, Portland VAMC, Portland
- MARIA CAROLINA HINESTROSA**,* Executive Vice President for Programs and Planning, National Breast Cancer Coalition, Co-Founder, Nueva Vida, Washington, DC
- GEORGE J. ISHAM**, Medical Director and Chief Health Officer, HealthPartners, Inc., Bloomington, MN
- ARTHUR A. LEVIN**, Director, Center for Medical Consumers, New York
- JOANN E. MANSON**, Professor of Medicine and the Elizabeth Fay Brigham Professor of Women's Health, Harvard Medical School, Chief of the Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA
- KATIE MASLOW**, Director, Policy Development, Alzheimer's Association, Washington, DC

*Deceased.

- MARK B. McCLELLAN**, Director, Engelberg Center for Health Care Reform, The Brookings Institution, Washington, DC
- SALLY C. MORTON**, Vice President for Statistics and Epidemiology, RTI International, Research Triangle Park, NC
- NEIL R. POWE**, Chief, Medical Services, San Francisco General Hospital Professor and Vice Chairman, Department of Medicine, University of California, San Francisco
- JOE V. SELBY**, Director, Division of Research, Kaiser Permanente, Oakland, CA
- LISA SIMPSON**, Director, Child Policy Research Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- SEAN TUNIS**, Founder and Director, Center for Medical Technology Policy, Baltimore, MD
- I. STEVEN UDVARHELYI**, Senior Vice President and Chief Medical Officer, Independence Blue Cross, Philadelphia, PA
- A. EUGENE WASHINGTON**, Executive Vice Chancellor and Provost, University of California, San Francisco
- JAMES N. WEINSTEIN**, Dartmouth College Third Century Professor, Director, The Dartmouth Institute for Health Policy and Clinical Practice; Professor and Chair, Department of Orthopedic Surgery, Dartmouth Medical School and Vice Chair, Board of Governors, Dartmouth-Hitchcock Medical Center, Lebanon, NH

Study Staff

- ROGER HERDMAN**, Board Director
- ROBERT RATNER**, Study Director
- JILL EDEN**, Senior Program Officer
- DIANNE MILLER WOLMAN**, Senior Program Officer
- SALLY ROBINSON**, Program Officer
- LAURA LEVIT**, Associate Program Officer
- LEA GREENSTEIN**, Research Associate
- MICHELLE MANCHER**, Research Associate
- ALLISON McFALL**, Senior Program Assistant
- REDA URMANAVICIUTE**, Administrative Assistant
- HARRIET CRAWFORD**, IT Project Manager
- DWAYNE BELL**, Programmer Analyst

Consultants

JOSHUA BENNER, The Brookings Institution

STEVEN PEARSON, Institute for Clinical and Economic Review,
Harvard Medical School

NEIL WEISFELD, NEW Associates

VICTORIA WEISFELD, NEW Associates

Reviewers

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:

RHONDA J. ROBINSON BEALE, United Behavioral Health
MARC BOUTIN, National Health Council
ELLEN WRIGHT CLAYTON, Center for Biomedical Ethics and
Society, Vanderbilt University
DON E. DETMER, American Medical Informatics Association
ERIC B. LARSON, Group Health, Center for Health Studies
DAVID O. MELTZER, Pritzker School of Medicine, University of
Chicago
GARY A. PUCKREIN, National Minority Quality Forum
RICHARD SCHILSKY, Biological Sciences Division, University of
Chicago Medical Center

J. SANFORD SCHWARTZ, School of Medicine and the Wharton School, University of Pennsylvania
GLENN D. STEELE, JR., Geisinger Health System
BRIAN L. STROM, University of Pennsylvania School of Medicine
JOHN A. WAGNER, Merck & Co., Inc.

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.

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

The committee and staff are indebted to a number of individuals and organizations for their contributions to this report.

We extend thanks to the following individuals for their assistance in gathering the objective data that the committee used in its voting and prioritization process.

Christina Bethell, Oregon Health & Science University, School of Medicine

James A. Schuttinga, Division of Program Coordination, Planning, and Strategic Initiatives, National Institutes of Health

Nancy Sonnenfeld, National Center for Health Statistics

Deborah A. Zarin, ClinicalTrials.gov, National Library of Medicine

We extend thanks to the following individuals who piloted and provided feedback on the web-based questionnaire.

Raymond J. Baxter, Kaiser Permanente

Melanie Bella, Center for Health Care Strategies

Kathleen Buto, Johnson & Johnson

Denis A. Cortese, Mayo Clinic

Nancy Derr, Food and Drug Administration

Daniel M. Fox, Milbank Memorial Fund

Jean Paul Gagnon, Sanofi Aventis

Mark Gibson, Oregon Health & Science University, Center for Evidence-based Policy

Carmen Hooker Odom, Milbank Memorial Fund
Richard A. Justman, United HealthCare
Michael S. Lauer, National Institutes of Health
Sandy Leonard, AstraZeneca
Samuel R. Nussbaum, WellPoint, Inc.
Steven D. Pearson, Institute for Clinical and Economic Review,
Harvard Medical School
John W. Rowe, Columbia University
Edward M. Rozyński, Stryker
John Santa, Consumers Union
Chad Shearer, Center for Health Care Strategies
Jeffrey Shuren, Food and Drug Administration
Jean Slutsky, Agency for Healthcare Research and Quality
Karen Smith, AstraZeneca
Stephen A. Somers, Center for Health Care Strategies
Frank Torres, Microsoft Corporation

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.

Funding for this study was provided by the National Academies President's Fund, the Agency for Healthcare Research and Quality, and the Robert Wood Johnson Foundation. The committee appreciates the opportunity and support for the development of this report.

Finally, many within the Institute of Medicine were helpful to the study staff. The staff would especially like to thank Clyde Behney, Patrick Burke, William McLeod, Abbey Meltzer, LeighAnne Olsen, Lauren Tobias, Jackie Turner, and Jordan Wyndelts.

Contents

SUMMARY	1
1 INTRODUCTION	21
Study Scope, 22	
Committee Formation and Procedures, 23	
Study Context, 24	
Organization of the Report, 26	
References, 27	
2 WHAT IS COMPARATIVE EFFECTIVENESS RESEARCH?	29
The Need for <i>More</i> and <i>Better</i> Evidence of What Works in Health Care, 30	
Defining Comparative Effectiveness Research, 33	
Characteristics of CER, 37	
Examples of CER Studies: Coronary Artery Disease, 42	
Existing CER Activity in the United States, 46	
Conclusion, 54	
References, 56	
3 OBTAINING INPUT TO IDENTIFY NATIONAL PRIORITIES FOR COMPARATIVE EFFECTIVENESS RESEARCH	61
Introduction, 61	
Invitations to Provide Input, 62	
Communications Directly to the Committee, 62	
Presentations at an Open Meeting of Stakeholders, 65	

	Input from a Web-Based Questionnaire, 68	
	Reference, 75	
4	THE CRITERIA AND PROCESS FOR SETTING PRIORITIES	77
	Introduction, 77	
	Portfolio Considerations, 78	
	Criteria Chosen for Priority Setting, 80	
	Data Collection to Aid Topic Selection, 83	
	Lessons from Previous Priority-Setting Processes, 84	
	Voting Procedures, 90	
	Lessons Learned from the Current Prioritization Process and Committee Recommendations, 92	
	References, 94	
5	PRIORITIES FOR STUDY	97
	Assembling a Diverse Portfolio, 98	
	Diversity of Research Areas, 99	
	Diversity of Populations, 102	
	Diversity of Interventions, 103	
	Diversity of Study Methodologies, 104	
	Introduction to Final List of Priority Topics, 105	
	Discussion of the Priority Topics by Research Area, 116	
	Timeliness and Limitations of the Committee's Priority List, 136	
	References, 137	
6	ESSENTIAL PRIORITIES FOR A ROBUST CER ENTERPRISE	139
	The Imperative for Effective Coordination of the CER Enterprise, 140	
	Meaningful Consumer, Patient, and Caregiver Engagement, 142	
	Robust Data and Information Systems, 146	
	Develop, Deploy, and Support a CER Workforce, 155	
	Bringing Knowledge into Practice, 159	
	Conclusion, 159	
	References, 160	

APPENDIXES

A	Public Meeting Agenda—March 20, 2009	167
B	Stakeholder Questionnaire	171
C	Data Tables: Burden of Disease and Variation of Care	189
D	Cardiovascular and Peripheral Vascular Cover Sheet	199
E	Definitions of Medical Terminology in CER Priority List	203
F	Committee Biographies	213

Boxes, Figures, and Tables

Summary

Table

- S-1 Final List of 100 Priority Topics, by Quartile Ratings, 3

Chapter 1

Box

- 1-1 Charge to the IOM Committee on Comparative Effectiveness Research Prioritization, 23

Chapter 2

Box

- 2-1 Methods Commonly Used in CER, 40

Tables

- 2-1 Definitions of CER, 35
2-2 Selected CER Studies of Management of Acute Coronary Syndrome, 44

Chapter 3

Box

- 3-1 Organizations Represented at the Stakeholder Meeting, 66

Figure

- 3-1 Stakeholder response to web-based questionnaire, 69

Tables

- 3-1 Solicited Stakeholder Groups, 63
 3-2 Respondents to the IOM Questionnaire by Stakeholder Category, 70
 3-3 Comparative Effectiveness Research Priorities Submitted by Primary Area of Study, 71
 3-4 Comparative Effectiveness Research Priorities by Proposed Population to Be Studied, 72
 3-5 Comparative Effectiveness Research Priorities by Proposed Intervention, 72
 3-6 Comparative Effectiveness Research Priorities by Proposed Study Methodology, 73

Chapter 4

Figure

- 4-1 Voting process and selection of priority topics, 91

Tables

- 4-1 Portfolio and Priorities Criteria, 79
 4-2 Criteria and Priorities for Quality Improvement, 86
 4-3 A Variety of Priority-Setting Initiatives and Their Selected Criteria, 87

Chapter 5

Box

- 5-1 Round 3 Voting Procedure, 106

Figure

- 5-1 Distribution of the recommended research priorities by primary and secondary research areas, 101

Tables

- 5-1 Recommended Research Priorities by Research Area, 100
 5-2 Committee's Recommended Research Priorities by Study Populations, 103
 5-3 Committee's Recommended Research Priorities by Types of Intervention, 104

- 5-4 Committee's Recommended Research Priorities by Study Methodology, 105
- 5-5 Results of the IOM Committee's Final Vote for Priority Topics, by Quartile, 106
- 5-6 Final List of Priority Topics, by Quartile Ratings, 107
- 5-7 Health Care Delivery Systems Priority Topics, 118
- 5-8 Cardiovascular and Peripheral Vascular Diseases Priority Topics, 121
- 5-9 Psychiatric Disorders Priority Topics, 122
- 5-10 Neurologic Disorders Priority Topics, 123
- 5-11 Oncology and Hematology Priority Topics, 124
- 5-12 Women's Health Priority Topics, 124
- 5-13 Musculoskeletal Disorders Priority Topics, 125
- 5-14 Infectious Disease and Liver and Biliary Tract Disorder Priority Topics, 126
- 5-15 Endocrinology and Metabolism Disorders and Geriatric Priority Topics, 127
- 5-16 Birth and Developmental Disorders Priority Topics, 128
- 5-17 Complementary and Alternative Medicine Priority Topics, 129
- 5-18 Nutrition Priority Topics, 130
- 5-19 Race and Ethnic Disparities Priority Topics, 130
- 5-20 Skin Disorders Priority Topics, 131
- 5-21 Alcoholism, Drug Dependency, and Overdose Priority Topics, 131
- 5-22 Functional Limitations and Disability Priority Topics, 132
- 5-23 Ears, Eyes, Nose, and Throat Disorders Priority Topics, 132
- 5-24 Kidney and Urinary Tract Disorders Priority Topics, 133
- 5-25 Oral Health Priority Topics, 133
- 5-26 Palliative and End-of-Life Care Priority Topics, 134
- 5-27 Gastrointestinal System Disorders Priority Topics, 134
- 5-28 Immune System, Connective Tissue, and Joint Disorders Priority Topics, 135
- 5-29 Pediatric Disorders Priority Topics, 135
- 5-30 Respiratory Disorders Priority Topics, 136
- 5-31 Trauma, Emergency Medicine, and Critical Care Medicine Priority Topics, 136

Chapter 6

Box

- 6-1 IOM Recommendations for Changes to the HIPAA Privacy Rule and Associated Guidance Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research, 156

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

(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

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*

First Quartile

(listed alphabetically by primary research area)

CAD	Compare the effectiveness of treatment strategies for atrial fibrillation including surgery, catheter ablation, and pharmacologic treatment.
DIS	Compare the effectiveness of the different treatments (e.g., assistive listening devices, cochlear implants, electric-acoustic devices, habilitation and rehabilitation methods [auditory/oral, sign language, and total communication]) for hearing loss in children and adults, especially individuals with diverse cultural, language, medical, and developmental backgrounds.
ENDO	Compare the effectiveness of primary prevention methods, such as exercise and balance training, versus clinical treatments in preventing falls in older adults at varying degrees of risk.
GI	Compare the effectiveness of upper endoscopy utilization and frequency for patients with gastroesophageal reflux disease on morbidity, quality of life, and diagnosis of esophageal adenocarcinoma.
HCDS	Compare the effectiveness of dissemination and translation techniques to facilitate the use of CER by patients, clinicians, payers, and others.
HCDS	Compare the effectiveness of comprehensive care coordination programs, such as the medical home, and usual care in managing children and adults with severe chronic disease, especially in populations with known health disparities.
IMUN	Compare the effectiveness of different strategies of introducing biologics into the treatment algorithm for inflammatory diseases, including Crohn's disease, ulcerative colitis, rheumatoid arthritis, and psoriatic arthritis.
INFD	Compare the effectiveness of various screening, prophylaxis, and treatment interventions in eradicating methicillin resistant <i>Staphylococcus aureus</i> (MRSA) in communities, institutions, and hospitals.

continued

TABLE S-1 Continued

INFD	Compare the effectiveness of strategies (e.g., bio-patches, reducing central line entry, chlorhexidine for all line entries, antibiotic impregnated catheters, treating all line entries via a sterile field) for reducing health care associated infections (HAI), including catheter-associated bloodstream infection, ventilator associated pneumonia, and surgical site infections in children and adults.
KUT	Compare the effectiveness of management strategies for localized prostate cancer (e.g., active surveillance, radical prostatectomy [conventional, robotic, and laparoscopic], and radiotherapy [conformal, brachytherapy, proton-beam, and intensity-modulated radiotherapy]) on survival, recurrence, side effects, quality of life, and costs.
MS	Establish a prospective registry to compare the effectiveness of treatment strategies for low back pain without neurological deficit or spinal deformity.
NEURO	Compare the effectiveness and costs of alternative detection and management strategies (e.g., pharmacologic treatment, social/family support, combined pharmacologic and social/family support) for dementia in community-dwelling individuals and their caregivers.
NEURO	Compare the effectiveness of pharmacologic and non-pharmacologic treatments in managing behavioral disorders in people with Alzheimer's disease and other dementias in home and institutional settings.
NUTR	Compare the effectiveness of school-based interventions involving meal programs, vending machines, and physical education, at different levels of intensity, in preventing and treating overweight and obesity in children and adolescents.
NUTR	Compare the effectiveness of various strategies (e.g., clinical interventions, selected social interventions [such as improving the built environment in communities and making healthy foods more available], combined clinical and social interventions) to prevent obesity, hypertension, diabetes, and heart disease in at-risk populations such as the urban poor and American Indians.
ONC	Compare the effectiveness of management strategies for ductal carcinoma in situ (DCIS).
ONC	Compare the effectiveness of imaging technologies in diagnosing, staging, and monitoring patients with cancer including positron emission tomography (PET), magnetic resonance imaging (MRI), and computed tomography (CT).
ONC	Compare the effectiveness of genetic and biomarker testing and usual care in preventing and treating breast, colorectal, prostate, lung, and ovarian cancer, and possibly other clinical conditions for which promising biomarkers exist.
ORAL	Compare the effectiveness of the various delivery models (e.g., primary care, dental offices, schools, mobile vans) in preventing dental caries in children.

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.

TABLE S-1 Continued

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.

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

PSYCH	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.
PSYCH	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.
RED	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.
SKIN	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.
Fourth Quartile (listed alphabetically by primary research area)	
ADDO	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.
CAD	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.
CAD	Compare the effectiveness of anticoagulant therapies (e.g., low-intensity warfarin, aspirin, injectable anticoagulants) for patients undergoing hip or knee arthroplasty surgery.
DIS	Compare the effectiveness of focused intense periodic therapy and usual weekly therapy in managing cerebral palsy in children.
ENDO	Compare the effectiveness of different disease management strategies in improving the adherence to and value of pharmacologic treatments for the elderly.
HCDS	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.

TABLE S-1 Continued

HCDS	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.
HCDS	Compare the effectiveness of minimally invasive abdominal surgery and open surgical procedures on post-operative infections, pain management, and recuperative requirements.
HCDS	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.
HCDS	Compare the effectiveness of diagnostic imaging performed by non-radiologists and radiologists.
HCDS	Compare the effectiveness of different techniques (e.g., audio, visual, written) for informing patients about proposed treatments during the process of informed consent.
HCDS	Compare the effectiveness of different disease management strategies for activating patients with chronic disease.
HCDS	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.
INFD	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).
MS	Compare the effectiveness of different treatment strategies in the prevention of progression and disability from osteoarthritis.
MS	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.
NEURO	Compare the effectiveness of different treatment strategies on the frequency and lost productivity in people with chronic, frequent migraine headaches.
NEURO	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.
ONC	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.

continued

TABLE S-1 Continued

PELC	Compare the effectiveness of hospital-based palliative care and usual care on patient-reported outcomes and cost.
PSYCH	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.
PSYCH	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.
PSYCH	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.
SKIN	Compare the effectiveness of different long-term treatments for acne.
WH	Compare the effectiveness of different strategies for promoting breastfeeding among low-income African American women.

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; IMUN = 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 many 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., cardiovascular 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 committee 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.

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.

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.

1

Introduction

***Abstract:** This chapter describes the legislative mandate and scope of work for the current study as well as previous Institute of Medicine (IOM) experience in methodologies for priority setting. The IOM Committee on Comparative Effectiveness Research Prioritization was charged with recommending national priorities—with stakeholder input—for the discretionary expenditure of \$400 million by the Secretary of Health and Human Services on comparative effectiveness research (CER), and with addressing the data and infrastructure needs to support and sustain this research. The formation of the committee is described as well as the procedures by which it operated. This report provides definitions for CER, mechanisms the committee used for obtaining public input into the process and the priorities, methodologies for priority setting, and, finally, a portfolio of research topics recommended for funding by the Secretary and recommendations for an infrastructure to facilitate a sustained research enterprise for CER and its translation and dissemination.*

In the midst of one of the nation's most serious economic crises, and in anticipation of major national health care reform, the 111th Congress acted to significantly expand public spending, particularly on the nation's capacity to conduct comparative effectiveness research (CER). The American Recovery and Reinvestment Act (ARRA) of 2009 (P.L. 111-5) defines CER (highlighted in the legislative language that follows) and provides \$1.1 billion in CER funding for the Agency for Healthcare Research and Quality (AHRQ), the National Institutes of Health (NIH), and the Secretary of Health and Human Services (HHS). More than one-third of the funds—\$400 million—is for discretionary spending by the Secretary:

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”) . . . 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.**¹

The legislation also directs the Secretary to enter into a contract with the Institute of Medicine (IOM), under which the IOM should make recommendations to guide the nation’s priorities for CER and specifically to be taken into consideration by the Secretary in decisions on expenditure of the \$400 million available for CER:

[T]he Secretary shall enter into a contract with the Institute of Medicine . . . 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.

This report is the IOM’s response to the congressional mandate. In addition to the federal support for the project, the IOM received support both from the National Academies President’s Fund to finance the project until the federal sponsor could contract with the IOM and to undertake the complete cost of the questionnaire process described in Chapter 3, and from the Robert Wood Johnson Foundation for support of the study director.

STUDY SCOPE

Pursuant to the congressional mandate, the IOM committee established to carry out the study was charged with obtaining extensive stakeholder input for the formulation of national priorities for the Secretary’s investment of the ARRA funds for CER. The Governing Board Executive Committee of the National Research Council, an arm of the National Academies, authorized the study emphasizing stakeholder input (Box 1-1). After consultation with congressional staff and AHRQ, the administrative sponsor of the study, the committee concluded that its scope of work encompassed three principal tasks:

¹ *American Recovery and Reinvestment Act of 2009*, P.L. 111-5, 111th Congress, 1st session (February 17, 2009).

BOX 1-1
Charge to the IOM Committee on Comparative Effectiveness Research Prioritization

An ad hoc committee will conduct a study to recommend national priorities for comparative effectiveness research to be conducted or supported with funds from the American Recovery and Reinvestment Act of 2009. The study will be informed by and extend the views of stakeholders and the recent and ongoing IOM work relevant to comparative effectiveness research such as that on the national capacity to identify what works in health care, standards for systematic reviews of evidence, and standards for developing trustworthy clinical practice guidelines.

1. To obtain national input from a wide variety of stakeholders, including the public, patients, families, and health care providers in order to develop a list of no fewer than 50 recommended priority CER topics.
2. To define how these recommended priorities could be incorporated in a balanced portfolio of priority research that encompasses all age groups, underrepresented subpopulations in clinical research, the full care continuum from prevention to diagnosis to monitoring to treatment to end-of-life care, the complete range of health care services from the least to the most invasive, and strategies to ensure rapid and effective translation of knowledge into practice.
3. To recommend priority actions for ensuring the infrastructure and workforce for a long-term, sustainable national CER enterprise.

COMMITTEE FORMATION AND PROCEDURES

The legislation was signed February 17, 2009, and the IOM appointed most of the Committee on Comparative Effectiveness Research Prioritization on February 28, 2009, with a final few members in mid-March. The 23-member committee included experts in behavioral health, bioethics, biostatistics, child health, clinical trials, consumer and patient perspectives, disabilities, drug development, geriatrics, health care delivery, health care policy, health economics, health insurance, internal medicine, prevention, public health, racial and ethnic disparities, surgery, systematic review methods, and women's health. Brief biographies of the committee members appear in Appendix F.

The study required an intense, focused effort across just 19 weeks from

the enactment of ARRA to release of a final, peer-reviewed report. The committee began by clarifying the scope of work and developing and implementing an approach to obtaining public and stakeholder suggestions for the Secretary's CER priorities. The committee identified three mechanisms feasible within its time constraints to achieve the requested stakeholder input (see Chapter 3 for details):

1. Direct input via email and letter correspondence through the IOM website
2. A web-based questionnaire, open to all, asking for specific priority research recommendations and their justification
3. A day-long public session for stakeholder presentations to the committee

By March 6, 2009, a web-based questionnaire had been developed and field tested to obtain public input into priorities. The questionnaire was active on the project's website starting that same day and a broadcast announcement was emailed on March 9 to approximately 20,000 recipients, including everyone on the IOM listservs and targeted organizations involved in health care announcing all three opportunities for public input. In particular, public, consumer, and patient input was solicited by direct contact with major consumer and patient advocacy organizations (e.g., AARP, Consumers Union, National Health Council, National Minority Quality Forum). Despite a very short period to notify the public of this process, and the equally short time for the public to submit information to the committee for consideration and voting, the committee received extensive input from more than 1,700 individuals. Although this input meets the requirements of the legislative language, the committee clearly concludes that future efforts to establish research priorities need to provide more extensive opportunities for public input and discussion (see Chapters 3, 4, 5, and 6).

Over the course of the study, the committee held two in-person meetings (one in conjunction with the public session, and one during an extended weekend retreat) and three phone conferences. Several workgroups of committee members also communicated by telephone conference and other electronic means to address specific tasks such as the committee's methods for incorporating public input, consideration of selection criteria for developing a list of priority CER questions, and assessment of key issues related to infrastructure and the long-term sustainability of a national CER enterprise.

STUDY CONTEXT

The IOM has been integrally involved in national priority setting in the past. Almost 20 years ago, the IOM addressed the clinical conditions that

the Health Care Financing Agency (now the Centers for Medicare & Medicaid Services [CMS]) should prioritize as part of their Effectiveness Initiative. The reports set priorities for effectiveness research on acute myocardial infarction, hip fractures, and breast cancer (IOM, 1990a,b,e). Subsequently, the IOM recommended methodologies that NIH should utilize to improve consensus development in evaluating biomedical technologies and practices. This study was one part of a three-part examination of group judgment methods for assessing medical technologies (IOM, 1990d). An additional report set forth criteria and methods for deciding which health care technologies to evaluate (IOM, 1992). A series of reports addressed methods for guideline development. These reports focused on the optimal methods for setting priorities for clinical guideline topics (IOM, 1990c, 1995). Priority setting in the allocation of NIH research funding and mechanisms of involving the public were addressed in a report examining how NIH should set its research priorities, looking at four issues: (1) allocation criteria, (2) the decision-making process, (3) mechanisms for public input, and (4) impact of congressional directives (IOM, 1998).

More recently, as part of the *Quality Chasm* series, the IOM dealt with shortfalls in the quality of health care in the United States (IOM, 2003). It recommended criteria for which priorities should be established for quality improvement efforts, as well as specific priority disease entities and conditions including care coordination, health literacy, and end-of-life issues. Much of the CER committee's efforts have been guided by the findings and recommendations of the IOM Committee on Reviewing Evidence to Identify Highly Effective Clinical Services found in *Knowing What Works in Health Care* (IOM, 2008). In addition, the CER committee took full advantage of the extensive work of the IOM Roundtable on Evidence-Based Medicine's experience in *The Learning Healthcare System* (IOM, 2007a) and *Learning What Works Best* (IOM, 2007b) in identifying the importance of public input for priority setting, potential models of governance for a national program of CER, potential methodologies for conducting CER, and the requisite workforce to accomplish the task at hand.

The Committee on Comparative Effectiveness Research Prioritization operated in parallel with the Federal Coordinating Council for CER, which was also authorized in ARRA. This council consists of 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."² Its charge, like that of this committee, is "not later than June 30, 2009, the Council shall submit to the President and the Congress a report containing information describing current federal

² *American Recovery and Reinvestment Act of 2009*, P.L. 111-5, 111th Congress, 1st session (February 17, 2009).

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.” Additionally, “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.” The IOM committee intends its report to serve as a complementary document to that of the Council, which may serve as the blueprint for federal efforts to develop a structure and process for the implementation of CER efforts.

ORGANIZATION OF THE REPORT

This introductory chapter has described the context for this report, including related past IOM studies, the committee’s charge, and the objectives, scope, and study methods for this report. Subsequent chapters address the following topics:

- **Chapter 2—What Is Comparative Effectiveness Research?** This chapter has two primary objectives: first, to establish a conceptual framework for CER by defining key terms and research methods, and second, to describe several current private and public CER programs.
- **Chapter 3—Obtaining Input to Identify National Priorities for Comparative Effectiveness Research** documents the committee’s methods for soliciting stakeholder input and nominations for priority CER topics. Direct communications by letter and email are described, presentations at the open meeting are reviewed, and the questionnaire soliciting nominations for priority topics is presented in detail. The distribution of the public nominations is presented with their clinical characteristics pertinent to the portfolio distribution.
- **Chapter 4—The Criteria and Process for Setting Priorities** describes priority selection criteria used in past IOM committee initiatives and presents the committee’s recommendations. It further lays out the concept of the “portfolio,” by which the committee proposes to establish balance and scope of the priorities. Finally, it describes the process by which more than 2,600 nominated CER topics were narrowed to the final list of 100 priority CER topics. Recommendations are presented for a sustained priority setting process moving forward.

- **Chapter 5—Priorities for Study** presents the committee’s portfolio and list of recommended national priority topics for CER to be conducted or supported with the Secretary’s portion of funds from ARRA 2009.
- **Chapter 6—Essential Priorities for a Robust CER Enterprise** explains the imperative for effective coordination of the HHS Secretary’s sustained CER strategy and outlines four essential program priorities: (1) ensuring meaningful consumer, patient, and caregiver participation; (2) building robust information systems including research and innovation in the methods of CER; (3) development and support of a highly skilled CER workforce; and (4) vigorous support of research and efforts to translate CER knowledge into everyday clinical practice.

REFERENCES

- IOM (Institute of Medicine). 1990a. *Acute myocardial infarction: Setting priorities for effectiveness research*. Edited by P. H. Mattingly and K. N. Lohr. Washington, DC: National Academy Press.
- . 1990b. *Breast cancer: Setting priorities for effectiveness research*. Washington, DC: National Academy Press.
- . 1990c. *Clinical practice guidelines: Directions for a new program*. Edited by M. J. Field and K. N. Lohr. Washington, DC: National Academy Press.
- . 1990d. *Consensus development at the NIH: Improving the program*. Washington, DC: National Academy Press.
- . 1990e. *Hip fracture: Setting priorities for effectiveness research*. Edited by K. A. Heithoff and L. K. N. Washington, DC: National Academy Press.
- . 1992. *Setting Priorities for Health Technology Assessment: A Model Process*. Edited by M. S. Donaldson and H. C. Sox. Washington, DC: National Academy Press.
- . 1995. *Setting priorities for clinical practice guidelines*. Edited by M. J. Field. Washington, DC: National Academy Press.
- . 1998. *Scientific opportunities and public needs: Improving priority setting and public input at the National Institutes of Health*. Washington, DC: National Academy Press.
- . 2003. *Priority areas for national action: Transforming health care quality*. Edited by K. Adams and J. Corrigan. *Quality chasm series; Variation: Quality chasm series*. Washington, DC: The National Academies Press.
- . 2007a. *The Learning healthcare system: Workshop summary*. The IOM Roundtable on Evidence-Based Medicine. Edited by L. Olsen, D. Aisner, and J. M. McGinnis. Washington, DC: The National Academies Press.
- . 2007b. Learning what works best: The nation’s need for evidence on comparative effectiveness in health care. <http://www.iom.edu/ebm-effectiveness> (accessed April 15, 2009).
- . 2008. *Knowing what works in health care: A roadmap for the nation*. Edited by J. Eden, B. Wheatley, B. J. McNeil, and H. Sox. Washington, DC: The National Academies Press.

2

What Is Comparative Effectiveness Research?

Abstract: *Comparative effectiveness research (CER) provides an opportunity to improve the quality and outcomes of health care by providing more and better information to support decisions by the public, patients, caregivers, clinicians, purchasers, and policy makers. Several organizations have developed definitions of CER; for purposes of this study, the Institute of Medicine committee has defined CER as “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.” CER’s distinguishing characteristics include informing a specific clinical or policy decision, comparing at least two approaches or interventions, describing results at the subgroup level, measuring benefits in real-world populations, and applying appropriate methods and data sources. Several federal agencies and many other organizations are involved in important CER activities, which are summarized in this chapter. However, the existing incentives for developing CER evidence are uneven, the infrastructure for supporting the development of such evidence has gaps, and better coordination of research and translation of evidence into clinical practice and health policy is needed.*

THE NEED FOR MORE AND BETTER EVIDENCE OF WHAT WORKS IN HEALTH CARE

While the U.S. health care system continues to make progress in improving health, there is wide agreement that large gaps remain in the quality and outcomes of health services delivered to many Americans (IOM, 2001; Orszag, 2007). Moreover, the need for better value in the health care system becomes apparent when overall health care spending and outcomes are considered. Health care expenditures were \$2.4 trillion in 2008 and are projected to grow by an average of 6.2 percent per year for the next 10 years, more than triple the projected rate of overall gross domestic product (GDP) growth (Sisko et al., 2009). The Congressional Budget Office (CBO) projects that under current law, health care will consume more than 30 percent of GDP by 2035 (CBO, 2008).

Regional variations in treatment patterns and cost growth provide deeper insight into the need for more informed medical decision making. Researchers at the Dartmouth Institute for Health Policy and Clinical Practice have shown that patients in the highest-spending regions of the country receive 60 percent more health services than those in the lowest-spending regions, yet this additional care is not associated with improved outcomes (Fisher et al., 2003). The Dartmouth research suggests that physicians in higher-spending areas are more likely than physicians in other regions to recommend costly interventions that have not been definitively shown to be effective (Fisher et al., 2009). Nationwide, the Institute of Medicine (IOM) has estimated that less than half of all treatments delivered today are supported by evidence (IOM, 2007). Even the most thoughtfully conceived and sophisticated practice guidelines have inadequacies in their evidence base, whereas many guidelines that are evidence-based and well-supported are often not translated into clinical practice. A recent review of practice guidelines developed by the American College of Cardiology and the American Heart Association found that relatively few recommendations were based on high-quality evidence—randomized controlled trials, for instance—and many were based solely on expert opinion, individual case studies, or standard of care (Tricoci et al., 2009). A similar study revealed that more than two-thirds of recommendations contained in 51 guidelines for treating lung cancer were not evidence-based (Harpole et al., 2003). Researchers assessing recommendations for preventing and treating breast and colorectal cancers concluded that the overall quality of available guidelines for these cancers was “modest” (Vigna-Taglianti et al., 2006). Thus, providers need better information to provide the appropriate care for their patients.

Providers, hospitals, and clinics are not the only groups with a stake in the evidence base for health care decisions. A growing movement of education and empowerment for consumers, as well as the public and patients

taking a more active role in making decisions about their own health care, has emerged together with health insurance plans shifting a greater share of expenses to patients. New models of shared decision making promise to bring greater emphasis to informed patient choice for “preference-sensitive” care (Wennberg et al., 2007). Indeed, new and better research could improve the quality, safety, and effectiveness of health care by providing both patients *and* their health care providers with the evidence to assist in informed decision making. To accomplish this, however, patient-focused research is needed to identify not only the population-level effects of health interventions, but also the patient-level predictors of both positive and negative outcomes and the role of patient preferences in making choices (CBO, 2008).

Beyond consumers and health care providers, those that bear substantial financial responsibility for the health care needs of populations need better evidence; they include employers, federal programs such as Medicare and Medicaid, and private insurers. These organizations must allocate resources across a panoply of medical services, procedures, and technologies in an attempt to maximize health benefits while keeping coverage affordable. Moreover, these organizations must function within a growing array of models for the delivery and financing of health care, many of which are not yet supported with robust evidence of effectiveness.

Optimizing Evidence

Study Populations Representative of Clinical Practice

Many studies of the effects of medical interventions on health address efficacy rather than effectiveness. Efficacy reflects the degree to which an intervention produces the expected result under carefully controlled conditions chosen to maximize the likelihood of observing an effect if it exists. Many randomized controlled trials—generally considered to be the gold standard—are efficacy studies, particularly those conducted to win regulatory approval. The study population and setting of efficacy studies may differ in important ways from those settings in which the interventions are likely to be used. By contrast, effectiveness research intends to measure the benefits and harms of an intervention in ordinary settings and broader populations, and therefore can often be more relevant to policy evaluation and the health care decisions of providers and patients. Care needs to be taken, however, in effectiveness research such as observational, database, registry, and other studies to recognize that without randomization, unidentified bias and confounders may weaken the level of evidence, and that efficacy studies may be strengthened by broadening eligibility of populations or settings for trials and other attempts to increase generalizability. Issues

regarding efficacy and effectiveness, and other aspects of CER studies are further examined below.

Focus on the Individual Rather Than the Average Patient

With the growing knowledge of disease mechanisms, systems biology, genomics, and other sciences that create the potential for more targeted therapies, patients and providers are increasingly seeking evidence not only from representative populations, but also from relevant subgroups. Increasing emphasis on patient-level attributes that may modify the balance of benefits or harms can lead to more personalized medicine, reducing the pressure to try alternatives found to be ineffective in similar subgroups.

Study Two or More Interventions in Direct Comparison

Randomized, placebo-controlled studies demonstrating safety and efficacy for the purpose of gaining approval from the Food and Drug Administration (FDA) frequently serve as the basis for informing clinical decisions. Although the FDA does require “active comparators” in some clinical circumstances, there is a paucity of head-to-head studies, and the public needs more studies that compare evidence-based alternatives (including usual care), particularly in subgroups that preapproval studies often omit.

Beyond specific medical interventions and technologies, there is a need for evidence evaluating the clinical and resource effects of innovations in health care delivery models, including new benefit designs, cost-sharing techniques, integrated organizational models, public health and population-level strategies, and interventions to improve the quality of care. Approaches to the organization, delivery, and payment for health care services are seldom evaluated for their impact on patient outcomes and overall value, yet they need to be studied directly using the same principles described previously. Because these interventions are often implemented at provider or regional levels, the methods required to evaluate them—such as cluster randomized trials—may differ from those used to evaluate patient-level interventions.

Finally, merely generating better evidence is not enough to meet the decision-making needs of consumers, patients, health care providers, and purchasers. To maximize its impact on the quality and value of health care, these parties must use evidence when making clinical and policy decisions. Disseminating evidence into clinical practice must be accompanied by ongoing evaluation and feedback to decision makers, the key characteristic of a true learning health care system. However, this is not happening consistently. In a review of adherence to 439 indicators of health care quality for 30 acute and chronic conditions as well as preventive care, McGlynn

and colleagues concluded that American adults received only 55 percent of recommended care (McGlynn et al., 2003). Similarly, another study found that children and youth received only 46.5 percent of recommended care (Mangione-Smith et al., 2007). Even proven screening tests and other preventive services—such as influenza vaccines and mammograms in adults—are utilized by only 75 percent of Medicare beneficiaries (GAO, 2002). Furthermore, only 77 percent of U.S. children aged 19-35 months received all of the recommended doses of six childhood vaccines in 2006 (CDC, 2007). This gap between evidence and execution underscores the need to identify more effective tools to help patients, providers, and policy makers to use the available evidence.

Indeed, as the number of elective treatments and procedures has grown, so has the need for patient-centered research that compares their effectiveness. The promise of comparative effectiveness research (CER) is that it provides evidence that is better focused on the decisions of daily medical practice than existing evidence and therefore helps patients, caregivers, providers, payers, and policy makers make informed decisions about health care.

DEFINING COMPARATIVE EFFECTIVENESS RESEARCH

CER can be very broad in scope depending on what is “compared,” how one defines “effectiveness,” and what constitutes “research.” Virtually any applied biomedical inquiry is fundamentally about improving health, avoiding unnecessary costs, or both. In the current public policy environment, defining and describing CER is important: the 111th Congress made a \$1.1 billion investment in CER and has created a Federal Coordinating Council to coordinate CER within the Department of Health and Human Services (HHS).¹ According to the American Recovery and Reinvestment Act (ARRA) of 2009 (P.L. 111-5), this Council must provide Congress and the Secretary of HHS with an annual report describing its activities and specific recommendations for infrastructure and coordination of CER activities within relevant federal departments and agencies.

Debate continues among stakeholders seeking to shape what will be studied, how it will be studied, and how the results will be applied—a debate reflected in the extensive response to the present study’s efforts to encourage stakeholder input to its assigned task of setting research priorities (as described in Chapter 3).

New and expanded CER efforts will build on a solid base that is gaining wider recognition for its importance and applicability to clinical decision

¹ *American Recovery and Reinvestment Act of 2009*, P.L. 111-5, 111th Congress, 1st session (February 17, 2009).

making. As expectations for CER rise, more and more gaps in both knowledge and research infrastructure appear. These gaps must be filled if CER is to fulfill its promise of more informed decisions and better outcomes. In this chapter, the committee takes inventory of different authoritative definitions of CER, derives from these the discipline's defining characteristics, and briefly describes the range of ongoing activities that offer a foundation for new investments in this rapidly evolving field.

Existing Definitions

Although research comparing the effectiveness of health care strategies and interventions has been conducted for more than a century,² the term “comparative effectiveness research” has taken on new meaning in recent years. Table 2-1 displays several definitions, all of which were developed by leading public and private-sector authorities in the United States.

These definitions all emphasize CER's role in helping to inform health care decisions. All denote the evaluation of at least two alternatives, each with the potential to represent best practice. Most CER definitions suggest that the objective is to learn what works best in actual practice for a defined population. CER includes both systematic reviews of existing data and the collection and analysis of primary data.

A contested issue in defining CER is whether costs or cost-effectiveness are appropriate outcomes of interest. 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. Another view is that CER in general, and the use of cost-effectiveness analysis in particular, will inevitably discourage the use of expensive forms of care and lead to denial of needed care. While CER may identify ways to obtain better outcomes for the same or lower spending, cost-effectiveness analysis and CER may also lead to the conclusion that the more expensive approach offers *better* value than lower-cost approaches. For example, in the setting of breast cancer, magnetic resonance imaging (MRI) screening was found to be cost-effective relative to mammography in carriers of the BRCA1/2 mutation (Plevritis et al., 2006). Similarly, adjuvant trastuzumab was found to be cost-effective compared to conventional chemotherapy without trastuzumab in early stage HER2/neu-positive breast cancer (Kurian et al., 2007). When CER examines differences in costs as well as outcomes, its aim is to identify the approach that offers the better value; it does not necessarily promote or favor low-cost care.

² Ernest Amory Codman, M.D. (1869–1940), was a Boston surgeon and pioneer in the study of quality and safety outcomes. According to one biographer, he never stopped in his effort to link care, errors, and end results and to measure, report, and improve.

TABLE 2-1 Definitions of CER

Organization	Definition
Congressional Budget Office	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. Related terms include cost-benefit analysis, technology assessment, and evidence-based medicine, although the latter concepts do not ordinarily take costs into account.
IOM Roundtable on Evidence-Based Medicine	The comparison of one diagnostic or treatment option to one or more others. In this respect, primary comparative effectiveness research involves the direct generation of clinical information on the relative merits or outcomes of one intervention in comparison to one or more others, and secondary comparative effectiveness research involves the synthesis of primary studies to allow conclusions to be drawn. Secondary comparisons of the relative merits of different diagnostic or treatment interventions can be done through collective analysis of the results of multiple head-to-head studies, or indirectly, in which the treatment options have not been directly compared to each other in a clinical evaluation, and inferences must be drawn based on the relative effect of each intervention to a specific comparison, often a placebo.
American College of Physicians	Comparative effectiveness analysis evaluates the relative (clinical) effectiveness, safety, and cost of two or more medical services, drugs, devices, therapies, or procedures used to treat the same condition. Although the use of the term <i>comparative effectiveness</i> broadly refers to the evaluation of both the relative clinical and cost differences among different medical interventions, it is notable that most comparative effectiveness research engaged in and used by stakeholders in this country focuses solely on evaluating relative clinical differences to the exclusion of cost factors.
IOM Committee on Reviewing Evidence to Identify Highly Effective Clinical Services	Comparison of . . . the impacts of different options for caring for a medical condition for a defined set of patients. 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). This report uses the terms “effectiveness,” “clinical effectiveness,” and “comparative effectiveness” interchangeably.

continued

TABLE 2-1 Continued

Organization	Definition
Medicare Payment Advisory Commission	Comparative-effectiveness analysis evaluates the relative value of drugs, devices, diagnostic and surgical procedures, diagnostic tests, and medical services. By value, we mean the clinical effectiveness of a service compared with its alternatives. Comparative-effectiveness information has the potential to promote care of higher value and quality in the public and private sectors.
Agency for Healthcare Research and Quality	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 direct comparison of existing health care interventions to determine which work best for which patients and which pose the greatest benefits and harms . . . the core question of comparative effectiveness research (is) which treatment works best, for whom, and under what circumstances.

SOURCES: AHRQ (2009a); American College of Physicians (2008); IOM (2007, 2008); Medicare Payment Advisory Commission (2008); Orszag (2007); Slutsky and Clancy (2009).

Ultimately, CER aims to provide data that can influence clinical decisions for the better. If CER results are integrated into health care delivery and facilitate improved decision making, health care outcomes can be expected to improve. The concept has been formalized as the value of information, or the difference between the value of the outcome given the decision one would make in the absence of additional information and the value of the outcome of the decision that would be made as additional information became available as a result of the research (Garber and Meltzer, 2009). In such a circumstance, value may be judged from the perspective of the patient, provider, or payer.

The Spine Patient Outcomes Research Trial (SPORT) provides several examples of the potential utility of CER. The investigators demonstrate the value of spinal stenosis surgery in subjects without degenerative spondylolisthesis compared to nonsurgical interventions, as well as to subjects with degenerative spondylolisthesis (Tosteson et al., 2008; Weinstein et al., 2008). The Veterans Administration instituted a variety of interventions based upon their initial observations following performance scores obtained from an external peer review program in the mid-1990s, demonstrating remarkable improvement in 12 of 13 quality indicators over a 5-year period (Jha et al., 2003).

