





Exploring the Map of Clinical Research for the Coming Decade: Symposium Summary, Clinical Roundtable, December 2000

ISBN

Board on Health Sciences Policy

16 pages
8 1/2 x 11
2001

 [More information](#)

 [Find similar titles](#)

 [Share this PDF](#)



Visit the National Academies Press online and register for...

- ✓ Instant access to free PDF downloads of titles from the
 - NATIONAL ACADEMY OF SCIENCES
 - NATIONAL ACADEMY OF ENGINEERING
 - INSTITUTE OF MEDICINE
 - NATIONAL RESEARCH COUNCIL
- ✓ 10% off print titles
- ✓ Custom notification of new releases in your field of interest
- ✓ Special offers and discounts

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

Exploring the Map of Clinical Research for the Coming Decade

Symposium Summary
Clinical Research Roundtable
December 2000

Andrea L. Kalfoglou, Program Officer
Douglas A. Boenning, Senior Program Officer
David Korn, Symposium Coordinator

Board on Health Sciences Policy

INSTITUTE OF MEDICINE

Washington, D.C.

INSTITUTE OF MEDICINE • 2101 Constitution Avenue, N.W. • Washington, DC 20418

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.

Support for this project was provided by the AMA, AAMC, AHRQ, VA, CDC, FDA, NIH, RWJ, Blue Cross/Blue Shield, Johnson & Johnson, Burroughs Wellcome Fund, Merck and Co., Pfizer, Inc., and the Doris Duke Charitable Foundation. The views presented in this report are those of the Institute of Medicine Clinical Research Roundtable and are not necessarily those of the funding agencies.

Additional copies of this report are available in limited quantities from the Board on Health Sciences Policy, 2101 Constitution Avenue, N.W., Washington, D.C. 20418. Call (202) 334-2653. The full text of this report is available at www.nap.edu.

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

Copyright 2001 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.

*"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe*



INSTITUTE OF MEDICINE

Shaping the Future for Health

THE NATIONAL ACADEMIES

National Academy of Sciences
National Academy of Engineering
Institute of Medicine
National Research Council

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. Bruce M. Alberts 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. William A. Wulf 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. Kenneth I. Shine 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. Bruce M. Alberts and Dr. William A. Wulf are chairman and vice chairman, respectively, of the National Research Council.

Clinical Research Roundtable

- WILLIAM GERBERDING**, (Chair), President Emeritus, University of Washington, Seattle, Washington
- TOM BEAUCHAMP**, Professor of Philosophy and Senior Research Scholar, Kennedy Institute of Ethics, Georgetown University, Washington, D.C.
- ENRIQUETA BOND**, President, Burroughs Wellcome Fund, Research Triangle Park, North Carolina
- VERONICA CATANESE**, Associate Dean, New York University School of Medicine, Director of Development, American Federation for Medical Research Foundation, New York, New York
- FRANCIS CHESLEY**, Director, Office of Research, Review, Education and Policy, Agency for Healthcare Research and Quality, Rockville, Maryland
- WILLIAM F. CROWLEY, JR.**, Professor of Medicine, Harvard University, Director of Clinical Research, Massachusetts General Hospital, Boston, Massachusetts
- ADRIAN DOBS**, Associate Professor of Medicine, Director, Clinical Research Unit, Johns Hopkins University School of Medicine, Baltimore, Maryland
- JOHN FEUSSNER**, Chief Research and Development Officer, Department of Veterans' Affairs, Washington D.C.
- MYRON GENEL**, Associate Dean, Office of Government and Community Affairs, Yale University School of Medicine, New Haven, Connecticut
- KENNETH GETZ**, President/Publisher, CenterWatch, Boston, Massachusetts
- JACK GREBB**, Senior Vice President, Johnson & Johnson, Global CNS/Analgesia Clinical Research and Development, Janssen Research Foundation, Titusville, New Jersey
- STEPHEN KATZ**, Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Chief, Dermatology Branch, National Cancer Institute, Bethesda, Maryland
- ALLAN M. KORN**, Senior Vice President, Chief Medical Officer, Blue Cross/Blue Shield Association, Chicago, Illinois
- DAVID KORN**, Senior Vice President for Biomedical and Health Sciences Research, Association of American Medical Colleges, Washington D.C.
- ELAINE L. LARSON**, Professor of Pharmaceutical and Therapeutic Research, Columbia University School of Nursing, New York, New York
- MARY LERCHEN**, Director, Prevention Research and Academic Partnerships, Center for Disease Control and Prevention, Atlanta, Georgia
- E. ALBERT REECE**, Abraham Roth Professor and Chairman, Department of Obstetrics, Gynecology, and Reproductive Sciences, Temple University School of Medicine, Philadelphia, Pennsylvania
- DAVID L. RIMOIN**, Chairman of Pediatrics and Director, Medical Genetics-Birth Defects Center Cedars-Sinai Medical Center, Los Angeles, California
- PATRICIA SALBER**, Medical Director for Managed Care Health Care Initiative, General Motors Co., The Permanente Company, Larkspur, California
- LEWIS SANDY**, Executive Vice President, Robert Wood Johnson Foundation, Princeton, New Jersey
- DAVID SCHEINBERG**, Doris Duke Clinical Science Professor Chief, Leukemia Service, Memorial Sloan-Kettering Cancer, New York, New York