CHARACTERISTICS OF CER

Six defining characteristics of CER may be drawn from these definitions and the committee's deliberations over national priorities:

1. **CER has the objective of directly informing a specific clinical decision from the patient perspective or a health policy decision from the population perspective.** The range of potential objectives for CER studies gives the field a broad scope. Clinical questions refer to the health care of individual patients, including preventive, screening, diagnostic, therapeutic, monitoring, or rehabilitative interventions. Policy questions refer to the health and health care of populations through knowledge synthesis and transfer strategies, public health programs, or initiatives involving the organization, delivery, or payment for health services. This characteristic has a major implication; because CER contributes to such important decisions, all relevant stakeholders (including patients and the public) and decision makers would reasonably be included throughout the CER process, including priority setting, study design, and implementation of results (Tunis et al., 2003). Consumer involvement in trials began in earnest in the AIDS era (Epstein, 1996). Early efforts in CER embraced involvement of patients, caregivers, clinicians, and other decision makers in setting research boundaries and in defining populations, settings, comparisons, and outcomes that should be addressed in the research (Helfand, 2005; Santaguida et al., 2005; Whitlock et al., 2009).
2. **CER compares at least two alternative interventions, each with the potential to be “best practice.”** Compared clinical strategies may be very similar (drug vs. drug) or very different (drug vs. surgery). For many clinical decisions, “optimal usual care” reflecting current standards is an appropriate potential comparator. CER studies may also include the alternative of “watchful waiting” when it is considered to be a reasonable strategy in the clinical context. CER highlights research that compares a test intervention with viable alternatives. Interventions are implemented in accord with usual practice, which includes co-interventions and practice preferences. For policy decisions, a comparator may be the status quo.
3. **CER describes results at the population and subgroup levels.** The primary outcome of a clinical trial is a measure of the “average effect” of an intervention, usually as estimated in the population assigned to the intervention in the trial. Even when selecting from

“proven” strategies, clinicians must judge whether a particular patient is sufficiently similar to the trial population or if technological or scientific advancement has outdated the empirical results. By its focus on subgroup results and clinical prediction rules to identify patients likely to benefit from an intervention, CER assists providers and patients in individualizing decisions—going beyond the average effects to the effect in subjects with common clinical characteristics. This focus of CER reflects the growing potential for individualized and predictive medicine—based on advances in genomics, systems biology, and other biomedical sciences—through the analysis of subgroups with demographic, ethnic, physiologic, and genetic characteristics that could be useful factors in clinical decisions.

4. **CER measures outcomes—both benefits and harms—that are important to patients.** The committee is using the term “effectiveness” in reference to the extent to which a specific intervention, procedure, regimen, or service does what it is intended to do when used under *real-world* circumstances. This can be contrasted with “efficacy,” which is the extent to which an intervention produces a beneficial result under controlled conditions (Cochrane, 1971; Higgins and Green, 2008). This implies an important distinction between much clinical research and CER, in that CER places high value on external validity, or the ability to generalize results to real-world decision making. Harms or risks of unintended consequences are also outcomes of interest, because they influence the net benefits³ of an intervention. Including and giving weight to patient-reported outcomes is particularly important for CER studies in which patient ratings of effectiveness or adverse events may differ from clinical measures. Finally, resource utilization may be highly relevant to net benefits when comparing the full clinical course of interventions over time. Cost-effectiveness analysis is a useful tool of CER, allowing evaluation of the full range of treatment outcomes in relationship to the difference in costs. Robust evidence of comparative clinical effectiveness is a building block necessary for resource allocation decisions. Moreover, just as clinical effects may vary in different settings, costs vary as well, so a given set of cost-effectiveness results is often not generalizable.
5. **CER employs methods and data sources appropriate for the decision of interest.** CER includes at least three broad categories of

³ The net benefit of a particular intervention is the balance of the harms and benefits.

research methods. Where evidence is lacking, CER may generate it either in *nonexperimental studies* (observational settings) or in *experiments* (randomized and cluster randomized, as well as non-randomized, controlled trials). For decisions that have been the topic of substantial previous research, *synthesis* of existing studies (systematic reviews and meta-analysis, technology assessments and decision analysis) may be appropriate. Box 2-1 describes these methods in greater detail. Data sources for CER may thus include published studies, existing data from the delivery of care (administrative claims, medical charts, electronic health records), clinical registries, and information collected by clinical investigators, either retrospectively or prospectively. To ensure the wide availability and use of these data sources will require new CER infrastructure to support a highly robust national CER program, including methods, workforce, and data networks. For example, multisite data networks, analyzed simultaneously via a distributed protocol (distributed network analysis), are needed. Considerations in the selection of methods and data sources for CER include the quality and relevance of previously published evidence, the availability and potential for confounding in observational data sources, and the time and resources available for primary data collection.

6. **CER is conducted in settings that are similar to those in which the intervention will be used in practice.** Consistent with the definition of effectiveness, the settings of CER studies are a defining characteristic. Studying interventions in a realistic practice setting has implications for both CER trials and observational studies. For experimental studies, investigators should deliver the intervention in settings that are as close to actual practice as possible, which is a strength of observational studies of actual clinical practice.

The call for CER should not be interpreted to mean that all research must have these characteristics. Early studies of an intervention are likely to compare it to a placebo, standard care, or no intervention. In fact, during early development of a new intervention, it is critical to determine safety and efficacy under a defined set of circumstances. For example, the Ischemic Optic Neuropathy Decompression Trial was a landmark examination of an innovative surgical technique used by ophthalmologists (Ischemic Optic Neuropathy Decompression Trial Research Group, 1995). It found no beneficial effect and possible harm compared to no therapy. Once an intervention has been shown to be effective against a placebo, head-to-head trials address the critical question “What works best for whom?”

BOX 2-1 Methods Commonly Used in CER

Experimental study—A category of studies in which the investigators actively intervene to test a hypothesis. **Controlled trials** are experimental studies in which an experimental group receives the intervention of interest while one or more comparison groups receive an active comparator, a placebo, no intervention, or the standard of care, and the outcomes are compared. In a **randomized controlled trial (RCT)**, the participants are randomly allocated to the experimental group or the comparison group. Because patients are enrolled prospectively, RCTs can require many years to enroll a sufficient number of subjects and observe the outcomes of interest. **Cluster randomized trials** are RCTs in which the subjects are assigned to intervention or control in groups (clusters) defined by a common feature, such as the same physician or health plan. **Head-to-head** trials are a method of CER, because they compare more than one active intervention.

Observational or nonexperimental study—A category of studies in which the investigators do not seek to intervene but simply observe the course of events. Observational studies may be prospective or retrospective. **Prospective observational** studies, such as registries, can require years to accumulate the needed numbers of patients and outcomes. In **cohort studies**, groups with certain exposures or characteristics are monitored over time to observe an outcome of interest. In retrospective **case-control studies**, groups with and without an event or condition are examined to see whether a past exposure or event is more prevalent in one group than in the other. **Cross-sectional studies** determine the prevalence of a condition or an exposure at a specific time or time period. **Case series** describe a group of patients with a characteristic in common, for example, individuals undergoing a new type of surgery or the users of a new device. Retrospective

CER is limited by the intrinsic methodologies it utilizes. In some cases, bias or confounders may limit the reliability of data obtained through retrospective means. Alternatively, prospective, randomized clinical trials may take so long or be so expensive as to render the study unfeasible or unethical. As a result, it is imperative that the specific methodology be matched to the question being asked and to the population and/or data base that is available. In order for CER to impact health care delivery or outcomes, the results must be integrated into the health care delivery system and be utilized by patients and providers. Failure to utilize the findings minimizes their potential impact. How the data are utilized has also been a matter of significant debate. Some have expressed concern that CER could be inappropriately used to limit access to care (Gottlieb, 2009), however, coverage decisions can only benefit from better information on what works (Avorn, 2009; Garber and Tunis, 2009).

observational studies can be designed and analyzed in existing databases within a matter of months, but provide more limited data.

Research Synthesis—A category of studies in which investigators seek to summarize the information from multiple studies addressing similar research questions.

A **comparative effectiveness systematic review** summarizes available scientific evidence in which investigators collect, evaluate, and synthesize studies in accordance with an organized, structured, explicit, and transparent methodology. They seek to provide decision makers with accurate, independent, scientifically rigorous information for comparing the effectiveness and safety of alternative clinical options, and have become a foundation for decision making in clinical practice and health policy, including informing coverage decisions for therapeutics in health care.

Meta-analysis is the process of using statistical methods to combine the results of similar studies quantitatively in an attempt to allow inferences to be made from the sample of studies and applied to the population of interest.

Technology assessments assess the effectiveness of medical technologies using either single studies or systematic reviews.

SOURCES: Adapted from IOM (2008). See also Chou et al. (2007); Cochrane Collaboration (2005); Haynes et al. (2006); Last (2001); West et al. (2002).

IOM National Priorities Committee Definition

Proceeding from the definitions in Table 2-1 and the preceding considerations, the committee developed the following working definition of CER to guide its deliberations:

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.

This definition is consistent both with the rationale for CER expressed by other groups and with federal legislation providing support for such

research. In addition, it encompasses the breadth of interventions that influence the individual and public health of Americans, whether through prevention, diagnosis, or management of disease. The fundamental principle underlying this definition is that CER must be relevant to decision makers, particularly patients and providers.

EXAMPLES OF CER STUDIES: CORONARY ARTERY DISEASE

A better understanding of the scope of and potential methodologies employed by CER is best illustrated by several examples. The selected methodology is based on the sources of information available to answer the question and dictates the rapidity and cost involved in study performance. Treatment of coronary artery disease has been the subject of numerous CER studies.

Table 2-2 provides four distinct examples of CER studies—employing very different methodologies—related to commonly performed interventions for coronary revascularization in patients with coronary artery disease. These procedures are among the most widely performed—and most costly—in patients with coronary heart disease, the leading cause of death in the United States. Numerous trials have addressed the efficacy of three alternative treatment modalities: drug therapies; percutaneous coronary intervention (PCI) with balloon angioplasty, stents, or both; and coronary artery bypass graft (CABG) surgery. Uncertainty remains about which modality is best for specific patient subgroups. Moreover, the question of how to manage a patient with myocardial ischemia is often urgent, requiring the cardiologist to quickly explain the risks and benefits of alternative interventions to a patient and then agree on a timely course of action. In this context, an individualized recommendation based on evidence from rigorous CER has the potential to improve outcomes.

Randomized Controlled Clinical Trial

The 5-year randomized controlled trial (RCT) comparing all three modalities at a single center in Brazil is an example of a comparative effectiveness trial with some significant limitations (Hueb et al., 2007). Its strengths include internally valid results (the most powerful advantage of a study that randomly assigns patients to one of the target interventions) and long-term follow-up (namely, no differences in mortality over 5 years), yet it had too few subjects for robust analyses of secondary endpoints and subgroups. Moreover, it took many years from design to publication of results, during which new modalities—including glycoprotein IIb/IIIa inhibitors, clopidogrel, and drug-eluting stents, none of which were included in the study—achieved routine use.

Systematic Review and Meta-Analysis of Existing Data

A systematic review of PCI and CABG reported in 2007 included a meta-analysis of 23 RCTs and a comparison of findings of five large observational studies (Bravata et al., 2007). While corroborating the earlier finding of no difference in survival after PCI or CABG, the study filled important gaps by offering, on a limited scale, analyses of subgroups and secondary endpoints. By combining many studies, the statistical power to detect or rule out relatively small but still clinically useful differences in subgroups can be determined. These analyses demonstrated that survival outcomes were equivalent in diabetic and non-diabetic patients, and that CABG tended to lead to angina relief, but to more procedure-related strokes, whereas repeat revascularization procedures were more common after PCI.

Pooled Analysis of Patient-Level Data from Many Clinical Trials

Even more recently, data from 10 RCTs were pooled to create one large dataset that included the patients from the 10 trials. The authors sought to identify patient-level predictors of outcomes (Hlatky et al., 2009). The study confirmed equivalent overall survival outcomes with PCI and CABG. However, it showed that CABG might be a better option for elderly and diabetic patients, because mortality was lower in these subgroups. By pooling individual-level data (in contrast to study-level data as in the systematic review by Bravata, described earlier), the authors were able to use powerful, statistically valid methods (such as Cox regression analysis with interaction terms) to identify subgroup effects.

Health Services Research

Finally, in an example of a policy-level CER study, researchers analyzed a Hospital Quality Incentive Demonstration Project, piloted by the Centers for Medicare & Medicaid Services (CMS), in the care of patients with acute myocardial infarction (AMI) (Glickman et al., 2007). The intervention offered pay-for-performance economic incentives to hospitals with the highest quality scores in five clinical conditions, including AMI. Using a database of administrative and clinical data from both incentivized hospitals and a control group of hospitals, the researchers found that the pay-for-performance economic incentives produced neither significant benefits nor unintended adverse consequences. This hospital-level observational study gave useful information about the effects of incentives on hospitals. Because the study used existing electronically stored data, it was relatively inexpensive and quick to perform. However, like all observational studies, the authors could

TABLE 2-2 Selected CER Studies of Management of Acute Coronary Syndrome

Type of CER Study (Authors)	Randomized Clinical Trial (Hueb et al., 2007)	Systematic Review (Bravata et al., 2007)
Objective	To compare relative effectiveness of CABG with that of PCI or MT in patients with symptomatic multivessel coronary artery disease requiring revascularization.	To compare the effectiveness of PCI and CABG in patients for whom coronary revascularization is clinically indicated.
Comparators	CABG, PCI, and MT (stepped care using nitrates, aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, lipid-lowering agents, or combination of these unless contraindicated).	PCI (including balloon angioplasty or coronary stents) and CABG (including standard or minimally invasive techniques).
Population and Subgroups Studied	Patients with angiographically documented proximal multivessel coronary stenosis of >70% and documented ischemia (but no prior revascularization or AMI), randomly assigned to undergo CABG (n = 203), PCI (n = 205), or MT (n = 203).	Twenty-three unique RCTs, which enrolled a total of 9,963 patients, met inclusion criteria; subgroups were defined by diabetes, age, sex, smoking, and number of diseased vessels; five major clinical registries met inclusion criteria.
Outcomes of Interest	Primary: overall mortality, Q-wave MI, or refractory angina requiring revascularization Secondary: angina status and stroke or cerebro-vascular accident.	Survival, myocardial infarction, stroke, angina, and use of additional revascularization procedures.
Methods and Data Source(s)	RCT—Multivariate Cox proportional hazards 5-year survival model to assess the relationship between pairwise treatment comparisons and primary endpoints.	Systematic review of aggregate data from published trials and large observational studies; meta-analysis of RCTs computed summary risk differences and odds ratios between PCI and CABG and the 95% CI for each outcome of interest at annual intervals; observational studies were summarized qualitatively.

NOTE: AMI = acute myocardial infarction; CABG = coronary artery bypass graft; CI = confidence interval; CMS = Centers for Medicare & Medicaid Services; MT = medical therapy; PCI = percutaneous coronary intervention.

Pooled Quantitative Analysis of Trials (Hlatky et al., 2009)	Observational Study (Policy) (Glickman et al., 2007)
To assess whether the effects of CABG and PCI on mortality are modified by patient characteristics.	To determine if pay-for-performance was associated with either improved processes of care and outcomes or unintended consequences for AMI at hospitals participating in the CMS pilot project.
CABG and PCI (balloon angioplasty and bare-metal stents).	Quality improvement intervention, including bonus payments to hospitals with performance scores in the top two deciles and potential future financial penalty for those with the poorest performance, compared to usual care.
Subgroups defined based on demographics, cardiac risk factors, clinical manifestations, and angiographic factors.	Patients with acute non-ST-segment elevation. MI enrolled in a national quality-improvement initiative at 54 program hospitals (n = 10,325) and 446 control hospitals (n = 95,058).
Primary: All-cause mortality Secondary: Death or myocardial infarction; death or repeat revascularization; death, myocardial infarction, or repeat revascularization.	Six process measures used by CMS to evaluate the care of patients with non-ST-segment elevation AMI, and eight process measures that are designated “useful and effective” by the American College of Cardiology and American Heart Association, but are not currently tracked by CMS.
Pooled analysis of individual patient data from 10 clinical trials that randomly assigned patients with multivessel coronary disease to either CABG or PCI and that reported at least 3 years of follow-up.	Observational, patient-level analysis of data abstracted from hospital administrative and clinical records; temporal trends in individual and composite processes of care for both CMS and non-CMS measures at pay-for-performance and control hospitals were identified using nonlinear mixed-effects models.

not be sure that they had adjusted statistically for unmeasured differences between rewarded hospitals and control hospitals; these unmeasured differences could affect the quality of care independently of the incentives and conceal true differences in this apparently negative study.

These examples illustrate both the breadth and diversity of CER methods applied to a single clinical context. Clearly, definitive answers relevant to specific clinical situations are difficult to obtain, and these studies remind us that CER may provide answers to very specific questions to assist in clinical decision making, but that clinical uncertainty may persist to the extent that the study fails to encompass all individual patient characteristics. The challenge is to increase the probability of an optimal outcome in a particular patient if it is a clinical decision or a population if it is a policy decision.

EXISTING CER ACTIVITY IN THE UNITED STATES

Many research activities in the United States have one or more of the six characteristics of CER described by the committee earlier in this chapter. Some activities are propelled by regulatory and reimbursement requirements, while others respond to public and private research funding opportunities. This section reviews some of those initiatives and derives lessons that can guide new investments in CER.

Federal Government-Sponsored CER Activities

To date, the federal government has sponsored a series of systematic comparative effectiveness reviews as well as a considerable amount of CER, primarily through the Agency for Healthcare Research and Quality (AHRQ) and the National Institutes of Health (NIH). CMS, the Veterans Administration (VA), and the FDA also support specific forms of CER. Additional agencies and departments, such as the Centers for Disease Control and Prevention and the Department of Defense, engage in research, some of which may meet the definition of CER.

Agency for Healthcare Research and Quality

AHRQ's Effective Health Care Program has been the federal government's leading effort to conduct systematic comparative effectiveness reviews and database studies that compare health care interventions. Created by Congress in 2003 under the Medicare Prescription Drug, Improvement, and Modernization Act, the Effective Health Care Program had a budget of \$30 million in 2008. Its research priorities are set by the Secretary of HHS

and informed by an explicit priority-setting process that includes nominations from all stakeholders.

The Effective Health Care Program uses existing studies to make head-to-head comparisons of treatment alternatives, including drugs, devices, surgical procedures, and other types of interventions. Its activities are conducted by 14 Evidence-based Practice Centers (EPCs), 13 Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) Centers, 14 Centers for Education and Research on Therapeutics (CERTs), and the John M. Eisenberg Clinical Decisions and Communications Science Center. This multicenter infrastructure is capable of a wide range of evidence development and synthesis activities.

The EPCs review relevant scientific literature on clinical, behavioral, and organization and financing topics to produce evidence reports and technology assessments. Reviews may be systematic reviews of a given intervention, or comparative effectiveness reviews of a disease entity. These reports are used for informing and developing coverage decisions, quality measures, educational materials and tools, guidelines, and research agendas. The EPCs also conduct research on the methodology of systematic reviews.

The DEcIDE network links research centers to generate new CER evidence. It conducts accelerated practical studies about the outcomes, comparative clinical effectiveness, safety, and appropriateness of health care products and services. The network comprises health system-based research organizations with access to electronic health information databases and the capacity to conduct distributed network analysis.

The mission of the CERTs is to conduct research and provide education that will advance the optimal use of drugs, devices, and biological products; increase awareness of the benefits and risks of therapeutics; and improve quality while cutting the costs of care. The CERTs program consists of 14 research centers and a coordinating center (AHRQ, 2009b).

The John M. Eisenberg Clinical Decisions and Communications Science Center translates complex scientific research produced in the Effective Health Care Program into publications that are intended for use by the public, clinicians, and policy makers. The Eisenberg Center creates and disseminates a variety of products for each audience, ranging from summary guides to decision aids and other materials.

To date, the AHRQ Effective Health Care Program has released approximately 30 products, including 14 comparative effectiveness reviews from the EPCs; 18 summary guides for clinicians, patients, and policy makers; and 10 reports from the program's DEcIDE research network.⁴

⁴ Many more projects are under way, and all of the program's products are publicly available at AHRQ's website: <http://www.effectivehealthcare.ahrq.gov>.

National Institutes of Health

NIH is the principal federal agency that performs and funds biomedical research, including clinical trials, systematic reviews, and observational studies. An internal survey to determine the extent of NIH funding of studies meeting the definition of CER is under way, but to date it has provided limited information. Numerous obvious examples of CER exist; for example, the National Heart, Lung, and Blood Institute has funded or co-funded numerous comparative trials, including the CASS (Coronary Artery Surgery Study), ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), and ACCORD (Action to Control Cardiovascular Risk in Diabetes) studies. The Cardiovascular Research Network is taking advantage of electronic data, covering more than 10 million patients, to do observational research to answer questions about hypertension detection and management in communities, warfarin use in atrial fibrillation and venous thromboembolism, and the outcomes and costs of implantable defibrillators for primary prevention of sudden cardiac death (Lauer, 2009).

The Cooperative Group Program housed within the National Cancer Institute was established in 1955 to promote and support clinical trials of new cancer treatments, explore methods of prevention and detection, and assess quality of life during and following treatment (NCI, 2006). Currently, 1,700 institutions contribute more than 22,000 new patients into sponsored clinical trials annually. Many of these studies meet strict criteria for CER and generate important data for subsequent patient-level therapeutic decision making. For example, a large study of paclitaxel adjuvant treatment in over 4,900 women with breast cancer demonstrated an improved disease-free survival and overall survival in women negative for human epidermal growth factor receptor type 2 (HER2), as compared to those who were HER2 positive, regardless of their hormone receptor status (Sparano et al., 2008).

The National Institute for Neurological Diseases and Stroke has funded several trials that could be described as CER because they compared interventions that were already employed by practicing physicians, a key characteristic of CER. Ongoing trials include the CREST trial (Carotid Revascularization Endarterectomy Versus Stenting Trial), which compares carotid endarterectomy to stenting; ARUBA trial (A Randomized Trial of Unruptured Brain Arteriovenous Malformations), which compares medical care to more invasive procedures in patients with arteriovenous malformations; a trial performed in the Clinical Research Collaboration comparing propranolol and topiramate for migraine prophylaxis; and the CombiRx trial, which compares the combination of glatiramer acetate and beta interferon to each therapy alone in patients with multiple sclerosis (Johnston and Hauser, 2009).

Another example of NIH-funded CER is a trial supported by the National Institute for Arthritis, Musculoskeletal and Skin Diseases, called the Spine Patient Outcomes Research Trial (SPORT), which is the largest study comparing operative to non-operative treatment for the three most common conditions for which spine surgery is performed in the United States (disc herniation, spinal stenosis, and degenerative spondylolithesis with stenosis). This study was carried out in actual clinical practices in 11 states and 13 centers (Birkmeyer et al., 2002).

The NIH Pharmacogenetics Research Network was established in 2000 to enable multi-disciplinary research groups to address questions in pharmacogenetics and pharmacogenomics. The goal is to populate a knowledge base for the purpose of identifying safe and effective drug therapies for individual patients (NIH PGRN, 2009).

Not all NIH trials that compare interventions completely meet the definition of CER. Trials of this type may, for example, restrict entry to a small subset of the population actually treated in practice, or monitor subjects in ways inconsistent with routine care, changing the focus of the research to efficacy rather than effectiveness. Pragmatic trials and other new methods are being developed to better evaluate treatments in routine use while attempting to control for the risk of introducing confounding factors that can occur in real-world settings (Lohr, 2007).

Food and Drug Administration

The FDA has had growing involvement in developing the standards and methods for comparative studies, as well as assessing them to support the regulation of medical products. In some clinical contexts, the FDA has required active comparators for product approval when existing treatments have demonstrated significant benefit for a “major disease.” In addition, the FDA Amendments Act (FDAAA) of 2007 (P.L. 110-85) enhanced the FDA’s ability to enforce requirements for post-approval studies. While many such studies are focused on safety concerns, some provide additional evidence about comparative effectiveness (for example, longer-term or more definitive comparisons of effectiveness, and analyses involving additional types or subtypes of patients).

In addition to exercising regulatory authority to ensure the safety and effectiveness of medical products, the FDA is developing standards and methods for CER studies, as well as their interpretation to support its regulatory mission. The FDA’s Critical Path Initiative seeks to identify predictors of response to therapy, a key characteristic of CER. For example, collaborations between FDA scientists and academic groups validated genetic predictors of enhanced sensitivity to warfarin and other drugs metabolized by liver enzymes. One of the statutory goals of the Reagan-Udall

Foundation, authorized under the FDAAA but not yet funded, is to support public-private collaborations on applied research questions relevant to CER, such as the Sentinel Program, which endeavors to link very large numbers of medical records and claims data to facilitate post-marketing surveillance for unusual complications of new therapies.⁵

Centers for Medicare & Medicaid Services

The mission of CMS is to “ensure effective, up-to-date health care coverage and to promote quality care for its beneficiaries” (CMS, 2009a). CMS is a key stakeholder in the health care system in general—its beneficiaries generate about one-third of national health expenditures (CMS, 2009b)—and in CER in particular. Although Medicare does not explicitly base coverage decisions on CER evidence, it uses such evidence in its coverage reviews. Medicare’s predominance in the U.S. health care market provides product developers with a strong incentive to tailor the evidence they produce to the needs of CMS reviewers. The Medicare Evidence Development and Coverage Advisory Committee, a large group of clinical experts, researchers, industry representatives, and consumer advocates, provides CMS with guidance on specific—usually controversial—national coverage decisions.

When CMS determines that the available evidence is insufficient to support a definitive coverage decision, it can employ a relatively new policy option, “Coverage with Evidence Development,” which authorizes CMS to cover items or services only if the patient participates in a registry or a clinical trial. This mechanism serves to expand coverage to unapproved interventions, giving them an opportunity to prove themselves while simultaneously enlarging the evidence base (Tunis and Pearson, 2006).

Department of Veterans Affairs

The Veterans Healthcare System at the VA is suited to both produce and apply evidence on treatment effectiveness because it cares for a very large patient population, has a sophisticated electronic health records system that supports clinical research, and provides an array of medical services. Through its Cooperative Studies Program (CSP), the VA provides support to its own investigators conducting multi-center, collaborative clinical trials. The program’s research infrastructure includes five Coordinating Centers that provide data management and analysis support, a Clinical Research Pharmacy, four epidemiological Research and Information Centers, and a

⁵ Food and Drug Administration Act of 2007, P.L. 110-85, 110th Congress, 2nd session (September 27, 2007) 121.

Health Economics Resource Center (Holve et al., 2008; Veteran's Health Administration, 2009). CSP trials study a range of conditions, from schizophrenia to stroke (Veteran's Health Administration, 2009), and have produced notable results—for instance, a large RCT with 38,546 participants demonstrated the effectiveness of a *Herpes zoster* vaccine (Oxman et al., 2005), and a very recent RCT of 1,791 diabetic military veterans showed that intensive control of blood glucose was not superior to usual care in preventing cardiovascular complications (Duckworth et al., 2009).

The VA conducts comparative effectiveness reviews and guides for policy makers through its Evidence-based Synthesis Program, which works directly with top clinical managers and the Office of Quality and Performance to select priorities (VA, 2009). The VA is well-suited for CER activities because it has broad clinical and research capacity and feeds patient data recorded in the VA electronic health record system into a data warehouse that contains health records on the entire VA population. These data capabilities are a major national resource and a model for other data research networks. As a result of the application of the above techniques, the VA system has modified practices to markedly improve both the process of health care delivery and its outcomes (Jha et al., 2003).

Nongovernmental CER Activities

The private sector contains the life sciences industry, a number of organizations with the capacity to conduct CER reviews, and some organizations focused on evidence development. However, not all of the work of these organizations meets the IOM definition of CER, and some of the work is proprietary, and available by contract or purchase, if at all. Representative nongovernmental organizations involved in CER are described briefly below.

Life Sciences Industry

Manufacturers of drugs, devices, and other medical products have made large investments in research on their products, motivated in part by regulatory requirements set by the FDA. While most studies submitted to the FDA compare the new drug to a placebo, manufacturers also submit to the FDA studies comparing the new treatment to previously approved products with increasing frequency. Head-to-head studies may be necessary when comparison to a placebo is unethical, or to understand how the new treatment compares to an existing standard of care. The latter may be used to influence the content of the package insert and subsequent marketing of the product. Consequently, the FDA has been developing the standards and methods for comparative studies, and using the results to support the regulation of medical products.

The second major motivation for manufacturers to conduct CER is to increase the likelihood that health systems will list their products in their formularies, and that payers will reimburse them. Determination of safety and efficacy does allow entry into the market, but it does not ensure that a third-party payer will cover a product, or that safety and efficacy will be the sole basis for determining payment levels. Health care payers asked to pay a higher price for a new product increasingly require evidence that the higher price buys additional clinical benefit. For example, drugs with similar risk-benefit profiles may end up on different formulary tiers, depending on their price.⁶ Consequently, reimbursement pressures may encourage manufacturers to support CER to demonstrate that their products provide benefit at the margin relative to existing products. Although these incentives may be important motivators to do CER related to particular products, they are less effective motivators to study medical practices and processes, products that are not “on patent,” novel uses of approved products, or “class effects” or combinations of products.

Blue Cross and Blue Shield Association Technology Evaluation Center

The Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) was established in 1985. Its mission is to provide health care decision makers with scientifically rigorous assessments that synthesize the available evidence on the prevention, diagnosis, treatment, and management of disease. Its assessments review the evidence that specific medical procedures, devices, and drugs improve health outcomes such as length of life, quality of life, and functional ability (Blue Cross and Blue Shield Association, 2009). TEC produces 20 to 25 assessments per year for clients including CMS, Kaiser Permanente, and other private health plans. Its reports are publicly available. TEC is an EPC of the AHRQ Effective Health Care Program.

Cochrane Collaboration

Established in 1993, the Cochrane Collaboration is an independent, multinational nonprofit organization that creates and distributes systematic reviews of health care interventions. These reviews are prepared by 52 Cochrane Review Groups. Quality standards, which are published regularly in a handbook, are maintained by editorial teams that oversee the preparation and maintenance of the reviews. Cochrane review abstracts and plain-

⁶ When a payer places a drug on a high tier in the payer’s formulary, the patient is charged a higher out-of-pocket co-payment when purchasing the drug and the drug is less likely to be prescribed.

language summaries are free and publicly available online, and complete reviews are available with a subscription (Cochrane Collaboration, 2001). As of April 2009, The Cochrane Database of Systematic Reviews contained a total of 5,785 systematic reviews of medical interventions, methodological studies, and diagnostic test accuracy (Cochrane Collaboration, 2009).

A number of smaller nonprofit and for-profit enterprises are actively involved in a variety of CER activities. A sampling of organizations includes The ECRI Institute and Hayes, Inc., which provide exclusive proprietary information and do not make their reports publicly available (ECRI Institute, 2009; Hayes Inc., 2009). The Drug Effectiveness Review Project (DERP) is a collaboration of public entities: the Center for Evidence-based Policy and the EPC at Oregon Health and Science University. These organizations produce systematic reviews of the comparative effectiveness and safety of drugs (Oregon Health and Science University, 2009), which served as a significant source for “Consumer Reports Best Buy Drugs” (Findlay, 2006). The Institute for Clinical and Economic Review produces publicly available assessments of new medical interventions to support value-based insurance benefit designs, coverage and reimbursement policy, and patient-clinician decision support tools (Institute for Clinical and Economic Review, 2009). The Center for Medical Technology Policy (CMTP) provides a forum for the collaborative design and implementation of CER, including pragmatic trials, adaptive designs, and clinical registries (CMTP, 2009).

Lessons from Ongoing CER Activities

This account of CER initiatives supports several conclusions. First, considerable CER is under way, often as a result of regulatory and reimbursement incentives, with the support of a variety of programs in the public and private sectors. Although these programs vary in scope, goals, and activities, all seek to provide timely and useful evidence to health care decision makers on questions of patient care *and* policy significance. In its report, the committee acknowledges that this is not an exhaustive description of the activities of U.S. organizations involved in CER. The Federal Coordinating Council’s June 30, 2009, report to the Secretary of HHS will also describe the CER activities of federal agencies. Even limiting itself to its description of federal CER activities and the study of systematic reviews in *Knowing What Works in Health Care*, the committee found considerable duplicated effort, which is one reason to propose a mechanism to coordinate CER activities throughout the nation. New public investments in CER should complement these ongoing initiatives. Federal coordination would allow for systematic identification and rapid dissemination of best practices, improved prioritization of research topics for future funding,

reduction of duplication, encouragement of collaboration, improvement and standardization of methodology, and generally leverage of private-sector initiatives with the goal of more rapidly and efficiently generating results on priority topics.

Second, leaders of CER must evaluate the present CER workforce in light of the requirements of an expanded, sustained program equal to the task of undertaking the priority research described in Chapter 5. Expansion of CER, as envisioned by ARRA, requires assessment of current capacity and planning to support a national CER program. For example, the size of the qualified CER workforce is not known and the workforce needed to perform CER must be defined, assessed, and trained. NIH, FDA, AHRQ's DEcIDE Research Network, CERTs, CMS, VA, and CMTP are among the organizations focused on the development of new evidence from well-designed comparative clinical trials and observational studies. Priorities for new CER must address the research infrastructure required to generate new data to answer questions of interest to patients and policy makers and must recommend investment in new capacity where needed.

Third, the United States lacks a large-scale national infrastructure for learning from the delivery of health care through observational research using existing clinical and administrative data sources. Moreover, a methodological framework is needed to guide the translation of clinical and policy relevant questions into answerable CER questions and to match CER questions to appropriate CER methods.

Finally, the value of high-quality CER depends on successfully disseminating and incorporating the results into routine practice. The means to the latter end include evidence-based guidelines, clinician and patient decision support tools, models of shared, informed decision making, reimbursement policy, and benefit design. Current law provides direct support for the synthesis and dissemination of CER (through the AHRQ-sponsored EPCs) to inform clinical and policy decision making—providing the building blocks for evidence-based policy.

CONCLUSION

Greater investment in CER has the potential to help improve the quality, outcomes, and value of health care in America. *But what exactly is CER?* The committee has derived from several existing definitions six characteristics of CER studies, as well as a new working definition to guide priority setting. CER is defined by the pragmatic aim of informing a specific health care or health policy decision, and the explicit comparison of clinically credible, alternative interventions in a representative study population. CER studies seek to inform population-level and subgroup-level decisions alike, using outcomes, methods, and data sources appropriate to answer

the specific question within the limitations of the study design. CER encompasses the collection of new experimental and observational data, the analysis of existing observational data, studies that synthesize completed research, and the translation and dissemination of research findings into clinical practice.

Past clinical effectiveness studies have sought to answer questions about the effectiveness of medical interventions and strategies, but not all clinical effectiveness studies are *comparative* effectiveness studies. CER studies compare the intervention under study against its best or most commonly used alternatives in practice or in development, rather than against a placebo. Furthermore, the studies address effectiveness (i.e., how the intervention performs with real-world patients) rather than assessing efficacy (i.e., how it performs in highly selected patient groups who receive study-related care in parallel with usual care).

CER techniques are varied. Although RCTs, prospective cohort studies, and patient registries are among its most important tools, CER also uses other forms of information, such as systematic reviews, electronic health records, patient registries, and other observational datasets.

Prospective studies based on new trials or primary analyses of patient-level data are a very important aspect of CER. However, CER also includes secondary analyses—such as meta-analyses, or formal pooled analyses of multiple studies. Pooled analyses are often critically important because they can be used to draw conclusions that could not be inferred from individual studies.

Besides helping health care providers and patients make better clinical decisions, CER information can improve care in other ways. For example, hospitals and health systems might organize their facilities and personnel to better support care that is revealed by CER to be superior. Professional societies are likely to be both sources of CER and users of the information, incorporating CER into the development of clinical guidelines (IOM, 2008).

A common misapprehension is that CER will lead to uniform, “one-size-fits-all” care that ignores the ways that patients differ. In fact, CER done well should give providers the means to tailor the choice of treatment to the individual patient’s characteristics and preferences. Better comparative effectiveness studies will make it possible to measure the implications of individual differences in disease severity and the presence of comorbidities, to identify predictors of response to treatment, and to incorporate other aspects of a person’s health and preferences. For example, CER might assess the added value of using genomic information in addition to traditional clinical predictors to determine the best treatment for a cancer in a particular patient. It might suggest formal assessment of patient preferences in those situations in which patient and caregiver desires might

alter the decision to proceed with one or another treatment strategy. These techniques might allow physicians to tailor therapy to reflect the goals and desires of each patient. Better information can only help physicians do a better job of matching their care to an individual patient's needs. Indeed, improvements in CER methods to support the use of targeted therapies are urgently needed.

CER has been under way in a number of venues in the United States and has received notable support from the private and public sectors. The committee's review of these initiatives indicates that there is considerable capacity for evidence synthesis. However, the incentives for doing primary CER are uneven, the infrastructure for supporting the development of new evidence is in an early stage of development, and a wide gap exists between CER results and their translation into consistent clinical practice and health policy. New federal investments in CER must address these infrastructure and translational priorities in addition to the information needs on specific clinical topics.

REFERENCES

- AHRQ (Agency for Healthcare Research and Quality). 2009a. *AHRQ Effective Health Care glossary* <http://effectivehealthcare.ahrq.gov/tools.cfm?tooltype=glossary&TermID=118> (accessed April 4, 2009).
- . 2009b. *Centers for Education & Research on Therapeutics (CERTs)* <http://www.certs.hhs.gov/> (accessed April 9, 2009).
- American College of Physicians. 2008. Improved availability of comparative effectiveness information: An essential feature for a high-quality and efficient United States health care system. Philadelphia, PA.
- Avorn, J. 2009. Debate about funding comparative-effectiveness research. *New England Journal of Medicine* 360(19):1927-1929.
- Birkmeyer, N. J. O., J. N. Weinstein, A. N. A. Tosteson, T. D. Tosteson, J. S. Skinner, J. D. Lurie, R. Deyo, and J. E. Wennberg. 2002. Design of the spine patient outcomes research trial (SPORT). *Spine* 27(12):1361-1372.
- Blue Cross and Blue Shield Association. 2009. *Technology Evaluation Center criteria* <http://www.bcbs.com/blueresources/tec/tec-criteria.html> (accessed May 1, 2009).
- Bravata, D. M., A. L. Gienger, K. M. McDonald, V. Sundaram, M. V. Perez, R. Varghese, J. R. Kapoor, R. Ardehali, D. K. Owens, and M. A. Hlatky. 2007. Systematic review: The comparative effectiveness of percutaneous coronary interventions and coronary artery bypass graft surgery. *Annals of Internal Medicine* 147(10):703-716.
- CBO (Congressional Budget Office). 2008. Technological change and the growth of health care spending. In *CBO paper*. Place Published: United States Congressional Budget Office. <http://www.cbo.gov/ftpdocs/89xx/doc8947/01-31-TechHealth.pdf> (accessed April 30, 2008).
- CDC (Centers for Disease Control and Prevention). 2007. Morbidity and mortality weekly report. 56:880-888.
- Chou, R., R. Fu, S. Carson, S. Saha, and M. Helfand. 2007. Methodological shortcomings predicted lower harm estimates in one of two sets of studies of clinical interventions. *Journal of Clinical epidemiology* 60(1):18-28.

- CMS (Centers for Medicare & Medicaid Services). 2009a. *Mission, vision and goals overview* <http://www.cms.hhs.gov/MissionVisionGoals/> (accessed May 22, 2009).
- . 2009b. *National health expenditures aggregate, per capita amounts, percent distribution, and average annual percent growth, by source of funds: Selected calendar years 1960-2007* <http://www.cms.hhs.gov/NationalHealthExpendData/downloads/tables.pdf> (accessed May 1, 2009).
- CMTF (Center for Medical Technology Policy). 2009. *Welcome to the Center for Medical Technology Policy* <http://www.cmtfnet.org/> (accessed April 9, 2009).
- Cochrane, A. L. 1971. *Effectiveness and efficiency: Random reflections on health services*. London: Nuffield Provincial Hospitals Trust.
- Cochrane Collaboration. 2001. *Cochrane Collaboration consumer network* <http://www.cochraneconsumer.com/> (accessed April 28, 2009).
- . 2005. *Glossary of terms in the Cochrane Collaboration. Version 4.2.5*. www.cochrane.org (accessed November 27, 2006).
- . 2009. *Product descriptions-record counts* <http://www.interscience.wiley.com/egibin/mrwhome/106568753/ProductDescriptions.html> (accessed April 24, 2009).
- Duckworth, W., C. Abaira, T. Moritz, D. Reda, N. Emanuele, P. D. Reaven, F. J. Zieve, J. Marks, S. N. Davis, R. Hayward, S. R. Warren, S. Goldman, M. McCarran, M. E. Vitek, W. G. Henderson, and G. D. Huang. 2009. Glucose control and vascular complications in veterans with type 2 diabetes. *New England Journal of Medicine* 360(2):129-139.
- ECRI Institute. 2009. *Pioneering applied scientific research in healthcare* <https://www.ecri.org/about/pages/default.aspx> (accessed April 24, 2009).
- Epstein, S. 1996. Impure science: AIDS, activism, and the politics of knowledge. In *Medicine and society*. Place Published: University of California Press. <http://www.loc.gov/catdir/bios/ucal051/96016805.html> (accessed April 21, 2009).
- Findlay, S. D. 2006. Bringing the DERP to consumers: 'Consumer Reports Best Buy drugs'. *Health Affairs* 25(4):w283-w286.
- Fisher, E. S., D. E. Wennberg, T. A. Stukel, D. J. Gottlieb, F. L. Lucas, and E. L. Pinder. 2003. The implications of regional variations in Medicare spending. Part 2: Health outcomes and satisfaction with care. *Annals of Internal Medicine* 138(4):288-298.
- Fisher, E. S., J. P. Bynum, and J. S. Skinner. 2009. Slowing the growth of health care costs—Lessons from regional variation. *New England Journal of Medicine* 360(9):849-852.
- GAO (Government Accountability Office). 2002. *Medicare: Beneficiary use of clinical preventive services*. Report to the Chairman, Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives. Washington, DC.
- Garber, A. M., and D. O. Meltzer. 2009. *Setting priorities for comparative effectiveness research*. Paper presented at Implementing Comparative Effectiveness Research: Priorities, Methods, and Impact, Engleberg Center for Health Care Reform at Brookings: Washington, DC.
- Garber, A. M., and S. R. Tunis. 2009. Does comparative-effectiveness research threaten personalized medicine? *New England Journal of Medicine* 360(19):1925-1927.
- Glickman, S. W., F. S. Ou, E. R. DeLong, M. T. Roe, B. L. Lytle, J. Mulgund, J. S. Rumsfeld, W. B. Gibler, E. M. Ohman, K. A. Schulman, and E. D. Peterson. 2007. Pay for performance, quality of care, and outcomes in acute myocardial infarction. *JAMA* 297(21):2373-2380.
- Gottlieb, S. 2009. Congress wants to restrict drug access: A bill in the House could tie your doctor's hands. *Wall Street Journal*, January 20, 2009.
- Harpole, L. H., M. J. Kelley, G. Schreiber, E. M. Toloza, J. Kolimaga, and D. C. McCrory. 2003. Assessment of the scope and quality of clinical practice guidelines in lung cancer. *Chest* 123(1 SUPPL.):7S-20S.

- Hayes Inc. 2009. *Hayes: Transforming healthcare with evidence* <http://www.hayesinc.com/hayes/> (accessed May 8, 2009).
- Haynes, R. B., D. L. Sackett, G. H. Guyatt, and P. Tugwell. 2006. *Clinical epidemiology: How to do clinical practice research*. 3rd ed. Philadelphia, PA: Lipincott Williams & Wilkins.
- Helfand, M. 2005. Using evidence reports: Progress and challenges in evidence-based decision making. *Health Affairs* 24(1):123-127.
- Higgins, J., and S. Green. 2008. *Cochrane handbook for systematic reviews of interventions: Version 5.0.1* Place Published: The Cochrane Collaboration, 2008. <http://www.cochrane.org/resources/handbook/index.htm> (accessed April 2, 2009).
- Hlatky, M. A., D. B. Boothroyd, D. M. Bravata, E. Boersma, J. Booth, M. M. Brooks, D. Carrié, T. C. Clayton, N. Danchin, M. Flather, C. W. Hamm, W. A. Hueb, J. Kähler, S. F. Kelsey, S. B. King, A. S. Kosinski, N. Lopes, K. M. McDonald, A. Rodriguez, P. Serruys, U. Sigwart, R. H. Stables, D. K. Owens, and S. J. Pocock. 2009. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: A collaborative analysis of individual patient data from ten randomised trials. *The Lancet* 373(9670):1190-1197.
- Holve, E., S. Mercer, J. Kupersmith, and S. Phurrough. 2008. Exploring comparative effectiveness: Activities of CDC, VA and CMS to advance evidenced-based health. *National Health Policy Forum* The George Washington University, <http://www.nhpf.org/library/details.cfm/2646> (accessed October 3, 2008).
- Hueb, W., N. H. Lopes, B. J. Gersh, P. Soares, L. A. C. Machado, F. B. Jatene, S. A. Oliveira, and J. A. F. Ramires. 2007. Five-year follow-up of the medicine, angioplasty, or surgery study (MASS II): A randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. *Circulation* 115(9):1082-1089.
- Institute for Clinical and Economic Review. 2009. *Mission*. <http://www.icer-review.org/index.php/about.html> (accessed April 9, 2009).
- IOM (Institute of Medicine). 2001. *Crossing the quality chasm: A new health system for the 21st century*, Edited by J. M. Corrigan. Washington, DC: National Academy Press. <http://www.nap.edu/catalog/10027.html> (accessed April 20, 2009).
- . 2007. *Learning what works best: The nation's need for evidence on comparative effectiveness in health care*. <http://www.iom.edu/ebm-effectiveness> (accessed April 15, 2009).
- . 2008. *Knowing what works in health care: A roadmap for the nation*. Edited by J. Eden, B. Wheatley, B. J. McNeil and H. Sox. Washington, DC: The National Academies Press.
- Ischemic Optic Neuropathy Decompression Trial Research Group. 1995. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION) is not effective and may be harmful. *JAMA* 273(8):625-632.
- Jha, A. K., J. B. Perlin, K. W. Kizer, and R. A. Dudley. 2003. Effect of the transformation of the Veterans Affairs health care system on the quality of care. *New England Journal of Medicine* 348(22):2218-2227.
- Johnston, S. C., and S. L. Hauser. 2009. Comparative effectiveness research in the neurosciences. *Annals of Neurology* 65(2):A6-A8.
- Kurian, A. W., R. N. Thompson, A. F. Gaw, S. Arai, R. Ortiz, and A. M. Garber. 2007. A cost-effectiveness analysis of adjuvant trastuzumab regimens in early HER2/neu-positive breast cancer. *Journal of Clinical Oncology* 25(6):634-641.
- Last, J. M. 2001. *A dictionary of epidemiology*. New York: Oxford University Press.
- Lauer, M. S. 2009. Comparative effectiveness research: The view from the NHLBI. *Journal of the American College of Cardiology* 53(12):1084-1086.

- Lohr, K. N. 2007. Emerging methods in comparative effectiveness and safety: Symposium overview and summary. *Medical Care* 45(10 SUPPL. 2):S5-S8.
- Mangione-Smith, R., A. H. DeCristofaro, C. M. Setodji, J. Keeseey, D. J. Klein, J. L. Adams, M. A. Schuster, and E. A. McGlynn. 2007. The quality of ambulatory care delivered to children in the United States. *New England Journal of Medicine* 357(15):1515-1523.
- McGlynn, E. A., S. M. Asch, J. Adams, J. Keeseey, J. Hicks, A. DeCristofaro, and E. A. Kerr. 2003. The quality of health care delivered to adults in the United States. *New England Journal of Medicine* 348(26):2635-2645.
- Medicare Payment Advisory Commission. 2008. *Report to the Congress: Reforming the delivery system*. Washington, DC.
- NCI (National Cancer Institute). 2006. *NCI's clinical trials cooperative group program* <http://cancertrials.nci.nih.gov/cancertopics/factsheet/nci/clinical-trials-cooperative-group> (accessed June 15, 2009).
- NIH PGRN (National Institutes of Health Pharmacogenetics Research Network). 2009. *PGRN mission statement* http://www.pharmgkb.org/network/pgrn_mission_statement.jsp (accessed June 12, 2009).
- Oregon Health and Science University. 2009. *Drug Effectiveness Review Project* <http://www.ohsu.edu/drugeffectiveness/> (accessed April 8, 2009).
- Orszag, P. R. 2007. Research on the comparative effectiveness of medical treatments: Options for an expanded federal role: CBO testimony before the Subcommittee on Health, Committee on Ways and Means, U.S. House of Representatives. U.S. Congressional Budget Office. <http://www.cbo.gov/ftpdocs/82xx/doc8209/Comparative%5FTestimony.pdf> (accessed April 28, 2009).
- Oxman, M. N., M. J. Levin, G. R. Johnson, K. E. Schmader, S. E. Straus, L. D. Gelb, R. D. Arbeit, M. S. Simberkoff, A. A. Gershon, L. E. Davis, A. Weinberg, K. D. Boardman, H. M. Williams, J. H. Zhang, P. N. Peduzzi, C. E. Beisel, V. A. Morrison, J. C. Guatelli, P. A. Brooks, C. A. Kauffman, C. T. Pachucki, K. M. Neuzil, R. F. Betts, P. F. Wright, M. R. Griffin, P. Brunell, N. E. Soto, A. R. Marques, S. K. Keay, R. P. Goodman, D. J. Cotton, J. W. Gnann Jr, J. Loutit, M. Holodniy, W. A. Keitel, G. E. Crawford, S. S. Yeh, Z. Lobo, J. F. Toney, R. N. Greenberg, P. M. Keller, R. Harbecke, A. R. Hayward, M. R. Irwin, T. C. Kyriakides, C. Y. Chan, I. S. F. Chan, W. W. B. Wang, P. W. Annunziato, and J. L. Silber. 2005. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *New England Journal of Medicine* 352(22):2271-2284+2365.
- Plevritis, S. K., A. W. Kurian, B. M. Sigal, B. L. Daniel, D. M. Ikeda, F. E. Stockdale, and A. M. Garber. 2006. Cost-effectiveness of screening BRCA1/2 mutation carriers with breast magnetic resonance imaging. *JAMA* 295(20):2374-2384.
- Santaguida, P. L., M. Helfand, and P. Raina. 2005. Challenges in systematic reviews that evaluate drug efficacy or effectiveness. *Annals of Internal Medicine* 142(12_Part_2):1066-1072.
- Sisko, A., C. Truffer, S. Smith, S. Keehan, J. Cylus, J. A. Poisal, M. K. Clemens, and J. Lizonitz. 2009. Health spending projections through 2018: Recession effects add uncertainty to the outlook. *Health Affairs* 28(2):w346-357.
- Slutsky, J. R., and C. M. Clancy. 2009. AHRQ's Effective Health Care Program: Why comparative effectiveness matters. *American Journal of Medical Quality* 24(1):67-70.
- Sparano, J. A., M. Wang, S. Martino, V. Jones, E. A. Perez, T. Saphner, A. C. Wolff, G. W. Sledge, Jr., W. C. Wood, and N. E. Davidson. 2008. Weekly paclitaxel in the adjuvant treatment of breast cancer. *New England Journal of Medicine* 358(16):1663-1671.
- Tosteson, A. N. A., J. D. Lurie, T. D. Tosteson, J. S. Skinner, H. Herkowitz, T. Albert, S. D. Boden, K. Bridwell, M. Longley, G. B. Andersson, E. A. Blood, M. R. Grove, and J. N. Weinstein for the SPORT Investigators. 2008. Surgical treatment of spinal stenosis with and without degenerative spondylolisthesis: Cost-effectiveness after 2 years. *Annals of Internal Medicine* 149(12):845-853.

- Tricoci, P., J. M. Allen, J. M. Kramer, R. M. Califf, and S. C. Smith, Jr. 2009. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA* 301(8):831-841.
- Tunis, S. R., and S. D. Pearson. 2006. Coverage options for promising technologies: Medicare's 'coverage with evidence development.' *Health Affairs* 25(5):1218-1230.
- Tunis, S. R., D. B. Stryer, and C. M. Clancy. 2003. Practical clinical trials: Increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 290(12):1624-1632.
- VA (Veterans Affairs). 2009. *Evidenced-based synthesis program* <http://www.hsrdr.research.va.gov/publications/esp/> (accessed May 22, 2009).
- Veteran's Health Administration. 2009. *Cooperative studies program (CSP)* <http://www.research.va.gov/programs/csrd/csp.cfm> (accessed May 1, 2009).
- Vigna-Taglianti, F., P. Vineis, A. Liberati, and F. Faggiano. 2006. Quality of systematic reviews used in guidelines for oncology practice. *Annals of Oncology* 17(4):691-701.
- Weinstein, J. N., T. D. Tosteson, J. D. Lurie, A. N. A. Tosteson, E. Blood, B. Hanscom, H. Herkowitz, F. Cammisa, T. Albert, S. D. Boden, A. Hilibrand, H. Goldberg, S. Berven, H. An, and the SPORT Investigators. 2008. Surgical versus nonsurgical therapy for lumbar spinal stenosis. *New England Journal of Medicine* 358(8):794-810.
- Wennberg, J. E., A. M. O'Connor, E. D. Collins, and J. N. Weinstein. 2007. Extending The P4P agenda, part 1: How Medicare can improve patient decision making and reduce unnecessary care. *Health Affairs* 26(6):1564-1574.
- West, S., V. King, T. Carey, K. Lohr, N. McCoy, S. Sutton, and L. Lux. 2002. *Systems to rate the strength of scientific evidence. Evidence Report/Technology Assessment No. 47.* (Prepared by the Research Triangle Institute-University of North Carolina Evidence-based Practice Center under Contract No. 290-97-0011). AHRQ Publication No. 02-E016. Rockville, MD: Agency for Healthcare Research and Quality.
- Whitlock, E. P., S. A. Lopez, S. Chang, M. Helfand, M. Eder, and N. Floyd. 2009. Identifying, selecting, and refining topics for comparative effectiveness systematic reviews: AHRQ and the effective health care program. <http://effectivehealthcare.ahrq.gov/repFiles/20090427IdentifyingTopics.pdf> (accessed June 5, 2009).

3

Obtaining Input to Identify National Priorities for Comparative Effectiveness Research

***Abstract:** Stakeholder input was one of the express requirements of the comparative effectiveness research priority study that Congress requested from the Institute of Medicine (IOM) in the American Recovery and Reinvestment Act of 2009. The committee concluded that such input should be invited and analyzed from direct communications to the IOM from an in-person stakeholder meeting before the committee and from a web-based questionnaire. Policy recommendations, general comments, and opinions were provided in direct communication before, during, and after the public meeting from the biomedical and health care communities and patients and families. More than 2,600 nominations representing a diversity of research topics, respondents, and perspectives from the public and private for-profit and not-for-profit sectors were submitted to the web-based questionnaire.*

INTRODUCTION

In response to the directive of the American Recovery and Reinvestment Act (ARRA) of 2009 (P.L. 111-5) to consider input from stakeholders,¹ the committee focused on three mechanisms for obtaining input on comparative effectiveness research (CER) from as wide an array as possible of stakeholders including patients, families, and consumers. This chapter

¹ *American Recovery and Reinvestment Act of 2009*, P.L. 111-5, 111th Congress, 1st session (February 17, 2009).

describes the process of soliciting the inputs that informed the committee in preparing its report.

INVITATIONS TO PROVIDE INPUT

More than 20,000 email announcements describing the Institute of Medicine (IOM) study and inviting stakeholder input were sent out the first week of March 2009. These announcements were directed to general lists maintained by the IOM, composed of IOM members and other individuals who signed up for the listserv because of an interest in the IOM and its work. The lists include members of the media, policy makers, academics, researchers, health care industry, physicians and other health care providers, students, former Robert Wood Johnson Foundation Health Policy fellows, and others in the public and private sectors interested in health policy, as well as those on listservs to congressional staff and congressional agency staff. Announcements were also sent specifically to seven categories of stakeholders (Table 3-1) with broad constituencies; they were requested to forward the announcement to their memberships. The committee concluded that these organizations, and their memberships and constituencies, were relevant to CER and could initiate further dissemination of the announcements to similar individuals and groups thus providing an opportunity for increased input to the committee. Invitations provided three distinct avenues for submitting advice on national priorities for CER to the committee:

1. Direct correspondence with the IOM committee
2. Oral and written presentations at an open stakeholders' meeting scheduled at the National Academy of Sciences Building in Washington, DC
3. Submission of specific CER topics, as well as general comments on the process of conducting CER via a web-based questionnaire

The committee's goal was to receive the most extensive advice and recommendations possible for national CER priorities from the widest possible array of stakeholders within the time and resources available. In the aggregate, useful advice and a list of national priorities emerged from these three steps that related well to selection criteria and 32 research areas as described below.

COMMUNICATIONS DIRECTLY TO THE COMMITTEE

The committee received approximately 90 emails and letters from a wide variety of stakeholders that ranged from pharmaceutical manufacturers to health profession associations, patient and consumer organizations, health

TABLE 3-1 Solicited Stakeholder Groups (including, but not limited to the examples shown)

Categories	Stakeholder Groups
Consumers/Patient Advocacy Groups	<ul style="list-style-type: none"> • AARP • Center for Advancement of Health • Consumers Union • National Health Council • National Minority Quality Forum
Federal Government Agencies	<ul style="list-style-type: none"> • Agency for Healthcare Research and Quality • Centers for Disease Control and Prevention • Centers for Medicare & Medicaid Services • Department of Veterans Affairs • Food and Drug Administration • National Institutes of Health
Health Care Providers and Researchers	<ul style="list-style-type: none"> • American Academy of Family Physicians • American Academy of Pediatrics • American College of Physicians • American Medical Association • American Nurses Association • American Psychological Association • National Medical Association
Insurers	<ul style="list-style-type: none"> • America's Health Insurance Plans • Blue Cross and Blue Shield Association • CIGNA
Integrated Health Systems	<ul style="list-style-type: none"> • Geisinger • HealthPartners • Kaiser Permanente
Manufacturers (including drugs, devices, and biotechnology)	<ul style="list-style-type: none"> • Advanced Medical Technology Association • Biotechnology Industry Organization • Pharmaceutical Research and Manufacturers of America
State Government Agencies	<ul style="list-style-type: none"> • Association of State and Territorial Health Officials • National Governors Association

services researchers, health plans, complementary and alternative medicine providers, patient advocates, and individual patients and consumers. Many of these made recommendations to include specific topics nominated as research priorities, as well as suggestions about the general process. A summary of the general stakeholder recommendations follows:

- **Transparency.** Many stakeholders recommended using a systematic and open process of setting priorities that would include patients and consumers, and would avoid conflicts of interest.
- **Research Design.** Some stakeholders favored encouraging new types of studies, adopting certain techniques to minimize research bias, incorporating quality measures and patient preferences in effectiveness studies, and focusing on real-world clinical situations rather than ideal conditions. Related suggestions called for improving existing databases, making databases more accessible to researchers, protecting patient privacy, and investing in health information technology designed to produce a robust, scalable, and open architecture capable of providing real-time data. They also suggested that CER should take into account special populations defined by such factors as race and ethnicity, gender, age, and socioeconomic status.
- **Translation and Dissemination.** Many stakeholders addressed issues of disseminating CER findings and converting them into changes in health care practice. These suggestions included providing feedback to physicians, improving decision support for clinicians, encouraging physicians to use best practices and clinical guidelines, conducting research on medical and surgical devices, enhancing patient adherence to regimens, developing user-friendly guides, testing alternative patient decision-making tools, and allowing public comment periods for comparative effectiveness study reports. Long-term issues that were addressed included revisiting research results when new information becomes available, expanding training programs for CER, and partnerships among professions.
- **Economics.** A number of stakeholders suggested expanding “coverage with evidence development” (i.e., Medicare reimbursement is conditioned on reporting results of use) to other payers in both the public and private sectors. They also suggested including consideration of the cost of an intervention as a secondary factor in evaluation. Some correspondents urged that incentives for innovation be preserved.

- *Advocacy.* Some stakeholders suggested advocating for specific groups, providers, conditions, or organizations; the committee reviewed and acted on these suggestions as appropriate.

PRESENTATIONS AT AN OPEN MEETING OF STAKEHOLDERS

An open stakeholders meeting was held March 20, 2009 in the auditorium of the National Academy of Sciences Building on Constitution Avenue in Washington, DC. Fifty-four speakers made 3-minute presentations (or 5-minute presentations if the individual represented a large membership organization) to the committee and a large public audience with approximately 25 percent of the day reserved for the committee to address questions to the presenters. Box 3-1 displays the list of speaker organizations and a full agenda from the meeting is available in Appendix A. Written statements from all 54 speakers were made publicly available on the committee website and are provided as an electronic appendix at www.iom.edu/cerpriorities. Word limits were not imposed on these written statements.²

Virtually all of the presenters addressed issues of public policy or methodology involving CER, rather than proposing specific research topics. Many presenters expressed support for CER in principle, while none expressed direct opposition. The representative from America's Health Insurance Plans asserted that some health care interventions are used without evidence or without recent reevaluation, and there is a need to know first, what works, and second, what works best.

Many presenters, such as the representatives from the Biotechnology Industry Organization and several physician societies, stated that evidence-based medicine should guide CER, and that CER should be accurate and rigorous. They emphasized that CER needs to be grounded in "real-world" conditions and that the public will require evidence of this as investments in CER increase. The representative from the Association of American Medical Colleges urged the committee to recommend investments in training researchers, in data resources, and in other CER infrastructure.

Some presenters, such as the representatives from the National Medical Association and the National Minority Quality Forum, expressed concern that CER might be used to generalize approaches to therapy, in a so-called one-size-fits-all approach to health care. Others, such as the representative from the National Health Council, strongly advocated for a patient-

² Federal agencies listed in Table 3-1 did not make presentations before the committee. Instead, these agencies participated in the federal response to the CER mandate of ARRA under the aegis of the Federal Coordinating Council on Comparative Effectiveness Research. This council heard 3-minute presentations and/or received a written statement from stakeholders over 3 hours on April 14, 2009, at a "public listening session" held in Washington, DC, and on May 13, 2009, in Chicago, IL.

BOX 3-1
Organizations Represented at the Stakeholder Meeting

- A Certified Nurse Midwife
- Advanced Medical Technology Association
- American Academy of Family Physicians
- American Academy of Pediatrics
- American Association for Dental Research
- American Association of Neurological Surgeons
- American College of Cardiology
- American College of Clinical Pharmacy
- American College of Occupation and Environmental Medicine
- American College of Surgeons
- American Heart Association
- American Medical Association
- American Nurses Association
- American Psychiatric Association
- American Psychological Association
- American Society of Clinical Oncology
- America's Health Insurance Plans
- Association of American Medical Colleges
- Association of Clinical Research Organizations
- Association of Schools of Public Health
- Biotechnology Industry Organization
- Blue Cross and Blue Shield Association
- California Department of Public Health
- Center for Advancement of Health
- Center for Science in the Public Interest
- CIGNA
- Consumers Union
- Developing Families Center
- Duke University Medical Center
- eHealth Initiative
- Focus on Therapeutic Outcomes, Inc.
- Friends of Cancer Research
- Frontier School of Midwifery & Family Nursing
- Health Care Consultancy
- HealthPartners Research Foundation
- International Society for Pharmacoeconomics & Outcomes Research
- The Lewin Group
- National Alliance for Hispanic Health
- National Alliance on Mental Illness
- National Health Council
- National Medical Association
- National Minority Quality Forum
- National Pharmaceutical Council
- Network for Regional Healthcare Improvement
- Oregon Health and Science University and Portland VA Medical Center
- Parkinson Pipeline Project
- Personalized Medicine Coalition
- Pharmaceutical Research and Manufacturers of America
- Society for Cardiovascular Angiography and Interventions
- The Society of Thoracic Surgeons
- United BioSource Corporation
- United States Pharmacopeia
- University of Iowa
- Washington State Health Care Authority

centered approach to health care delivery and CER. Still, others, such as the presenter from the Lewin Group, offered a set of principles to guide research, which included transparency, public input, a broad scope, careful definitions of comparisons, support for personalized medicine, and evolution of innovation supported by explicit ground rules for review.

Speakers identified the inclusion of cost considerations in the outcomes of CER as controversial. At least nine speakers expressly supported the inclusion of costs in the comparison of health interventions, and many more advocated establishing the relative value of different interventions, services, and care models by comparing costs to clinical benefits for two or more alternatives. At least four others, however, recommended against the use of cost comparisons for fear that the availability of drugs on formularies or coverage decisions would be unduly influenced. One speaker suggested that cost be taken into account only when the alternative interventions are clinically equivalent. Another advocated a focus on enhancing value for patients rather than minimizing costs.

Many groups spoke in favor of personalized or individualized care, taking into consideration the varying concerns and clinical and genetic diversity of patients. This concept was expressed in different ways, but it reflected an overall concern that general research results should not be applied in a way that overlooks the specific needs and preferences of individual patients.

Strategic targeting of CER frequently arose as a topic of discussion. Key topics for investigation identified by the speakers included diabetes, coronary heart disease, chronic obstructive pulmonary disease, depression, common spinal disorders, childhood asthma, obesity, early brain development, family services and midwifery, oral health, minimally invasive surgery, chronic disease in general, and complementary and alternative medicine, among others. Specific modalities of health care delivery that were proposed included behavioral health, medical homes, multi-professional teams, and expanded roles for non-physician health professionals. Some also suggested starting with research that was “shovel-ready”—that is, likely to be accomplished and yield results quickly. There was general agreement that areas to be targeted included high-prevalence conditions, services with high variation in use, conditions with major public health consequences such as those involving health disparities, high-cost conditions, conditions not covered by existing clinical guidelines, and research directed at disease prevention. In addition, there was widespread agreement that effectiveness must be assessed in racial and ethnic minorities to help remedy health disparities.

A number of suggestions regarding research methods came from groups such as the National Alliance on Mental Illness, the American Heart Association, Friends of Cancer Research, the Association of Clinical Research

Organizations, and the Washington State Health Care Authority, among others. They recommended improvements in defining the populations used in randomized clinical trials, avoiding treatment and publication bias by considering completed but unpublished studies, and collecting and storing biospecimens. They also suggested the establishment of a process for timely reconsideration of CER results.

Many presenters discussed sources of information, databases, and other aspects of CER infrastructure. Some professional groups reported joining together to help develop CER standards, registries, and procedures. Some organizations, such as the Advanced Medical Technology Association and Blue Cross and Blue Shield Association, indicated that they might be willing to support projects materially. The American College of Surgeons and other professional groups said their members would be supportive, participate in studies, and likely to incorporate CER results into their practices.

Stakeholders at the meeting generally concluded that there was a need for full transparency in the prioritization process. This encompasses the ongoing participation of stakeholders, the avoidance or strict management of potential conflicts of interest, and the establishment of rigorous scientific standards and methods.

INPUT FROM A WEB-BASED QUESTIONNAIRE

At a very early stage, the committee concluded that substantial and meaningful stakeholder input and specific recommendations for CER priorities to the committee required a web-based questionnaire³ designed to elicit such recommendations. As described earlier, announcement notices of this questionnaire were circulated through a wide distribution of emails to about 20,000 individuals and organizations, and through these organizations to their memberships. In addition, notice was disseminated through the IOM website (www.iom.edu/cerpriorities). The questionnaire was open for 3 weeks, from March 6 to March 27, 2009, which included 1 week following the open stakeholders meeting. The questionnaire is available in Appendix B.

Priority Topic Nominations

There were 1,758 respondents to the questionnaire and 2,606 nominations for CER topics. Initial review showed many duplicated entries and

³ The questionnaire was not requested by the federal sponsor nor was there time for approval by the Office of Management and Budget. This situation did not allow payment for the questionnaire and associated analysis from federal funds, but because the committee concluded it was essential, the IOM took the unusual step of supporting the costs associated with the questionnaire from National Academies funds.

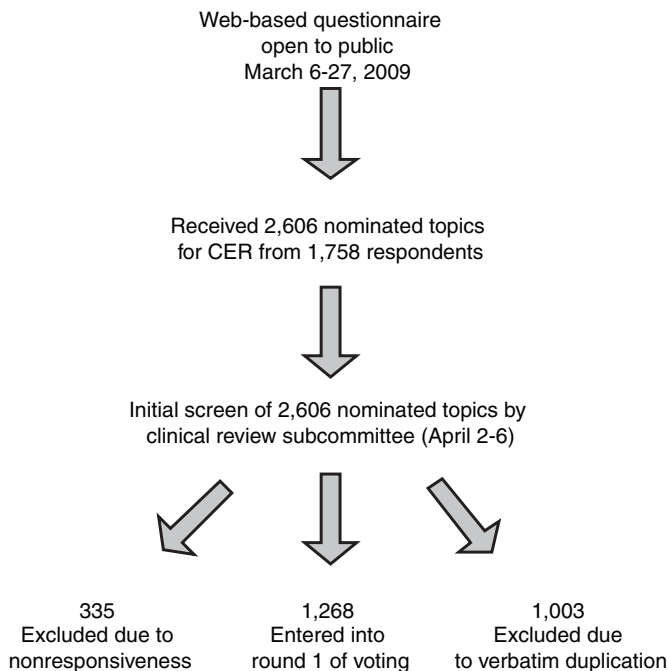


FIGURE 3-1 Stakeholder response to web-based questionnaire.

nonresponsive submissions.⁴ The initial entries were screened by staff to identify unique submissions and were confirmed by two committee members in independent review. Figure 3-1 shows the review and screening process of the questionnaire submissions that resulted in the 1,268 topics that entered the first round of voting. Table 3-2 displays the distribution of respondents by self-identified stakeholder category. While approximately 75 percent of respondents identified themselves as either providers or researchers (which includes the following categories: Health Care Provider, Researcher, Government—Research, Government—Programs, and Health Plan/Insurance Carrier), there was also representation from other categories in the public and private for-profit and not-for-profit sectors, and nearly 10 percent of respondents identified themselves as patients, families, or consumers (which includes the following categories: Patient/Family, Public/Consumer, and Employer). More than 300 respondents self-identified as members of more than

⁴ Nonresponsive submissions were either nonsense answers such as entering “aaaa” so that the respondent could browse through the questionnaire without inserting answers, were not complete responses, or were just general comments to the committee rather than topics for CER.

TABLE 3-2 Respondents to the IOM Questionnaire by Stakeholder Category

Self-Identified Stakeholder Categories	Number of Responders*
Health Care Provider	797
Researcher	416
Professional Association	229
Other	212
Nonprofit/Policy Institute	95
Patient/Family (including family caregiver)	77
Public/Consumer	76
Medical Administrator	40
Government—Research	39
Employer	26
Government—Programs (e.g., Medicare, Medicaid)	26
Manufacturer (Device)	17
Health Plan/Insurance Carrier	12
Manufacturer (Drug or Biologic)	11
Total	2,073

*315 respondents self-identified with more than one category.

one category. Although respondents were primarily from the biomedical and health care communities, the committee concluded that a fair degree of diversity of perspective was represented within those communities.

The questionnaire asked each respondent to submit up to three nominations for priority research topics. Respondents were further asked to support each nominated topic with specific information, including data to justify the importance of the proposed research, assignment of the topic to a single primary research area, identification of appropriate study populations, specification of interventions being compared, and the proposed study methodology. In an effort to be as broad and inclusive as possible, the committee identified the primary research areas from the 17th edition of *Harrison's Principles of Internal Medicine* (Fauci et al., 2008). In addition, the committee added the following research areas to the questionnaire: birth and developmental disorders, functional limitations and disabilities, and pediatrics. Stakeholders pointed out during the public meeting on March 20, 2009, that oral health had been omitted as a distinct category. Therefore, the committee reassigned those nominated topics clearly belonging in this category. The complete listing of named research area categories totaled 32, with an additional category for “other.” The breakdown of the questionnaire nominations by research area, study population, proposed intervention, and study methodology appear in Tables 3-3 through 3-6. The tables display results for the 1,268 topics that emerged after consolidating

TABLE 3-3 Comparative Effectiveness Research Priorities Submitted by Primary Area of Study

Category	Number of Submissions
Alcoholism, Drug Dependency, and Overdose	31
Birth and Developmental Disorders	73
Cardiovascular and Peripheral Vascular Disease	50
Complementary and Alternative Medicine	19
Endocrinology and Metabolism Disorders	33
Eyes, Ears, Nose, and Throat Disorders	50
Functional Limitations and Disabilities	55
Gastrointestinal System Disorders	15
Genetics and Disease	11
Geriatrics	35
Health Care Delivery System*	156
Immune System, Connective Tissue, and Joint Disorders	12
Infectious Diseases	37
Kidney and Urinary Tract Disorders	23
Liver and Biliary Tract Disorders	0
Medical Aspects of Bioterrorism	2
Musculoskeletal Disorders	36
Neurologic Disorders	81
Nutrition (including obesity)	47
Oncology and Hematology	57
Oral Health	15
Other	3
Palliative and End-of-Life Care	20
Pancreatic Disorders	2
Pediatrics	89
Psychiatric Disorders	127
Racial and Ethnic Disparities	19
Regenerative Medicine	2
Respiratory Disease	29
Sexual Function and Reproductive Disorders	4
Skin Disorders	19
Trauma, Emergency Medicine, and Critical Care Medicine	79
Women's Health	37
Total	1,268

NOTE: Secondary and comorbid conditions were also provided but not included in this table.

*Although this category was described as “Safety and Quality of Health Care” in the web-based questionnaire, the category was relabeled by the committee as “Health Care Delivery System” to be more accurate.

TABLE 3-4 Comparative Effectiveness Research Priorities by Proposed Population to be Studied

Population	Count
Adults (excluding elderly)	120
Adults (including elderly)	381
Children/Adolescents Only	448
Elderly Only	193
Ethnic Subpopulations Only	72
Long-Term Care	124
Women	299
Men	242
Population at Large (general population)	336
Rare Diseases	25
Special Populations (e.g., pregnant women, low income, patients with disabilities)	333
Total	2,573

NOTE: The total exceeds the total number of nominations because respondents were allowed to select multiple populations.

TABLE 3-5 Comparative Effectiveness Research Priorities by Proposed Intervention

Comparators	Count
Alternative Treatment	171
Behavioral Treatment	421
Devices	114
Pharmacological Treatment	306
Prevention	452
Procedures (including surgery)	136
Provider-Patient Relationships	304
Standard of Care	458
Systems of Care	508
Testing, Monitoring, and Evaluation	398
Treatment Pathways	305
Total	3,573

NOTE: The total exceeds the total number of nominations because respondents were allowed to select multiple interventions.

TABLE 3-6 Comparative Effectiveness Research Priorities by Proposed Study Methodology

Methodology	Count
Database Review	295
Prospective Observational Study	593
Randomized Clinical Trial	676
Systematic Review	253
Total	1,817

NOTE: The total exceeds the total number of nominations because respondents were allowed to select multiple methodologies.

the 2,606 nominated topics to eliminate verbatim duplicates and nonresponsive submissions, described in greater detail in Chapter 4.

Public Responses on Their Priority-Setting Process

In addition to making specific recommendations for comparative effectiveness priorities and providing supporting information, many of the questionnaire respondents provided information on how they developed their topic nominations, what were their principal priority-setting criteria, and what new or enhanced infrastructure would be needed to sustain a CER enterprise. Regarding the development of CER topics, the largest number of respondents indicated that they nominated topics based on professional experience, both clinical and classroom, and often of many years' duration. Many others developed topics based on literature reviews; conferences attended (such as a National Institutes of Health [NIH] state-of-the-science review); suggestions of specific organizations, such as NIH or the Centers for Disease Control and Prevention (CDC); or their own professional associations such as the American Medical Association, the American Diabetes Association, or Blue Cross and Blue Shield Association. Others reported consulting with colleagues and stakeholders, including a hospital, health system, or consumer group. A small number reported using personal experience to make their nominations, such as being the mother of a deaf child.

The most common priority-setting criteria identified by the respondents can be classified into three broad categories: patient need, quality of care, and cost and reimbursement issues. Patient need was ranked as the top criterion; 23 percent of respondents ranked it in first place, and 14 percent ranked it in second place. Patient need referred primarily to disease burden, including prevalence, morbidity, mortality, and family and social impact, as

well as risk factors such as obesity and substance abuse. Conditions supporting the use of this criterion included speech or hearing problems, autism and traumatic brain injury, chronic diseases including HIV, cancer, asthma, cardiovascular disease, birth outcomes, smoking and alcohol abuse, mental health, and dental disease. The remaining specific criteria—decreasing variability in care, the potential to act on the information, and cost, all received about 13 percent of the support from respondents.

With respect to quality of care-related criteria, many self-identified clinicians said they sought better information for making clinical decisions in order to deliver the best or evidence-based treatment, to reduce treatment variation, and to promote quality of care for their patients, including safety and improved outcomes. Clinicians sought better aids in making clinical decisions; they expressed a need for help in delivering the best care when there were many confusing alternatives.

Cost and reimbursement issues may reflect that research would lead to cost management, better resource use, a decrease in societal costs, and elimination of waste. Respondents stated that if research could lead to deploying health care resources more effectively, costs would decrease. Others thought CER might persuade payers to support or improve reimbursement for particular services, such as integrative care, complementary and alternative medicine, improved doctor-patient communication, caregiver education, specific diagnostic services, and strategies to improve adherence to treatment regimens, among others.

Other comments justifying priority nominations included closing information gaps, countering misinformation, addressing specific areas of research deemed underfunded, assessing new service delivery models, improving public interest, minimizing controversy, reducing disproportionate impact on subpopulations, focusing on research that could deliver quick results, that is low cost, and that is feasible to implement, focusing on psychosocial and educational factors, including family dysfunction that affects health outcomes, and developing new research methods.

In addition, 650 respondents answered the question about enhancing CER infrastructure. Some called for either sufficient, high, or permanent funding for CER, commenting that a public and business case needs to be made to overcome the strong opposition to CER. Important attributes were listed, such as a public-private partnership, methodological rigor, a focus on outcomes, facilitating innovation in interventions and approaches, and broad stakeholder involvement. Some respondents noted that CER is related to health reform or Food and Drug Administration reform, or changes in state licensure of health professions. While some respondents recommended privatizing or decentralizing CER or using existing resources, others suggested that a CER program could be located within the Agency for Healthcare Research and Quality, NIH, or the CDC. It was suggested that

funding be available to individually initiated, multicenter, or non-university-based investigators. Simplification of participation in randomized controlled clinical trials, or in institutional review board processes, and prohibition of conflicts of interest were also recommended. Specific proposals were made for openness, including a national conference, a national committee, local research efforts, and scientific input. Identified needs included registries, longitudinal studies, data availability and access provisions, development of clinical guidelines, examination of subpopulations, reduction in disparities, ways of widely disseminating results, and public and professional education and communication of findings.

The committee was impressed by the value, breadth, and common themes that characterized these inputs from stakeholders and the public. While the committee concluded that many of the original topics nominated by respondents to the web-based questionnaire were thoughtful and worthy, as described in Chapter 4, some topics were edited to be broader and more inclusive of multiple patient populations. In addition, the committee nominated several topics to fill gaps in the portfolio. Through the selection process described in Chapter 4, the topics nominated by the stakeholders, the public, and the committee members were reduced to the final list of 100 national priority topics for CER listed in Chapter 5. The publically nominated topics served as the basis for the majority (82 percent) of the list, and the remaining 18 percent were nominated by the committee. These responses also allayed committee concerns that the 3-week window for the questionnaire that was necessary to meet the short turnaround time for this report may have unduly limited public input. Furthermore, answers to questions on the questionnaire, and input from letters, e-mails, and stakeholder presentations, informed the committee in several other ways—for example, the suggestions on infrastructure were considered in drafting Chapter 6.

Learning from this experience, the committee concluded that an ongoing process for citizens to express themselves and provide priorities for CER would be worthwhile. See Chapter 4 for further discussion of how this input could be collected. This process might also serve an educational role by informing the public that CER is aimed to improve the quality of clinical care delivered to patients not a sub rosa scheme to ration it.

REFERENCE

- Fauci, A. S., E. Braunwald, D. L. Kasper, S. L. Hauser, D. L. Longo, J. L. Jameson, and J. Loscalzo. 2008. *Harrison's principles of internal medicine*, 17th edition. Place Published: McGraw-Hill Companies. <http://www.accessmedicine.com/resourceTOC.aspx?resourceID=4> (accessed May 21, 2009).

4

The Criteria and Process for Setting Priorities

Abstract: *This chapter describes the prioritization criteria and process the committee used in its review of the nominated research topics. The committee considered the balance of the portfolio of nominated research topics across research areas, populations to be studied, types of interventions, and methodologies. In establishing prioritization and portfolio criteria, the committee had the benefit of examining methods and criteria used in several past priority-setting exercises. The committee developed two types of criteria: (1) condition-level criteria that relate to the significance of specific conditions or diseases for the population as a whole or certain age groups, and (2) priority topic-level criteria that include the appropriateness of the nominated research topics for CER, information gaps, variability in care, and gaps in translation. The committee used three rounds of voting to narrow the list of nominated topics to a manageable, high priority portfolio. Based on this experience, the committee made recommendations for future priority-setting projects. Prioritization of CER topics should be a sustained and continuous process that requires the prioritizing body to make regular reports to the Secretary of Health and Human Services, involves the public in a transparent process, and is informed by robust topic briefs and background information.*

INTRODUCTION

The previous chapter described the committee's method of obtaining the nominated topics from stakeholders and the public, while this chapter describes the prioritization criteria and process the committee used in its

review of the nominated topics. The first half of the chapter outlines the various types of prioritizing criteria. The committee developed the concept of portfolio criteria that were intended to ensure that the final priority comparative effectiveness research (CER) topics reflect a balance of CER questions across research area (e.g., geriatrics, neurology, psychiatry), study populations (e.g., women, children, elderly), type of intervention (e.g., surgical, pharmaceutical), and study methodology (e.g., randomized trial, observational study). The committee also developed two sets of criteria for committee members to use in evaluating the specific nominated priority topics: (1) condition-level criteria, including data on burden of disease and variability in care, and (2) priority topic-level criteria, including the appropriateness of the nominated research topics for CER, existing information gaps, variability in care, and gaps in translation.

The second section of the chapter includes an overview of the Institute of Medicine's (IOM's) previous recommendations, criteria, and procedures for setting research priorities, as well as the criteria and methodologies used by other prioritization projects. The committee relied on these past IOM and external reports to develop the criteria it used in the voting process that established the final priority CER topics. The committee's voting process that was used to narrow the list of nominated topics to a manageable, high priority portfolio is also described in detail.

The chapter concludes with a description of the lessons learned from the committee's priority-setting exercise and provides recommendations for future prioritization processes in CER. The final results of the committee's deliberations and voting are presented in Chapter 5.

PORTFOLIO CONSIDERATIONS

As described in Chapter 3, the committee developed the majority of its priority CER topics from the public input gathered through the web-based questionnaire. The questionnaire required the respondents to provide detailed information about each of their nominated priority topics. Respondents were required to identify the primary area of study of their nominated topic from among the 32 disease classifications, patient conditions, and systems of care categories provided. Research areas included categories such as oncology and hematology, geriatrics disorders, neurologic disorders, and so on.

Respondents were also asked to identify the proposed population to be studied, ranging from categories based on gender, age, race, special populations, and rare diseases, as well as the proposed comparators, such as alternative and complementary treatments, behavior intervention, devices, and pharmacological therapy. In addition, the respondents were requested to identify a proposed methodology for their nominated research topic.

TABLE 4-1 Portfolio and Priorities Criteria

Portfolio Criteria	Condition-Level Criteria	Priority Topic-Level Criteria
<ul style="list-style-type: none"> • Research area • Population to be studied • Interventions • Proposed methodology 	<ul style="list-style-type: none"> • Prevalence • Mortality • Morbidity • Cost • Variability 	<ul style="list-style-type: none"> • Appropriateness of topic for CER • Information gaps and duplication • Gaps in translation

Potential methodologies included database review, prospective observational study, randomized clinical trial, or systematic review.

As part of the process of prioritizing the nominated research topics, the committee, with the financial support provided by the Agency for Healthcare Research and Quality (AHRQ), created a portfolio of CER topics that was balanced and diverse across the characteristics previously described and listed in Table 4-1 (see next section for discussion of criteria for priority setting). The distribution of the nominated research topics according to the portfolio's characteristics was provided to the committee throughout each step in the voting process. The committee weighed the balance of the portfolio in its deliberations and selection of the final priority CER topics.

The committee selected the following four characteristics for balancing the portfolio after careful consideration of the goals of CER. The committee determined that it is important to have a portfolio balanced in terms of research areas because it did not want to study only those diseases and conditions with the greatest effects on the health of the U.S. population. It determined that it is also important to study rare diseases and conditions that disproportionately and seriously affect subgroups of the population, partly because the scientific opportunity may be greatest for some of these conditions. Similarly, the committee determined that it is essential for the portfolio to be balanced across populations to be studied. The priority CER topics should include populations and subpopulations representing minority, racial and ethnic groups, all genders, and different age groups ranging from infancy to the elderly.

The committee determined that the portfolio should also include a diversity of interventions. Traditionally, much of CER has focused on head-to-head comparisons of pharmaceutical treatments. However, the committee saw great value in extending the concept of comparison to include a variety of interventions, including tests to screen for or monitor diseases (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. surgical vs. radiotherapy for prostate cancer). This diversity

helps ensure that the portfolio covers the entire continuum of health care, including screening and prevention, treatment of acute health problems, chronic health problems, and palliative and end-of-life care. 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.

The committee also decided that the portfolio should include a diversity of methodologies. This is especially important in light of the committee's charge to develop a portfolio of topics that will lead to an appropriate expenditure of the \$400 million for CER in the American Recovery and Reinvestment Act (ARRA) of 2009 (P.L. 111-5). The different methodologies vary widely in terms of resource requirements, time lines, and types of infrastructure necessary to conduct the research. Varying these methodologies in the portfolio ensures that some relatively inexpensive and easy results will be generated early on, and within the scope of ARRA. Performance of randomized controlled trials or prospective observational trials will have to extend well beyond the 2-year focus of ARRA.

CRITERIA CHOSEN FOR PRIORITY SETTING

In addition to the portfolio criteria intended to assess the balance of all the priority CER topics, the committee also concluded that criteria were needed to evaluate the individual nominated research topics. The committee reviewed the criteria used for priority setting by other projects and the two IOM reports discussed below, but it developed its own set of criteria that applied specifically to setting priorities for CER. After careful consideration, the committee recognized two levels of criteria to assess the nominated CER research topics: (1) condition-level criteria, and (2) priority topic-level criteria.

Condition-Level Criteria

The condition-level criteria focus on burden of disease indicators that could be readily obtained by the committee. The committee recognized the importance of selecting priority topics that affected a large portion of the population (prevalence), were the leading causes of death and disease (mortality and morbidity), imposed serious costs on patients, families, payers, and society (costs), and had the greatest differences in treatment used by practitioners (variability). The committee would have also liked to include work loss due to disability as a criterion, but it could not find data to support that criterion within the time frame of the study. Data on the following criteria were provided to the committee for consideration in the prioritizing and voting process:

- *Prevalence*: The number or percentage of people with a specified condition in the United States at a given time (Appendix C, Table C-1).
- *Mortality*: The number or percentage of deaths due to a specified condition in the United States in a given time period (Appendix C, Table C-2).
- *Morbidity*: The extent of illness, injury, or disability in a defined population (Appendix C, Table C-3).
- *Cost*: The total treatment expenses for selected conditions (Appendix C, Table C-4).
- *Variability*: A measure of the dispersion of data. In the context of Appendix C, Table C-5, it refers to the pattern of variation in admissions for specific procedures among hospital referral regions. In the context of Appendix C, Table C-6, it refers to the pattern of variation in admission for treatment of conditions among hospital referral regions.

Priority Topic-Level Criteria

The committee made a distinction between condition-level criteria and the criteria that could be applied to individual topics involving those conditions (Table 4-1). For example, as shown in Appendix C, the prevalence data provided to the committee identified the top 20 conditions for adults and the top five for children. From this information, committee members might determine that a particular condition targeted in a proposed research topic is widespread and so it may be of importance to study; however, they had little or no information on other aspects of the topic such as whether particular procedures, clinical decisions, or delivery models were also prevalent or appropriate for CER. The specific priority topic-level criteria considered by the committee were intended to help assess the particular questions identified in the nominated research topics, not just the conditions and diseases. The priority topic-level criteria used by the committee include the following:

- Appropriateness of topic for CER
 - *Utility for decision making*—Does the proposed topic include populations previously excluded from trials, clinically meaningful comparisons, or patient-important outcomes rather than markers or intermediate outcomes? Does it involve direct, head-to-head comparisons to inform the decisions of daily practice? Is it patient-centered so that it tailors the test or treatment to the specific characteristics of the patient? Will it enhance clinical

- practice decision making by patients and physicians in everyday circumstances and help policy makers?
- *Risks associated with care*—There may be risks as well as benefits associated with particular treatments/methods of care either in current practice or the comparator that should be considered.
 - Information gaps and duplication. CER should address gaps left by existing research. Research gaps for selected topics can be identified by Cochrane or Evidence-based Practice Center (EPC) systematic reviews on the subject, which compare “what we need to know” to make good decisions with “what we know now” from existing studies. The description of gaps should follow the logic of the previously outlined criteria for utility in decision making:
 - *For suggested comparative effectiveness systematic reviews, are there recent EPC or Cochrane reviews on the same subject?*
 - *For suggested CER studies or trials, do recent EPC or Cochrane reviews on the same subject identify the suggested research as needed research (evidence gaps)?*
 - *Have previous studies ignored patients with comorbidities? Does the proposed study explicitly include them?*
 - *Have previous studies ignored patients from special populations? Does the proposed study include them?*
 - *Have previous studies made meaningful comparisons? Does the proposed study include head-to-head comparisons?*
 - *Have previous studies fully explored benefits and harms?*
 - *Is the proposed topic redundant with current research?* Data derived from a check of the short list against www.clinicaltrials.gov and answers to the above questions.
 - *Variability*
 - The data requested from Dartmouth indicate rates of hospitalizations and common procedures with high variability across the country.
 - Health care delivery—Does the proposed study address the effectiveness of different strategies for delivering the intervention? Strategies may include organization characteristics, work patterns, or work processes.
 - Gaps in translation
 - *Moving from research to practice*—Has CER been conducted on the topic and recommendations made, but with limited impact on practice? Will the proposed study be likely to improve the implementation of the recommendations? Or identify improved strategies for research translation?

DATA COLLECTION TO AID TOPIC SELECTION

The committee was unable to collect priority topic-level data relating to the significance of the 1,268 nominated research topics to be assessed initially, and instead, focused mainly on data to support criteria at the condition level.