BERNARD SCHWETZ, Acting Deputy Commissioner and Senior Advisor for Science,
Food and Drug Administration, Rockville, Maryland

LOUIS SHERWOOD, Senior Vice President for Medical and Scientific Affairs, Merck and
Co., West Point, Pennsylvania

WILLIAM SIGMUND, Vice President for Medical Affairs, Pfizer Pharmaceuticals Group,
Pfizer, Inc., New York, New York

LANA SKIRBOLL, Director, Office of Science Policy, National Institutes of Health,
Rockville, Maryland

HAROLD SLAVKIN, Dean, G. Donald and Marian James Montgomery Professor of
Dentistry, School of Dentistry, University of Southern California, Los Angeles,
California

MYRL WEINBERG, President, National Health Council, Washington D.C.

MICHAEL J. WELCH, Co-Director, Division of Radiological Sciences, The Edward
Mallinckrodt Institute of Radiology, Washington University School of Medicine, St.
Louis, Missouri

Liaisons to the Roundtable

DAVID BLUMENTHAL, Liaison to the Board on Health Sciences Policy; Director,
Institute for Health Policy, Massachusetts General Hospital/Partners HealthCare System

STEVEN PAUL, Liaison to the Board on Neuroscience and Behavioral Health; Vice
President, Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center

HUGH TILSON, Liaison to the Board on Health Promotion and Disease Prevention; Senior
Advisor to the Dean, School of Public Health, University of North Carolina, Global
Health Outcomes, Glaxo Wellcome Company

MARY WOOLLEY, Liaison to the Board on Health Sciences Policy; President,
Research!America

Study Staff

ANDREW M. POPE, Director, Board on Health Sciences Policy

ALEX OMMAYA, Project Director (May 2001-Current)

ANDREA KALFOGLOU, Program Officer

DOUGLAS BOENNING, Project Director (June 2000-March 2001)

CURT TAYLOR, Senior Project Assistant (July 2000-March 2001)

Contributing Staff

FREDERICK J. MANNING, Senior Program Officer

CHARLES EVANS, Senior Advisor for Biomedical and Clinical Research

ALDEN CHANG, Administrative Assistant

REVIEWERS

The report was reviewed 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 to assist the authors and the Institute of Medicine in making the 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 content of the review comments and the draft manuscript remain confidential to protect the integrity of the deliberative process. The committee wishes to thank the following individuals for their participation in the report review process:

James Curran, Chair, Rollins School of Public Health, Atlanta, Georgia

Hugh Tilson, Liaison to the Board on Health Promotion and Disease Prevention; Senior Advisor to the Dean, School of Public Health, University of North Carolina, Global Health Outcomes, Glaxo Wellcome Company

Myrl Weinberg, President, National Health Council, Washington D.C.

Mary Woolley, President, Research America!, Alexandria, Virginia

Mel Worth, M.D., Scholar-in-Residence, Institute of Medicine, Washington, D.C.

While the individuals listed above provided many constructive comments and suggestions, responsibility for the final content of the report rests solely with the authoring committee and the Institute of Medicine.

Exploring the Map of Clinical Research for the Coming Decade

Symposium Summary
Clinical Research Roundtable
December 2000

Andrea L. Kalfoglou, Program Officer
Douglas A. Boenning, Senior Program Officer
David Korn, Symposium Coordinator

Board on Health Sciences Policy

INSTITUTE OF MEDICINE

Washington, D.C.

Abstract. During its third meeting in December 2000, the Clinical Research Roundtable held a symposium entitled Exploring the Map of Clinical Research for the Coming Decade. Speakers were asked to describe the infrastructure needs and clinical research environment of the next 10 years. Topics included the role and impact of genomics, bioinformatics, and clinical information systems on clinical research, as well as the future of evidence-based medicine. The symposium concluded with a panel of private and public health care purchasers, who discussed their interest and role in clinical research. Repeated themes included the need to encourage collaboration among researchers and between academic health centers and for-profit companies; the need to develop ways of rewarding collaborative research, particularly in academia; the need to develop good data and information management systems that can support huge databases and facilitate mining of clinical information while protecting patient privacy; and the need for more consistent standards for these highly valuable, large, automated population-based research resources, which could permit more effective cross-data system record linkages for population based research.