The committee selected individual data tables to aid in the voting process. The Medical Expenditure Panel Survey (MEPS) (AHRQ, 2009) provided proxy indicators for information on prevalence, morbidity and cost, and the National Vital Statistics Report on mortality (Kung et al., 2008). The Dartmouth Institute for Health Policy and Clinical Practice analyzed clinical practice data according to variation in treatment for medical conditions and surgical procedures at the IOM's request (Wennberg, 2009). Data sources were chosen based on their year of production (with preference given to the most recent reports), representativeness of the whole population, and ability to provide age stratification.

Data pertaining to knowledge gaps (areas of scientific uncertainty in terms of treatment strategies for the population as a whole or for subpopulations) and funding gaps (areas with a dearth of recent or existing research studies) were feasible to use after the first round of voting on the 1,268 nominated topics had narrowed to the list of 145. For the second round of voting, the committee was provided several proxy indicators for knowledge and information gaps, including the most recent systematic reviews as well as the funding source and number of recent and ongoing clinical trials. The AHRQ Effective Health Care Program's issue briefs and the National Institutes of Health's registry of privately and publicly supported clinical trials in the United States and abroad supplied data on perceived knowledge gaps remaining to be addressed. Many of the second-round research topic nominations for CER were not covered in the AHRQ issue briefs, and committee members were informed of the unevenness of the supporting data across topics.

The committee used the criteria and data tables as guided in voting instructions and as summarized in cover sheets for each of the 32 broad research areas. The cover sheets for each research area indicated whether specified conditions within that research area were among the top-ranked conditions by each condition-level criterion (as ranked in the tables in Appendix C), and if the topic was listed by other national priority-setting projects. For instance, in the cardiovascular and peripheral vascular disease category, hypertension and hyperlipidemia were 2 among the top 20 most prevalent diseases across all conditions for all age groups, and hypertension along with heart conditions were 2 of the top 12 diseases according to the morbidity proxy table, number of events, for all ages. Cardiovascular disease including stroke and hypertension were listed among the top priorities

of AHRQ's Effective Health Care Program (Whitlock et al., 2009), Healthy People 2010 (HHS, 2000), and the Cochrane Collaboration (Doyle et al., 2005). The cover sheets were designed to be a quick reference to highlight more specific subcategories or conditions within each broad research area. An example of a cover sheet for cardiovascular and peripheral vascular disease is presented in Appendix D. All 32 cover sheets are available at www.iom.edu/cerpriorities.

The voting instructions for the committee listed and, if necessary, defined the condition-level and priority topic-level criteria for the committee to consider. However, there was no explicit direction on how to weigh criteria, except that members should decide based on their own expertise and preferences.

The selected criteria provided the committee with a framework for their voting decisions. However, individual committee member expertise played an important role in the decision-making process. Consequently, although committee members were instructed to take into account quantitative data such as prevalence, morbidity, and cost where such data were available, the voting process had subjective elements in terms of how each member selected their top priorities.

LESSONS FROM PREVIOUS PRIORITY-SETTING PROCESSES

IOM Reports

For this project, the most relevant IOM reports concerning priority setting, *Priority Areas for National Action* (IOM, 2003) and *Knowing What Works in Health Care* (IOM, 2008), provided the initial basis for the methodology and criteria used by this committee in setting priorities for CER.

In *Priority Areas for National Action*, AHRQ tasked an earlier IOM committee with recommending a list of 20 priority conditions whose improvement would help the nation achieve significant advances in health care quality over the next 5 years, and then with establishing a process and set of criteria for determining those priorities. The study committee chose a framework, initially designed to assess care across the lifespan, developed by the Foundation for Accountability (FACCT, which closed its operations in 2004) to organize all potential high priority conditions (Markle Foundation, 2008). This framework consisted of four "domains of care": preventive, acute, chronic, and palliative; the committee also considered system-wide interventions that would cut across these domains (FAACT, 1997). The goal was to create a final portfolio of priorities for quality improvement that touched on the full continuum of care. Members of that committee nominated most of the topics with the aid of stakeholder input

through presentations at a public workshop and a review of other relevant priority lists (IOM, 2003).

That committee then applied three sets of criteria to the suggested topics. The criteria reflected potential *impact* (disease burden variables), *improvability* (the likelihood the priority would address one of the six quality aims in the 2001 *Quality Chasm* report), and *inclusiveness* (relevance to a broad range of patients, conditions, and health care settings). The committee ranked the topic suggestions within their respective domains of care categories and then determined the complete list, which is shown in Table 4-2 (IOM, 2003).

The committee that produced *Knowing What Works in Health Care* provided further research and recommendations on the topic of setting priorities. In a detailed assessment of methods used by other organizations to identify topics for systematic reviews,¹ the committee found little guidance for designing an optimal priority-setting process. However, it did establish several principles for future priority-setting committees (IOM, 2008):

- The process should be open, transparent, efficient, and timely.
- It should consider how evidence-based practice could help reduce burden of disease.
- It should include cost considerations in the decision-making process.
- Its membership should include people with a broad base of interests and expertise to minimize bias and conflicts of interest.

Knowing What Works in Health Care also identified the most common criteria used in other priority-setting efforts (IOM, 2008):

- Burden of disease (prevalence, disability, mortality, morbidity, etc.)
- Public controversy (uncertainty around the topic and supporting data)
- Cost
- Potential impact
- New evidence that might change previous conclusions
- Existence of an evidence gap
- Unexplained variation in the use of healthcare services

¹ The list of organizations includes the Agency for Healthcare Research and Quality, Blue Cross and Blue Shield Association Technology Evaluation Center, Centers for Medicare & Medicaid, the Cochrane Collaboration, Drug Effectiveness Review Project, Medicare Evidence Development and Coverage Advisory Committee, the National Institute for Health and Clinical Excellence, National Institutes of Health Office of Medical Applications of Research, and the U.S. Preventive Services Task Force.

TABLE 4-2 Criteria and Priorities for Quality Improvement

Criteria	Priority List
Impact —disease burden (disability, mortality, and economic costs affecting patients, families, communities and society)	<ul style="list-style-type: none"> • Asthma • Cancer screening that is evidence-based • Care coordination • Children with special health care needs • Diabetes
Improvability —the likelihood that systemic changes in health system could improve priorities in the six quality aims listed in the <i>Quality Chasm</i> report	<ul style="list-style-type: none"> • End of life with advanced organ system failure • Frailty associated with old age • Hypertension • Immunization
Inclusiveness —equity (across ages, races, gender, and socioeconomic status), representativeness (across spectrum of healthcare conditions); reach (across spectrum of healthcare settings and providers); also, later included four care domains (preventive, acute, chronic, and palliative), or crosscutting	<ul style="list-style-type: none"> • Ischemic heart disease • Major depression • Medication management • Nosocomial infections • Pain control in advanced cancer • Pregnancy and childbirth • Self-management/health literacy • Severe and persistent mental illness • Stroke • Tobacco dependence treatment in adults • Obesity

SOURCE: IOM (2003).

External Priority-Setting Initiatives

In addition to the two IOM reports, the CER committee reviewed the following external priority-setting initiatives to select the condition-level criteria and priority topic-level criteria: AHRQ's Effective Health Care Program, which identified topics for comparative effectiveness systematic reviews (Whitlock et al., 2009); Healthy People 2010, an alliance of national and state public health agencies that developed a list of leading health indicators and priority focus areas to set a prevention agenda for the nation (HHS, 2000); the Cochrane Collaboration, which identified global priorities for Cochrane systematic reviews of public health topics (Doyle et al., 2005); the World Health Organization (WHO) Advisory Committee, which reviewed the literature on priority setting for health care guidelines, recommendations, and technology assessments (Oxman et al., 2006); and the National Quality Forum (NQF), which convened the National Priorities Partnership (NPP) to set national priorities and goals for performance improvement efforts in potentially fruitful areas (NPP, 2008); among others.

These external priority-setting programs identified additional criteria, including appropriateness of a topic for CER research, feasibility of study design, potential for change, and potential risk from inaction (Whitlock et

al., 2009); research that is not duplicative (Doyle et al., 2005); priorities that are likely to improve quality of life and reduce health disparities (HHS, 2000); priorities that address the major challenges of eliminating harm and removing waste (NPP, 2008); and interventions that would likely require systems change (Oxman et al., 2006). Criteria chosen by the priority-setting organizations are summarized in Table 4-3. As described above, the committee incorporated the appropriateness of the topic for CER and information gaps and duplication into the priority topic-level criteria.

The Committee on Comparative Effectiveness Research Prioritization also considered the methodology used by the other priority-setting groups to arrive at its final priority CER topics including the following:

- The creation of a specific taskforce or committee to oversee and ultimately vote on the priority questions
- An invitation for stakeholders to submit comments and priority agendas via written or oral testimony to committee members
- The establishment of explicit priority criteria (and gathering of data sources/information relevant to criteria) on which the committee members were to base their decisions
- A process to refine submitted questions and gain feedback on the revisions
- A recommendation to continuously evaluate and improve upon the inherently dynamic and subjective priority-setting process

TABLE 4-3 A Variety of Priority-Setting Initiatives and Their Selected Criteria

Name Study/ Priority List	Source	Criteria
Identifying, Selecting and Refining Topics for Comparative Effectiveness Systematic Reviews: AHRQ and Effective Health Care Program	AHRQ	<ul style="list-style-type: none"> • <i>Appropriateness</i>—applies to Medicare and/or Medicaid populations, HHS priority condition • <i>Importance</i>—disease burden, cost, strong stakeholder support, uncertainty or controversy surrounding issue • <i>Desirability of New Research/Duplication</i> • <i>Feasibility</i> • <i>Potential Value</i>—potential for significant health and economic impact, change, and risk of inaction

continued

TABLE 4-3 Continud

Name Study/ Priority List	Source	Criteria
Healthy People 2010	U.S. Department of Health and Human Services (HHS)	<ul style="list-style-type: none"> • <i>Goal 1: Increase Quality and Years of Healthy Life</i>—Life expectancy, quality of life: looked at global assessments, healthy days, and years of healthy life • <i>Goal 2: Eliminate Health Disparities</i>—In terms of gender, race and ethnicity, income and education, disability, geographic location, and sexual orientation • <i>Leading Health Indicators considered when choosing focus areas</i>—physical activity, overweight and obesity, tobacco use, substance abuse, responsible sexual behavior, mental health, injury and violence, environmental quality, immunization, access to health care
National Priorities and Goals: Aligning Our Efforts to Transform America's Healthcare	NPP/NQF	<ul style="list-style-type: none"> • <i>Eliminating harm</i> • <i>Eradicating disparities</i> • <i>Reducing disease burden</i> • <i>Removing waste</i>
Improving the Use of Research Evidence in Guideline Development: 2 Priority Setting	WHO Advisory Committee on Health Research	<ul style="list-style-type: none"> • <i>Problems associated with a high burden of illness</i>—in low- and middle-income countries, or new and emerging diseases • <i>No existing guidelines or recommendations of good quality</i> • <i>Feasibility of developing recommendations</i>—that will improve health outcomes, reduce inequities or reduce unnecessary costs if they are implemented • <i>Implementation is feasible</i>—will not exhaustively use available resources, and barriers to change are not likely to be so high they cannot be overcome • <i>Interventions that will likely require systems changes</i> • <i>Interventions where there might be a conflict in choices between individual and societal perspectives</i>

TABLE 4-3 Continued

Name Study/ Priority List	Source	Criteria
Global Priority Setting for Cochrane Systematic Reviews of Health Promotion and Public Health Research	The Cochrane Health Promotion and Public Health Field	<ul style="list-style-type: none"> • <i>Burden of disease, magnitude of problem, urgency</i> • <i>Importance to developing countries</i> • <i>Avoidance of duplication</i> • <i>Opportunity for action</i>
Recommendations for the Framework and Format of Healthy People 2010	Healthy People 2020 (HHS)	<ul style="list-style-type: none"> • <i>The overall burden of the risk factor or disease</i> • <i>The extent the burden may be preventable or reducible</i> • <i>Cost-effectiveness of alternate opportunities</i> • <i>The net health benefit</i> • <i>The synergy of different interventions that target the same disease</i> • <i>The likely timeframe to observe the impact</i> • <i>The potential to reduce health inequities among populations</i> • <i>The willingness of public health, private organizations, and other collaborating entities to address a particular health problem and to accept accountability for convening multisectoral stakeholders to effect changes in these areas.</i>

SOURCES: Doyle et al. (2005); HHS (2000, 2008); NPP (2008); Oxman et al. (2006); Whitlock et al. (2009).

Several groups used a two-step process to arrive at their ultimate list. For example the AHRQ program first decided on broad priority areas and then selected specific research questions that fit in those areas (Whitlock et al., 2009). Similarly, the Cochrane Collaboration first chose a list of eight broad priority topics and then formulated a longer list of more specific review priorities (Doyle et al., 2005).

The committee incorporated the lessons learned by the IOM and external priority-setting projects whenever possible, including maintaining a transparent and systematic process, involving stakeholder input, and using many of their suggested criteria. The committee also recognized that each

priority-setting enterprise has its own unique needs, and so it developed its own priority-setting process and criteria to meet the needs specified in the ARRA legislation.

VOTING PROCEDURES

The committee used three rounds of voting, illustrated in Figure 4-1, to establish the CER priority topics listed in Chapter 5. Each round was conducted using a web-based data entry system. The first round included the 1,268 unique nominated research topics submitted by the public and screened by the committee for nonresponsive and verbatim duplicates (as discussed in Chapter 3). In this round, the committee was divided into five groups and given 3 days to vote. Each group voted on the nominated research topics categorized into several of the 32 unique research areas, with each group voting on approximately 20 percent of the total nominated research topics, and each committee member voting independently. This design was intended to ensure that the leading nominated research topics from each of the 32 research areas were likely to be retained in the next round of voting, thus preserving the balance of the portfolio.

Committee members were given points equal to the number of nominated research topics assigned to their group. They were required to allocate all of their points, and they could give as many as 10 percent of those points to any one topic. This design allowed committee members to indicate the strength of their preference for specific topics. The score for each nominated topic was tallied as a percentage of allocatable points received, because the five groups had an unequal distribution of topics and, thus, of points.

After the initial voting, raw data distributions of scores were reviewed by the committee without knowledge of the topics or portfolio distribution. Of the 1,268 that were voted on, 200 topics received at least 1 percent of the available points and included 60 percent of the topics that received at least one point by any committee member. The committee concluded that the top 200 nominated topics represented a natural statistical break for the second round of voting.

Three clinicians on the committee reviewed these 200 topics again for duplications. Any topic that all three clinicians agreed was a duplicate was removed from consideration for the second round of voting. Fifty-five topics were consolidated in this process. The committee assessed the remaining 145 topics against the portfolio criteria and determined that the portfolio was sufficiently balanced across research areas—only 3 of 32 designated research areas were eliminated (see Table 5-1 in the next chapter).

In the second round of voting, committee members received the scores from the first round of voting for each of the nominated topics, as well as expanded information on research and funding gaps related to those topics.

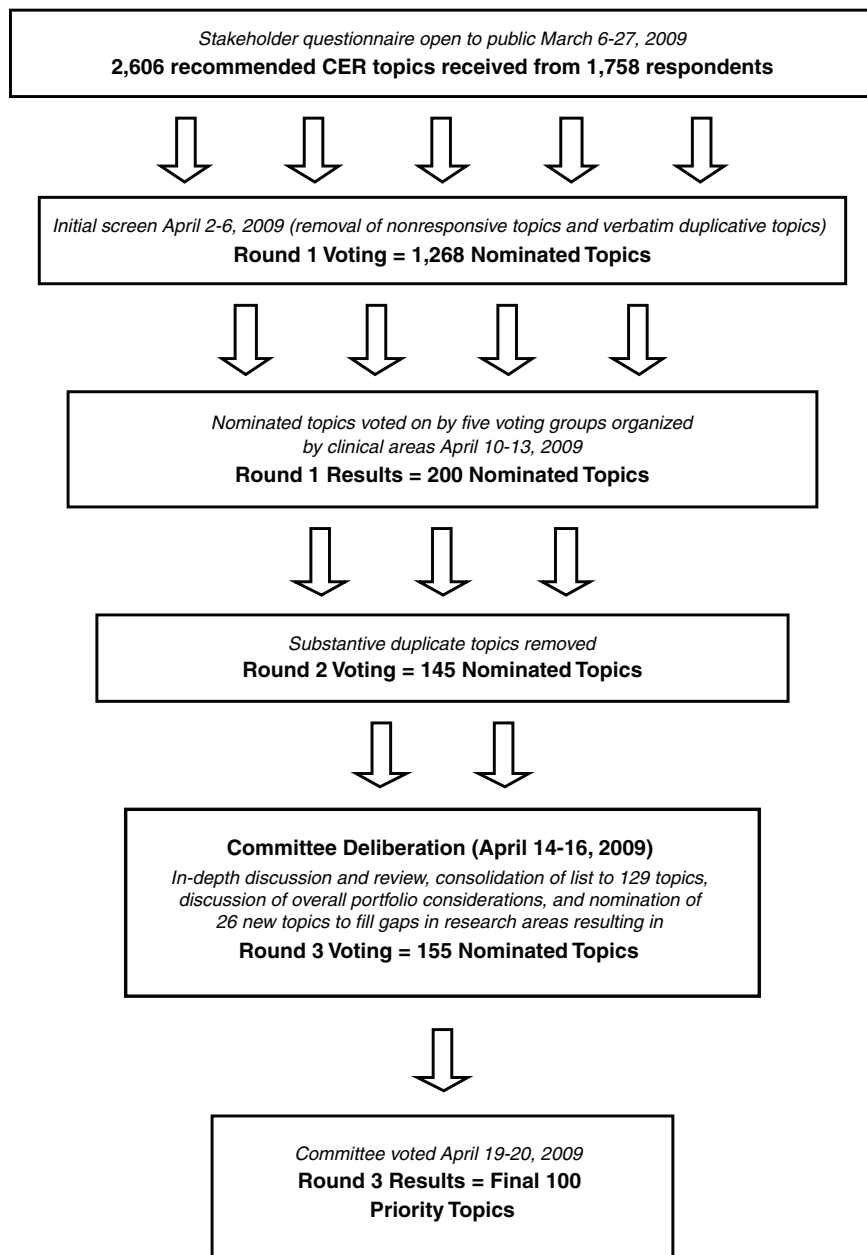


FIGURE 4-1 Voting process and selection of priority topics.

Unlike the first round of voting, in the second round all committee members voted on all 145 remaining nominated topics. Each committee member was allocated 145 total points and could give a maximum of 14 points to any individual topic.

At a 3-day retreat, the entire committee reviewed and discussed the nominated topics in priority order following the second round voting. The leading topics were discussed in detail to clarify the topics. The discussion also allowed committee members to share their opinions and expertise about the individual nominated topics. Through the discussion process, the committee combined 16 of the 145 nominated topics and expanded several of them beyond the scope of their original condition or population. For example, topics addressing mental health issues or obesity in adults were extended to include children and adolescents. Health care delivery topics examining care of a single chronic disease were expanded to cover multiple chronic diseases. In general, the committee decided that it was useful to broaden the nominated research topics at this stage because agencies spending the CER funds will later be issuing their own more detailed requests for proposals as part of the grant applications process, and researchers will define the questions further when applying for those funds.

At the retreat, the committee also reached consensus on topics to fill out 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. Committee members were allocated 300 total points for voting, with a maximum of 30 points allowed for any particular topic. Web-based voting took place over a day and a half. The raw scores were reviewed by the committee, and the distribution of the scores provided a natural cutoff at 100 topics, 18 of which had been proposed by the committee. The top 100 topics all received a mean of at least 1.0 points. Topics that fell below this threshold received zero scores from at least 60 percent of the committee members. The final results of the voting process are presented in Chapter 5.

LESSONS LEARNED FROM THE CURRENT PRIORITIZATION PROCESS AND COMMITTEE RECOMMENDATIONS

The IOM committee developed several recommendations to set future priorities based on the experience of this project.

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

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 evidence is produced and gaps in evidence are diminished, CER will need to go in new directions. New scientific tools and techniques may open opportunities for CER where none previously existed. A continuous process is necessary to update funding priorities as conditions change and the impact of previous CER becomes evident. The criteria used in the prioritization process may also need to be evaluated on a regular basis. The prioritizing body may consider additional criteria, such as evaluating levels of uncertainty and potential for future funding from various stakeholders.

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.

An ongoing process of CER prioritization will need to engage the public more completely. Efficiency requires that representative stakeholder perspectives be engaged at the most critical time points rather than every possible step in the research process. With respect to prioritizing topics, there are two key stages. The first is in setting criteria for choosing topics and balancing the overall portfolio. While the committee has set forth criteria here, these criteria should be revisited to ensure that they reflect the public's goals and values.

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.

“Topic nomination development” is the second critical stage in the prioritization process for public input (Whitlock et al., 2009). Many potentially important nominations delivered through the web-based questionnaire would have benefited from further development before voting so that the voters had a better idea of what motivated the nomination and the nominator and so that other contributors had a chance to expand on the patients, interventions, comparators, and outcomes to be considered by the research. In the future, the topic brief preparation process should be an interactive one in which the prioritizing body gains the perspective of the nominator and other stakeholders to better convey the context and main points of the nomination to the voters.

The process should allow sufficient time to develop robust, consistent

topic briefs for use in voting in order to “level the playing field.” The process should provide background information on the condition, address current practice and policy, and document existing research in order to allow explicit consideration of each topic against pre-specified prioritization criteria.

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 believes that increased transparency of the overall process and documentation of decision making for each topic would allow improved public participation and allow the public to revise and resubmit rejected research suggestions for future consideration. This type of transparency is needed for any ongoing process to be responsive to public concerns and interests and to enhance its legitimacy. Thus, the prioritization process should produce regular reports evaluating its portfolio of potential and selected topics for CER against a variety of criteria, including type of service domain, clinical domain, population characteristics, and other policy priorities such as addressing vulnerable populations and health disparities. 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. Ultimately, any prioritization process for a CER Program will be evaluated by the impact of the funded research on improving health decision making, health outcomes, and reducing unnecessary variation in health care.

REFERENCES

- AHRQ (Agency for Healthcare Research and Quality). 2009. Medical Expenditure Panel Survey. <http://www.meps.ahrq.gov/mepsweb/> (accessed March 10, 2009).
- Doyle, J., E. Waters, D. Yach, D. McQueen, A. De Francisco, T. Stewart, P. Reddy, A. M. Gulmezoglu, G. Galea, and A. Portela. 2005. Global priority setting for Cochrane systematic reviews of health promotion and public health research. *Journal of Epidemiology and Community Health* 59:193-197.
- FAACT. 1997. *The FACCT consumer information framework: Comparative information for better health care decisions* <http://www.facct.org/information.html> (no longer accessible).
- HHS (Department of Health and Human Services). 2000. *Healthy People 2010: Understanding and improving health*. U.S. Government Printing Office. <http://purl.access.gpo.gov/GPO/LPS4217> (accessed April 3, 2009).

- . 2008. Recommendations for the framework and format of Healthy People 2020. http://www.healthypeople.gov/HP2020/advisory/PhaseI/sec5.htm#_Toc211942927 (accessed June 12, 2009).
- IOM (Institute of Medicine). 2003. *Priority areas for national action: Transforming health care quality*. Edited by K. Adams and J. Corrigan. Washington, DC: The National Academies Press.
- . 2008. *Knowing what works in health care: A roadmap for the nation*. Edited by J. Eden, B. Wheatley, B. J. McNeil and H. Sox. Washington, DC: The National Academies Press.
- Kung, H.-C., D. L. Hoyert, J. Xu, S. L. Murphy, and Division of Vital Statistics. 2008. *Deaths: Final data for 2005. National vital statistics reports* National Center for Health Statistics.
- Markle Foundation. 2008. *FACCT legacy documents* <http://www.markle.org/archives/facct/> (accessed May 12, 2009).
- NPP (National Priorities Partnership). 2008. *National priorities and goals*. Washington, DC: National Quality Forum.
- Oxman, A., H. Schunemann, and A. Fretheim. 2006. Improving the use of research evidence in guideline development: 2. Priority setting. *Health Research Policy and Systems* 4(1):14.
- Wennberg, J. E. 2009 (unpublished). *Recommendations to the Institute of Medicine on comparative effectiveness research priorities*. Submitted in response to a request from the Institute of Medicine Committee on Comparative Effectiveness Research Prioritization. The Dartmouth Institute for Health Policy and Clinical Practice.
- Whitlock, E. P., S. A. Lopez, S. Chang, M. Helfand, M. Eder, and N. Floyd. 2009. Identifying, selecting, and refining topics for comparative effectiveness systematic reviews: AHRQ and the effective health care program. <http://effectivehealthcare.ahrq.gov/repFiles/20090427IdentifyingTopics.pdf> (accessed June 5, 2009).

5

Priorities for Study

Abstract: *The Institute of Medicine Committee on Comparative Effectiveness Research Prioritization was charged with developing a portfolio of priority topics that reflected balance across research areas, populations, type of interventions, and methodologies. The final list of 100 priority CER topics includes a large number addressing health care delivery systems, and a large number that consider racial and ethnic disparities. All but 3 of the 32 originally delineated research areas are represented. Similarly, the priority research topics include studies examining various special population categories, including individuals with rare diseases. This chapter presents the full list of priority CER topics.*

As explained in detail in Chapter 1, the Institute of Medicine (IOM) committee's statement of task charged the committee with developing a list of priority comparative effectiveness research (CER) topics and presenting those recommendations for the Secretary to consider. To develop the list, the committee obtained substantial public input (described in Chapter 3) and followed a multistage process of individual and collective deliberation (described in Chapter 4). The final portfolio, described in this chapter, contains 100 priority topics. The first half of the chapter is a "portfolio analysis," which shows the representation of research areas, study populations, comparators, and study methodologies within the final 100 topics. The second half of the chapter presents the specific CER topics prioritized by the committee, together with a description of their relevance.

ASSEMBLING A DIVERSE PORTFOLIO

As described in Chapter 4, the committee utilized the concept of a diverse research portfolio, meaning that the committee's priority topics reflect a balance of CER questions across research area (i.e., disorders by organ systems, specific populations, systems of care), study populations (i.e., men, women, children, minority groups), types of interventions (i.e., comparators, such as surgical or pharmaceutical treatments), and study methodologies (i.e., randomized controlled trials, registry studies, systematic reviews). The committee wanted to ensure that the final list of topics represents not only those diseases and conditions with the greatest effects on the health of the U.S. population, but also that it includes other diseases and conditions that disproportionately and seriously affect subgroups of the population (such as women, minorities, and children and adolescents). In addition, the committee wanted to ensure its priority topics examine a variety of interventions, including studies examining prevention, systems of care, pharmacological treatments, devices, surgery, and monitoring of disease. The committee also sought to achieve balance in the distribution of proposed methodologies so that some answers could be obtained within the 2-year framework specified by the American Recovery and Reinvestment Act (ARRA) of 2009, while other research questions would require a longer timeframe. For example, CER conducted from established databases and from systematic reviews of the current literature holds the potential to provide information relatively rapidly, whereas performance of randomized controlled clinical trials or prospective observational trials would extend well beyond the 2-year focus of the ARRA.

The committee strongly believes that CER should be conducted using “real-world” patients, so that results are readily generalizable across populations. Therefore, it is important that sponsors design CER studies to ensure adequate numbers of all relevant population and patient subgroups, including all genders and patients representing a wide range of races, ethnicities, levels of health literacy, and ages, as well as those with multiple chronic conditions.

The following sections conduct a “portfolio analysis”—an analysis of the distribution of the committee's final 100 priority topics across the portfolio variables, including (1) research areas, (2) study populations, (3) interventions, and (4) study methodologies. A successful portfolio is one that is widely distributed across these dimensions. It is important to recognize that the precision of the information in this section was limited by the procedures that were required to meet the committee's deadline. In the future, thorough topic nomination development requires interaction with the nominators and other stakeholders to sufficiently develop the nomination

and to ensure that the supporting evidence accurately conveys the context and the main points of the nomination (Whitlock et al., 2009).

The following sections display the distribution of the committee's priority list by the portfolio criteria: research area, population, intervention, and methodology. In addition, an interactive electronic file providing search capabilities for priority topics by portfolio criteria is available at www.iom.edu/cerpriorities. This spreadsheet will allow the reader to search, for example, all cardiovascular disease topics affecting women and children, or to study the effectiveness of procedures for their treatment. The search will also indicate which quartile the committee assigned each topic.

DIVERSITY OF RESEARCH AREAS

As described earlier, one of the committee's main methods of categorizing the proposed priority topics was by research area. The committee identified 32 categories of research areas based on disease classification, other patient conditions, and systems of care.¹ However, because many of the conditions co-occur frequently (e.g., obesity and osteoarthritis), and many of the nominated priorities mentioned both a disease and a system of care (e.g., Alzheimer's disease and nursing home care), most of the priority topics could be classified according to two or more research areas.² For example, a topic to study alternative strategies for treating heart disease in African American patients with diabetes could have been classified as cardiovascular disease, endocrinology (which includes diabetes care), and racial and ethnic disparities. In addition, if that research question involved comparing alternative organizational approaches to care, such as coordinated disease management programs or remote monitoring of patients' symptoms, the topic could also be classified under the health care delivery system area. In fact, among the final 100 priority topics, the average number of assignable research categories was three.

To determine whether the committee's priority list was balanced across research areas, each priority was categorized by all of the possible research areas that reasonably described it. For the purposes of this exercise, one area was designated as the primary topic. Table 5-1 and Figure 5-1 show the breakdown of the 100 final priority topics categorized by research area. In Table 5-1, the topic's primary research area is shown with assigned secondary research areas, if reported. Several areas are prominently represented.

¹ Refer to Chapter 3 to see how the committee developed the list of 32 research area categories.

² In the classification exercise that took place at each stage of the IOM committee's deliberations, however, each nominated recommendation was placed into only one area, which was considered its primary research area.

TABLE 5-1 Recommended Research Priorities by Research Area

Category	Primary Research Area	Secondary Research Area	Total
Health Care Delivery Systems*	23	27	50
Racial and Ethnic Disparities	3	26	29
Cardiovascular and Peripheral Vascular Disease	8	13	21
Geriatrics	2	19	21
Functional Limitations and Disabilities	2	20	22
Neurologic Disorders	6	11	17
Psychiatric Disorders	7	10	17
Pediatrics	1	15	16
Endocrinology and Metabolism Disorders	2	12	14
Musculoskeletal Disorders	5	7	12
Oncology and Hematology	6	5	11
Women's Health	5	2	7
Alcoholism, Drug Dependency, and Overdose	2	4	6
Infectious Diseases	3	2	5
Skin Disorders	3	1	4
Birth and Developmental Disorders	3	1	4
Nutrition (including obesity)	3	1	4
Immune System, Connective Tissue, and Joint Disorders	1	3	4
Eyes, Ears, Nose, and Throat Disorders	2	1	3
Trauma, Emergency Medicine, and Critical Care Medicine	1	2	3
Complementary and Alternative Medicine	3	0	3
Kidney and Urinary Tract Disorders	2	1	3
Oral Health	2	1	3
Respiratory Disease	1	2	3
Genetics and Disease	0	3	3
Gastrointestinal System Disorders	1	1	2
Palliative and End-of-Life Care	2	0	2
Sexual Function and Reproductive Disorders	0	2	2
Liver and Biliary Tract Disorders	1	1	2
Total	100	193	293

*Although this category was described as “Safety and Quality of Health Care” in the web-based questionnaire, the category was re-labeled by the committee as “Health Care Delivery Systems” to be more accurate.

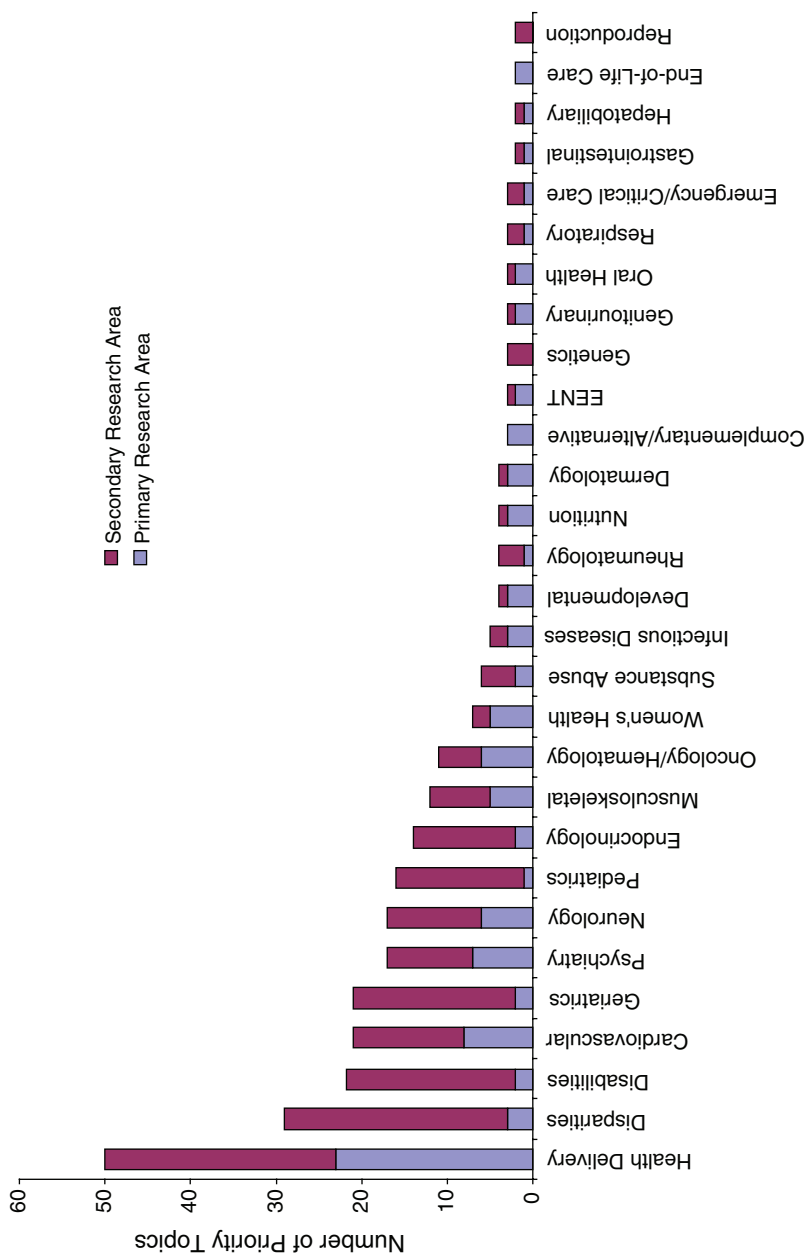


FIGURE 5-1 Distribution of the recommended research priorities by primary and secondary research areas.

Half of all topics involve a comparison to some aspect of the health care delivery system. Research topics categorized in this group focus on comparing *how* or *where* services are provided, rather than *which* services are provided. The prominence of health care delivery systems in the portfolio primarily reflects the interest of the public in this area, as well as the committee's belief that an early investment in CER should focus on learning how to make services more effective. Nearly one-third of the total recommended topics involve research that addresses racial and ethnic disparities and nearly one-fifth address functional limitations and disabilities. Other frequently represented areas are cardiovascular disease, geriatrics, psychiatric disorders, neurologic disorders, and pediatrics.

Twenty-nine out of the original 32 research areas are represented in the final portfolio. The missing categories include medical aspects of bioterrorism, pancreatic disorders, and regenerative medicine. The fact that there are no topics from any of these categories in the final list is less of a reflection of these categories' importance than of the fact that these categories only received 2 nominations out of the total 1,268 topics that entered the first round of voting and that the committee did not score the particular topics nominated within these categories as highly as topics in other categories. The portfolio's inclusion of 29 out of the original 32 research areas suggests that an investment in CER based on the committee's portfolio recommendations would comprehensively explore a broad spectrum of disease. It is interesting to note that, when asked for input, the public responded with recommendations that spanned a full portfolio of research areas.³

DIVERSITY OF POPULATIONS

A balanced portfolio should include a consideration of the demographic characteristics of the populations and subpopulations to be studied, including minority, racial, and ethnic groups; gender; and different age groups ranging from infancy to the elderly. It should also consider less obvious factors that affect health care, such as geographic location, socioeconomic status, educational achievement, and cultural differences; and it should be proportionately representative of those factors. Table 5-2 displays the 100 final priority topics categorized by study population. Many of the nominators of the priority topics selected more than one population as appropriate for the proposed research. Adults, including the elderly and the general population, are the most frequently represented study populations in the committee's portfolio. Other populations well represented in

³ As discussed in Chapter 3, 82 percent of the committee's final priority list were nominated by the public; 18 percent were nominated by the committee during its in-depth discussion of the priority list.

TABLE 5-2 Committee's Recommended Research Priorities by Study Populations

Study Population	Number of Topics
Adults (including elderly)	36
Population at Large (general population)	28
Women	27
Special Populations (e.g., pregnant women, low income, patients with disabilities)	24
Men	22
Children and Adolescents Only	20
Elderly Only	15
Other	12
Long-Term Care	7
Ethnic Subpopulations Only	5
Adults (excluding elderly)	4
Rare Diseases	2
Total	202

NOTE: The total exceeds the total number of priority topics because respondents were allowed to select multiple populations for each topic.

the committee's portfolio are women, special populations (such as pregnant women and low-income families and individuals), men, and children and adolescents.

Based on the answers to the open-ended questions given by the questionnaire respondents, the "other" category in the table encompasses a wide variety of study populations, such as those with chronic conditions, cancer survivors, persons with psychiatric and mental disabilities, and persons at risk of developing heart disease.

DIVERSITY OF INTERVENTIONS

Another component of a balanced portfolio is that it should cover all steps in the trajectory of health care, from prevention and screening to diagnosis and treatment of acute and chronic health problems to palliative and end-of-life care. It should also reflect the full range of care modalities, from behavioral changes to pharmacological treatment to radiation to surgery. Table 5-3 displays the 100 final priority topics categorized by type of intervention or strategy proposed for the CER study. Types of comparators represented in the portfolio range from institutional and organization-based, such as management and delivery of health care, to patient-centered interventions. The patient-centered interventions range from completely

TABLE 5-3 Committee’s Recommended Research Priorities by Types of Intervention

Types of Interventions	Number of Topics
Systems of Care	43
Pharmacological Treatment	36
Standard of Care	33
Behavioral Treatment	29
Prevention	24
Procedures	23
Provider-Patient Relationships	20
Treatment Pathways	19
Testing, Monitoring, and Evaluation	17
Devices	13
Alternative Treatment	9
Other	18
Total	284

NOTE: The total exceeds the total number of priority topics because respondents were allowed to select multiple interventions to be compared for each topic.

noninvasive approaches, such as ways to persuade patients to adopt healthier behavior, to major surgical procedures.

The interventions most strongly represented in the committee’s portfolio are systems of care, pharmacologic treatment, and standard of care comparisons. Other frequently proposed types of interventions include behavioral treatments, disease prevention modalities, medical or surgical procedures (including radiological procedures), provider-patient forms of communication or other features of provider-patient relations, and treatment pathways (or clinical guidelines).

The list includes a broad array of diagnostic and therapeutic actions taken by primary care physicians and specialists. It also includes actions taken by other health professionals, ancillary service providers, administrators, and, importantly, health care leaders—for example, professional associations that develop treatment pathways. The “other” category includes interventions such as complementary care and economic incentives.

DIVERSITY OF STUDY METHODOLOGIES

Table 5-4 displays the division of the 100 final priority topics by study methodology. The four major methodologies identified by the committee as appropriate for CER are well represented on the committee’s portfolio. Thus, the committee’s portfolio provides a list of CER questions that vary

TABLE 5-4 Committee's Recommended Research Priorities by Study Methodology

Methodology	Number of Topics
Randomized Trial	49
Prospective Observational Study	46
Database Research	27
Systematic Review	23
TOTAL	145

NOTE: The total exceeds the total number of priority topics because respondents were allowed to select multiple methodologies for each topic.

widely in terms of resource requirements, timelines, and types of infrastructure necessary to conduct the research. For example, a database study using existing databases could be performed more rapidly and economically than a randomized clinical trial, but its findings and conclusions may be less definitive. The appropriate choice of method depends on the nature of the research, on whether the intervention is currently in use, on whether sufficient data are available to identify a large group of persons receiving the intervention and suitable unbiased comparator groups, and whether a range of patient outcomes is recorded.

INTRODUCTION TO FINAL LIST OF PRIORITY TOPICS

In preparing the list for presentation in this report, the committee refined the wording of each priority topic to fit a common format that indicates the research area, two or more interventions to be compared, the population, and, where appropriate and feasible, the outcomes of interest. The committee did not attempt to change the essence of the research question, or to change or add specific outcomes, nor did the committee attempt to refine the topics by specifying methodologies or comparators that the nominator did not provide. The committee fully anticipates that funding agencies, when preparing their Requests for Applications based on these priority topics, will provide details on the scope of the clinical problem, the current best practices, and the potential alternative approaches. It is ultimately the responsibility of the research teams applying for funding to propose the precise population, comparators, outcomes, and methodologies to be undertaken in the studies attempting to answer the priority questions. Moreover, a single priority topic is likely to generate alternative designs, so the committee's 100 priorities will likely provide the opportunity for many more than 100 specific research studies.

BOX 5-1
Round 3 Voting Procedures

One hundred fifty-five nominated research topics were considered in the committee's third round of voting. Each committee member was allocated 300 total points to distribute among the 155 topics but could not award more than 30 points to any one topic. The mean score for each topic was calculated by dividing the total points that each topic received by the number of committee members voting. The raw scores were reviewed by the committee, and the distribution of the scores provided a natural cutoff at 100 topics. The top 100 topics all received a mean of at least 1.0 points.

TABLE 5-5 Results of the IOM Committee's Final Vote for Priority Topics, by Quartile

Quartile	Mean Score	Standard Deviation	Range	
			Low	High
1	4.6	1.0	3.5	7.4
2	2.9	0.3	2.5	3.4
3	2.0	0.3	1.5	2.4
4	1.3	0.1	1.0	1.4

The voting process (described in detail in Chapter 4) introduced a substantial degree of subjectivity and variable weighting of topics. The committee felt that this imprecision reduced the reliability of relative rankings. Therefore, the 100 priority topics are presented grouped into quartiles, listed alphabetically by primary area of research.⁴ The first quartile contains all topics with a mean score between 3.5 and 7.4 (see Box 5-1 for a brief recap of how the voting was conducted). The second quartile contains all topics with a mean score between 2.5 and 3.5. The third quartile contains all topics with a mean score between 1.5 and 2.5. The fourth quartile contains all topics with a mean score between 1 and 1.5. Refer to Table 5-5 to see the variability and ranges of the committee's votes across quartile. Table 5-6 displays the 100 priority topics by quartile. The medical terminology used in the list of priorities is defined in Appendix E.

⁴ Note that 55 of the 155 nominated recommendations that appeared on the final ballot did not score high enough to be included in the final list. These 55 items are not represented in the quartiles.

TABLE 5-6 Final List of Priority Topics, by Quartile Ratings
**display within quartile does not indicate priority rank—topics are listed alphabetically by primary research area*

First Quartile (listed alphabetically by primary research area)	
CAD	Compare the effectiveness of treatment strategies for atrial fibrillation including surgery, catheter ablation, and pharmacologic treatment.
DIS	Compare the effectiveness of the different treatments (e.g., assistive listening devices, cochlear implants, electric-acoustic devices, habilitation and rehabilitation methods [auditory/oral, sign language, and total communication]) for hearing loss in children and adults, especially individuals with diverse cultural, language, medical, and developmental backgrounds.
ENDO	Compare the effectiveness of primary prevention methods, such as exercise and balance training, versus clinical treatments in preventing falls in older adults at varying degrees of risk.
GI	Compare the effectiveness of upper endoscopy utilization and frequency for patients with gastroesophageal reflux disease on morbidity, quality of life, and diagnosis of esophageal adenocarcinoma.
HCDS	Compare the effectiveness of dissemination and translation techniques to facilitate the use of CER by patients, clinicians, payers, and others.
HCDS	Compare the effectiveness of comprehensive care coordination programs, such as the medical home, and usual care in managing children and adults with severe chronic disease, especially in populations with known health disparities.
IMUN	Compare the effectiveness of different strategies of introducing biologics into the treatment algorithm for inflammatory diseases, including Crohn's disease, ulcerative colitis, rheumatoid arthritis, and psoriatic arthritis.
INFID	Compare the effectiveness of various screening, prophylaxis, and treatment interventions in eradicating methicillin resistant <i>Staphylococcus aureus</i> (MRSA) in communities, institutions, and hospitals.
INFID	Compare the effectiveness of strategies (e.g., bio-patches, reducing central line entry, chlorhexidine for all line entries, antibiotic impregnated catheters, treating all line entries via a sterile field) for reducing health care associated infections (HAI), including catheter-associated bloodstream infection, ventilator associated pneumonia, and surgical site infections in children and adults.
KUT	Compare the effectiveness of management strategies for localized prostate cancer (e.g., active surveillance, radical prostatectomy [conventional, robotic, and laparoscopic], and radiotherapy [conformal, brachytherapy, proton-beam, and intensity-modulated radiotherapy]) on survival, recurrence, side effects, quality of life, and costs.

continued

TABLE 5-6 Continued

MS	Establish a prospective registry to compare the effectiveness of treatment strategies for low back pain without neurological deficit or spinal deformity.
NEURO	Compare the effectiveness and costs of alternative detection and management strategies (e.g., pharmacologic treatment, social/family support, combined pharmacologic and social/family support) for dementia in community-dwelling individuals and their caregivers.
NEURO	Compare the effectiveness of pharmacologic and non-pharmacologic treatments in managing behavioral disorders in people with Alzheimer's disease and other dementias in home and institutional settings.
NUTR	Compare the effectiveness of school-based interventions involving meal programs, vending machines, and physical education, at different levels of intensity, in preventing and treating overweight and obesity in children and adolescents.
NUTR	Compare the effectiveness of various strategies (e.g., clinical interventions, selected social interventions [such as improving the built environment in communities and making healthy foods more available], combined clinical and social interventions) to prevent obesity, hypertension, diabetes, and heart disease in at-risk populations such as the urban poor and American Indians.
ONC	Compare the effectiveness of management strategies for ductal carcinoma in situ (DCIS).
ONC	Compare the effectiveness of imaging technologies in diagnosing, staging, and monitoring patients with cancer including positron emission tomography (PET), magnetic resonance imaging (MRI), and computed tomography (CT).
ONC	Compare the effectiveness of genetic and biomarker testing and usual care in preventing and treating breast, colorectal, prostate, lung, and ovarian cancer, and possibly other clinical conditions for which promising biomarkers exist.
ORAL	Compare the effectiveness of the various delivery models (e.g., primary care, dental offices, schools, mobile vans) in preventing dental caries in children.
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.

TABLE 5-6 Continued

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.
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.

continued

TABLE 5-6 Continued

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.
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.

TABLE 5-6 Continued

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.
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.

continued

TABLE 5-6 Continued

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.
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.

TABLE 5-6 Continued

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.
PSYCH	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.
PSYCH	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.

continued

TABLE 5-6 Continued

RED	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.
SKIN	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.
Fourth Quartile (listed alphabetically by primary research area)	
ADDO	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.
CAD	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.
CAD	Compare the effectiveness of anticoagulant therapies (e.g., low-intensity warfarin, aspirin, injectable anticoagulants) for patients undergoing hip or knee arthroplasty surgery.
DIS	Compare the effectiveness of focused intense periodic therapy and usual weekly therapy in managing cerebral palsy in children.
ENDO	Compare the effectiveness of different disease management strategies in improving the adherence to and value of pharmacologic treatments for the elderly.
HCDS	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.
HCDS	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.
HCDS	Compare the effectiveness of minimally invasive abdominal surgery and open surgical procedures on post-operative infections, pain management, and recuperative requirements.
HCDS	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.

TABLE 5-6 Continued

HCDS	Compare the effectiveness of diagnostic imaging performed by non-radiologists and radiologists.
HCDS	Compare the effectiveness of different techniques (e.g., audio, visual, written) for informing patients about proposed treatments during the process of informed consent.
HCDS	Compare the effectiveness of different disease management strategies for activating patients with chronic disease.
HCDS	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.
INFID	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).
MS	Compare the effectiveness of different treatment strategies in the prevention of progression and disability from osteoarthritis.
MS	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.
NEURO	Compare the effectiveness of different treatment strategies on the frequency and lost productivity in people with chronic, frequent migraine headaches.
NEURO	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.
ONC	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.
PELC	Compare the effectiveness of hospital-based palliative care and usual care on patient-reported outcomes and cost.
PSYCH	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.

continued

TABLE 5-6 Continued

PSYCH	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.
PSYCH	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.
SKIN	Compare the effectiveness of different long-term treatments for acne.
WH	Compare the effectiveness of different strategies for promoting breastfeeding among low-income African American women.

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; IMUN = Immune System, Connective Tissue, and Joint Disorders; INFID = 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.

DISCUSSION OF THE PRIORITY TOPICS BY RESEARCH AREA

The following discussion presents the items contained in the final list of 100 priority topics, grouped by primary research area. The importance of the research area is explained, with reference to the criteria used by the IOM committee members in voting.

For voting purposes, each nominated priority topic was assigned to a primary research area.⁵ The remainder of this section presents the priority topics by research areas. The areas containing the most topics are presented first.

⁵ As discussed in Chapter 4, the committee's subgroup reviewed all of the nominated priorities and assigned each topic to a primary research area.

Health Care Delivery Systems⁶

Almost one-fourth of the committee's recommended priority topics are classified primarily in the health care delivery system (HCDS) research area. This is a broad category that includes topics related to dissemination of CER study results; patient decision making, health behavior and care management, comparing settings of care, and utilization of surgical, radiological, and medical procedures (Table 5-7). Different dissemination techniques are proposed for study (HCDS-A) to ensure that interventions are widely adopted in practice once CER studies prove them effective. Five priority topics focus on patient decision making (HCDS-B-F) involving decision support tools and other mechanisms, such as electronic health records, to help patients make informed choices about their care. Health behaviors, such as smoking, are the subject of four topics (HCDS-G-J), which involve disease management (a comprehensive approach to caring for patients with chronic diseases), clinical guidelines (as followed by both clinicians and patients), information about genetic biomarkers and their impact on patient choice of diagnostic and therapeutic approaches, and economic incentives to adopt a healthier lifestyle. Health care management (HCDS-K-P) specifically addresses quality improvement, post-hospital transition support, hospital formularies for medical devices, comprehensive care coordination, population-based "accountable care," and certain health system strategies (such as revising health insurance policies). Settings of care topics (HCDS-Q-S) address remote patient monitoring, care that is not structured around office visits to physicians, including community and home-based care for elderly and chronic disease patients. Certain procedures included in the health care delivery system research area (HCDS-T-W) address robotic surgery, minimally invasive surgery, scanning and imaging performed by physicians other than radiologists, and methods of controlling hypertension.

Other groups have set a high priority on studying health care delivery topics. Several aspects of this expansive topic were identified as important by *Healthy People 2010*, the National Quality Forum, and the Cochrane Collaboration (Doyle et al., 2005; HHS, 2000; NPP, 2008). These aspects include access to quality health services, education and community-based programs, environmental health, food safety, health communication, medical product safety, occupational safety and health, public health infrastructure, safety and reliability of the health care system, integration and coordination of care, overuse and misuse of care, and organizational capacity.

The large number of recommended topics addressing health care and delivery reflects the dramatic variability of care from region to region, the

⁶ Described in the questionnaire as "Safety and Quality of Health Care."

TABLE 5-7 Health Care Delivery Systems Priority Topics

HCDS-A	Compare the effectiveness of dissemination and translation techniques to facilitate the use of CER by patients, clinicians, payers, and others.
HCDS-B	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-C	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-D	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.
HCDS-E	Compare the effectiveness of different techniques (e.g., audio, visual, written) for informing patients about proposed treatments during the process of informed consent.
HCDS-F	Compare the effectiveness of strategies for enhancing patients' adherence to medication regimens.
HCDS-G	Compare the effectiveness of different disease management strategies for activating patients with chronic disease.
HCDS-H	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.
HCDS-I	Compare the effectiveness of adding information about new biomarkers (including genetic information) with standard care in motivating behavior change and improving clinical outcomes.
HCDS-J	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.
HCDS-K	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.

TABLE 5-7 Continued

HCDS-L	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-M	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-N	Compare the effectiveness of comprehensive care coordination programs, such as the medical home, and usual care in managing children and adults with severe chronic disease, especially in populations with known health disparities.
HCDS-O	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-P	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).
HCDS-Q	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-R	Compare the effectiveness of different residential settings (e.g., home care, nursing home, group home) in caring for elderly patients with functional impairments.
HCDS-S	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.
HCDS-T	Compare the effectiveness of robotic assistance surgery and conventional surgery for common operations, such as prostatectomies.
HCDS-U	Compare the effectiveness of minimally invasive abdominal surgery and open surgical procedures on post-operative infections, pain management, and recuperative requirements.
HCDS-V	Compare the effectiveness of diagnostic imaging performed by non-radiologists and radiologists.
HCDS-W	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.

lack of clarity of what constitutes best practice, and the desire to identify optimal systems for providing health care.

Cardiovascular and Peripheral Vascular Disease

Cardiovascular and Peripheral Vascular disease was the second-ranked topic category among the committee's top 100 priority topics. Diseases of the heart were ranked as the leading cause of death in 2005 according to the Centers for Disease Control and Prevention's (CDC's) National Vital Statistics Reports (Kung et al., 2008). Such diseases are associated with multiple comorbidities that are becoming increasingly prevalent, such as diabetes and obesity. The final priority list had eight topics (Table 5-8) dealing with ischemic heart disease (CAD-A–D) and heart failure (CAD-E), which are among the leading causes of death in all age groups (Kung et al., 2008) together with cardiac arrhythmias (CAD-F), which are among the most variably treated conditions (Wennberg, 2009). In addition, the AHRQ Effective Health Care program, *Healthy People 2010*, and the Cochrane Collaboration rank cardiovascular disease among the highest national priorities for health (Doyle et al., 2005; HHS, 2000; Whitlock et al., 2009). The committee's list also had two topics that focused on the treatment and management of peripheral vascular disorders (CAD-G–H).

Psychiatric Disorders

Across the nation, the prevalence of mental health disorders is high, and the cost of treating such disorders is substantial. The committee recommended that CER address several important psychiatric disorders (Table 5-9). AHRQ's Effective Health Care Program, *Healthy People 2010*, and the Cochrane Collaboration agree that mental health disorders are a priority research area for the nation (Doyle et al., 2005; HHS, 2000; Whitlock et al., 2009). Three topics address various strategies for managing and treating mental health disorders (ranked among the most prevalent, the most costly, and the leading causes of morbidity across all age groups) (AHRQ, 2009a,c; Kung et al., 2008) by specifically studying location of care, provider training, and various pharmacologic treatments (PSYCH-A–C). Depression contributes to suicidal ideation and suicide and is one of the leading causes of mortality across all age groups (Kung et al., 2008). The final list includes two topics addressing depression (PSYCH-D–E), and two that address early mortality (PSYCH-F) and suicide (PSYCH-G).

TABLE 5-8 Cardiovascular and Peripheral Vascular Diseases Priority Topics

CAD-A	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-B	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-C	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.
CAD-D	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.
CAD-E	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-F	Compare the effectiveness of treatment strategies for atrial fibrillation including surgery, catheter ablation, and pharmacologic treatment.
CAD-G	Compare the effectiveness of treatment strategies for vascular claudication (e.g., medical optimization, smoking cessation, exercise, catheter-based treatment, open surgical bypass).
CAD-H	Compare the effectiveness of anticoagulant therapies (e.g., low-intensity warfarin, aspirin, injectable anticoagulants) for patients undergoing hip or knee arthroplasty surgery.

Neurologic Disorders

The final priority list includes six topics in the area of neurologic disorders (Table 5-10). These address imaging used for diagnosing neurologic conditions (NEURO-A), treatment of headaches (NEURO-B), multiple sclerosis (NEURO-C), epilepsy (NEURO-D), and the detection, treatment, and management of dementia (NEURO-E) and Alzheimer's disease (NEURO-F). Epilepsy is one of the most costly disorders affecting adolescents (AHRQ, 2009a), while dementias disproportionately affect the elderly, and are considered national priorities by the AHRQ Effective Health Care Program (Whitlock et al., 2009).

TABLE 5-9 Psychiatric Disorders Priority Topics

PSYCH-A	Compare the effectiveness of wraparound home and community-based services and residential treatment in managing serious emotional disorders in children and adults.
PSYCH-B	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.
PSYCH-C	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.
PSYCH-D	Compare the effectiveness of pharmacologic treatment and behavioral interventions in managing major depressive disorders in adolescents and adults in diverse treatment settings.
PSYCH-E	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.
PSYCH-F	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.
PSYCH-G	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.

Oncology and Hematology

Cancer is a leading cause of death and among the most costly conditions to treat (AHRQ, 2009a; Kung et al., 2008). Cancer is also listed as a national priority by the AHRQ Effective Health Care Program and *Healthy People 2010* (HHS, 2000; Whitlock et al., 2009). The final priority list includes six topics in this research area (Table 5-11). These include two topics involving screening technologies for colorectal and breast cancer (ONC-A–B). Breast cancer is among the most variably treated diseases, due in part to the large number of subtypes of breast cancer (Wennberg, 2009). One topic specifically addresses strategies for managing one of those

TABLE 5-10 Neurologic Disorders Priority Topics

NEURO-A	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-B	Compare the effectiveness of different treatment strategies on the frequency and lost productivity in people with chronic, frequent migraine headaches.
NEURO-C	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.
NEURO-D	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.
NEURO-E	Compare the effectiveness and costs of alternative detection and management strategies (e.g., pharmacologic treatment, social/family support, combined pharmacologic and social/family support) for dementia in community-dwelling individuals and their caregivers.
NEURO-F	Compare the effectiveness of pharmacologic and non-pharmacologic treatments in managing behavioral disorders in people with Alzheimer's disease and other dementias in home and institutional settings.

subtypes, ductal carcinoma in situ (ONC-C). The topics also address the use of imaging technologies for diagnosing, staging, and monitoring all cancers (ONC-D), the use of biomarker analysis in risk assessment and treatment strategies for common cancers (ONC-E), and comparing treatment strategies for liver metastases (ONC-F).

Women's Health

Three of the five priority topics in the area of women's health emphasize conditions of particular importance among minority and underserved populations (Table 5-12). One topic addresses the prevention of unplanned pregnancies (WH-A), focusing on the effectiveness of strategies to expand access to care and systems of health care delivery. One topic focuses on alternative interventions to ensure healthy pregnancies and manage risky pregnancies in minority populations, including behavioral interventions to reduce infant mortality, preterm birth, and low birth weight (WH-B). One topic examines the optimal use of ultrasound during pregnancy (WH-C). The use of ultrasound scanning throughout gestation in both normal and

TABLE 5-11 Oncology and Hematology Priority Topics

ONC-A	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-B	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.
ONC-C	Compare the effectiveness of management strategies for ductal carcinoma in situ (DCIS).
ONC-D	Compare the effectiveness of imaging technologies in diagnosing, staging, and monitoring patients with cancer including positron emission tomography (PET), magnetic resonance imaging (MRI), and computed tomography (CT).
ONC-E	Compare the effectiveness of genetic and biomarker testing and usual care in preventing and treating breast, colorectal, prostate, lung, and ovarian cancer, and possibly other clinical conditions for which promising biomarkers exist.
ONC-F	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.

TABLE 5-12 Women's Health Priority Topics

WH-A	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).
WH-B	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-C	Compare the effectiveness and outcomes of care with obstetric ultrasound studies and care without the use of ultrasound in normal pregnancies.
WH-D	Compare the effectiveness of birthing care in freestanding birth centers and usual care of childbearing women at low and moderate risk.
WH-E	Compare the effectiveness of different strategies for promoting breastfeeding among low-income African American women.

high-risk pregnancies is highly variable, and it is not yet known whether frequency of use affects pregnancy outcomes or safety. One topic addresses the impact of birthing location on outcomes (WH-D) and, finally, the committee recommended examination of programs to promote breastfeeding in African American women (WH-E). Topics related to metabolic bone disease and cardiovascular disease as they affect women are discussed within those specific research areas.

Musculoskeletal Disorders

Although musculoskeletal disorders produce a very broad range of health problems, the committee's topics focused on two primary disorders: (1) neck and back pain, and (2) osteoarthritis, both considered to be priorities in *Healthy People 2010* (HHS, 2000). The committee recommended four priorities focusing on back problems (Table 5-13), which are listed among the most prevalent, most costly, most variable, and most morbid conditions (AHRQ, 2009a,b,c; Wennberg, 2009). Two of these topics focus on management and treatment strategies for low back pain and cervical spondylotic myelopathy (compression of the spinal cord) (MS-A–B), including identification of patient-specific biomarkers to help predict outcome and inform treatment strategies. The others focus on surgical and nonsurgical treatment strategies for cervical disc and neck pain (MS-C–D). The remaining topic in this research area addresses interventions to prevent disability and progression of osteoarthritis (MS-E).

TABLE 5-13 Musculoskeletal Disorders Priority Topics

MS-A	Establish a prospective registry to compare the effectiveness of treatment strategies for low back pain without neurological deficit or spinal deformity.
MS-B	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.
MS-C	Compare the effectiveness of treatment strategies (e.g., artificial cervical discs, spinal fusion, pharmacologic treatment with physical therapy) for cervical disc and neck pain.
MS-D	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.
MS-E	Compare the effectiveness of different treatment strategies in the prevention of progression and disability from osteoarthritis.

Infectious Diseases and Liver and Biliary Tract Disorders

Infectious diseases carry risks for infected patients and also constitute a significant public threat because they can be transmitted from person to person through a variety of mechanisms. Once detected, effective treatments can be applied and transmission of many infectious diseases can be mitigated. The committee's topics focus on screening for detection, interventions to reduce transmission, and clinical management of chronic infectious diseases (Table 5-14). The specific diseases highlighted by the committee's topics include methicillin resistant *Staphylococcus aureus* (MRSA) (INFD-A), hepatitis C (INFD-B), human immunodeficiency virus (HIV) (INFD-C), and more generally hospital acquired infections (HAI) (INFD-D). Hospital acquired infections can be deadly if not treated properly—in fact, septicemia and pneumonia, two diseases commonly transmitted in hospital settings are among the most variably treated conditions according to the Dartmouth Atlas (Wennberg, 2009). Finding effective methods to reduce such infections is critically important to the health of the nation. Chronic infections with HIV and hepatitis C can now be treated so that people live decades. However, identifying optimal treatment strategies, particularly in African American populations and at-risk populations, such as intravenous drug users, require more research. Both infectious diseases generally, and HIV/AIDS in particular, are listed by AHRQ's Effective

TABLE 5-14 Infectious Disease and Liver and Biliary Tract Disorder Priority Topics

INFD-A	Compare the effectiveness of various screening, prophylaxis, and treatment interventions in eradicating methicillin resistant <i>Staphylococcus aureus</i> (MRSA) in communities, institutions, and hospitals.
INFD-B	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).
INFD-C	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.
INFD-D	Compare the effectiveness of strategies (e.g., bio-patches, reducing central line entry, chlorhexidine for all line entries, antibiotic impregnated catheters, treating all line entries via a sterile field) for reducing health care associated infections (HAI), including catheter-associated bloodstream infection, ventilator associated pneumonia, and surgical site infections in children and adults.

Health Care Program and *Healthy People 2010* as conditions of national importance (HHS, 2000; Whitlock et al., 2009).

Endocrinology and Metabolism Disorders and Geriatrics

Diabetes, which ranks among the most prevalent and most costly diseases throughout the nation, is associated with multiple comorbidities including heart disease, stroke, and obesity (AHRQ, 2009a,c). In addition, it is among the leading causes of morbidity and mortality (AHRQ, 2009b; Kung et al., 2008). Determining the effectiveness and cost effectiveness of alternative strategies to treat type 2 diabetes in adolescents and adults has the potential to dramatically improve health and reduce health care costs across the country. As such, the committee recommended it as a priority (ENDO-A), as did AHRQ's Effective Health Care Program and *Healthy People 2010* (AHRQ Effective Health Care Program, 2009; HHS, 2000) (Table 5-15).

As the baby boomer generation continues to age, it will be important to determine the effectiveness of strategies to reduce hip and vertebral fractures in patients both with and without osteopenia and osteoporosis. The committee concluded that falls, which are a contributing factor to fractures, should also be among its list of national priorities (ENDO-B-C).

Many older Americans take multiple medications on a routine basis. The committee recommends performing studies to evaluate the impact of

TABLE 5-15 Endocrinology and Metabolism Disorders and Geriatric Priority Topics

ENDO-A	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.
ENDO-B	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.
ENDO-C	Compare the effectiveness of primary prevention methods, such as exercise and balance training, versus clinical treatments in preventing falls in older adults at varying degrees of risk.
ENDO-D	Compare the effectiveness of different disease management strategies in improving the adherence to and value of pharmacologic treatments for the elderly.

disease management strategies on the efficiency and value of pharmacological treatments (ENDO-D). There are multiple other topics that affect the elderly population; these topics are listed according to the specific organ system or disease area to which they pertain.

Birth and Developmental Disorders

The uncertainty surrounding the root causes of social-emotional disorders in infants and toddlers, as well as autism spectrum disorder, has resulted in a lack of effective treatment options for these individuals. As a result, AHRQ's Effective Health Care Program recommended this as a national priority area for CER (Whitlock et al., 2009). The final list includes two priority topics focused on identifying effective treatment strategies for these disorders (BDEV-A–B) (Table 5-16). With the remarkable improvement in survival and attendant costs for premature infants, the impact of support programs on child and family outcomes after a child is discharged from a neonatal intensive care unit (NICU) (BDEV-C) was felt to be of significant value. For specific topics related to pregnancy, refer to the Women's Health category.

Complementary and Alternative Medicine

The widespread use of complementary and alternative methodologies (including yoga, meditation, acupuncture, and nutraceuticals [CAM-A–C]) in managing a broad array of disorders (e.g., anxiety and depression, pain, cardiovascular risk factors, chronic diseases, other prevalent conditions)

TABLE 5-16 Birth and Developmental Disorders Priority Topics

BDEV-A	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-B	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-C	Compare the effectiveness of diverse models of comprehensive support services for infants and their families following discharge from a neonatal intensive care unit.

TABLE 5-17 Complementary and Alternative Medicine Priority Topics

CAM-A	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.
CAM-B	Compare the effectiveness of acupuncture for various indications using a cluster randomized trial.
CAM-C	Compare the effectiveness of dietary supplements (nutriceuticals) and usual care in the treatment of selected high-prevalence conditions.

provides the impetus to compare their effectiveness to more conventional approaches to care (Table 5-17).

Nutrition

Obesity is a growing epidemic with medical consequences that extend to multiple chronic conditions, such as diabetes, hypertension, heart disease, and arthritis. Within the medical community, there is currently uncertainty regarding effective strategies for preventing and treating obesity. The committee recommended priorities that compare strategies for improving social conditions to reduce obesity (NUTR-A), including various school policies (NUTR-B) (Table 5-18). Both of these priorities include a focus on populations with varying risk rates. Identifying effective methods for treating obese populations could significantly improve health in this country. As such, the committee recommends comparing the effectiveness of surgical procedures, such as bariatric surgery (gastric bypass), behavior modification, and medication (NUTR-C).

Racial and Ethnic Disparities

Disparities in access to care and in clinical outcomes between different populations were of considerable concern for the committee. Some minority populations, such as African Americans, Asian Pacific Islanders, Latinos, and Native Americans, have higher rates of chronic diseases and also experience greater barriers to obtaining care. Together, these factors contribute to creating disparities in health status and clinical outcomes. The committee recommends comparing the effectiveness of several strategies aimed at reducing these disparities, including community-based and multi-level interventions (RED-A), providing literacy sensitive disease management programs (RED-B), and strategies to improve engagement and retention (RED-C) (Table 5-19).

TABLE 5-18 Nutrition Priority Topics

NUTR-A	Compare the effectiveness of various strategies (e.g., clinical interventions, selected social interventions [such as improving the built environment in communities and making healthy foods more available], combined clinical and social interventions) to prevent obesity, hypertension, diabetes, and heart disease in at-risk populations such as the urban poor and American Indians.
NUTR-B	Compare the effectiveness of school-based interventions involving meal programs, vending machines, and physical education, at different levels of intensity, in preventing and treating overweight and obesity in children and adolescents.
NUTR-C	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.

Skin Disorders

Skin disorders across the country are widespread, cause a high degree of morbidity, and are among the most costly disorders in children and adolescents between ages 1 and 17 (AHRQ, 2009a,b,c). The committee's priorities on skin disorders include chronic conditions such as lower extremity wounds (common complications in patients with diabetes, peripheral vascular disease, and paralysis) (SKIN-A), and acne—specifically comparing the long-term safety and effectiveness of alternative treatments (SKIN-B) (Table 5-20). Another topic focused on reducing skin disease and comparing treatments to improve quality of life for chronic psoriatic disease (SKIN-C).

TABLE 5-19 Race and Ethnic Disparities Priority Topics

RED-A	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-B	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).
RED-C	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.

TABLE 5-20 Skin Disorders Priority Topics

SKIN-A	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.
SKIN-B	Compare the effectiveness of different long-term treatments for acne.
SKIN-C	Compare the effectiveness (including effects on quality of life) of treatment strategies (e.g., topical steroids, ultraviolet light, methotrexate, biologic response modifiers) for psoriasis.

Alcoholism, Drug Dependency, and Overdose

The harms of tobacco smoking are well known and well documented. Yet, roughly one-fifth of the nation's population continues to smoke. The committee recommended that a national priority for comparative effectiveness should be to examine alternative smoking cessation strategies in understudied populations such as minorities, individuals with mental illness, and adolescents (ADDO-A) (Table 5-21). The Cochrane Collaboration and *Healthy People 2010* also include tobacco use as national priorities (Doyle et al., 2005; HHS, 2000).

The increasing prevalence of abuse of and dependency on pain medications led the committee to recommend an examination of treatment and prescribing practices to reduce substance dependence for patients with non-cancer chronic pain and acute pain (ADDO-B).

Functional Limitations and Disabilities

While many of the committee's priority topics affect patients with disabilities, the following topics specifically address two populations: (1) the

TABLE 5-21 Alcoholism, Drug Dependency, and Overdose Priority Topics

ADDO-A	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.
ADDO-B	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.

TABLE 5-22 Functional Limitations and Disability Priority Topics

DIS-A	Compare the effectiveness of the different treatments (e.g., assistive listening devices, cochlear implants, electric-acoustic devices, habilitation and rehabilitation methods [auditory/oral, sign language, and total communication]) for hearing loss in children and adults, especially individuals with diverse cultural, language, medical, and developmental backgrounds.
DIS-B	Compare the effectiveness of focused intense periodic therapy and usual weekly therapy in managing cerebral palsy in children.

hearing-impaired, and (2) children with cerebral palsy (Table 5-22). The committee recommended one priority focus on treatment strategies for hearing loss among those with diverse cultural/linguistic and medical/developmental backgrounds (DIS-A) and another on usual care compared to focused and intense periodic therapy sessions to manage symptoms related to cerebral palsy (DIS-B).

Eyes, Ears, Nose, and Throat Disorders

The committee included two topics on eye disorders: (1) comparing the effectiveness of alternative treatment strategies for diabetic retinopathy, macular degeneration, and retinal vein occlusion (EENT-A), and (2) comparing strategies for treatment of primary open-angle glaucoma (EENT-B), including a focus on minority populations (Table 5-23).

Kidney and Urinary Tract Disorders

The committee identified prostate cancer and renal replacement therapies as priority areas for comparative effectiveness research (Table 5-24). Because prostate cancer is the second leading cause of cancer death in men

TABLE 5-23 Ears, Eyes, Nose, and Throat Disorders Priority Topics

EENT-A	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-B	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.

TABLE 5-24 Kidney and Urinary Tract Disorders Priority Topics

KUT-A	Compare the effectiveness of management strategies for localized prostate cancer (e.g., active surveillance, radical prostatectomy [conventional, robotic, and laparoscopic], and radiotherapy [conformal, brachytherapy, proton-beam, and intensity-modulated radiotherapy]) on survival, recurrence, side effects, quality of life, and costs.
KUT-B	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.

(U.S. Cancer Statistics Working Group, 2009), the committee recommended that all aspects of managing the disease be studied (KUT-A).

Renal failure is among the leading causes of mortality across all age groups (Kung et al., 2008). It is also one of the most costly diseases in adults over 65 years of age (AHRQ, 2009a). As such, the committee recommended comparing alternative renal replacement therapies with an emphasis on determining the effectiveness differences among different ages, race, and ethnicities (KUT-B).

Oral Health

The committee recommended two priority topics within oral health for CER, one comparing prevention to surgery in adults with periodontal disease (ORAL-A), and the other in children comparing delivery model approaches for preventing dental caries (cavities) (ORAL-B) (Table 5-25).

Palliative and End-of-Life Care

Effective management and delivery of palliative and end-of-life care is a challenge as the elderly population grows in the United States. Palliative and

TABLE 5-25 Oral Health Priority Topics

ORAL-A	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.
ORAL-B	Compare the effectiveness of the various delivery models (e.g., primary care, dental offices, schools, mobile vans) in preventing dental caries in children.

TABLE 5-26 Palliative and End-of-Life Care Priority Topics

PELC-A	Compare the effectiveness of coordinated care (supported by reimbursement innovations) and usual care in long-term and end-of-life care of the elderly.
PELC-B	Compare the effectiveness of hospital-based palliative care and usual care on patient-reported outcomes and cost.

end-of-life care services must be effective for a variety of populations, and in a variety of environments, including hospitals, long-term care facilities, and homes. The committee specifically recommends research comparing strategies to improve delivery of long-term and end-of-life care, including reimbursement models to support coordinated care (PELC-A) and comparing hospital-based palliative care services with standard care to standard care alone (PELC-B) (Table 5-26).

Gastrointestinal System Disorders

Disorders of the upper gastrointestinal tract, such as gastroesophageal reflux disease (GERD), are among the most prevalent disorders in the nation, and they are particularly prevalent among the elderly (AHRQ, 2009c). They are also among the most costly conditions for infants less than 1 year old (AHRQ, 2009a). The committee specifically recommends the research of the effects of endoscopy on the management and outcomes of patients with GERD as a priority (GI-A) (Table 5-27).

Immune System, Connective Tissue, and Joint Disorders

Conditions of the immune system, connective tissue, and joints such as arthritis and connective tissue disorders are some of the most prevalent and costly diseases in all age groups, especially in the elderly (AHRQ, 2009a,c). Both AHRQ's Effective Health Care Program and *Healthy People 2010* list arthritis and non-traumatic joint disorders as national research priorities (HHS, 2000; Whitlock et al., 2009). The committee recommended comparing the effectiveness of different strategies, including biologics, in the treatment of these diseases (IMUN-A) (Table 5-28).

TABLE 5-27 Gastrointestinal System Disorders Priority Topics

GI-A	Compare the effectiveness of upper endoscopy utilization and frequency for patients with gastroesophageal reflux disease on morbidity, quality of life, and diagnosis of esophageal adenocarcinoma.
------	---

TABLE 5-28 Immune System, Connective Tissue, and Joint Disorders
Priority Topics

IMUN-A	Compare the effectiveness of different strategies of introducing biologics into the treatment algorithm for inflammatory diseases, including Crohn's disease, ulcerative colitis, rheumatoid arthritis, and psoriatic arthritis.
--------	--

Pediatrics

There are a variety of alternative and pharmacological treatments available for children with attention deficit hyperactivity disorder (ADHD), but more research is needed to compare their effectiveness. In fact, AHRQ's Effective Health Care Program lists ADHD as a national priority (Whitlock et al., 2009). The committee recommended more research that addresses the comparative effectiveness of these treatments in decreasing the symptoms of ADHD in children (PEDS-A) (Table 5-29). There are a number of other important pediatric topics that are discussed under the research area categories eyes, ears, nose and throat; functional limitations and disabilities; birth and developmental disorders; nutrition; and respiratory disease.

Respiratory Disease

Chronic Obstructive Pulmonary Disease (COPD) and asthma are among the most prevalent, most costly, and morbid conditions for all age groups (AHRQ, 2009a,c; Kung et al., 2008). Asthma is especially common in children and is the leading condition in terms of cost (AHRQ, 2009a). In addition, AHRQ's Effective Health Care Program lists asthma as a priority research area (Whitlock et al., 2009). The committee recommended alternative strategies for managing asthma be studied through CER (RD-A) (Table 5-30).

Trauma, Emergency Medicine, and Critical Care Medicine

Accidents are a leading cause of death for all ages in the United States, and trauma-related disorders are listed as one of the most prevalent and

TABLE 5-29 Pediatric Disorders Priority Topics

PEDS-A	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.
--------	---

TABLE 5-30 Respiratory Disorders Priority Topics

RD-A	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.
------	--

TABLE 5-31 Trauma, Emergency Medicine, and Critical Care Medicine Priority Topics

TEMC-A	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.
--------	--

costly (AHRQ, 2009a,c). While there are many disorders that arise from trauma and emergencies, the committee focused on the treatment of Post-traumatic Stress Disorder (PTSD) in all populations and from all sources of trauma. With the large number of veterans returning from the wars in Iraq and Afghanistan, and increased recognition of the inadequacies of the nation's health system to effectively treat patients with mental health conditions, it is important to identify effective treatment strategies. The committee recommended that PTSD be studied as part of a balanced portfolio of CER (TEMC-A) (Table 5-31).

TIMELINESS AND LIMITATIONS OF THE COMMITTEE'S PRIORITY LIST

The committee believes that the priority list presented in this chapter is relevant to the needs and conditions of today. New questions in CER will continue to appear. However, the balance of topics across the portfolio, the correlation with established priorities by other groups, and the good fit between the topics and the pre-established, pre-specified criteria suggest that the process used by the committee was effective. As discussed in Chapters 4 and 6, this process requires modification if it is to be continued in the future.

Recognizing the dynamic nature of disease and the rapid technologic and therapeutic advancements in health care, these priorities may very well be answered by ongoing research or be superseded by new disorders in the near future. In fact, that is the committee's hope and expectation. Recognition of priorities and initiation of new research should provide answers to the clinical dilemmas identified. Therefore, an ongoing and active process

of priority setting using stakeholder input is imperative. The previous two chapters described systems for continuous stakeholder input, together with methodologies for identifying which of these topics deserve priority. However, the committee emphasizes the importance of repeating this exercise on a regular basis or of integrating aspects of the process described here into the routine determination of CER funding in order to sustain the effort to discover what works best and for whom.

REFERENCES

- AHRQ (Agency for Healthcare Research and Quality). 2009a. Medical Expenditure Panel Survey. Total expenses for conditions by site of service: United States <http://www.meps.ahrq.gov/mepsweb/> (accessed March 10, 2009).
- . 2009b. Total number of events accounting for expenditures by site of service: United States, 2006. In *Medical Expenditure Panel Survey Component Data*.
- . 2009c. Total number of people accounting for expenditures (deduplicated) by site of service: United States, 2006. In *Medical Expenditure Panel Survey Component Data*.
- AHRQ Effective Health Care Program. 2009. *Effective Health Care: Topic triage cover sheets*.
- Doyle, J., E. Waters, D. Yach, D. McQueen, A. De Francisco, T. Stewart, P. Reddy, A. M. Gulmezoglu, G. Galea, and A. Portela. 2005. Global priority setting for Cochrane systematic reviews of health promotion and public health research. *Journal of Epidemiology and Community Health* 59:193-197.
- HHS (Department of Health and Human Services). 2000. *Healthy People 2010: Understanding and improving health*. Place Published: U.S. Government Printing Office. <http://purl.access.gpo.gov/GPO/LPS4217> (accessed April 3, 2009).
- Kung, H.-C., D. L. Hoyert, J. Xu, S. L. Murphy, and Division of Vital Statistics. 2008. *Deaths: Final data for 2005*. *National vital statistics reports* National Center for Health Statistics.
- NPP (National Priorities Partnership). 2008. *National priorities and goals*. Washington, DC: National Quality Forum.
- U.S. Cancer Statistics Working Group. 2009. United States cancer statistics: 1999–2005 Incidence and mortality web-based report. Atlanta: Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute.
- Wennberg, J. E. 2009 (unpublished). *Recommendations to the Institute of Medicine on comparative effectiveness research priorities*. Submitted in response to a request from the Institute of Medicine Committee on Comparative Effectiveness Research Prioritization. The Dartmouth Institute for Health Policy and Clinical Practice.
- Whitlock, E. P., S. A. Lopez, S. Chang, M. Helfand, M. Eder, and N. Floyd. 2009. Identifying, selecting, and refining topics for comparative effectiveness systematic reviews: AHRQ and the Effective Health Care Program. <http://effectivehealthcare.ahrq.gov/repFiles/20090427IdentifyingTopics.pdf> (accessed June 5, 2009).

6

Essential Priorities for a Robust CER Enterprise

Abstract: *This chapter presents the committee’s findings and recommendations for ensuring effective implementation of comparative effectiveness research (CER) and its translation into health care delivery. A short-term priority research agenda alone will not fulfill the potential of CER to improve the health of Americans and the quality of health care in the United States. The committee strongly recommends that Congress and the Secretary of Health and Human Services act to establish a sustainable strategy to coordinate government CER activity. The organizational and scientific challenges of CER are immense and the case for a strong, coordinating authority is compelling. Effective implementation of the CER agenda will involve collaboration among multiple government agencies and numerous professional disciplines and areas of expertise. The relevant areas of research encompass the complete continuum of health care services, all age groups, numerous disease conditions and health technologies, diverse health care settings, and the organization of health care delivery itself. No single U.S. research agency or organization possesses the breadth of expertise necessary to address this considerable scientific challenge. Four CER program priorities merit high-level attention and coordination: (1) meaningful participation of consumers, patients, and caregivers; (2) building of robust data and information systems as well as research and innovation in the methods of CER research; (3) development and support of a highly skilled CER workforce; and (4) vigorous support of research and efforts to translate CER knowledge into everyday clinical practice.*

Early in its deliberations, the Institute of Medicine (IOM) committee agreed that the nation’s investment in comparative effectiveness research

(CER) should go beyond recommending the individual CER topics suggested in the previous chapter. A short-term priority research agenda alone will not fulfill the potential of CER to improve the health of Americans and the quality of health care in the United States. The most important priority of all should be the building of a broad and supportive infrastructure to carry out a sustainable national CER strategy. Congress and the Secretary of Health and Human Services (HHS) must take concerted steps to establish a robust CER enterprise. This chapter refers to this effort, its coordination, and its recommended tasks as the “CER Program.”

Rather than develop a comprehensive blueprint, the committee focused on four essential program priorities that the HHS Secretary should embrace: (1) meaningful consumer, patient, and caregiver participation (in addition to other stakeholders); (2) investing in building robust data and information systems and in strengthening the research infrastructure for conducting new prospective CER studies; (3) investing in development, deployment, and support of a highly skilled CER workforce; and (4) supporting a vigorous translational effort to help bring CER knowledge into everyday clinical decision making.

The objective of this chapter is to describe these essential priorities. It begins with a section outlining the imperative for effective coordination of CER activities. The rest of the chapter reviews the other four program priorities listed above. See Chapter 4 for the committee’s recommendations for CER priority setting.

THE IMPERATIVE FOR EFFECTIVE COORDINATION OF THE CER ENTERPRISE

The committee strongly agreed that Congress should direct the HHS Secretary to implement a sustainable strategy to coordinate government CER activity including the Agency for Healthcare Research and Quality (AHRQ), Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services (CMS), National Institutes of Health (NIH), Food and Drug Administration (FDA), Department of Defense (DOD), and Veterans Administration.

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.

Organizational Challenges

Broad Research Scope

The organizational and scientific challenges of CER are immense and the case for a strong, coordinating authority is compelling. This report's recommended research topics¹ encompass not only the complete continuum of health care services (prevention, early detection, diagnosis, treatment, rehabilitation, palliation, end-of-life care), but also the effective organization of health care delivery itself. The high priority CER topics also span all age groups, from infants to adolescents to young, middle age, and older adults; numerous disease conditions; health care technologies (drugs, imaging, surgery, devices); and diverse health care settings. And, the investigative means include an array of complex methods including randomized clinical trials and observational studies.

No current research organization in the United States possesses the breadth of expertise necessary to address this considerable scientific challenge. High-level coordination and funding authority across this broad front is of paramount importance.

Scientific Rigor

An essential component of CER is the study of representative populations in real-world clinical settings. This demands a wide array of study designs including systematic reviews and meta-analysis, observational analytic methods, modeling, clinical trials, and others. The field must set uniform quality standards at each phase (i.e., priority setting, design and analysis of observational and experimental studies, interpretation and dissemination) and maintain a highly skilled workforce.

Objectivity

Objectivity will be central to the public's trust and confidence in the integrity of the CER Program. Conflict of interest and bias in clinical research—published in even the most respected medical journals—is well-documented (IOM, 2009b). Selective reporting or publication bias is common. Positive findings are more likely to be published than negative results (Chan et al., 2004; Dickersin, 2005; Dickersin and Min, 1993; Rising et al., 2008; Turner et al., 2008). In addition, there have been significant instances in which leading journals have not sufficiently enforced disclosure

¹ See Chapter 5.

requirements for authors and reviewers (Schwartz et al., 2008; Weinfurt et al., 2008).

CER is as vulnerable to bias and conflict of interest as any other area of medical research. The ultimate value of the CER enterprise will rest, in part, on vigilant attention to these issues. 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.

Public-Private Collaboration

The U.S. health care system has substantial resources—both public and private—to contribute to the CER effort. These resources include the private health care organizations that provide care for potential enrollees in CER studies. At present, experience in developing and maintaining such collaborative relationships is very limited within the federal government. To lead this coordinated effort, the committee agreed, will require an organization that is highly, preferably solely, focused on achieving the goals of CER. A national program of CER must engage the public—including all of the stakeholders—at all levels of its organization if it is to fulfill its potential to improve health care outcomes and to reduce unnecessary health care costs, which are both urgent needs.

Sustainability

The CER Program needs sustained and predictable funding beyond the American Recovery and Reinvestment Act (ARRA) of 2009 (P.L. 111-5) to achieve its objectives. To ensure research activities that truly embrace the definition of CER, the ARRA funds—and subsequent funding to support CER—should flow through a CER coordinating authority directly to grantees, through federal agencies, or both.

MEANINGFUL CONSUMER, PATIENT, AND CAREGIVER ENGAGEMENT²

In Chapter 4, the committee urged that consumers, patients, and caregivers be active participants in setting research priorities. In this chapter, the committee recommends that consumers also be integrally involved in

² In this chapter, the term “consumer” is used to represent not only consumers, but also patients and their families and caregivers.

the governance of the CER Program, the framing of research questions and research protocols, peer review of systematic reviews and monitoring of trials, and interpreting and disseminating the results of CER studies to ensure that new knowledge improves everyday clinical practice. CER will not achieve its basic objectives unless it embraces—and acts upon—a patient-centered mindset.

Centering on the patient is fundamental to high-quality health care (IOM, 2001). Patient-centered health care demands that CER be developed and applied with respect to each patient's unique needs, beliefs, and values. There is strong evidence that many consumers want to be involved in decision making about their care (President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 1982). Many—but not all—patients expect to make their own decisions about diagnosis and treatments and look to their health providers for support in interpreting and assessing the available information (Deber et al., 1996; Degner and Russell, 1988; Guadagnoli and Ward, 1998; Mansell et al., 2000; Mazur and Hickam, 1997). Yet, even the most sophisticated health care consumers often struggle to find the information that is relevant to their specific health-related questions and particular clinical circumstances (IOM, 2008).

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.

Consumers' Role in Informing and Framing the Research

Experts and consumers often have different perspectives on the questions that research should answer. Clinicians and patients do not always consider the same factors when weighing the tradeoffs posed by important health care alternatives (Entwistle et al., 1998). To ensure that the fruits of CER support consumers' health care decision making, the CER Program should focus on the questions and perspectives of patients as well as their health care providers.

Many researchers, acknowledging the importance of consumers' contribution to framing research questions, advocate for decision makers to participate directly in formulating research questions (IOM, 2008). Consumers can inform investigators' decisions about which patient outcomes to measure, patient populations to study (including important subgroups and relevant comorbidities), and interventions to compare, among other issues (Andejaski et al., 2002a,b; Hubbard et al., 2008; Saunders et al., 2008). Diabetes researchers, for example, have reported that involving patients is particularly helpful at keeping their research relevant and applicable to real-world settings (Lindenmeyer et al., 2007). Researchers responding to a survey on consumer involvement in randomized controlled studies in the United Kingdom reported that involving consumers helped to refine research questions and make the trials more relevant to patients' needs (Hanley et al., 2001). Nevertheless, opportunities for public input into clinical research remain rare.

In breast cancer, the involvement of consumers at all levels of decision making at the DOD Breast Cancer Research Program including vision setting, and peer and programmatic review, has proven valuable to the research process, resulted in an educated and engaged consumer force, and influenced clinical research beyond the DOD research program and beyond breast cancer (IOM, 1997).

Cultivating Consumers', Patients', and Caregivers' Participation in CER

Community-based participatory research refers to research that involves community members or recipients of interventions in all phases of the research process, starting with a research topic of importance to the community. Numerous researchers have advocated that community-based participatory research is key to improving the relevance of clinical research, especially research on health care disparities (Faridi et al., 2007; Fretheim et al., 2006; Jones and Wells, 2007; Minkler et al., 2003; Omenn, 1999; Zerhouni, 2005). Nevertheless, consumer participation in research is not the norm and there is no agreed-upon model for conducting community-based research effectively (Johnson et al., 2008). Researchers do not know how to meaningfully engage consumers in their work or to whom to turn for advice on a consumer representative. If scientists choose the consumer representatives, the representatives may not represent the consumer viewpoint. In addition, independent consumer groups face numerous challenges when their members want to contribute to research. The CER Program should identify best practices for consumer involvement and set standards for the key competencies required for consumer participation in CER.

Consumers will likely need appropriate information and education about CER to contribute meaningfully (Hubbard et al., 2008; Saunders

et al., 2008). The CER Program must reach out first to engage consumers and then to support, educate, and, as necessary, prepare them for their roles. Several programs have already been developed for this purpose. For example, a special initiative of the U.S. Cochrane Center, Consumers United for Evidence-based Healthcare, has developed a web-based course to help consumers understand the fundamentals of evidence-based health care (United States Cochrane Center Consumers United for Evidence-based Healthcare, 2009). Other programs include the National Breast Cancer Coalition's Project LEAD Institute, a science education program for breast cancer advocates, and Quality Care Project LEAD; the DOD Breast Cancer Research Program's peer review process, which involves consumer advocates; the FDA's Office of Special Health Initiatives, which trains patient representatives to participate on Advisory Panels (FDA, 2009); and the United Kingdom's national advisory group, which educates the public about involvement in research (INVOLVE, 2009).³

To achieve meaningful consumer participation, the CER program should incorporate the following:

- Substantial consumer representation in program governance
- Focus groups, forums, and citizen juries. Public meetings should be well-publicized and held at convenient times and locations
- Well-publicized web-based surveys (see Chapter 4 for how the committee solicited public nominations of CER topics)
- Educational programs offered through public symposia and seminars. Active consumer participants should have formal training opportunities and be compensated for their time

Public Trust

Some members of the public have voiced concerns that CER research may lead to health care rationing and inappropriate limits on patients' treatment choices (Meier, 2009). Engaging consumers in CER, and building the case for the value of CER, could help improve the public's trust in the U.S. research enterprise, because the communication is expanded to be inclusive, rather than exclusive, among the key decision makers (IOM, 2002). In fact, consumers may have the most credibility in conveying information about CER back to the general public and help in explaining health and health care delivery (Oliver et al., 2008).

A public that is more informed about the processes and value of CER is likely to have greater enthusiasm and confidence in both the research

³ See http://www.stopbreastcancer.org/index.php?option=com_content&task=view&id=395 for further information on Project LEAD.

and the research community (Academy of Medical Sciences, 2006) and may be more likely to participate in CER, either actively or passively as research subjects. The CER Program should, therefore, work to lower barriers to active public participation in planning research, such as the lack of adequate financial support to allow for travel and to compensate for the time required to participate (Staniszewska et al., 2007).

ROBUST DATA AND INFORMATION SYSTEMS

As noted earlier and described in greater detail in Chapter 2, CER comprises a broad spectrum of established and emerging research methods including systematic reviews of existing evidence, observational research, and experimental studies such as clinical trials (each described in this section). A critical first step in launching a comparative effectiveness study is to identify the most appropriate design for the type of research question being asked (IOM, 2008). Every study design has limitations and no single method is ideal for addressing questions of comparative effectiveness. Each study should be well-designed to ensure scientific rigor and minimal bias.

Systematic Reviews

Systematic reviews address a specific research question by identifying, selecting, assessing, and summarizing the existing body of evidence. Individual research studies often do not provide definitive answers to clinical effectiveness questions (IOM, 2008). If conducted properly, a systematic review should make obvious the gap between what is known about the effectiveness of an intervention and what clinicians and patients want to know. Thus, systematic reviews provide a central link between research evidence and clinical decision making. If the systematic review is both scientific and transparent, researchers and decision makers should be able to interpret the evidence, to know what is not known, and to describe the extent to which the evidence is applicable to clinical practice and particular patients. As such, systematic reviews are integral to framing research questions for future study regarding comparative effectiveness.

To date, the quality of systematic reviews has been variable and some published reviews have been unreliable. Criticisms include a confusing array of schemes for grading evidence in the literature, hierarchies of evidence that may not account for the true quality of studies, no disclosure of potential bias or conflict of interest, and a failure to use existing standards for reporting methods and results in systematic reviews. In *Knowing What Works in Health Care*, the IOM recommended that the HHS Secretary only fund systematic reviews that commit to and consistently meet evidence-

based, methodologic standards (IOM 2008).⁴ This principle should also be followed in HHS funding of CER studies.

Clinical Trials

Fundamental questions of comparative effectiveness often require head-to-head comparisons of alternative interventions using randomized assignment to the interventions to be compared. Randomized controlled trials (RCTs) are the gold standard for determining effectiveness because they minimize selection bias, that is, the likelihood that study participants will be given a treatment related to their prognosis such as comorbidities. RCTs have answered many important comparative effectiveness questions. The ALLHAT trial, for example, compared the benefits and harms of different forms of antihypertensive therapies (Furberg et al., 2002).

Clinical trials, however, cannot address many comparative effectiveness questions because of cost, ethical considerations, or other issues. RCTs are expensive because they involve careful follow-up of study participants as well as multiple clinical centers and investigators and centralized data coordination. Ethical considerations preclude trials of many types of interventions. For example, a randomized study comparing prophylactic mastectomy to “watchful waiting” in women positive for BRCA1 is very unlikely.

Smaller scale trials with small study populations conducted at a single site are often not representative of real-world clinical settings. This is not to say that small single center studies should never be done. For example, entirely new research questions should be addressed using observational studies to begin with, progressing to small scale trials and finally testing in the context of large scale trials and real-world settings.

Studies of intervention effectiveness and prognosis often require years of follow-up (e.g., interventions for chronic diseases and interventions in children). As a result, such research is subject to high drop-out rates and missing data. The findings must be interpreted cautiously. Moreover, as time goes by, the technology being studied may change, its use may improve, or, in the case of medications, the indications for use may broaden (Kent and Hayward, 2007).

Registration trials conducted for the purpose of FDA approval are unlikely to detect uncommon adverse effects because they typically involve relatively few subjects and often address short-term outcomes. The study

⁴ The Medicare Improvements for Patients and Providers Act of 2008 (P.L. 110-275 Sec. 304) directed the HHS Secretary to contract with the IOM for the purpose of identifying such standards and reporting the results of this effort to Congress. This study is scheduled to begin the summer of 2009.

population for FDA pre-approval and marketing trials is often younger and healthier than the target population of the health care intervention. Comparator interventions in these trials may not reflect the comparisons of interest to clinicians and patients because the comparator is often a placebo or an atypical dose of a competing drug.

Increasingly, trialists are applying methods to adapt clinical trials to real-world conditions. Methods to recruit and follow patients efficiently and to adapt trial designs to accommodate changing technologies are being incorporated in the design of randomized trials (Berry, 2003; Godwin et al., 2003). These methodologies should be refined and applied to meet the need for stronger, more applicable comparative effectiveness trials.

Observational Research

Observational studies can address gaps in the evidence when a randomized trial design is not practical. Observational research includes prospective and retrospective cohort studies, case-control studies, and case series analyses. In observational studies, the researcher does not intervene in patient care but observes the process of patient care and its outcomes as they occur in everyday life. Well-characterized cohort studies are particularly useful. In the Women's Health Initiative, for example, this method was used to identify predictors of disease, medication-related outcomes, and factors associated with health disparities in women ages 50 to 79 years old (National Heart, Lung, and Blood Institute, 2009). Case-control studies are useful for identifying risk factors for rare events such as deep venous thrombosis during long-distance travel or harm from interventions (Aryal and Al-khaffaf, 2006).

Observational studies are typically most appropriate for answering questions related to prognosis, diagnostic accuracy, incidence, prevalence, and etiology (Chou and Helfand, 2005; Tatsioni et al., 2005). They have the potential to address gaps in randomized trial evidence by including larger, more representative populations to identify rare or long-term adverse effects.

Observational studies that link process of care datasets (such as administrative claims data) to outcomes datasets (such as national death indexes) provide excellent opportunities to study both health services utilization and health outcomes, as discussed in the next section.

Despite their potential advantages, however, observational studies are more subject to bias than randomized trials, and the decision to rely on data from observational studies must be weighed against the possibility of misleading results. The main form of bias (selection bias) occurs when the factors causing a person to experience the intervention are associated with the patient's prognosis.

Innovation Is Needed in CER Methods

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.

There is a significant need for new and better research methods for studying comparative effectiveness (IOM, 2007; McClellan and Benner, 2009; Rawlins, 2008; Tunis, 2009). Current study designs, both experimental and nonexperimental, must be further refined if CER is to be scientifically valid, efficient, and credible. 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 (IOM, 2008). New analytic techniques are needed to evaluate the effects of bias due to confounding when assessing comparative effectiveness using large observational datasets. Many fundamental questions of comparative effectiveness relate to small but clinically important differences in treatment effects that cannot be detected by current nonexperimental methods (Tunis, 2009). Clinical trials will always be essential to CER, but more efficient, larger, simpler, and pragmatic designs are needed.

The Potential of Existing Data

CER may also draw from analyses of existing data, such as that held by payers, health care delivery systems, and electronic health records. ARRA's \$40 billion support for advancing health information technology and implementing an interoperable electronic health record system with compatible data definitions and formats can help make these ambitious aspirations a reality (Office of National Coordinator for Health Information Technology, 2009).

Claims data from large national insurers, electronic health records maintained by large integrated health systems, data collected through practice-based research networks, and patient registry data hold tremendous potential for CER. Harnessing these sources of *existing* data could markedly enhance the timeliness and value of CER. Existing data sources can be used for many research purposes: to study prognosis, risks and harms, and etiology of disease (Cupples et al., 1988); to analyze trends over time and capture long-term outcomes (Fung et al., 2004); to examine the causes of geographic variation (Wennberg and Fisher, 2008); to analyze racial and ethnic disparities in both access to and outcomes of health care (Peterson and Yancy, 2009); to study low prevalence conditions (many

occurring in pediatric populations) (Merlini et al., 2008); to assess clinical effectiveness in populations and subpopulations, such as minority groups and people with comorbidities (Bell et al., 2009); and to generate hypotheses for experimental research (de Simone et al., 2009). Such data sources can also provide efficient sampling frames for recruitment to experimental studies, such as large practical individual-level RCTs, cluster randomized trials,⁵ and other prospective studies (Sabin et al., 2008).

Researchers can use existing data from larger clinical populations to assess whether the benefits of interventions suggested in smaller clinical trials persist in the broader populations to which treatments are applied in practice. For example, non-Whites have been underrepresented in clinical research compared to white Americans (Braunstein et al., 2008; Brown et al., 2000; Farmer et al., 2007; Giuliano et al., 2000; Wendler et al., 2006; Williams and Corbie-Smith, 2006). Older patients, patients with many comorbid conditions and/or disabilities, children, and other subpopulations are also underrepresented in most clinical trials (Van Spall et al., 2007). Existing data sources can also help generate hypotheses about the characteristics of patients who are most likely to benefit from a therapy, as well as the characteristics of patients who are more likely to have adverse reactions to otherwise safe and effective drugs.

Administrative Claims Data

Administrative claims data comprise data obtained to support claims for reimbursement from insurers for services rendered. They include information on diagnoses, treatments (both medications and procedures), as well as many outcomes from millions of insured members. Claims data typically lack detailed information on clinical variables, such as laboratory results, lifestyle factors, and other physiological measures (e.g., height, weight, blood pressure, health status). The nation's largest and most representative claims database is held by CMS. Medicare now covers more than 45 million Americans, mostly over age 64. Information on drugs paid for under Medicare Part D, available since 2006, covers nearly 27 million people (CMS, 2009). Medicaid data and data from the Children's Health Insurance Program (CHIP) include younger Americans of lower socioeconomic status and individuals with significant comorbid conditions (The Henry J. Kaiser Foundation, 2009). In 2005, Medicaid provided coverage to 29.4 million children and 15.2 million adults (primarily poor working parents), and CHIP covered an additional 7 million children by 2007 (The Henry

⁵ Cluster randomized trials are RCTs in which the participants are assigned to the experimental or comparison groups (clusters) defined by a common feature, such as the same physician or health plan.

J. Kaiser Foundation, 2009). However, there is significant variation in the quality of Medicaid claims data and the difficulties that researchers face in securing these data—often requiring inquiries to multiple states and their Institutional Review Boards (IRBs)—have greatly constrained the use of Medicaid and CHIP data for research.

Electronic Health Records

Several large health delivery systems have used their electronic health records to build clinical datasets for research. These include the Veterans Health Administration's VISTA system, Kaiser Permanente, Group Health Cooperative of Puget Sound, Intermountain Healthcare, and Geisinger Health System. The clinical data in electronic health records collected by these organizations are more comprehensive than claims data and can be used for detailed management of chronic disease and some prospective studies of treatment outcomes. Large health care systems, however, may have restricted drug formularies that do not cover newer, non-evidence-based medications, which limits the data available for analysis and reduces the generalizability of findings. To date, the adoption of fully functional electronic health records has been slow (Ford et al., 2009); however, the incentives provided under ARRA should spur more rapid uptake, which could benefit the conduct of CER if the deployment is undertaken with systems capable of interoperability and connectivity for data sharing with repositories and if the electronic health records have the capability of clinical decision support and opportunities for patients to add relevant information into their records via secure web portals. Without these considerations, a major public investment will fall short of meeting the needs of CER and our nation will miss an opportunity to enhance its capacity to dramatically improve system performance through the benefit of CER.

Practice-Based Research Networks

Practice-based research networks are designed for research on clinical practices and quality improvement activities. These networks generate both primary and specialty care data, often using data gathered prospectively for the purpose of research (in contrast to most existing data from practice, which document routine clinical care and may have important limitations for research purposes). These data may thus provide detailed clinical information from settings not captured in large integrated systems (Westfall et al., 2007). A limitation of most current practice-based research networks is that they typically enroll relatively small numbers of patients and may not be representative of the population as a whole, a problem that could be overcome with larger networks and/or integration across networks.

Disease- and Treatment-Specific Registries

Patient registries can be a valuable data source for research on the real-world effectiveness of health care interventions. A patient registry is an organized system, designed for a predetermined purpose (e.g., clinical or policy research), that employs observational research methods to collect standardized clinical and other data in order to evaluate specific outcomes for a population defined by a specific disease, condition, or exposure (Gliklich and Dreyer, 2007). The data may be exclusively drawn from existing electronic sources or may also include primary data provided by clinicians. Many registries have preexisting IRB review and approvals that can facilitate data sharing and reduce concerns related to patient consent and privacy (Gliklich and Dreyer, 2007).

At present, there are hundreds of patient registries in the United States. Many are designed around specific diseases; others are product registries maintained for post-marketing surveillance (IOM, 2007). The Clozapine registry, for example, was mandated by the FDA to detect adverse events associated with use of the drug (Teva Pharmaceuticals, 2008). The Cystic Fibrosis Foundation has sponsored a national patient registry for more than 40 years to enable clinicians and researchers to observe trends in the health of people with cystic fibrosis, create clinical care guidelines, design clinical trials to test new therapies, and improve the delivery of care (Cystic Fibrosis Foundation, 2009).

Registries have two major drawbacks: first, their restriction to patient populations who undergo a particular intervention (e.g., immunization registries) or who have a condition of interest (e.g., cystic fibrosis) and, second, they may not collect all the data needed to answer specific comparative effectiveness questions. An advantage of registries is that they can centralize data collection for rare conditions or procedures in order to improve the likelihood of observing trends.

Challenges to Using Existing Data

The CER Program will have to overcome three critical hurdles to reap the potential contribution of existing datasets to CER: (1) linking patient-level data from multiple sources, (2) protection of the privacy and security of patient data, and (3) ensuring that holders of large datasets actively participate in the CER enterprise. These are described below.

Data Linkage

CER often requires data to be linked at the individual patient level from multiple large-scale, clinical research networks. Datasets may be

duplicative or complementary. A single database may not provide a large enough patient cohort or a sufficiently complete picture of a patient's condition or health history, whereas several complementary datasets may be needed to meet the needs of CER.

In order to link data across databases, the data must have standardized definitions and be electronically compatible. Moreover, different individual patient identifier codes in different datasets must recognize each other—requirements that also apply to linkage and pooling of data from two or more similar observational cohorts or the complementary linkage of a clinically defined cohort with a payer's data. Patient identifiers in pharmaceutical dispensing, hospital discharges, and diagnosis and procedure codes are standardized across most systems. However, information from laboratory results, enrollment, and utilization data usually require significant harmonization of patient identifiers to link the information from multiple sources into an analyzable, single patient record.

The FDA's 2008 Sentinel Initiative is the most ambitious linkage proposal to date. Its ultimate goal is the creation and implementation of the Sentinel System—a national, integrated, electronic database to detect adverse effects of drugs and other medical products. The system, which will eventually monitor as many as 100 million individuals, will be built from participating electronic health record or claims databases. The Sentinel Initiative system could also be used to study questions of comparative effectiveness. Because of concerns related to patient privacy and to health care systems' proprietary interests, the Sentinel System has proposed to use the tools and processes of distributed network analysis. In a distributed network, all clinical data remain with the source systems' databases. Centralized software is used to query each networked system, provided that system has approved the query. Transfer of identifiable data from the source health care systems to a central location is eliminated—a large advantage for adherence to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule regulations and protection of privacy (FDA, 2008).

Data Privacy and Security

Individuals are more likely to participate in research and to support using medical records in research if they are convinced that their personal health information will remain confidential. Highly publicized privacy and security breaches undermine public trust in the research community, hinder recruitment of research participants, and threaten the overall research enterprise (IOM, 2009a).

Under the HIPAA Privacy Rule, researchers must obtain an informed consent for every use of an individual's protected health information. However, the Privacy Rule acknowledges that obtaining informed consent from

every research participant in every research situation is not always feasible. Thus, the Privacy Rule specifies several situations, including using “deidentified” patient data, in which researchers can use protected health information without each patient’s consent.⁶

A recent IOM committee concluded that the HIPAA Privacy Rule does not protect privacy as well as it should and, as currently implemented, it impedes important health research (IOM, 2009a). That committee’s principal recommendation proposed congressional authorization of HHS and other relevant federal agencies to develop a comprehensive, new approach to ensuring privacy while facilitating health research. Recognizing that this ambitious recommendation might be controversial and difficult to implement, that committee also provided a set of more limited recommendations that addressed particular provisions of the HIPAA Privacy Rule, involving issues such as accounting for disclosures, authorizations for specified future research, activities preparatory to research, and mechanisms for linking multisource data, among others (Box 6-1). This committee views these recommendations as crucial to enabling robust CER.

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.

The committee also agreed that the federal government should support the development of privacy-enhancing technologies for sharing health information for CER, including methods that minimize or eliminate transfer of protected health information. Distributed research networks, as noted earlier, are designed to keep clinical data within and under the control of the source data systems participating in the network (Brown et al., 2009). With the permission of a system authority, researchers can extract deidentified data from the source system and export it to a central site where the data are pooled with data from other network participants. While this technology does require further refinement before it can be fully exploited

⁶ Deidentified data are stripped of information that could be used to identify individuals.

in CER, work is under way in groups like the HMO Research Network and similar emerging research networks.

Widespread Participation by Data Holders

To develop the concepts of shared data research networks to their potential for advancing health care, the CER Program must address both data holder's proprietary interests and the costs that they incur in order to share data. Patterns of medication use, rates of use of various procedures, organizational performance with respect to quality, and complications of therapy are all subjects of intense proprietary interest to competing health care organizations. These organizations may not share their information if doing so threatens a competitive advantage. Privacy-enhancing technologies, such as distributed networks, may successfully address these proprietary concerns because users cannot identify the source of the patient data.

Holders of data will incur costs setting up and maintaining databases that are usable for CER research. The CER Program will need to create financial incentives that effectively offset these costs to encourage health systems to participate in CER research. The Medicare program's "coverage with evidence development" initiative is an example and adaptation to Medicaid and CHIP programs that could be explored. Other types of incentives to share data may also be helpful. For instance, organizations might provide data and analysis in return for periodic reports—suitably deidentified—comparing their data (e.g., on drug utilization or performance metrics) with that of other participants.

DEVELOP, DEPLOY, AND SUPPORT A CER WORKFORCE

Health interventions are inherently complex and often involve multiple systems and diverse patients, providers, health care organizations, financing mechanisms, communities, and sociodemographic factors. Research that addresses the functions of complex systems—such as CER—requires collaboration between many disciplines and also continual methods innovation.

CER researchers come from a range of professional disciplines, including clinical medicine, epidemiology, biomedical informatics, biostatistics, health services research, economics, methods research, decision and cognitive sciences, genomics, proteomics, library science, communications, as well as other areas (IOM, 2009c). They may have medical or other clinical degrees, doctoral degrees in public health specialties, specific training in systematic reviews and clinical trials, and/or post-doctoral or master's-level training. The CER workforce needs individuals with expertise in designing and conducting trials, statistical modeling, conducting systematic reviews and meta-analysis, quasi-experimental design and other observational

BOX 6-1**IOM Recommendations for Changes to the HIPAA Privacy Rule and Associated Guidance Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health through Research****A. HHS should reduce variability in interpretations of the HIPAA Privacy Rule in health research by covered entities, Institutional Review Boards (IRBs) and Privacy Boards through revised and expanded guidance and harmonization.**

1. HHS should develop a dynamic, ongoing process to increase empirical knowledge about current “best practices” for privacy protection in responsible research using protected health information (PHI), and promote the use of those best practices.
2. HHS should encourage greater use of partially deidentified data called “limited datasets” and develop clear guidance on how to set up and comply with the associated data use agreements more efficiently and effectively, in order to enhance privacy in research by expanding use and usability of data with direct identifiers removed.
3. HHS should clarify the distinctions between “research” and “practice” to ensure appropriate IRB and Privacy Board oversight of PHI disclosures for these activities.
4. HHS guidance documents should simplify the HIPAA Privacy Rule’s provisions regarding the use of PHI in activities preparatory to research and harmonize those provisions with the Common Rule, in order to facilitate appropriate IRB and Privacy Board oversight of identification and recruitment of potential research participants.

B. HHS should develop guidance materials to facilitate more effective use of existing data and materials for health research and public health purposes.

methods, use and analysis of large datasets, cost-effectiveness analysis, clinical prediction rules, measurement of patient-reported and clinical outcomes, and communicating research findings to patients, providers, and others. The CER Program will have to ensure the participation of individuals with a sound foundation in these areas.

Current Workforce Capacity

The significant increase in CER activity will create a substantial need for the types of expertise just described. Gauging the capacity of the current CER workforce is difficult because so many disciplines are involved and so

1. HHS should develop guidance that clearly states that individuals can authorize use of PHI stored in databases or associated with biospecimen banks for specified future research under the HIPAA Privacy Rule with IRB/Privacy Board oversight, as is allowed under the Common Rule, in order to facilitate use of repositories for health research.
2. HHS should develop clear guidance for use of a single form that permits individuals to authorize use and disclosure of health information in a clinical trial and to authorize the storage of their biospecimens collected in conjunction with the clinical trial, in order to simplify authorization for interrelated research activities.
3. HHS should clarify the circumstances under which DNA samples or sequences are considered PHI, in order to facilitate appropriate use of DNA in health research.
4. HHS should develop a mechanism for linking data from multiple sources so that more useful datasets can be made available for research in a manner that protects privacy, confidentiality, and security.

C. HHS should revise provisions of the HIPAA Privacy Rule that entail heavy burdens for covered entities and impede research without providing substantive improvements in patient privacy.

1. HHS should reform the requirements for the accounting of disclosures of PHI for research.
2. HHS should simplify the criteria that IRBs and Privacy Boards use in making determinations for when they can waive the requirements to obtain authorization from each patient whose PHI will be used for a research study, in order to facilitate appropriate authorization requirements for responsible research.

SOURCE: IOM (2009a).

many educational pathways to the field exist. For these reasons, no one has yet analyzed the current workforce to see if it is sufficient to respond to the ARRA mandate for expanding CER. Nonetheless, ARRA's infusion of \$1.1 billion into CER will clearly stress the limits of the current CER workforce. ARRA appropriations increased AHRQ's CER budget tenfold. Aggregate current NIH spending on CER is not known, but the Institutes will receive at least an additional \$400 million to conduct CER.

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

Ensuring a Highly Skilled CER Workforce

The committee agreed that, at the outset, the CER Program should develop a strategic plan for research workforce development. The plan should include assessments of both the capacity of the current workforce to carry out the Program's research agenda and the capacity and effectiveness of current training programs for producing researchers with the relevant skills. Developing an adequate CER workforce will involve the training, deployment, and collaboration of a significant number of professional disciplines. Data on education paths and training programs for CER investigators are scarce.

The NIH Roadmap for Medical Research, together with the Clinical and Translational Science Consortium are two mechanisms by which workforce development can be efficiently achieved (National Center for Research Resources, 2009; NIH, 2009). Training grants, such as K12, K30, and T32, should incorporate concepts of CER in their curricula exposing young scientists to CER and expanding the opportunities for participation in CER.

CER is a fast-growing field that has experienced changes over time. At the present state of development of CER, it appears to be growing as a cohesive discipline. However, the career path is ill defined, and other areas of clinical research compete for the best and the brightest investigators. To be attractive to them, the field needs sustainable research funding and must adhere to high standards of research quality and scientific integrity, be open to new ideas and people, and provide excitement about the potential to contribute to health research and health care practice overall. The CER Program should secure long-term, sufficient funding for 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. Without adequate training and secure, stable financial support, talented investigators are likely to pursue other areas of research. Undoubtedly, a stable funding stream for CER will attract investigators to CER, as will a sense that the nation places a high priority on CER as a partial but important part of paying for health care reform and improving the quality of care.

BRINGING KNOWLEDGE INTO PRACTICE

Many stakeholders and members of the public asked the committee to prioritize CER topics related to the comparative effectiveness of methods for bringing proven health care interventions into everyday clinical practice (see Chapter 5). Dougherty and Conway have proposed that three steps in knowledge translation must occur before research can improve health care quality and value: (1) translation of basic biomedical science into clinical efficacy knowledge, (2) translation of clinical efficacy knowledge into clinical effectiveness knowledge, and (3) translation of clinical effectiveness knowledge into health system improvement (Dougherty and Conway, 2008). Biomedical research has traditionally focused on steps one and two. The Clinical and Translational Science Consortium is now beginning to expand research networks and emphasize community engagement. But, the health care system will not benefit from CER without the third translational step, and more effort can be made by the Consortium to assess the integration of new findings into practice and their impact on health outcomes.

The CER Program should require researchers to publish all federally funded CER studies and make the research readily available to the public. Health care professionals and patients must use CER results to make informed decisions that integrate the best available evidence, the patients' preferences, and specific characteristics of the patient (Matthews, 2009; Weinstein et al., 2007).

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.

The American health research infrastructure lacks a systematic way to translate knowledge from research to practice. 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 reluctance to question clinicians (Shojania and Grimshaw, 2005). These barriers and others should be addressed and, insofar as possible, overcome. Knowledge translation research must be a high priority.

CONCLUSION

In summary, the HHS Secretary's CER agenda will fall far short of its potential without effective coordination and governance of the enterprise.

The research agenda will involve a broad array of study designs, the full range of health care services, and an extensive corps of experts in diverse professional disciplines. However, an ambitious research enterprise alone will not improve health care in the United States without the Secretary's attention to high fidelity translation of knowledge into practice. Moreover, consumers, patients, and caregivers as well as their health care providers must be involved in all aspects of CER to ensure its relevance to everyday health care delivery.

The \$1.1 billion ARRA investment in CER is an unprecedented vote of confidence in patient-centered research. The CER program should be held accountable to its mission. Sustained program evaluation and continuous quality improvement must be a bedrock feature of the enterprise.

REFERENCES

- Academy of Medical Sciences. 2006. Personal data for public good: Using health information in medical research. <http://www.acmedsci.ac.uk/images/project/Personal.pdf> (accessed August 28, 2008).
- Andejeski, Y., I. T. Bisceglia, K. Dickersin, J. E. Johnson, S. I. Robinson, H. S. Smith, F. M. Visco, and I. M. Rich. 2002a. Quantitative impact of including consumers in the scientific review of breast cancer research proposals. *Journal of Women's Health & Gender-Based Medicine* 11(4):379-388.
- Andejeski, Y., E. S. Breslau, E. Hart, N. Lythcott, L. Alexander, I. Rich, I. Bisceglia, H. S. Smith, and F. M. Visco. 2002b. Benefits and drawbacks of including consumer reviewers in the scientific merit review of breast cancer research. *Journal of Women's Health & Gender-Based Medicine* 11(2):119-136.
- Aryal, K. R., and H. Al-khaffaf. 2006. Venous thromboembolic complications following air travel: What's the quantitative risk? A literature review. *European Journal of Vascular and Endovascular Surgery* 31(2):187-199.
- Bell, C. L., J. Davis, R. C. Harrigan, E. Somogyi-Zalud, M. K. G. Tanabe, and K. H. Masaki. 2009. Factors associated with place of death for elderly Japanese American men: The Honolulu heart program and Honolulu-Asia aging study. *Journal of the American Geriatrics Society* 57(4):714-718.
- Berry, D. A. 2003. Statistical innovations in cancer research. In *Cancer Medicine 6th Edition*, Edited by J. Holland, E. Frei, D. W. Kufe, R. E. Pollock, R. R. Weichselbaum, R. C. Bast and T. S. Gansler. Hamilton: BC Decker. Pp. 465-478.
- Braunstein, J. B., N. S. Sherber, S. P. Schulman, E. L. Ding, and N. R. Powe. 2008. Race, medical researcher distrust, perceived harm, and willingness to participate in cardiovascular prevention trials. *Medicine* 87(1):1-9.
- Brown, D. R., M. N. Fouad, K. Basen-Engquist, and G. Tortolero-LUa. 2000. Recruitment and retention of minority women in cancer screening, prevention and treatment trials. *Annals of Epidemiology* 10:S13-S21.
- Brown, J., J. Holmes, J. Maro, B. Syat, K. Lane, R. Lazarus, and R. Platt. 2009. Developing a distributed research network and cooperative to conduct population-based studies and safety surveillance. In *Report 1: Design Specifications for Network Prototype and Research Cooperative*.

- Chan, A. W., A. Hrobjartsson, M. T. Haahr, P. C. Gøtzsche, and D. G. Altman. 2004. Empirical evidence for selective reporting of outcomes in randomized trials: Comparison of protocols to published articles. *JAMA* 291:2457-2465.
- Chou, R., and M. Helfand. 2005. Challenges in systematic reviews that assess treatment harms. *Annals of Internal Medicine* 142(12 [Part 2]):1090-1099.
- CMS (Centers for Medicare & Medicaid). 2009. Prescription drug coverage general information: Overview. <http://www.cms.hhs.gov/PrescriptionDrugCovGenIn/> (accessed May 9, 2009).
- Cupples, L., R. D'Agostino, and D. Kiely. 1988. The Framingham heart study. *Section 35. An Epidemiological Investigation of Cardiovascular Disease Survival Following Cardiovascular Events: 30 Year Follow-up*.
- Cystic Fibrosis Foundation. 2009. *Patient registry report*. <http://www.cff.org/treatments/Care-CenterNetwork/PatientRegistryReport/> (accessed June 16, 2009).
- de Simone, G., R. B. Devereux, M. Chinali, M. J. Roman, E. T. Lee, H. E. Resnick, and B. V. Howard. 2009. Metabolic syndrome and left ventricular hypertrophy in the prediction of cardiovascular events: The strong heart study. *Nutrition, Metabolism and Cardiovascular Diseases* 19(2):98-104.
- Deber, R. B., N. Kraetschmer, and J. Irvine. 1996. What role do patients wish to play in treatment decision making. *Archives of Internal Medicine* 156:1414-1420.
- Degner, L. F., and C. A. Russell. 1988. Preferences for treatment control among adults with cancer. *Research in Nursing & Health* 11:367-374.
- Dickersin, K. 2005. Publication bias: Recognizing the problem, understanding its origins and scope, and preventing harm. In *Publication Bias in Meta-analysis: Prevention, Assessment, and Adjustments*, Edited by H. Rothstein, A. Sutton and M. Borenstein. London, UK: John Wiley and Sons, Ltd.
- Dickersin, K., and Y.-I. Min. 1993. Publication bias: The problem that won't go away. In *Doing More Good than Harm: The Evaluation of Health Care Interventions*. Edited by K.S. Warren and F. Mosteller. New York Academy of Sciences. 135-148.
- Dougherty, D., and P. H. Conway. 2008. The "3T's" road may transform US health care: The "how" of high-quality care. *JAMA* 299(19):2319-2321.
- Entwistle, V. A., M. J. Renfrew, S. Yearley, J. Forrester, and T. Lamont. 1998. Lay perspectives: Advantages for health research. *BMJ* 316:463-366.
- Faridi, Z., J. Grunbaum, B. S. Gray, A. Franks, and E. Simoes. 2007. Community-based participatory research: Necessary next steps. *Preventing Chronic Disease: Public Health Research, Practice and Policy* 4(3):1-5.
- Farmer, D., S. A. Jackson, F. Camacho, and M. A. Hall. 2007. Attitudes of African American and low socioeconomic status White women toward medical research. *Journal of Health Care for the Poor and Underserved* 18:85-99.
- FDA (Food and Drug Administration). 2008. FDA's Sentinel Initiative. <http://www.fda.gov/oc/initiatives/advance/sentinel/> (accessed May 5, 2009).
- . 2009. Information for patient advocates <http://www.fda.gov/oashi/home.html> (accessed May 13, 2009).
- Ford, E. W., N. Menachemi, L. T. Peterson, and T. R. Huerta. 2009. Resistance is futile: But it is slowing the pace of EHR adoption nonetheless. *Journal of the American Medical Informatics Association* 16(3):274-281.
- Fretheim, A., H. J. Schanemann, and A. D. Oxman. 2006. Improving the use of research evidence in guideline development: 3. Group composition and consultation process. *Health Research Policy and Systems* 4.
- Fung, M. M., R. Bettencourt, and E. Barrett-Connor. 2004. Heart disease risk factors predict erectile dysfunction 25 years later: The rancho bernardo study. *Journal of the American College of Cardiology* 43(8):1405-1411.

- Furberg, C. D., J. T. Wright Jr, B. R. Davis, J. A. Cutler, M. Alderman, H. Black, W. Cushman, R. Grimm, L. J. Haywood, F. Leenen, S. Oparil, J. Probstfield, P. Whelton, C. Nwachuku, D. Gordon, M. Proschan, P. Einhorn, C. E. Ford, L. B. Piller, I. K. Dunn, D. Goff, S. Pressel, J. Bettencourt, B. DeLeon, L. M. Simpson, J. Blanton, T. Geraci, S. M. Walsh, C. Nelson, M. Rahman, A. Juratovac, R. Pospisil, L. Carroll, S. Sullivan, J. Russo, G. Barone, R. Christian, S. Feldman, T. Lucente, D. Calhoun, K. Jenkins, P. McDowell, J. Johnson, C. Kingry, J. Alzate, K. L. Margolis, L. A. Holland-Klemme, B. Jaeger, J. Williamson, G. Louis, P. Ragusa, A. Williard, R. L. S. Ferguson, J. Tanner, J. Eckfeldt, R. Crow, and J. Pelosi. 2002. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT). *JAMA* 288(23):2981-2997.
- Giuliano, A. R., N. Mokuau, C. Hughes, G. Tortelero-Luna, B. Risendal, R. C. S. Ho, T. E. Prewitt, and W. J. McCaskill-Stevens. 2000. Participation of minorities in cancer research: The influence of structural, cultural, and linguistic factors. *Annals of Epidemiology* 10:S22-S34.
- Gliklich, R. E., and N. A. Dreyer. 2007. *Registries for evaluating patient outcomes: A user's guide*. Rockville, MD: Agency for Healthcare Research and Quality.
- Godwin, M., L. Ruhland, I. Casson, S. MacDonald, D. Delva, R. Birtwhistle, M. Lam, and R. Seguin. 2003. Pragmatic controlled clinical trials in primary care: The struggle between external and internal validity. *BMC Medical Research Methodology* 3:1-7.
- Guadagnoli, E., and P. Ward. 1998. Patient participation in decision-making. *Social Science & Medicine* 47(3):329-339.
- Hanley, B., A. Truesdale, A. King, D. Elbourne, and I. Chalmers. 2001. Involving consumers in designing, conducting and interpreting randomised controlled trials: Questionnaire survey. *BMJ* 322:519-523.
- The Henry J. Kaiser Foundation. 2009. Medicaid & CHIP. <http://www.statehealthfacts.org/comparecat.jsp?cat=4> (accessed May 9, 2009).
- Hubbard, G., L. Kidd, and E. Donaghy. 2008. Involving people affected by cancer in research: A review of literature. *European Journal of Cancer Care* 17(3):233-244.
- INVOLVE. 2009. Promoting public involvement in NHS, public health and social care research. <http://www.invo.org.uk/> (accessed May 13, 2009).
- IOM (Institute of Medicine). 1997. *A review of the Department of Defense's program for breast cancer research*. Washington, DC: National Academy Press.
- . 2001. *Crossing the quality chasm: A new health system for the 21st century*, National Academy Press. <http://www.nap.edu/catalog/10027.html> (accessed April 20, 2009).
- . 2002. *Responsible research: A systems approach to protecting research participants*. Washington, DC: The National Academies Press.
- . 2007. Learning what works best: The nation's need for evidence on comparative effectiveness in health care. <http://www.iom.edu/ebm-effectiveness> (accessed April 15, 2009).
- . 2008. *Knowing what works in health care: A roadmap for the nation*. Edited by J. Eden, B. Wheatley, B. J. McNeil and H. Sox. Washington, DC: The National Academies Press.
- . 2009a. *Beyond the HIPAA privacy rule: Enhancing privacy, improving health through research*. Edited by Nass, S. J., L. A. Levit and L. O. Gostin. Washington, DC: The National Academies Press.
- . 2009b. *Conflict of interest in medical research, education, and practice*. Edited by B. Lo, and M. J. Field. Washington, DC: The National Academies Press.

- . 2009c. A framework for the workforce required for comparative effectiveness research. In *Learning What Works Infrastructure Required to Learn Which Care is Best* (in press). Washington, DC: The National Academies Press.
- Johnson, B., M. Abraham, J. Conway, L. Simmons, S. Edgman-Levitan, P. Sodomka, J. Schlucter, and D. Ford. 2008. *Partnering with patients and families to design a patient- and family-centered health care system: Recommendations and promising practices*. <http://www.ihl.org/NR/rdonlyres/C810CCBB-2DEB-4678-994A-57D9B703F98D/0/PartneringwithPatientsandFamiliesRecommendationsApr08.pdf> (accessed June 12, 2009).
- Jones, L., and K. Wells. 2007. Strategies for academic and clinician engagement in community-participatory partnered research. *JAMA* 297(4):407-410.
- Kent, D. M., and R. A. Hayward. 2007. Limitations of applying summary results of clinical trials to individual patients. *JAMA* 298:1209-1212.
- Lindenmeyer, A., H. Hearnshaw, J. Sturt, R. Ormerod, and G. Altchison. 2007. Assessment of the benefits of user involvement in health research from the Warwick Diabetes Care Research User Group: A qualitative case study. *Health Expectations* 10:268-277.
- Mansell, D., R. M. Poses, L. Kazis, and C. A. Duefield. 2000. Clinical factors that influence patients' desire for participation in decisions about illness. *Archives of Internal Medicine* 160:2991-2996.
- Mattews, S. C. 2009. Physician autonomy and informed decision making: Finding the balance for patient safety and quality. *JAMA* 300(24):2913-2915.
- Mazur, D. J., and D. H. Hickam. 1997. Patients' preferences for risk disclosure and role in decision making for invasive medical procedures. *Journal of General Internal Medicine* 12:114-117.
- McClellan, M., and J. Benner. 2009. Comparative effectiveness research: Will it bend the health care cost curve and improve quality? In *Implementing Comparative Effectiveness Research: Priorities, Methods, and Impact*. Washington, DC: Brookings.
- Meier, B. 2009. New effort reopens a medical minefield *The New York Times*, B1.
- Merlini, L., P. Kishnani, B. Byrne, W. Maller-Felber, L. Case, and A. v. d. Ploeg. 2008. The Pompe registry: Centralized data collection to track the natural course of Pompe disease. *Clinical Therapeutics* 30(SUPPL. 1).
- Minkler, M., A. G. Blackwell, M. Thompson, and H. Tamir. 2003. Community-based participatory research: Implications for public health funding. *American Journal of Public Health* 93(8):1210-1213.
- National Center for Research Resources. 2009. *Clinical and translational science awards*. http://www.ncrr.nih.gov/clinical_research_resources/clinical_and_translational_science_awards/ (accessed June 16, 2009).
- National Heart, Lung, and Blood Institute. 2009. *Women's health initiative: Observational fact sheet*. <http://www.nhlbi.nih.gov/whi/os.htm> (accessed May 23, 2009).
- NIH (National Institutes of Health). 2009. *NIH roadmap for medical research*. <http://nihroadmap.nih.gov/> (accessed June 16, 2009).
- Office of National Coordinator for Health Information Technology. 2009. Information related to the Economic Recovery Act of 2009. www.HealthIT.hhs.gov (accessed May 11, 2009).
- Oliver, S. R., R. W. Rees, L. Clarke-Jones, R. Milne, A. R. Oakley, J. Gabbay, K. Stein, P. Buchanan, and G. Gyte. 2008. A multidimensional conceptual framework for analysing public involvement in health services research. *Health Expectations* 11:72-84.
- Omenn, G. S. 1999. Caring for the community: The role of partnerships. *Academic Medicine* 74(7):782-789.
- Peterson, E., and C. W. Yancy. 2009. Eliminating racial and ethnic disparities in cardiac care. *New England Journal of Medicine* 360(12):1172-1174.

- President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. 1982. *Making health care decisions: The ethical and legal implications of informed consent in the patient-provider relationship*. http://bioethics.gov/reports/past_commissions/making_health_care_decisions.pdf (accessed June 25, 2009).
- Rawlins, M. 2008. De testimonio: On the evidence for decisions about the use of therapeutic interventions. *The Lancet* 372(9656):2152-2161.
- Rising, K., P. Bacchetti, and L. Bero. 2008. Reporting bias in drug trials submitted to the food and drug administration: Review of publication and presentation. *Public Library of Science Medicine* 5(11):e217.
- Sabin, J. E., K. Mazor, V. Meterko, S. L. Goff, and R. Platt. 2008. Comparing drug effectiveness at health plans: The ethics of cluster randomized trials. *Hastings Center Report* 38(5):39-48.
- Saunders, C., A. Girgis, P. Butow, S. Crossing, and A. Penman. 2008. From inclusion to independence—Training consumers to review research. *Health Research Policy and Systems* 6(3).
- Schwartz, R. S., G. D. Curfman, S. Morrissey, and J. M. Drazen. 2008. Full disclosure and the funding of biomedical research. *New England Journal of Medicine* 358(17):1850-1851.
- Shojania, K. G., and J. M. Grimshaw. 2005. Evidence-based quality improvement: The state of the science. *Health Affairs* 24(1):138-150.
- Staniszewska, S., N. Jones, M. Newburn, and S. Marshall. 2007. User involvement in the development of a research bid: Barriers, enablers and impacts. *Health Expectations* 10:173-183.
- Tatsioni, A., D. A. Zarin, N. Aronson, D. J. Samson, C. R. Flamm, C. Schmid, and J. Lau. 2005. Challenges in systematic reviews of diagnostic technologies. *Annals of Internal Medicine* 142(12 Part 2):1048-1055.
- Teva Pharmaceuticals. 2008. *Teva clozapine patient registry*. <https://clozapineregistry.com/AboutRegistry/GeneralOverview.aspx> (accessed June 16, 2009).
- Tunis, S. 2009. Strategies to improve comparative effectiveness research methods and data infrastructure. In *Implementing Comparative Effectiveness Research: Priorities, Methods, and Impact*. Washington, DC: Brookings.
- Turner, E. H., A. M. Matthews, E. Linardatos, R. A. Tell, and R. Rosenthal. 2008. Selective publication of antidepressant trials and its influence on apparent efficacy. *New England Journal of Medicine* 358(3):252-260.
- United States Cochrane Center Consumers United for Evidence-based Healthcare. 2009. *Understanding evidence-based healthcare: A foundation for action*. <http://apps1.jhsph.edu/cochrane/CUEwebcourse.htm> (accessed May 23, 2009).
- Van Spall, H. G. C., A. Toren, A. Kiss, and R. A. Fowler. 2007. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: A systematic sampling review. *JAMA* 297(11):1233-1240.
- Weinfurt, K. P., D. M. Seils, J. P. Tzeng, L. Lin, K. A. Schulman, and R. M. Califf. 2008. Consistency of financial interest disclosures in the biomedical literature: The case of coronary stents. *PLoS ONE* 3(5).
- Weinstein, J. N., K. Clay, and T. S. Morgan. 2007. Informed patient choice: Patient-centered valuing of surgical risks and benefits. *Health Affairs* 26(3):726-730.
- Wendler, D., R. Kington, J. Madans, G. Van Wye, H. Christ-Schmidt, L. A. Pratt, O. W. Brawley, C. P. Gross, and E. Emanuel. 2006. Are racial and ethnic minorities less willing to participate in health research? *PLoS Medicine* 3(2):201-210.
- Wennberg, J. E., and E. S. Fisher. 2008. Tracking the care of patients with severe chronic illness: The Dartmouth Atlas of health care 2008. Dartmouth Institute for Health Policy and Clinical Practice, Center for Health Policy Research. <http://www.dartmouthatlas.org/atlas/2008%5FChronic%5FCare%5FAtlas.pdf> (accessed June 8, 2009).

- Westfall, J. M., J. Mold, and L. P. Fagnan. 2007. Practice-based research—"Blue highways" on the NIH roadmap. *JAMA* 297:403-406.
- Williams, I. C., and G. Corbie-Smith. 2006. Investigator beliefs and reported success in recruiting minority participants. *Contemporary Clinical Trials* 27:580-586.
- Zerhouni, E. A. 2005. Translational and clinical science—Time for a new vision. *New England Journal of Medicine* 353(15):1621-1623.

Appendix A

Public Meeting Agenda— March 20, 2009



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION

PUBLIC AGENDA—FRIDAY, MARCH 20, 2009

FRIDAY, MARCH 20 — OPEN SESSION Stakeholder's Presentations — Auditorium

- 8:30am Welcome to Public Session (Dr. Sox)
- Mechanisms of announcement (email, website)
 - Mechanisms of input (meeting and call-in presentations, web submissions)
- 9:00am Invited presentations from stakeholders
- Myrl Weinberg, National Health Council
 - Nancy Nielsen, American Medical Association
 - Carmella Bocchino, America's Health Insurance Plans
 - Ted Buckley, Biotechnology Industry Organization
 - Mary Jean Schumann, American Nurses Association
 - William Vaughan, Consumers Union
 - Ted Epperly, American Academy of Family Physicians
 - Randy Burkholder, Pharmaceutical Research and Manufacturers of America
- Question and Answer Session

- 10:00am
- Naomi Aronson, Blue Cross/Blue Shield Association
 - Mohammad Akhter, National Medical Association
 - Dorothy Jeffress, Center for Advancement of Health
 - Robert Hall, American Academy of Pediatrics
 - Teresa Lee, Advanced Medical Technology Association
 - Antonio C. Wolff, American Society of Clinical Oncology
 - Jack Lewin, American College of Cardiology
 - Harold Miller, Network for Regional Healthcare Improvement
- Question and Answer Session
- 11:00am
- Bryan Luce, United BioSource Corporation
 - Leah Hole-Curry, WA State Health Care Authority
 - Erick Turner, Oregon health and Science University and Portland VA Medical
 - Robert Harrison, California Dept of Public Health
 - Gary Puckrein, National Minority Quality Forum
 - Marilyn Dix Smith, International Society for Pharmacoeconomics & Outcomes Research
 - Frederick Grover, Society of Thoracic Surgeons
 - Douglas Hadley, CIGNA
 - Adolph Falcon, National Alliance for Hispanic Health
 - Roger Williams, United States Pharmacopeia
- Question and Answer Session
- 12:00pm
- Lunch Break
- 1:00pm
- Nada Stotland, American Psychiatric Association
 - Ruth Lubic, Developing Families Center
 - William Weintraub, American Heart Association
 - Eugene Rich, Association of American Medical Colleges
 - Merrill Goozner, Center for Science in the Public Interest
 - Jeff Allen, Friends of Cancer Research
 - Les Paul, National Pharmaceutical Council
 - Steven Bailey, Society for Cardiovascular Angiography and Interventions
- Question and Answer Session
- 2:00pm
- Clifford Goodman, The Lewin Group
 - Amy Abernethy, Duke University Medical Center
 - Katie Orrico, American Association of Neurological Surgeons

- Christopher Fox, American Association for Dental Research
 - Amy Miller, Personalized Medicine Coalition
 - Douglas Peddicord, Association of Clinical Research Organizations
 - Patrick O'Connor, HealthPartners Research Foundation
 - Janet Marchibroda, eHealth Initiative
- Question and Answer Session
- 3:00pm
- James Bray, American Psychological Association
 - C. Edwin Webb, American College of Clinical Pharmacy
 - Harrison Spencer, Association of Schools of Public Health
 - Andrew Sperling, National Alliance on Mental Illness
 - John Brooks, University of Iowa
 - Marty Makary, American College of Surgeons
 - Perry D. Cohen, Parkinson Pipeline Project
 - Morgan Downey, Health Care Consultancy
 - Dennis Hart, Focus On Therapeutic Outcomes, Inc.
 - Eunice K. M. Ernst, Frontier School of Midwifery & Family Nursing
 - Carolyn Curtis
 - Patrick O'Connor, American College of Occupational and Environmental Medicine
- Question and Answer Session
- 3:50pm Concluding remarks (Dr. Sox)
- 4:00pm Adjourn

Appendix B

Stakeholder Questionnaire

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**Welcome to the Institute of Medicine's Questionnaire on Comparative Effectiveness Research Priorities**

BACKGROUND: The Institute of Medicine (IOM) requests your input for consideration of priorities for comparative effectiveness research (CER) as called for in the American Recovery and Reinvestment Act of 2009 (Stimulus Bill). In addition to allocating \$400 million to the Secretary of Health and Human Services for CER, the legislation mandates that the IOM produce and submit a consensus report by June 30, 2009, that provides specific recommendations to Congress and the Secretary for expenditure of these funds. The legislation also requires the IOM committee to solicit and consider public input as it develops its recommendations.

This questionnaire is a primary vehicle by which the committee will collect information on the priorities of all stakeholders in health care (e.g., patients, consumers, providers, state and federal agencies, employers, manufacturers, policy makers).

PUBLIC INPUT OPPORTUNITIES:

- **Questionnaire:** This questionnaire will be active from March 6 - March 27, 2009. All responses will be compiled into a database that will be reviewed by the committee. Please note that with the exception of individuals' email addresses and phone numbers, all responses will also be placed in a public access file as required by federal legislation. If you choose to omit contact information, your response will still be given full consideration.
- **Public Meeting:** A public meeting will be convened on March 20, 2009 in Washington, DC, during which stakeholders, including members of the public, will be invited to present to the committee, as time allows. Information and registration instructions are provided at the committee's website (www.iom.edu/cerpriorities).

SAVING AND SUBMITTING YOUR RESPONSE:

- **Saving:** You will be able to leave the questionnaire and then return to it later; however, you must complete an entire page and move on to the next page to save your work.
- **Submitting:** When you have completed the questionnaire you will see a confirmation page and will then be taken back to the committee's website where you can find additional information about the committee's work.
- **Printing:** Please note that if you wish to print your responses, you must print each page when you are finished with it by using your web browser's print menu options.

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**Instructions**

In the next 3 pages, you will have the opportunity to submit up to 3 comparative effectiveness studies for the committee's consideration. Please rank your suggested CER priorities as first, second, and third by entering them in that order.

Once you have submitted your top 3 priorities, you will be asked what criteria you feel are most important in establishing a national set of priorities for CER. You will be asked to select and rank criteria (e.g., disease burden, disease severity, variation in care, cost, public interest, information gap) as well as identify other criteria for the committee to consider.

Lastly, you will be asked to provide recommendations to the committee regarding what new or enhanced capacities and infrastructure are needed to sustain a national CER enterprise.

CER Scope

The committee's working definition for CER is: "The generation and synthesis of evidence that compares the effectiveness of alternative methods to prevent, diagnose, treat, monitor, and improve delivery of care for a clinical condition. The purpose of CER is to assist patients, clinicians, purchasers, and policy makers in making informed health decisions."

Please consider the following as you develop your suggested priority areas for study:

- **Study Population:** Identify a study population by disease entity, condition, susceptible population, or population affected.
- **Alternative Interventions:** Comparators might include systems of care as well as specific interventions to address the prevention, diagnosis, treatment, monitoring, or delivery of care. One comparator could be the current standard of care or usual care.
- **Outcome of Interest:** Please identify the health related risk, side effect or harm of greatest concern, and/or the health related benefit of greatest interest (e.g., patient-reported outcomes, surrogate endpoints [such as change in tumor size or laboratory parameters], clinical event, death).
- **Study Methods:** CER can include analyses of existing data, observational studies (e.g., Framingham study), prospective trials, and systematic reviews of published studies.

Overview of requested information

We anticipate a high response rate to this questionnaire. Therefore, to facilitate the committee's review of each response, we ask that you characterize each of your priorities by specifying the following:

- **A single sentence that frames your research question** (include condition, comparison, and outcome of interest)
- **Justification for why the question should be a national priority**
- **Area to be studied** (e.g., cardiovascular and peripheral vascular disease, racial and ethnic disparities in health care, nutrition)
- **Comparators** (i.e., include a comparison of two or more alternatives for the prevention, diagnosis, treatment, monitoring, or delivery of care for a clinical condition)
- **Study design** (e.g., analyses of existing data [systematic review], observational studies [such as the Framingham study], and prospective trials)
- **Study population** (e.g., children/adolescents, elderly, special populations)

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**CER Priority (1 of 3)**

Describe your **first priority** by answering the following questions.

***1. Please submit a single sentence that frames your research question. We request that your response specify a condition; a comparison of 2 or more alternatives for the prevention, diagnosis, treatment, monitoring, or delivery of care of the condition; and the study outcome(s) to be assessed (e.g., patient-reported outcomes, surrogate endpoints [such as change in tumor size or laboratory parameters], clinical event, death).**

For example: Compare the effectiveness of identifying pre-malignant lesions and early colon cancer by either virtual or actual colonoscopy in individuals at low to moderate risk of colon cancer.

***2. Please provide justification for why this study should be a priority. Please consider the following criteria in your justification:**

- disease burden
- increasing prevalence
- morbidity and mortality
- variability in care
- cost
- information gap (e.g., little is know about this topic)
- funding gap (e.g., minimal research is being done on this topic)
- public interest
- controversy
- disproportionate impact by subpopulation
- potential to act on the information once generated
- utility of the answer for decision making

Please limit your response to 100 words. To verify that your text is within the limits, use this [word count](#) link.

For example: Screening for colon cancer by colonoscopy identifies pre-malignant lesions and early cancers allowing for both prevention and cure. Many people needlessly delay this procedure because of perceived inconveniences or pain, and thus miss the potential benefits. Virtual colonoscopy may increase the number of people undergoing screening compared to the current number having colonoscopy, increase the number of pre-malignant and early cancers found, and reduce the death rate from colon cancer.

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:

3. Please specify the primary area to be studied in the left hand column. If your study involves multiple conditions, please mark the associated conditions in the right hand column. If you are unsure of how to characterize the condition described in questions 1 and 2 above, please indicate the specific condition/disease in the "other" box.

	Primary Condition (please select only one)	Comorbidity (associated conditions—you may select more than one)
Sexual Function and Reproductive Disorders	<input type="radio"/>	<input type="radio"/>
Skin Disorders	<input type="radio"/>	<input type="radio"/>
Cardiovascular and Peripheral Vascular Disease	<input type="radio"/>	<input type="radio"/>
Eyes, Ears, Nose, and Throat Disorders	<input type="radio"/>	<input type="radio"/>
Gastrointestinal System Disorders	<input type="radio"/>	<input type="radio"/>
Immune System, Connective Tissue, and Joint Disorders	<input type="radio"/>	<input type="radio"/>
Kidney and Urinary Tract Disorders	<input type="radio"/>	<input type="radio"/>
Pancreatic Disorders	<input type="radio"/>	<input type="radio"/>
Endocrinology and Metabolism Disorders (includes Diabetes)	<input type="radio"/>	<input type="radio"/>
Infectious Diseases (including HIV/AIDS)	<input type="radio"/>	<input type="radio"/>
Liver and Biliary Tract Disease	<input type="radio"/>	<input type="radio"/>
Musculoskeletal Disorders	<input type="radio"/>	<input type="radio"/>
Neurologic Disorders	<input type="radio"/>	<input type="radio"/>
Oncology and Hematology	<input type="radio"/>	<input type="radio"/>
Psychiatric Disorders	<input type="radio"/>	<input type="radio"/>
Respiratory Disease	<input type="radio"/>	<input type="radio"/>
Trauma, Emergency Medicine, Critical Care Medicine	<input type="radio"/>	<input type="radio"/>
Medical Aspects of Bioterrorism	<input type="radio"/>	<input type="radio"/>
Nutrition (includes Obesity)	<input type="radio"/>	<input type="radio"/>
Complementary and Alternative Medicine	<input type="radio"/>	<input type="radio"/>
Alcoholism, Drug Dependency, and Overdosage	<input type="radio"/>	<input type="radio"/>
Functional Limitation and Disabilities	<input type="radio"/>	<input type="radio"/>
Birth and Developmental Disorders	<input type="radio"/>	<input type="radio"/>
Genetics and Disease	<input type="radio"/>	<input type="radio"/>
Regenerative Medicine (e.g., stem cell research)	<input type="radio"/>	<input type="radio"/>
Safety and Quality of Health Care (e.g., delivery and organization of care)	<input type="radio"/>	<input type="radio"/>
Racial and Ethnic Disparities	<input type="radio"/>	<input type="radio"/>
Women's Health (including disorders during pregnancy)	<input type="radio"/>	<input type="radio"/>
Pediatrics	<input type="radio"/>	<input type="radio"/>
Geriatric Medicine	<input type="radio"/>	<input type="radio"/>
Palliative and End-of-Life Care	<input type="radio"/>	<input type="radio"/>
Other (please specify)	<input type="text"/>	

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**4. For this priority, please select the type(s) of interventions to be compared. You may select more than one.**

- | | |
|---|---|
| <input type="checkbox"/> Prevention | <input type="checkbox"/> Procedures – Surgery |
| <input type="checkbox"/> Testing, monitoring, and evaluation (e.g., lab, imaging, psychosocial and functional assessments) | <input type="checkbox"/> Devices (e.g., artificial joint, spinal cage, stent, pacemaker, breast implants) |
| <input type="checkbox"/> Standard of care/usual care (please elaborate on the specific elements of standard of care in the "other" box) | <input type="checkbox"/> Systems of Care (e.g., organization, management, delivery of healthcare services) |
| <input type="checkbox"/> Treatment – Behavioral | <input type="checkbox"/> Provider/Patient Relationships (e.g., counseling, education) |
| <input type="checkbox"/> Treatment – Alternative | <input type="checkbox"/> Treatment pathways (e.g., strategy for early stage prostate cancer, team approach to diabetes care vs. general care) |
| <input type="checkbox"/> Treatment – Pharmacological | |

Other (please specify)

5. For the topic you suggested, which of the following types of research would be most effective in providing the needed evidence?

- Synthesis of existing evidence (e.g., qualitative review, meta-analysis)
- Primary research using existing health care databases (might include electronic health record data or other clinical data)
- Primary research using prospective data collection without randomization (e.g., observational study, registry)
- Primary research through a prospective randomized trial

Other (please specify)

6. Please describe the study population(s). You may select more than one.

- | | |
|---|---|
| <input type="checkbox"/> Population at Large | <input type="checkbox"/> Elderly |
| <input type="checkbox"/> Men | <input type="checkbox"/> Long-term care (institutionalized and home care) |
| <input type="checkbox"/> Women | <input type="checkbox"/> Ethnic sub-populations only |
| <input type="checkbox"/> Children/Adolescents | <input type="checkbox"/> Rare Diseases |
| <input type="checkbox"/> Adults (excluding elderly) | <input type="checkbox"/> Special Populations (e.g., pregnant women, prisoners, low income, persons with disability)—please elaborate in the "other" box |
| <input type="checkbox"/> Adults (including elderly) | |

Other (please specify)

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:

***7. Would you like to submit another priority?**

Yes

No

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**CER Priority (2 of 3)**

Describe your **second priority** by answering the following questions.

***8. Please submit a single sentence that frames your research question. We request that your response specify a condition; a comparison of 2 or more alternatives for the prevention, diagnosis, treatment, monitoring, or delivery of care of the condition; and the study outcome(s) to be assessed (e.g., patient-reported outcomes, surrogate endpoints [such as change in tumor size or laboratory parameters], clinical event, death).**

A text input field with a light gray background and a thin black border. It contains no text. On the right side, there are two small vertical arrows (up and down) for scrolling. On the bottom left and right sides, there are small horizontal arrows (left and right) for scrolling.

***9. Please provide justification for why this study should be a priority. Please consider the following criteria in your justification:**

- disease burden
- increasing prevalence
- morbidity and mortality
- variability in care
- cost
- information gap (e.g., little is know about this topic)
- funding gap (e.g., minimal research is being done on this topic)
- public interest
- controversy
- disproportionate impact by subpopulation
- potential to act on the information once generated
- utility of the answer for decision making

Please limit your response to 100 words. To verify that your text is within the limits, use this [word count](#) link.

A text input field with a light gray background and a thin black border. It contains no text. On the right side, there are two small vertical arrows (up and down) for scrolling. On the bottom left and right sides, there are small horizontal arrows (left and right) for scrolling.

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:

10. Please specify the primary area to be studied in the left hand column. If your study involves multiple conditions, please mark the associated conditions in the right hand column. If you are unsure of how to characterize the condition described in questions 8 and 9 above, please indicate the specific condition/disease in the "other" box.

	Primary Condition (please select only one)	Comorbidity (associated conditions—you may select more than one)
Sexual Function and Reproductive Disorders	<input type="radio"/>	<input type="radio"/>
Skin Disorders	<input type="radio"/>	<input type="radio"/>
Cardiovascular and Peripheral Vascular Disease	<input type="radio"/>	<input type="radio"/>
Eyes, Ears, Nose, and Throat Disorders	<input type="radio"/>	<input type="radio"/>
Gastrointestinal System Disorders	<input type="radio"/>	<input type="radio"/>
Immune System, Connective Tissue, and Joint Disorders	<input type="radio"/>	<input type="radio"/>
Kidney and Urinary Tract Disorders	<input type="radio"/>	<input type="radio"/>
Pancreatic Disorders	<input type="radio"/>	<input type="radio"/>
Endocrinology and Metabolism Disorders (includes Diabetes)	<input type="radio"/>	<input type="radio"/>
Infectious Diseases (including HIV/AIDS)	<input type="radio"/>	<input type="radio"/>
Liver and Biliary Tract Disease	<input type="radio"/>	<input type="radio"/>
Musculoskeletal Disorders	<input type="radio"/>	<input type="radio"/>
Neurologic Disorders	<input type="radio"/>	<input type="radio"/>
Oncology and Hematology	<input type="radio"/>	<input type="radio"/>
Psychiatric Disorders	<input type="radio"/>	<input type="radio"/>
Respiratory Disease	<input type="radio"/>	<input type="radio"/>
Trauma, Emergency Medicine, Critical Care Medicine	<input type="radio"/>	<input type="radio"/>
Medical Aspects of Bioterrorism	<input type="radio"/>	<input type="radio"/>
Nutrition (includes Obesity)	<input type="radio"/>	<input type="radio"/>
Complementary and Alternative Medicine	<input type="radio"/>	<input type="radio"/>
Alcoholism, Drug Dependency, and Overdosage	<input type="radio"/>	<input type="radio"/>
Functional Limitation and Disabilities	<input type="radio"/>	<input type="radio"/>
Birth and Developmental Disorders	<input type="radio"/>	<input type="radio"/>
Genetics and Disease	<input type="radio"/>	<input type="radio"/>
Regenerative Medicine (e.g., stem cell research)	<input type="radio"/>	<input type="radio"/>
Safety and Quality of Health Care (e.g., delivery and organization of care)	<input type="radio"/>	<input type="radio"/>
Racial and Ethnic Disparities	<input type="radio"/>	<input type="radio"/>
Women's Health (including disorders during pregnancy)	<input type="radio"/>	<input type="radio"/>
Pediatrics	<input type="radio"/>	<input type="radio"/>
Geriatric Medicine	<input type="radio"/>	<input type="radio"/>
Palliative and End-of-Life Care	<input type="radio"/>	<input type="radio"/>
Other (please specify)	<input type="text"/>	

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**11. For this priority, please select the type(s) of interventions to be compared. You may select more than one.**

- | | |
|---|---|
| <input type="checkbox"/> Prevention | <input type="checkbox"/> Procedures – Surgery |
| <input type="checkbox"/> Testing, monitoring, and evaluation (e.g., lab, imaging, psychosocial and functional assessments) | <input type="checkbox"/> Devices (e.g., artificial joint, spinal cage, stent, pacemaker, breast implants) |
| <input type="checkbox"/> Standard of care/usual care (please elaborate on the specific elements of standard of care in the "other" box) | <input type="checkbox"/> Systems of Care (e.g., organization, management, delivery of healthcare services) |
| <input type="checkbox"/> Treatment – Behavioral | <input type="checkbox"/> Provider/Patient Relationships (e.g., counseling, education) |
| <input type="checkbox"/> Treatment – Alternative | <input type="checkbox"/> Treatment pathways (e.g., strategy for early stage prostate cancer, team approach to diabetes care vs. general care) |
| <input type="checkbox"/> Treatment – Pharmacological | |

Other (please specify)

12. For the topic you suggested, which of the following types of research would be most effective in providing the needed evidence?

- Synthesis of existing evidence (e.g., qualitative review, meta-analysis)
- Primary research using existing health care databases (might include electronic health record data or other clinical data)
- Primary research using prospective data collection without randomization (e.g., observational study, registry)
- Primary research through a prospective randomized trial

Other (please specify)

13. Please describe the study population(s). You may select more than one.

- | | |
|---|---|
| <input type="checkbox"/> Population at Large | <input type="checkbox"/> Elderly |
| <input type="checkbox"/> Men | <input type="checkbox"/> Long-term care (institutionalized and home care) |
| <input type="checkbox"/> Women | <input type="checkbox"/> Ethnic sub-populations only |
| <input type="checkbox"/> Children/Adolescents | <input type="checkbox"/> Rare Diseases |
| <input type="checkbox"/> Adults (excluding elderly) | <input type="checkbox"/> Special Populations (e.g., pregnant women, prisoners, low income, persons with disability)—please elaborate in the "other" box |
| <input type="checkbox"/> Adults (including elderly) | |

Other (please specify)

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:

***14. Would you like to submit another priority?**

Yes

No

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**CER Priority (3 of 3)**

Describe your **third priority** by answering the following questions.

***15. Please submit a single sentence that frames your research question. We request that your response specify a condition; a comparison of 2 or more alternatives for the prevention, diagnosis, treatment, monitoring, or delivery of care of the condition; and the study outcome(s) to be assessed (e.g., patient-reported outcomes, surrogate endpoints [such as change in tumor size or laboratory parameters], clinical event, death).**

***16. Please provide justification for why this study should be a priority. Please consider the following criteria in your justification:**

- disease burden
- increasing prevalence
- morbidity and mortality
- variability in care
- cost
- information gap (e.g., little is know about this topic)
- funding gap (e.g., minimal research is being done on this topic)
- public interest
- controversy
- disproportionate impact by subpopulation
- potential to act on the information once generated
- utility of the answer for decision making

Please limit your response to 100 words. To verify that your text is within the limits, use this [word count](#) link.

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:

17. Please specify the primary area to be studied in the left hand column. If your study involves multiple conditions, please mark the associated conditions in the right hand column. If you are unsure of how to characterize the condition described in questions 15 and 16 above, please indicate the specific condition/disease in the "other" box.

	Primary Condition (please select only one)	Comorbidity (associated conditions—you may select more than one)
Sexual Function and Reproductive Disorders	<input type="radio"/>	<input type="radio"/>
Skin Disorders	<input type="radio"/>	<input type="radio"/>
Cardiovascular and Peripheral Vascular Disease	<input type="radio"/>	<input type="radio"/>
Eyes, Ears, Nose, and Throat Disorders	<input type="radio"/>	<input type="radio"/>
Gastrointestinal System Disorders	<input type="radio"/>	<input type="radio"/>
Immune System, Connective Tissue, and Joint Disorders	<input type="radio"/>	<input type="radio"/>
Kidney and Urinary Tract Disorders	<input type="radio"/>	<input type="radio"/>
Pancreatic Disorders	<input type="radio"/>	<input type="radio"/>
Endocrinology and Metabolism Disorders (includes Diabetes)	<input type="radio"/>	<input type="radio"/>
Infectious Diseases (including HIV/AIDS)	<input type="radio"/>	<input type="radio"/>
Liver and Biliary Tract Disease	<input type="radio"/>	<input type="radio"/>
Musculoskeletal Disorders	<input type="radio"/>	<input type="radio"/>
Neurologic Disorders	<input type="radio"/>	<input type="radio"/>
Oncology and Hematology	<input type="radio"/>	<input type="radio"/>
Psychiatric Disorders	<input type="radio"/>	<input type="radio"/>
Respiratory Disease	<input type="radio"/>	<input type="radio"/>
Trauma, Emergency Medicine, Critical Care Medicine	<input type="radio"/>	<input type="radio"/>
Medical Aspects of Bioterrorism	<input type="radio"/>	<input type="radio"/>
Nutrition (includes Obesity)	<input type="radio"/>	<input type="radio"/>
Complementary and Alternative Medicine	<input type="radio"/>	<input type="radio"/>
Alcoholism, Drug Dependency, and Overdosage	<input type="radio"/>	<input type="radio"/>
Functional Limitation and Disabilities	<input type="radio"/>	<input type="radio"/>
Birth and Developmental Disorders	<input type="radio"/>	<input type="radio"/>
Genetics and Disease	<input type="radio"/>	<input type="radio"/>
Regenerative Medicine (e.g., stem cell research)	<input type="radio"/>	<input type="radio"/>
Safety and Quality of Health Care (e.g., delivery and organization of care)	<input type="radio"/>	<input type="radio"/>
Racial and Ethnic Disparities	<input type="radio"/>	<input type="radio"/>
Women's Health (including disorders during pregnancy)	<input type="radio"/>	<input type="radio"/>
Pediatrics	<input type="radio"/>	<input type="radio"/>
Geriatric Medicine	<input type="radio"/>	<input type="radio"/>
Palliative and End-of-Life Care	<input type="radio"/>	<input type="radio"/>
Other (please specify)	<input type="text"/>	

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**18. For this priority, please select the type(s) of interventions to be compared. You may select more than one.**

- | | |
|---|---|
| <input type="checkbox"/> Prevention | <input type="checkbox"/> Procedures – Surgery |
| <input type="checkbox"/> Testing, monitoring, and evaluation (e.g., lab, imaging, psychosocial and functional assessments) | <input type="checkbox"/> Devices (e.g., artificial joint, spinal cage, stent, pacemaker, breast implants) |
| <input type="checkbox"/> Standard of care/usual care (please elaborate on the specific elements of standard of care in the "other" box) | <input type="checkbox"/> Systems of Care (e.g., organization, management, delivery of healthcare services) |
| <input type="checkbox"/> Treatment – Behavioral | <input type="checkbox"/> Provider/Patient Relationships (e.g., counseling, education) |
| <input type="checkbox"/> Treatment – Alternative | <input type="checkbox"/> Treatment pathways (e.g., strategy for early stage prostate cancer, team approach to diabetes care vs. general care) |
| <input type="checkbox"/> Treatment – Pharmacological | |

Other (please specify)

19. For the topic you suggested, which of the following types of research would be most effective in providing the needed evidence?

- Synthesis of existing evidence (e.g., qualitative review, meta-analysis)
- Primary research using existing health care databases (might include electronic health record data or other clinical data)
- Primary research using prospective data collection without randomization (e.g., observational study, registry)
- Primary research through a prospective randomized trial

Other (please specify)

20. Please describe the study population(s). You may select more than one.

- | | |
|---|---|
| <input type="checkbox"/> Population at Large | <input type="checkbox"/> Elderly |
| <input type="checkbox"/> Men | <input type="checkbox"/> Long-term care (institutionalized and home care) |
| <input type="checkbox"/> Women | <input type="checkbox"/> Ethnic sub-populations only |
| <input type="checkbox"/> Children/Adolescents | <input type="checkbox"/> Rare Diseases |
| <input type="checkbox"/> Adults (excluding elderly) | <input type="checkbox"/> Special Populations (e.g., pregnant women, prisoners, low income, persons with disability)—please elaborate in the "other" box |
| <input type="checkbox"/> Adults (including elderly) | |

Other (please specify)

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**Criteria for Establishing Priorities**

***21. Briefly describe the process used to develop your priorities. Please limit your response to 100 words. To verify that your text is within the limits, use this [word count link](#).**

***22. Please rank what criteria you, or your organization view as most important for setting national priorities for CER.**

Criteria in order of importance

1st	<input type="text"/>
2nd	<input type="text"/>
3rd	<input type="text"/>
4th	<input type="text"/>
5th	<input type="text"/>

Other(s) (specify and include rank)

NOTE: The drop down choices for question 22 included the following:

- Disease burden
- Increasing prevalence
- Morbidity and mortality
- Variability in care
- Cost
- Information gap
- Funding gap
- Public interest
- Controversy
- Disproportionate impact by subpopulation
- Potential to act on the information
- Utility of the answer for decision making

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**Additional Input Regarding CER Infrastructure**

Effective implementation of CER priorities may require investments in infrastructure. If you have suggestions on specific investments necessary to support expanded CER research, please submit your recommendations for the committee's consideration.

***23. What are the highest priorities for developing new or enhanced systems, alliances, or capacities to sustain a national comparative effectiveness research enterprise? You may select up to four.**

- Increased workforce training (e.g., clinical researchers, epidemiologists, statisticians, informatics)
- Clinical trials support (e.g., ad hoc collaborations)
- Clinical data pooling and mining support
- Novel method development for data analysis and modeling
- Clinical registry development, application, and networking
- Creation of robust national registries for tracking both short- and long-term performance of therapeutic strategies, drugs, or devices
- Capacity to use electronic health records for safety and effectiveness monitoring
- Inclusion or creation of direct patient data entry (e.g., questionnaires, surveys, personal health records to provide patient-reported outcomes)
- Increased coordination of CER through existing Health and Human Services entities
- Creation of an independent institute for CER

24. Additional suggestions for infrastructure development for committee consideration. Please limit your response to 100 words. To verify that your text is within the limits, use this [word count](#) link.

 A rectangular text input field with a light gray background and a thin border. On the right side of the field, there are two small, vertically stacked buttons: a top button with an upward-pointing arrow and a bottom button with a downward-pointing arrow. Below the input field, there is a horizontal bar with a dotted pattern, containing a left-pointing arrow on the left and a right-pointing arrow on the right.

IOM COMMITTEE ON COMPARATIVE EFFECTIVENESS RESEARCH PRIORITIZATION:**Demographic Information**

The following questions will help ensure that the committee has gathered input from a broad range of perspectives.

25. Please select a description that best describes your role or perspective:

- | | |
|---|--|
| <input type="checkbox"/> Employer | <input type="checkbox"/> Medical Administrator |
| <input type="checkbox"/> Government - Programs (e.g., Medicare, Medicaid) | <input type="checkbox"/> Nonprofit/Policy Institute |
| <input type="checkbox"/> Government - Research | <input type="checkbox"/> Patient/Family (including family caregiver) |
| <input type="checkbox"/> Health Care Provider | <input type="checkbox"/> Professional Association |
| <input type="checkbox"/> Health Plan/Insurance Carrier | <input type="checkbox"/> Public/Consumer |
| <input type="checkbox"/> Manufacturer (Device) | <input type="checkbox"/> Researcher |
| <input type="checkbox"/> Manufacturer (Drug or Biologic) | |

Other (please specify)

***26. Who are you representing with your response?**

- Self
- Organization

27. Please provide your contact information (optional).

Note that your email address and phone number will not be released to the public. If you choose to omit contact information, your response will still be given full consideration.

Name:

Organization:

Title:

Email Address:

Phone Number:

Appendix C

Data Tables: Burden of Disease and Variation of Care

As discussed in Chapter 3, the committee selected published data tables to use in the voting process to provide proxy indicators for burden of disease and variation in care. The Medical Expenditure Panel Survey (MEPS) provided information on prevalence (Table C-1), morbidity (Table C-3) and cost (Table C-4), and the National Vital Statistics Report on mortality (Table C-2). The Dartmouth Institute for Health Policy and Clinical Practice analyzed clinical practice data according to variation in treatment for surgical procedures (Table C-5) and medical conditions (Table C-6) at the Institute of Medicine's request. Data sources were chosen based on their year of production (with preference given to the most recent reports), representativeness of the nation's entire population, and ability to provide age stratification.

TABLE C-1 Number of People Receiving Care for Selected Conditions in the U.S. Civilian Noninstitutionalized Population in 2006

Conditions	Total Persons (in thousands)
<i>People of all ages</i>	
Chronic Obstructive Pulmonary Disease (COPD), asthma	48,455
Hypertension	45,795
Mental disorders	36,246
Trauma-related disorders	34,899
Acute Bronchitis and URI	33,869
Hyperlipidemia	29,884
Skin disorders	22,700
Disorders of the upper GI	21,602
Osteoarthritis and other non-traumatic joint disorders	21,491
Back problems	20,487
Heart conditions	19,711
Residual Codes	19,149
Diabetes mellitus	18,268
Other eye disorders	16,403
Infectious diseases	16,254
Systemic lupus and connective tissues disorders	15,113
Female genital disorders, and contraception	14,998
Other CNS disorders	14,540
Cancer	11,114
Otitis media	10,951
Other bone and musculoskeletal disease	10,069
<i>People ages <1 year</i>	
Otitis media	1,893
Acute Bronchitis and URI	1,641
COPD, asthma	1,063
Infectious diseases	820
Other eye disorders	591

TABLE C-1 Continued

Conditions	Total Persons (in thousands)
<i>People ages 1-17 years</i>	
COPD, asthma	12,588
Acute Bronchitis and URI	12,221
Otitis media	7,595
Trauma-related disorders	6,687
Mental disorders	4,570
Infectious diseases	4,222
Skin disorders	4,067
Other eye disorders	3,469
Intestinal infection	2,899
Other CNS disorders	1,853
Allergic reactions	1,783
<i>People ages 65+ years</i>	
Hypertension	19,844
Hyperlipidemia	13,201
Heart conditions	10,242
COPD, asthma	9,002
Osteoarthritis and other non-traumatic joint disorders	8,881
Diabetes mellitus	7,436
Mental disorders	7,393
Disorders of the upper GI	7,044

SOURCE: AHRQ (2009c).

TABLE C-2 Number of Deaths for People in the United States by Age in 2005

Cause of Death	Number of Deaths
<i>People of all ages</i>	
Ischemic heart diseases	445,687
Malignant neoplasms of trachea, bronchus and lung	159,292
Acute myocardial infarction	151,004
Cerebrovascular diseases	143,579
Chronic lower respiratory diseases	130,933
Accidents (unintentional injuries)	117,809
Diabetes mellitus	75,119
Alzheimer's disease	71,599
Influenza and pneumonia	63,001
Pneumonia	61,189
Heart failure	58,933
Malignant neoplasms of lymphoid, hematopoietic and related tissue	55,028
Malignant neoplasms of colon, rectum and anus	53,252
Renal failure	42,868
Malignant neoplasm of breast	41,491
Septicemia	34,136
Malignant neoplasm of pancreas	32,760
Intentional self-harm (suicide)	32,637
Hypertensive heart disease	29,282
Malignant neoplasm of prostate	28,905
<i>People age <1 year</i>	
Congenital malformations, deformations and chromosomal abnormalities	5,552
Disorders related to length of gestation and fetal malnutrition	4,798
Sudden infant death syndrome	2,230
Other respiratory conditions originating in the perinatal period	1,160
Accidents (unintentional injuries)	1,083
Infections specific to the perinatal period	1,039
Respiratory distress of newborn	860
Bacterial sepsis of newborn	834

TABLE C-2 Continued

Cause of Death	Number of Deaths
<i>People age 1-14 years</i>	
Accidents (unintentional injuries)	4079
Malignant neoplasms	1377
Congenital malformations, deformations and chromosomal abnormalities	918
Assault (homicide)	716
Major cardiovascular diseases	584
Diseases of heart	403
<i>People age 65+ years</i>	
Ischemic heart diseases	365,491
Cerebrovascular diseases	123,881
Acute myocardial infarction	119,164
Malignant neoplasms of trachea, bronchus and lung	112,826
Chronic lower respiratory diseases	112,716
Alzheimer's disease	70,858
Influenza and pneumonia	55,453
Diabetes mellitus	55,222
Heart failure	54,740
Malignant neoplasms of lymphoid, hematopoietic and related tissue	40,267
Malignant neoplasms of colon, rectum and anus	39,100
Accidents (unintentional injuries)	36,729
Renal failure	35,642
Malignant neoplasm of prostate	26,327
Septicemia	26,243
Malignant neoplasm of breast	23,747
Malignant neoplasm of pancreas	23,397
Hypertensive heart disease	20,295
Parkinson's disease	19,030

SOURCE: Kung et al. (2008).

TABLE C-3 The Number of Events for People in the U.S. Civilian Noninstitutionalized Population in 2006

Condition	Number of Events (in thousands)
<i>People of all ages</i>	
Hypertension	246,722
Mental disorders	244,543
COPD, asthma	225,990
Trauma-related disorders	186,155
Diabetes mellitus	162,113
Back problems	160,397
Heart conditions	129,160
Osteoarthritis and other non-traumatic joint disorders	121,942
Acute Bronchitis and URI	94,124
Systemic lupus and connective tissues disorders	83,307
Cancer	74,611
Skin disorders	70,517
<i>People ages 0-17 years</i>	
COPD, asthma	54,354
Mental disorders	42,212
Acute Bronchitis and URI	33,931
Otitis media	24,568
Trauma-related disorders	18,899
Skin disorders	11,339
Infectious diseases	10,425
Other eye disorders	7,887
Other CNS disorders	7,010
Intestinal infection	5,798
Other endocrine, nutritional, and immune disorder	4,835
Allergic reactions	4,828

SOURCE: AHRQ (2009b).

TABLE C-4 Total Expenses for People for Selected Conditions in the U.S. Civilian Noninstitutionalized Population in 2006

Condition	Total Expenses (in millions)
<i>People of all ages</i>	
Heart conditions	\$ 78,032
Trauma-related disorders	\$ 68,142
Cancer	\$ 57,501
Mental disorders	\$ 57,452
COPD, asthma	\$ 51,320
Hypertension	\$ 48,507
Diabetes mellitus	\$ 48,341
Osteoarthritis and other non-traumatic joint disorders	\$ 37,538
Normal birth/live born	\$ 37,499
Back problems	\$ 35,015
<i>People age <1 year</i>	
Perinatal conditions	\$ 3,727
COPD, Asthma	\$ 1,227
Congenital anomalies	\$ 1,035
Otitis media	\$ 883
Acute Bronchitis and URI	\$ 743
Infectious diseases	\$ 716
Disorders of the upper GI	\$ 510
Gallbladder, pancreatic, and liver disease	\$ 393
Intestinal infection	\$ 383
Trauma-related disorders	\$ 310
<i>People ages 1-17 years</i>	
Mental disorders	\$ 8,834
COPD, asthma	\$ 7,080
Trauma-related disorders	\$ 5,890
Acute Bronchitis and URI	\$ 2,730
Infectious diseases	\$ 2,720
Otitis media	\$ 2,451
Skin disorders	\$ 1,305
Other eye disorders	\$ 1,197
Tonsillitis	\$ 1,119
Epilepsy and convulsions	\$ 985

TABLE C-4 Continued

Condition	Total Expenses (in millions)
<i>People age 65+ years</i>	
Heart conditions	\$ 46,151
Diabetes mellitus	\$ 21,420
Cancer	\$ 21,299
Hypertension	\$ 20,432
Trauma-related disorders	\$ 20,327
COPD, asthma	\$ 20,295
Osteoarthritis and other non-traumatic joint disorders	\$ 17,217
Mental disorders	\$ 13,598
Kidney disease	\$ 13,331
Back problems	\$ 10,462

SOURCE: AHRQ (2009a).

TABLE C-5 Pattern of Variation in Admissions for Procedures Among Hospital Referral Regions

Condition	Coefficient of Variation
Septicemia	34.1
COPD	34.0
Back Surgery	32.8
Congestive Heart Failure	27.3
Gastroenteritis	27.0
Simple Pneumonia	24.1
Knee Replacement	21.4
Cardiac Arrhythmia	20.6
Gastrointestinal Hemorrhage	16.3
Stroke	16.0
Hip Fracture Discharge	14.4

NOTE: Coefficient of variation is calculated as the ratio of the standard deviation to the mean (multiplied by 100, so expressed as a percent) across geographic units in the United States.

SOURCE: Wennberg (2009).

TABLE C-6 Pattern of Variation in Admission for Treatment of Conditions Among Hospital Referral Regions

Procedure	Coefficient of Variation
Percutaneous Interventions (PCI)	34.0
Lower Extremity Bypass	33.6
Carotid Endarterectomy	33.2
Back Surgery	32.8
TURP for BPH	31.7
Mastectomy for Cancer	30.4
CABG	26.7
Hip Replacement	26.4
Cholecystectomy	21.5
Knee Replacement	21.4
Hip Fracture discharge	14.4

NOTE: Coefficient of variation is calculated as the ratio of the standard deviation to the mean (multiplied by 100, so expressed as a percent) across geographic units in the United States.

SOURCE: Wennberg (2009).

REFERENCES

- AHRQ (Agency for Healthcare Research and Quality). 2009a. Medical Expenditure Panel Survey: Total expenses for conditions by site of service: United States <http://www.meps.ahrq.gov/mepsweb/> (accessed March 10, 2009).
- . 2009b. Total number of events accounting for expenditures by site of service: United States, 2006. In *Medical Expenditure Panel Survey Component Data*.
- . 2009c. Total number of people accounting for expenditures (deduplicated) by site of service: United States, 2006. In *Medical Expenditure Panel Survey Component Data*.
- Kung, H.-C., D. L. Hoyert, J. Xu, S. L. Murphy, and Division of Vital Statistics. 2008. *Deaths: Final data for 2005*. *National Vital Statistics Reports* National Center for Health Statistics.
- Wennberg, J. E. 2009 (unpublished). *Recommendations to the Institute of Medicine on comparative effectiveness research priorities*. Submitted in response to a request from the Institute of Medicine Committee on Comparative Effectiveness Research Prioritization. The Dartmouth Institute for Health Policy and Clinical Practice.

Appendix D

Cardiovascular and Peripheral Vascular Cover Sheet

This is one of 32 cover sheets addressing the research areas represented by the nominated topics provided to the committee to guide their prioritization process. The data included the committee's condition-level criteria pertinent to the specific research area.

(n) the number in parenthesis signifies the number of conditions on the particular list

X signifies condition appears on the list of the top (n) conditions

Blank signifies that condition does not appear on the list of the top (n) conditions

Prevalence—Number of people receiving care for selected conditions, 2006

MEPS Survey Data

Condition	All age groups (20)	Age 0-1 years (5)	Ages 1-17 years (11)	65+ years (8)
Hypertension	X			X
Hyperlipidemia	X			X
Heart conditions	X			X

Mortality—Number of deaths, 2005

National and Vital Statistics Report

Condition	All age groups (20)	Age 0-1 years (8)	Ages 1-14 years (6)	65+ years (20)
Ischemic heart diseases	X			X
Acute myocardial Infarction	X			X

Condition	All age groups (20)	Age 0-1 years (8)	Ages 1-14 years (6)	65+ years (20)
Cerebrovascular diseases	X			X
Heart failure	X			X
Hypertensive heart disease	X			X
Major cardiovascular diseases			X	
Diseases of heart			X	

Morbidity—Number of events for selected conditions including: Hospital outpatient or office based, Hospital inpatient, ER, Home health visits, and Prescribed medicines, 2006

MEPS Survey Data

Condition	All age groups (12)	Ages 0-17 years (12)
Hypertension	X	
Heart conditions	X	

Cost—Total expenses for selected conditions including: Hospital outpatient or office based, Hospital inpatient, ER, Home health visits, and Prescribed medicines, 2006

MEPS Survey Data

Condition	All ages (10)	Age 0-1 years (10)	Age 1-17 years (10)	Age 65+ years (10)
Heart conditions	X			X
Hypertension	X			X

Variability—The Dartmouth Institute for Health Policy and Clinical Practice Data, 2005

Condition	Variation of hospitalization for procedure (11)	Variation in treatment for conditions (11)
Congestive heart failure		X
Cardiac arrhythmia		X
Stroke		X
PCI	X	
Lower extremity bypass	X	
Carotid endarterectomy	X	
CABG	X	

Condition Appears on Other Priority Lists

Condition	AHRQ Effective Health Care program (19)	Healthy People 2010 (32)	National Quality Forum (5)	Cochrane (15)
Cardiovascular disease, including stroke and hypertension	X	X		X

Funding Gap—Number of Trials by Sponsor Type, February 2000 to April 2009
Clinicaltrials.gov

Condition	NIH	Industry	Other Federal Agencies	Universities/Organizations	Total
Anticoagulant therapy for myocardial infarction	6	43	1	37	74
Anticoagulant therapy for stroke	9	43	0	44	81
Cardiac imaging	107	154	3	287	537

Condition	NIH	Industry	Other Federal Agencies	Universities/Organizations	Total
Congestive heart failure	87	227	35	268	537
Hyperlipidemia	103	365	22	257	666
Hypertension	535	1080	74	1211	2616
Stable angina pectoris or acute coronary syndrome	93	151	6	262	439

REFERENCES

- AHRQ (Agency for Healthcare Research and Quality). 2009. Medical Expenditure Panel Survey. <http://www.meps.ahrq.gov/mepsweb/> (accessed March 10, 2009).
- Doyle, J., E. Waters, D. Yach, D. McQueen, A. De Francisco, T. Stewart, P. Reddy, A. M. Gulmezoglu, G. Galea, and A. Portela. 2005. Global priority setting for Cochrane systematic reviews of health promotion and public health research. *Journal of Epidemiology and Community Health* 59:193-197.
- HHS (Department of Health and Human Services). 2000. Healthy People 2010: Understanding and improving health. Place Published: U.S. Government Printing Office. <http://purl.access.gpo.gov/GPO/LPS4217> (accessed April 3, 2009).
- Kung, H.-C., D. L. Hoyert, J. Xu, S. L. Murphy, and Division of Vital Statistics. 2008. *Deaths: Final data for 2005. National Vital Statistics Reports* National Center for Health Statistics.
- NIH (National Institutes of Health). 2009. Clinicaltrials.Gov. <http://www.clinicaltrials.gov/> (accessed June 5, 2009).
- NPP (National Priorities Partnership). 2008. *National priorities and goals*. Washington, DC: National Quality Forum.
- Wennberg, J. E. 2009 (unpublished). *Recommendations to the Institute of Medicine on comparative effectiveness research priorities*. Submitted in response to a request from the Institute of Medicine Committee on Comparative Effectiveness Research Prioritization. The Dartmouth Institute for Health Policy and Clinical Practice.
- Whitlock, E. P., S. A. Lopez, S. Chang, M. Helfand, M. Eder, and N. Floyd. 2009. Identifying, selecting, and refining topics for comparative effectiveness systematic reviews: AHRQ and the Effective Health Care Program. <http://effectivehealthcare.ahrq.gov/repFiles/20090427IdentifyingTopics.pdf> (accessed June 5, 2009).

Appendix E

Definitions of Medical Terminology in CER Priority List

Ablative techniques	Removal of tissue by vaporization, abrasion, or destruction.
Active surveillance	The systematic collection, analysis, interpretation, and dissemination of health data on an ongoing basis to gain knowledge of the pattern of disease occurrence and potential in a community in order to control and prevent disease in the community.
Activities of daily living (ADL)	The performance of the basic activities of self care, such as dressing, ambulation, eating, and so on, in rehabilitation.
Angiography	X-ray of blood vessels after injection of a contrast medium.
Anticoagulant therapy	Agents that prevent blood clotting.
Anti-VEGF (vascular endothelial growth factor)	Anti-VEGF drugs work by blocking VEGF, a protein that helps the formation of new blood vessels.

Atypical antipsychotics	New generation of drugs for treatment of psychosis and schizophrenia.
Biologic response modifiers	Treatment of diseases with biological materials such as the use of genes, cells, tissues, organs, serum, vaccines, and humoral agents.
Biologics	Complex pharmaceutical substances, preparations, or agents of organic origin, usually obtained by biological methods or assay (e.g., monoclonal antibodies, recombinant proteins).
Biomarkers	Measurable and quantifiable biological parameters which serve as indices for health- and physiology-related assessments, such as disease risk, psychiatric disorders, environmental exposure and its effects, disease diagnosis, metabolic processes, substance abuse, pregnancy, cell line development, and epidemiologic studies.
Body mass index (BMI)	An indicator of body density as determined by the relationship of body weight to body height. For adults, BMI falls into these categories: below 18.5 (underweight); 18.5-24.9 (normal); 25.0-29.9 (overweight); 30.0 and above (obese).
Cardiac resynchronization	A treatment for selected patients with heart failure-induced conduction disturbances and ventricular dyssynchrony.
Catheter ablation	Removal of tissue with electrical current delivered via electrodes positioned at the distal end of a catheter.
Central line entry	A long, thin, flexible tube inserted into a major central vein used to give medicines, fluids, nutrients, or blood products over a long period of time, usually several weeks or more.

Cervical spondylotic myelopathy	The most common cause of spinal cord dysfunction in older persons. The aging process results in degenerative changes in the cervical spine that, in advanced stages, can cause compression of the spinal cord.
Chlorhexidine	A disinfectant and topical anti-infective agent also used as mouthwash to prevent oral plaque.
Clinical decision support system	Computer-based information systems used to integrate clinical and patient information and provide support for decision making in patient care.
Cluster randomized trial	A trial in which individuals are randomized in groups (i.e., the group is randomized, not the individual).
Cochlear implants	Electronic hearing devices typically used for patients with normal outer and middle ear function, but defective inner ear function.
Colonoscopy	Procedure in which a long flexible viewing tube (a colonoscope) is threaded up through the rectum for the purpose of inspecting the entire colon and rectum and, if there is an abnormality, taking a biopsy of it or removing it.
Comorbidity	The presence of co-existing or additional diseases.
Compendia	A collection.

Comprehensive care coordination program	Primary care is considered comprehensive when the primary provider takes responsibility for the overall coordination of the care of the patient's health problems, be they biological, behavioral, or social. The appropriate use of consultants and community resources may be an important part of the comprehensive care program. Such care is generally provided by physicians but is increasingly provided by other personnel such as nurse practitioners or physician assistants.
Computed tomography (CT) angiography	A noninvasive imaging method that uses computed x-ray data combined with specialized imaging software to examine blood vessels.
Continuous ambulatory peritoneal dialysis (CAPD)	Portable peritoneal dialysis using the continuous (24 hours a day, 7 days a week) presence of peritoneal dialysis solution in the peritoneal cavity except for periods of drainage and instillation of fresh solution.
Coronary stenosis	Narrowing or constriction of a coronary artery.
CRF2 receptors (Corticotropin-releasing factor)	A receptor subtype from mammalian brain.
Crohn's disease	A chronic inflammation that may involve any part of the digestive tract from mouth to anus, mostly found in the ileum, the cecum, and the colon.
CT colonography	A noninvasive imaging method that uses computed x-ray data combined with specialized imaging software to examine the colon.

Diabetic retinopathy	Disease of the retina as a complication of diabetes mellitus. It is characterized by progressive microvascular complications.
Diagnostic and Statistical Manual of Mental Disorders (DSM)	Categorical classification of mental disorders based on criteria sets with defining features. It is produced by the American Psychiatric Association.
Digital mammography	Digital (computerized) mammography is similar to standard mammography in that x-rays are used to produce detailed images of the breast.
Disease management programs	A mechanism to provide long-term case management for individuals with chronic or expensive conditions (e.g., diabetes, asthma, burn recovery).
Ductal carcinoma in situ	A noninvasive (noninfiltrating) cancer of the breast characterized by a proliferation of malignant cells confined to the mammary ducts or lobules.
Electronic health record	Electronic recording of pertinent information concerning patient's illness or illnesses.
Esophageal adenocarcinoma	A malignant epithelial tumor with a glandular organization of the esophagus.
Fecal immunochemical tests	Screen for lower gastrointestinal bleeding associated with colorectal cancer, adenomas, polyps, and other lower gastrointestinal conditions.
Fecal occult blood test (FOBT)	A test to examine evidence of gastrointestinal bleeding. May be done to check for some intestinal conditions or colorectal cancer.

Gastroesophageal reflux disease	Retrograde flow of gastric juice (gastric acid) and/or duodenal contents (bile acids; pancreatic juice) into the distal esophagus, commonly due to incompetence of the lower esophageal sphincter.
Hemodialysis	Therapy for the insufficient cleansing of the blood by the kidneys.
Hyperbaric oxygen	The therapeutic intermittent administration of oxygen in a chamber at greater than sea-level atmospheric pressures (three atmospheres).
Hyperlipidemia	Condition with excess lipids in the blood.
Hypertension	Persistently high systemic arterial blood pressure.
Iatrogenic	Due to the action of a physician or a therapy the doctor prescribed. An iatrogenic disease may be inadvertently caused by a physician or surgeon or by a medical or surgical treatment or a diagnostic procedure.
Incidence	A measure of the frequency with which an event, such as a new case of illness, occurs in a population over a defined period of time.
Infant mortality	Postnatal deaths from birth to 365 days after birth in a given population.
Intractable epilepsy	Epilepsy refractive to treatment.
Intravitreal steroids	Direct injection of glucocorticoids into the gel of the eye.
Knee arthroplasty surgery	Replacement of the knee joint.

Low birth weight	An infant having a birth weight of 2,500 g (5.5 lb.) or less.
Macular degeneration	Deterioration in the macula lutea of the retina.
Medical home	There is no single definition or medical home model, but is generally described as a model of delivering primary care that is accessible, continuous, comprehensive, family-centered, coordinated, compassionate, and culturally effective care.
Methicillin resistant <i>Staphylococcus aureus</i> (MRSA)	A strain of <i>Staphylococcus aureus</i> that is non-susceptible to the action of methicillin.
Methotrexate	An antimetabolite drug used in the treatment of cancer and autoimmune diseases.
Migraine prophylaxis	Prevention of severe headaches.
Negative pressure wound therapy	The application of a vacuum across the surface of a wound through a foam dressing cut to fit the wound. This removes wound exudates, reduces build-up of inflammatory mediators, and increases the flow of nutrients to the wound thus promoting healing.
Off-label use	The practice of using medicines for non-Food and Drug Administration approved reasons.
Open-angle glaucoma	Increased pressures within the eye in which the angle of the anterior chamber is open and the trabecular meshwork does not encroach on the base of the iris.
Osteopenia	Metabolic bone disease with mild decrease in bone density.

Osteoporosis	Reduction of bone mass without alteration in the composition of bone, leading to fractures.
PCI/PTCA (Percutaneous coronary intervention/ Percutaneous transluminal coronary angioplasty)	A variety of procedures used to treat patients with diseased arteries of the heart.
Pervasive developmental disorder, not otherwise specified (PDD-NOS)	A “subthreshold” condition in which some—but not all—features of autism or another explicitly identified developmental disorder are identified.
Pharmacological	Drug metabolism and drug interactions.
Preterm births	Childbirth before 37 weeks of pregnancy.
Prophylaxis	Use of therapy to prevent the occurrence of symptoms or disease.
Prospective registry	A place where data, records, or laboratory samples are kept and usually made available for research or comparative study.
Radical prostatectomy	Complete or partial surgical removal of the prostate.
Radiotherapy	The use of ionizing radiation to treat cancers and some benign conditions.
Remote physiologic monitoring/remote sensing	Tracking patients’ vital signs and health status without physical presence.
Retinal vein occlusion	Blockage of the central vein of the eye. Those at high risk for this condition include patients with hypertension, diabetes mellitus, atherosclerosis, and other cardiovascular diseases.

Risk assessment	The measure of the association between exposure to something and the outcome.
Risk factors	A characteristic of a person that affects that person's chance of having a disease.
Screening outcomes	Using tests or other methods of diagnosis to find out whether or not a person has a specific disease or condition before it causes any symptoms.
Surgical bypass	Surgical repair of an obstructive lesion.
Surgical resection	Surgical removal of part of an organ or a structure.
Symptomatic cervical disc herniation	Symptoms stemming from pressure on the spinal cord due to protrusion of a disc between the spinal vertebrae in the neck.
Telemedicine	Delivery of health services via telecommunications. This includes interactive consultative and diagnostic services.
Thromboembolic disease	Obstruction of a blood vessel by a blood clot in the bloodstream either originating at the site or migrating from a separate site of origin.
Ulcerative colitis	Inflammation of the colon that is predominantly confined to the inner lining. Its major symptoms include diarrhea, rectal bleeding, the passage of mucus, and abdominal pain.
Upper endoscopy	Examination involving passing an optical instrument along natural body pathways such as the digestive tract for disease diagnosis and treatment.

Vascular claudication	Pain resulting from limited blood flow to the lower extremities usually due to atherosclerosis.
Viral genomic profile	Determination of the specific genes (genetic material) in a given virus in order to characterize behavior.

NOTE: Definitions adapted from the National Library of Medicine's Medical Subject Headings (MeSH), WebMD, MedicineNet, National Center for Health Statistics, National Institute of Health Policy, Imaginis, Quest Diagnostics, the Centers for Disease Control and Prevention Reproductive Health Glossary, The National Center for Medical Home Implementation, Yale School of Medicine Child Study Center, Merriam-Webster Online, The American Heart Association, and The Free Dictionary by Farlex.

Appendix F

Committee Biographies

Harold C. Sox, M.D., M.A.C.P. (Co-Chair), is the editor of *Annals of Internal Medicine*. He graduated from Stanford University (B.S. in physics) and Harvard Medical School and served as a medical intern and resident at Massachusetts General Hospital. He spent 15 years on the faculty of the Stanford University School of Medicine, where he was the chief of the division of general internal medicine and director of ambulatory care at the Palo Alto VA Medical Center. In 1988, he returned to Dartmouth where he served for 13 years as Joseph M. Huber Professor and chair of the department of medicine before taking his present position with the American College of Physicians. Dr. Sox was the President of the American College of Physicians from 1998 to 1999. He chaired the U.S. Preventive Services Task Force from 1990 to 1995, the Institute of Medicine Committee to Study HIV Transmission through Blood Products, and the Institute of Medicine Committee on Health Effects Associated with Exposures Experienced in the Gulf War. He chaired the Medicare Coverage Advisory Committee of the Center for Medicare Services from 1999 to 2003. He currently chairs the National Advisory Committee for the Robert Wood Johnson Foundation Physician Faculty Scholars Program and is a member of the Board of Directors of the Foundation for Informed Medical Decision Making. He was elected to the Institute of Medicine of the National Academies in 1993. His books include *Medical Decision Making*, *Common Diagnostic Tests: Selection and Interpretation*, and *HIV and the Blood Supply: An Analysis of Crisis Decision Making*.

Sheldon Greenfield, M.D. (Co-Chair), an internationally recognized leader in quality of care and health services research, is the Donald Bren Professor of Medicine and executive director of the Health Policy Research Institute, University of California at Irvine. Dr. Greenfield's research has focused on primary care outcomes, quality of chronic disease care, patient participation in care, and assessment of comorbidity. He was the 1995 recipient of the PEW Health Professions Commission Award for lifetime achievement in Primary Care Research. Dr. Greenfield is a recipient of the Glaser Award of the Society of General Internal Medicine and the 1999 Novartis Global Outcomes Leadership Award. Dr. Greenfield is the 2006 recipient of the Founders Award by the American College of Medical Quality (ACMQ). Dr. Greenfield was elected to the Institute of Medicine (IOM) in 1996. He chaired the IOM Committee on Guidance for Designing a National Health Care Disparities Report, and was chair of the IOM Cancer Survivorship Report. He was the chair of the National Diabetes Quality Improvement Alliance. His current research focus is on performance assessment at the individual physician level, heterogeneity of treatment effects, and quality of chronic disease care for ethnic and racial minorities. He received his undergraduate degree from Harvard College and his medical degree from the University of Cincinnati College of Medicine.

Christine K. Cassel, M.D., M.A.C.P., is president and CEO of the American Board of Internal Medicine (ABIM) and the ABIM Foundation, and an expert in geriatric medicine, bioethics and quality of care. Dr. Cassel, board certified in internal medicine and geriatric medicine, was the first female board chair of the ABIM and the first female president of the American College of Physicians. She chaired influential Institute of Medicine reports on end-of-life care and public health. In April 2009, Dr. Cassel was appointed by President Obama to the President's Advisory Council on Science and Technology. She has also held leadership positions in academic medicine, including the University of Chicago, Mount Sinai Medical Center in New York City, and Oregon Health & Science University. An active scholar and lecturer, Dr. Cassel is the author or coauthor of 14 books and more than 150 journal articles on geriatric medicine, aging, bioethics and health policy. Her most recent book is *Medicare Matters: What Geriatric Medicine Can Teach American Health Care*.

Kay Dickersin, M.A., Ph.D., is Professor of Epidemiology at Johns Hopkins Bloomberg School of Public Health, and Director of the Center for Clinical Trials. She is also the director of the U.S. Cochrane Center (USCC) and is director of the Cochrane Eyes and Vision Group US Satellite. The USCC supports Consumers United for Evidence-based Healthcare (CUE), a partnership with health and consumer advocacy organizations, started

in 2003. Dr. Dickersin's main research contributions have been in clinical trials, systematic reviews, publication bias, trials registers, and the development and utilization of methods for the evaluation of medical care and its effectiveness. Dr. Dickersin currently is engaged in or has recently completed projects funded by the National Institutes of Health, the Agency for Healthcare Research and Quality, Blue Shield California, the Cochrane Collaboration, and the Center for Medical Technology Policy. At the Institute of Medicine (IOM), she has been a member of many committees, including the Committee on Reviewing Evidence to Identify Highly Effective Clinical Services. Dr. Dickersin received a Master's Degree in zoology, specializing in cell biology, from the University of California, Berkeley, and a Ph.D. in epidemiology from Johns Hopkins University's School of Hygiene and Public Health. Among her honors, Kay served as president of the Society for Clinical Trials (2008-2009) and has been elected to membership in the American Epidemiology Society and the IOM.

Alan M. Garber, M.D., Ph.D., is the Henry J. Kaiser Jr. Professor and a professor of medicine at Stanford, where he directs the Center for Health Policy and the Center for Primary Care and Outcomes Research. He is a staff physician at the Palo Alto VA and directs the Health Care Program of the National Bureau of Economic Research (NBER). He is a member of the Panel of Health Advisers of the Congressional Budget Office, the American Society for Clinical Investigation, the Association of American Physicians, and the Institute of Medicine of the National Academy of Sciences. He served as the chair of the Medicare Evidence Development and Coverage Advisory Committee (Centers for Medicare & Medicaid Services), as a member of the National Advisory Council on Aging (National Institutes of Health), and as a member of many committees of the National Institutes of Health and of the National Academies. His work addresses methods for improving health care delivery and financing, particularly for the elderly. It encompasses technology evaluation, analysis of the causes of health expenditure growth, and health care productivity. A summa cum laude graduate of Harvard College, he received his Ph.D. in economics from Harvard and an M.D. with research honors from Stanford, and trained in medicine at Brigham and Women's Hospital.

Constantine Gatsonis, Ph.D., is professor of medical science (Biostatistics) and founding director of the Center for Statistical Sciences at Brown University. Dr. Gatsonis is a leading authority on the evaluation of diagnostic and screening tests and has extensive involvement in methodologic research in medical technology assessment and in health services and outcomes research. He is Group Statistician of the American College of Radiology Imaging Network (ACRIN), a National Cancer Institute funded

collaborative group conducting multicenter studies of diagnostic imaging and image-guided therapy for cancer. A major focus of the research publications and current interests of Dr. Gatsonis is on Bayesian inference and its applications to problems in biostatistics, with emphasis on the evaluation of diagnostic imaging and health services and outcomes research. Dr. Gatsonis has served on the Institute of Medicine Immunization Safety Review Committee, the National Academy of Sciences (NAS) Committee on Identifying the Needs of the Forensic Sciences Community (co-chair), the NAS Committee to Study Engineering Aviation Security Environments, the NAS Committee on Applied and Theoretical Statistics, the Commission on Technology Assessment of the American College of Radiology, the Research Development Committee of the Radiology Society of North America, the HSDG Study Section of the Agency for Health Care Policy Research review panels of the Center for Devices and Radiological Health of the Food and Drug Administration, and technical expert panels for Health Care Financing Administration/Centers for Medicare & Medicaid Services. He is the founding editor in chief of *Health Services and Outcomes Research Methodology*, an associate editor of *the Annals of Applied Statistics*, *Bayesian Analysis*, *Statistics and Probability Letters*, and *Clinical Trials* and convenor of the Diagnostic and Screening Test Methods Working Group, Cochrane Collaboration. Dr. Gatsonis was elected fellow of the American Statistical Association and the Association for Health Services Research. He received his BA in mathematics, magna cum laude, from Princeton and his PhD in mathematical statistics from Cornell.

Gary L. Gottlieb, M.D., M.B.A., serves as president of Brigham and Women's/Faulkner Hospitals, a position he has held since March 1, 2002. He is a professor of psychiatry at the Harvard Medical School. Partners Health-Care recruited Dr. Gottlieb to become the first chairman of Partners Psychiatry in 1998 and he served in that capacity through 2005. In 2000, he added the role of president of the North Shore Medical Center where he served until early 2002. Prior to coming to Boston, Dr. Gottlieb spent 15 years in positions of increasing leadership in health care in Philadelphia. In 1983, he arrived at the University of Pennsylvania as a Robert Wood Johnson Foundation Clinical Scholar. Through that program, he earned an M.B.A. with distinction in Health Care Administration from Penn's Wharton Graduate School of Business Administration. He credits the program with building a foundation of interest in health policy, management, and academic leadership. Dr. Gottlieb went on to establish Penn Medical Center's first program in geriatric psychiatry and developed it into a nationally recognized research, training, and clinical program. Dr. Gottlieb rose to become executive vice chair and interim chair of Penn's Department of Psychiatry and the Health System's Associate Dean for Managed Care. In

1994, he became director and CEO of Friends Hospital in Philadelphia, the nation's oldest, independent, freestanding psychiatric hospital. In addition to his noteworthy academic, clinical and management record, Dr. Gottlieb has published extensively in geriatric psychiatry and health care policy. He is a past president of the American Association of Geriatric Psychiatry. Dr. Gottlieb also was a director of NASDAQ-traded OVID Technologies from 1997 to 1998 and participated in its acquisition by Wolters Kluwer Publishing. Dr. Gottlieb received his B.S. cum laude from the Rensselaer Polytechnic Institute and his M.D. from the Albany Medical College of Union University in a 6-year accelerated biomedical program. He completed his internship and residency and served as Chief Resident at New York University/Bellevue Medical Center. Now, as a recognized community leader in Boston, Dr. Gottlieb also focuses his attention on workforce development and disparities in health care. He was appointed by Mayor Thomas Menino as chairman of the Private Industry Council, the city's workforce development board, which partners with education, labor, higher education, the community, and government to provide oversight and leadership to public and private workforce development programs. In 2004-2005, he served as co-chair of the Mayor's Task Force to Eliminate Health Disparities. Dr. Gottlieb is slated to become the president and CEO of Partners HealthCare System in January 2010.

James A. Guest, J.D., became president and CEO of Consumers Union in February 2001 after a long career in public service and the consumer interest, including 21 years as chair of Consumers Union's Board of Directors. Consumers Union is the expert, independent, nonprofit organization that publishes *Consumer Reports* magazine, *ConsumerReports.org*, *Consumer Reports on Health*, and other special publications. Consumers Union operates the Consumer Reports Health Ratings Center, the Best Buy Drugs Program, which was supported initially, in part, by a grant from the National Library of Medicine, and other programs relating to health care quality and safety for which it also may seek federal grants. Consumers Union has a public policy and advocacy division which advocates for governmental and marketplace policies in the consumer interest. Mr. Guest is a member of the Institute of Medicine Roundtable on Evidence-Based Medicine, the Quality Alliance Steering Committee, and the Lucian Leape Institute of the National Patient Safety Foundation. He has spoken before various health stakeholder groups including the Association of Academic Health Centers, America's Health Insurance Plans, the World Health Care Congress, the National Business Group on Health, and others. Mr. Guest also serves as vice president of Consumers International, a federation of more than 225 consumer organizations from 115 countries that serves as the global campaigning voice for consumers around the world. Mr. Guest's public service career

spans more than three decades. After graduating from Amherst College, studying economics at MIT as a Woodrow Wilson Fellow, and graduating from Harvard Law School, he worked as a legislative assistant to Senator Edward Kennedy. In the early 1970s, Mr. Guest moved to Vermont, where he served as Banking and Insurance Commissioner, Secretary of State, and Secretary of Development and Community Affairs. Over the past 20 years, he has served as CEO of several service organizations and advocacy groups including Planned Parenthood of Maryland, Handgun Control, Inc. and the Center to Prevent Handgun Violence, and the American Pain Foundation, a national consumer information, education, and advocacy organization for pain prevention and management.

Mark Helfand, M.D., M.P.H., M.S., is a professor in the Departments of Medicine and Medical Informatics and Clinical Epidemiology at Oregon Health & Science University and a practicing physician at the Portland VA Medical Center. He has directed the Oregon Evidence-based Practice Center since 1997 and is also editor in chief of the journal *Medical Decision Making*. Dr. Helfand received his A.B. and B.S. from Stanford University and his M.D. and MPH from the University of Illinois School of Medicine. He specialized in internal medicine at Stanford, where he also completed a fellowship and earned an M.S. in health services research. Dr. Helfand has been a leader in methods for comparative effectiveness research. From 1998 to 2002, Dr. Helfand led a team that helped the U.S. Preventive Services Task Force prioritize topics and develop evidence-based guidelines. In the area of comparative effectiveness, he was a founder of the Drug Effectiveness Review Project (2003-2006) and, since 2004, has served as director of the Scientific Resource Center for AHRQ's Effective Health Care program. In addition to AHRQ, Dr. Helfand's work is funded by the Veterans Administration, the National Library of Medicine, Consumers Union, and the Society for Medical Decision Making.

Maria Carolina Hinestrosa, M.P.H.,* is the executive vice president for Programs and Planning at the National Breast Cancer Coalition (NBCC), and founder and former executive director of Nueva Vida, a support organization for Latinas with cancer. She is a breast cancer survivor, having been diagnosed with this disease in 1994 and in 2000. In 2008, she was diagnosed with a radiation-induced sarcoma, a consequence of her prior breast cancer treatment. Ms. Hinestrosa chairs the Integration Panel of the Department of Defense Breast Cancer Research Program, serves on the National Advisory Council and on the Stakeholder Group of the Effective

*Deceased.

Health Care Program at the Agency for Healthcare Research and Quality; on the Roadmap and the Communications Groups of the Institute of Medicine's (IOM's) Roundtable on Evidence-Based Medicine, and on the Oversight Body of the Ethical Force of the American Medical Association, among other national committees. She has served on the IOM's committees on Technologies for the Early Detection of Breast Cancer (Mammography and Beyond) and Reauthorization of MQSA (Improving the Quality of Breast Imaging Standards), as well as on the Breast Cancer Technical Panel of the National Quality Forum, on the National Action Plan on Breast Cancer and on the National Cancer Institute's Central Institutional Review Board. Ms. Hinestrosa is an economist from Universidad del Rosario in Bogota, Colombia; obtained a masters degree in economics from Western Illinois University as a Fulbright Scholar, and a Masters of Public Health from the George Washington University in Washington, DC. Prior to her service as a consumer advocate, she worked as a business economist and strategic planner in Colombia and New Zealand.

George J. Isham, M.D., M.S., chief health officer and plan medical director, is responsible for health promotion and disease prevention, research, and health professionals' education. He is also responsible for the health dimension of HealthPartners' strategic plan and is active in state and national health policy issues. As plan medical director, he is responsible for quality and utilization management for HealthPartners Health Plan. He is a founding board member of the Institute for Clinical Systems Improvement, a collaborative of Twin Cities medical groups and health plans that is implementing clinical practice guidelines in Minnesota. Dr. Isham is currently a co-chair of a State of Minnesota Health Care Reform Task Force that is working on defining episodes of care. Dr. Isham provides leadership to other care delivery systems through service on the board of directors for Presbyterian Health Services in Albuquerque, New Mexico and the External Advisory board of the Marshfield Clinic in Marshfield, Wisconsin. Dr. Isham is active nationally as a member of the board of directors of the American's Health Insurance Plans, the Alliance of Community Health Plans, the Accreditation Association for Ambulatory Care, and Bridges to Excellence. He is past co-chair and current member of the National Committee for Quality Assurance's (NCQA) Committee on Performance Measurement which oversees the Health Plan quality measurement standards and currently chairs the NCQA's committee on Physician Recognition Programs. He is a member of the National Priority Partners effort convened by the National Quality Forum, chairing the population health workgroup of that effort. He has served on the Centers for Disease Control and Prevention's (CDC) Task Force on Community Preventive Services, on the Agency for Healthcare Research and Quality's Advisory

Board for the National Guideline Clearinghouse, and currently is a member of the U.S. Task Force on Clinical Preventive Services. He currently serves on the advisory board for the Institute for Clinical and Economic Review at Harvard. Dr. Isham has served on the Institute of Medicine's (IOM) Board on Population Health and Public Health Practice and chaired the IOM committees that authored the reports *Priority Areas for National Action: Transforming Health Care Quality* and *The State of the USA Health Indicators*. Dr. Isham currently chairs the IOM Roundtable on Health Literacy. He was invited to present the IOM's Rosenthal Lecture for 2005 on "Next Steps Toward Higher Quality Health Care." In addition, he has served on a number of committees, has presented to a number of workshops, and has served as a reviewer of reports and workshop proceedings. In 2003, Dr. Isham was appointed as a lifetime National Associate of the National Academies of Science in recognition of his contributions to the work of the IOM.

Arthur A. Levin, M.P.H., is co-founder and the director of the Center for Medical Consumers, a New York City based nonprofit organization committed to informed consumer and patient health care decision making, patient safety, evidence-based, high-quality medicine and health care system transparency. It receives no funding from the drug, device or health care industry. Mr. Levin was a member of the Institute of Medicine's (IOM) Committee on the Quality of Health Care that published the *To Err is Human* and *Crossing the Quality Chasm* reports. He also served on a number of other IOM committees, most recently one that released its report *Knowing What Works in Health Care: A Roadmap for the Nation*, published last winter. He is a member of the IOM Board for Health Care Services. Mr. Levin is co-chair of the National Committee for Quality Assurance Committee on Performance Measures and a member of the National Quality Forum Consensus Standards Approval Committee (CSAC). Levin is also on the Board of the Foundation for Informed Medical Decision Making, dedicated to supporting patients and families in their health care decision making. Levin has served as the consumer representative on the FDA's Drug Safety and Risk Management Advisory Committee (DSaRM). On the health information and exchange technology front, Levin is on the board of THINC, a not-for-profit regional health information organization located in the mid-Hudson Valley and is a founding board member of the public-private partnership coordinating statewide HIT development and implementation, the New York State E-Health Collaborative (NYeC). Levin earned his M.P.H. degree in health policy from Columbia University School of Public Health and a B.A. degree in philosophy from Reed College.

JoAnn E. Manson, M.D., Dr.P.H., M.P.H., is professor of medicine and the Elizabeth Fay Brigham Professor of Women's Health at Harvard Medical School, chief of the Division of Preventive Medicine at Brigham and Women's Hospital (BWH), and co-director of the Connors Center for Women's Health and Gender Biology at BWH. An endocrinologist and epidemiologist, Dr. Manson is actively involved in women's health research, including several large-scale clinical trials and observational studies of cardiovascular disease (CVD), diabetes, and cancer. Her research has focused on the role of reproductive and hormonal factors, lifestyle and behavioral variables that influence chronic disease risk, health promotion and research translation, clinical trial methodology, and novel plasma and genetic markers as predictors of CVD, diabetes, and cancer. Dr. Manson is Principal Investigator of the Boston center for the Women's Health Initiative (WHI), the CVD component of the Harvard Nurses' Health Study, the Women's Antioxidant and Folic Acid Cardiovascular Trial, the Vitamin D and Omega-3 Trial, and other studies. She has published more than 700 articles in medical and scientific journals. Dr. Manson is the recipient of numerous awards, including the "Woman In Science Award" from the American Medical Women's Association, the Harvard College "Women's Professional Achievement Award," the Bowditch Award for Excellence in Public Health, the Postmenopausal Cardiovascular Health Research Award from the North American Menopause Society, the International Menopause Society's Henry Burger Prize, and others. She is an elected member of the Association of American Physicians, the American Epidemiological Society, and an elected Fellow of the American Association for the Advancement of Science, and she serves on a number of editorial and advisory boards, including the Board of the North American Menopause Society and the Scientific Advisory Board of the *Harvard HealthLetter* and *Nutrition Action HealthLetter*. Dr. Manson received her A.B. from Harvard University, her M.D. from Case Western Reserve University School of Medicine, and her M.P.H. and Dr.P.H. from the Harvard School of Public Health. Researchers at Brigham and Women's Hospital and Harvard University apply for and receive grants from the federal government and industry on health-related issues, including comparative effectiveness.

Katie Maslow, M.S.W., graduated from Stanford and received her M.S.W. degree from Howard University. She is the director for Policy Development at the Alzheimer's Association. Her various projects at the Association encompass project management and advocacy on the national level on many aspects of Alzheimer's and dementia care. She directed the Association's initiatives on managed care and co-directed its multisite demonstration project, Chronic Care Networks for Alzheimer's Disease. She also directed the Association's demonstration project on improving hospital care for

people with dementia, which included the development of training materials for hospital nurses caring for this population in partnership with the John A. Hartford Institute for Geriatric Nursing. She represented the Association on the National Assisted Living Workgroup and is the primary author of the Association's Alzheimer's Facts and Figures, 2008. Before joining the Alzheimer's Association, Ms. Maslow worked for 12 years at the U.S. Office of Technology Assessment, studying policy issues in aging, Alzheimer's disease, long-term care, end-of-life, and case management. Ms. Maslow's current employer, the Alzheimer's Association, receives grants from the U.S. Department of Justice, the U.S. Administration on Aging, the Centers for Disease Control and Prevention, long-term care provider organizations, and pharmaceutical and other private companies. Ms. Maslow has served on numerous government and non-government advisory panels on aging, Alzheimer's disease, dementia, family caregiving, home care, assisted living, nursing home care, and care coordination. She has served on the national board of the American Society of Aging (ASA) and won the Society's ASA award in 2003. She is a member of the American Geriatrics Society, the Gerontological Society of America, and the National Association of Social Workers.

Mark B. McClellan, M.D., Ph.D., is currently the director of the Engelberg Center for Health Care Reform, senior fellow in economic studies, and Leonard D. Schaeffer Director's Chair in Health Policy Studies at the Brookings Institution in Washington, DC. Before joining Brookings he was the administrator of the federal Centers for Medicare & Medicaid Services and the commissioner of the U.S. Food and Drug Administration. He is an internist and economist with an interest in developing innovative statistical methods for using observational data to estimate the effects of medical interventions. His research studies have focused on the economic and policy factors influencing medical treatment decisions and health outcomes; technological change in health care and its consequences for health and medical expenditures; and the relationship between health and economic well-being. He has previously served as a visiting scholar at the American Enterprise Institute, a member of the National Academy of Sciences' National Cancer Policy Board, associate editor of the *Journal of Health Economics*, and co-principal investigator of the Health and Retirement Study, a longitudinal study of the health and economic well-being of older Americans. During 2001 and 2002 he served in the White House as a senior policy director for health care and related economic issues. He has twice received the Arrow Award for Outstanding Research in Health Economics. He earned his Ph.D. in economics from the Massachusetts Institute of Technology, his M.D. from the Harvard-MIT Division of Health Sciences and Technology,

and completed a residency in internal medicine at Brigham and Women's Hospital.

Sally C. Morton, Ph.D., M.S., is vice president for Statistics and Epidemiology at RTI International. RTI receives funding from the federal government, foundations, and industry for research on health-related issues, including comparative effectiveness. Dr. Morton is the 2009 president of the American Statistical Association (ASA) and a member of the National Academy of Sciences Committee on National Statistics (CNSTAT). She served as a member of the Institute of Medicine (IOM) Committee on Reviewing Evidence to Identify Highly Effective Clinical Services. She does not receive compensation for any professional activity. Dr. Morton is an Adjunct Professor of Biostatistics at the UNC-Chapel Hill School of Public Health, and is a fellow of the ASA and of the American Association for the Advancement of Science (AAAS). She is a meta-analytic expert for the RTI-University of North Carolina (UNC) Evidence-based Practice Center (EPC), which receives funding from the Agency for Healthcare Research and Quality (AHRQ). Her research focuses on synthesis in evidence-based medicine, and surveys of vulnerable populations, and she has received of the AHSR Article-of-the-Year Award, and the AAPOR Policy Impact Award. Dr. Morton received a Ph.D. in statistics, an M.S. in operations research, a B.S. in mathematical sciences from Stanford, and an M.Sc. in statistics from the London School of Economics. Prior to joining RTI, Dr. Morton was the chair in Statistics and head of the Statistics Group at the RAND Corporation.

Neil R. Powe, M.D., M.P.H., M.B.A., is the Constance B. Wofsy Distinguished Professor and vice chair of medicine at the University of California San Francisco and chief of the Medical Service at San Francisco General Hospital. Until recently, he was the James F. Fries Distinguished Service Professor in the Department of Medicine at the Johns Hopkins University School of Medicine and Director of the Welch Center for Prevention, Epidemiology and Clinical Research, a multidisciplinary research and training center at Johns Hopkins focused on clinical and population-based research. He also was professor of epidemiology and health policy and management at Hopkins' Bloomberg School of Public Health and founding director of the Johns Hopkins Evidence-based Practice Center. He has published over 300 articles on the prevention, diagnosis and treatment of diseases, value of health care technologies, and the effectiveness of the health care system. His major areas of interest and expertise are kidney and cardiovascular diseases, effectiveness and outcomes research, and economic evaluations in health care. He has studied physician decision making and other determinants of use of medical practices including payers' decisions about insurance

coverage for new medical technologies, the effect of financial incentives on the use of technology, efficiency and outcomes in for-profit versus nonprofit health care institutions, and the relation between hospital volume, technology and outcomes. Dr. Powe receives major funding for his work from the National Institutes of Health and the Centers for Disease Control and Prevention. His work is also currently being supported by research grants from the Foundation for Informed Medical Decision Making and other charitable organizations. Among Dr. Powe's many honors are membership in the Institute of Medicine, the John M. Eisenberg National Award for Career Achievement in Research from the Society of General Internal Medicine and the Distinguished Educator Award from the Association of Clinical Research Training.

Joe V. Selby, M.D., M.P.H., is the director of the Division of Research, Kaiser Permanente, Northern California. He conducts research in the areas of cancer screening, diabetes outcomes and quality improvement research. He is a family physician, clinical epidemiologist and health services researcher. He also serves as lecturer in the Department of Epidemiology and Biostatistics, University of California, San Francisco School of Medicine, and as a Consulting Professor, Health Research and Policy, Stanford University School of Medicine. Dr. Selby was a member of the Agency for Healthcare Policy and Research study section for Health Care Quality and Effectiveness from 1999 through 2003. He is past chair and a member of Kaiser Permanente's National Research Council and of the Governing Board of the HMO Research Network. He was a commissioned officer in the Public Health Service from 1976 to 1983 and received the Commissioned Officer's Award in 1981. Dr. Selby has authored or co-authored over 200 peer-reviewed scientific publications, as well as numerous editorials and book chapters. His publications cover a spectrum of topics from colon cancer screening and diabetes outcomes research to the delivery of primary care, quality measurement and quality improvement. Dr. Selby's current research includes clinical comparative effectiveness studies in the areas of diabetes and hypertension care, with funding from the Agency for Healthcare Research and Quality, the National Heart, Lung, and Blood Institute, and the Centers for Disease Control and Prevention. He also serves as the director of a large research center in which a number of researchers apply for funding to conduct comparative effectiveness studies across a variety of clinical and programmatic areas.

Lisa Simpson, M.B., B.Ch., M.P.H., FAAP, is director of the Child Policy Research Center at Cincinnati Children's Hospital Medical Center and a professor of pediatrics in the Division of Health Policy and Clinical Effectiveness, Department of Pediatrics, University of Cincinnati. Dr. Simpson,

a board-certified pediatrician, also serves as the national director for Child Health Policy at the National Initiative for Children's Healthcare Quality, an education and research organization dedicated solely to improving the quality of health care provided to children. A nationally recognized health services and policy researcher, Dr. Simpson has led studies of the safety, quality and effectiveness of care for children and adolescents, the role of health information technology in improving care for children, disparities in care for children and youth, the health policy response to childhood obesity, and the role of policies in advancing child health at both state and national levels. She was formerly the deputy director of the Agency for Healthcare Research and Quality and the Maternal and Child Health Director in Hawaii. Dr. Simpson earned her undergraduate and medical degrees at Trinity College (Dublin, Ireland) and an M.P.H. at the University of Hawaii, and she completed a post-doctoral fellowship in health services research and health policy at the University of California, San Francisco. She is also an elected member of three organizations' Board of Directors, AcademyHealth, the Coalition for Health Services Research, and the National eHealth Collaborative, as well as numerous other national committees. She previously served on an Institute of Medicine Committee on improving the evidence base for health care (2008) and has recently been appointed by Governor Beshear to co-chair the Committee on Child Health and Wellbeing of the Commonwealth of Kentucky's Commission on Philanthropy. She has received numerous awards including the Excellence in Public Service Award from the American Academy of Pediatrics, the Senior Executive Service Meritorious Presidential Rank Award, the Health and Human Services Secretary's Distinguished Service Award, and, most recently, the 2007 Health Policy Researcher of the Year award from the Health Policy Institute of Ohio.

Sean Tunis, M.D., M.Sc., is the founder and director of the Center for Medical Technology Policy (CMTP) in San Francisco, where he works with health care decision makers, experts and stakeholders to develop methods, strategies and policies for comparative effectiveness research. CMTP receives support for this work from a number of foundations, government grants, as well as health plans, life sciences companies, and medical professional societies. Through September 2005, Dr. Tunis was the director of the Office of Clinical Standards and Quality and chief medical officer at the Centers for Medicare & Medicaid Services (CMS). In this role, he had lead responsibility for clinical policy and quality for the Medicare and Medicaid programs, which provide health coverage to over 100 million U.S. citizens. Dr. Tunis supervised the development of national coverage policies, quality standards for Medicare and Medicaid providers, quality measurement and public reporting initiatives, and the Quality Improvement Organization

program. As chief medical officer, Dr. Tunis served as the senior advisor to the CMS Administrator on clinical and scientific policy. He also co-chaired the CMS Council on Technology and Innovation. Dr. Tunis joined CMS in 2000 as the director of the Coverage and Analysis Group. Before joining CMS, Dr. Tunis was a senior research scientist with the Technology Assessment Group, where his focus was on the design and implementation of prospective comparative effectiveness trials and clinical registries. Dr. Tunis also served as the director of the Health Program at the Congressional Office of Technology Assessment and as a health policy advisor to the U.S. Senate Committee on Labor and Human Resources, where he participated in policy development regarding pharmaceutical and device regulation. He received a B.S. in biology and history of science from the Cornell University School of Agriculture, and a medical degree and masters in health services research from the Stanford University School of Medicine. Dr. Tunis did his residency training at UCLA and the University of Maryland in Emergency Medicine and Internal Medicine. He is board certified in Internal Medicine and holds adjunct faculty positions at Johns Hopkins and Stanford University Schools of Medicine.

I. Steven Udvarhelyi, M.D., M.Sc., is senior vice president and chief medical officer for Independence Blue Cross and its affiliated companies (IBC). In this role, Dr. Udvarhelyi has overall responsibility for medical management programs and policies, provider contracting and provider relations, pharmacy services, and informatics. Specific areas of responsibility in medical management include utilization management, case management, disease management, quality management, prevention and wellness, claim payment policy, and member and provider appeals and grievances. In overseeing informatics, Dr. Udvarhelyi is responsible for corporate-wide information management and reporting activities. Dr. Udvarhelyi also has oversight over IBC's pharmacy benefit management subsidiary. Dr. Udvarhelyi is a board-certified internist and has over 15 years of experience in the managed care industry. He received an A.B. from Harvard College, an M.D. from the Johns Hopkins University School of Medicine, and an M.S. in Health Services Administration from the Harvard School of Public Health. Prior to his career in the managed care and insurance industry, Dr. Udvarhelyi was a faculty member at Harvard Medical School and has published numerous articles on quality in health care. He currently serves on the Board of Directors of the National Committee for Quality Assurance, the National Council of Physician Executives of the Blue Cross Blue Shield Association, and on the Chief Medical Officers Committee of America's Health Insurance Plans. He is also a member of the Institute of Medicine (IOM)

Roundtable on Evidence-Based Medicine, and has served on other IOM committees in the past.

A. Eugene Washington, M.D., M.Sc., is executive vice chancellor and provost at the University of California, San Francisco (UCSF), where he is also professor of gynecology, epidemiology, and health policy in the School of Medicine. He has been a national leader in assessing medical technologies and shaping health policy. He has published extensively in his major areas of research, which include prenatal genetic testing, cervical cancer screening and prevention, noncancerous uterine conditions management, quality of health care, and racial/ethnic disparities in health outcomes. Dr. Washington co-founded UCSF's Medical Effectiveness Research Center for Diverse Populations in 1993 and served as the director from its establishment through July 2005, was chair of the Department of Obstetrics, Gynecology, and Reproductive Sciences from 1996 to 2004, and also co-founded the UCSF-Stanford Evidence-based Practice Center and served as its first director from 1997-2002. He is a member of the Institute of Medicine (IOM) of the National Academy of Sciences, where he serves on the governing Council of the IOM, and he also currently serves on the Scientific Management Review Board of the National Institutes of Health.

James N. Weinstein, D.O., M.S., is the Dartmouth College Third Century Professor and director of the Dartmouth Institute for Health Policy and Clinical Practice, professor and chair, Department of Orthopedic Surgery, Dartmouth Medical School, and vice chair, Board of Governors, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire. He is an internationally renowned spine surgeon and health services researcher. He is a leader in advancing "informed choice" to ensure that patients receive evidence-based, safe, effective, efficient and appropriate care. With Dr. John Wennberg, he established the first-in-the-nation Center for Shared Decision-Making. He also founded the multidisciplinary Spine Center, which has become an international model for patient-centered health care delivery, using patient-generated outcomes data to measure and inform clinical practice. He has recently been appointed vice chair of the Dartmouth-Hitchcock Board of Governors, with responsibility for oversight of operations for New Hampshire's only academic medical center, the largest supplier of health services in Northern New England. Dr Weinstein serves on the Institute of Medicine standing committee Social Security Administration Disability Determination, and is on the National Institutes of Health Council for NIAMS, and serves as a director for the American Board of Orthopaedic Surgery.