The Clinical Research Roundtable (CRR) of the National Academies held its third meeting on December 12-13, 2000 at the National Academy of Sciences in Washington, D.C. A public symposium, entitled Exploring the Map of Clinical Research for the Coming Decade, was hosted by the CRR as part of its meeting, and was chaired by CRR member David Korn, Senior Vice President for Biomedical and Health Sciences Research of the Association of American Medical Colleges. There were four panels: (1) The Impact of Genomics and Bioinformatics on Clinical Research, (2) The Role of Clinical Information Systems in Clinical Research, (3) What Is Evidence-Based Medicine, and How Do We Get There?, and (4) Should Purchasers of Health Care Be Concerned About Clinical Research?

Speakers were asked to describe the infrastructure needs and research environment of the next 10 years. Much of the discussion among the speakers and roundtable members revolved around the need for collaboration among researchers and the need to develop new ways of evaluating and rewarding this collaborative research, particularly in academic health centers. This report summarizes the general content of each presentation and discussions that occurred at the symposium.

Panel 1: The Impact of Genomics and Bioinformatics on Clinical Research

The first panel discussed the fields of genomics and bioinformatics, which refers to the computational biology tools required to analyze and statistically model genomic data. Eric Green, M.D., Ph.D., senior investigator, Chief of the Genome Technology Branch, and Director of the National Institutes of Health (NIH) Intramural Sequencing Center of the National Human Genome Research Institute at NIH, opened the first panel with a presentation on the history and background of the Human Genome Project (HGP). Dr. Green reviewed the past 30 years of DNA sequencing to demonstrate how the HGP has led to revolutionary technological improvements that have sped up the sequencing process. To date, 85-90 percent of the human genome has been sequenced. The next step will be to analyze all this data and then translate it into information that is useful in clinical practice. During a discussion with CRR members, Dr. Green stressed that research on the human genome requires a marriage between information technology, engineering, and molecular biology. He discussed a number of public- and private-sector training initiatives to help develop researchers with a knowledge base in all three areas. He recognizes that the centers that are now involved in sequencing will not be sequencing forever. He believes the next step is to figure out how to redistribute the tools and technology infrastructure to address a "broader array of biological problems."

Judith Vaitukaitis, M.D., Director of the National Center for Research Resources at the NIH, outlined the steps the NIH is taking to "Address the Infrastructure Needs for Clinical Research." She echoed Dr. Green's assertion that clinical research in the 21st century will depend on access to complex, expensive research tools, a multidisciplinary and collaborative approach, and good information management systems. She described a future in which clinical research centers form the core set of resources (research participants, human resources and technical assistance, bioinformatics, and specialized laboratories and equipment) that are available as national resources. The private sector must be included in network of resources. Next, she described national resources currently available to facilitate clinical research, such as research networks, tissue banks, and internet-based databases and networks. She concluded with the different types of grant support NIH is offering to enhance both researchers' and health care providers' career development.

John Gallin, M.D., director of the NIH Warren Grant Magnuson Clinical Center and NIH Associate Director for Clinical Research, stated that the biggest challenge facing clinical research in the coming decade is data management. He described a vision for a national and even international research enterprise in which clinical research centers are linked electronically. Next, he discussed NIH efforts to develop a new electronic data system called the Clinical Research Information System (CRIS), for the NIH Clinical Center, due to be implemented by the end of FY 2002. The goals of this system are (1) to provide tools for world-class clinical

research, (2) to improve the quality of patient care, and (3) to improve the cost-effectiveness of clinical care operations. An article describing this system is available on the NIH website. The system would assist clinical researchers with protocol writing, protocol review, protocol mapping, data capture for care/research, data management, adverse event detection/reporting, data presentation, and training and outreach. According to Dr. Gallin, "data coordination with a standardized vocabulary, to integrate patient care, research, and management, is a pressing need." Identifying and prioritizing informatics needs at national and institutional levels as well as increased federal and private funding to study and develop informatics support for clinical research are top priorities. Dr. Gallin handed out a pamphlet entitled "Standards for Clinical Research Within the NIH Intramural Research Program," which is available through the NIH Clinical Center's Office of Clinical Center Communications.

In her presentation on "Genomics and Human Genetics in Medicine," Vivian Cheung, M.D., Assistant Professor of Pediatrics in the Division of Neurology at the University of Pennsylvania, explained that genetics is the study of heredity or variation while genomics is the study of the global approach to cells, organs, and organisms at the DNA, RNA, and protein levels. Today, we are able to describe genetic variants that influence disease and drug metabolism and we are sequencing the genome of a number of different organisms. Tomorrow, we may be able to use genomics to diagnose, treat, and prevent disease. Dr. Cheung used the disease ataxia telangiectasia as an illustration.

In his presentation on "Genomic Approaches to the Genetics of Common Disease," David Altshuler, M.D., Ph.D., Assistant Professor of Genetics and Medicine, Harvard Medical School and Massachusetts General Hospital, and Director, Medical and Population Genetics, Whitehead/MIT Center for Genome Research, discussed the opportunities and challenges to using genetics to understand disease. He believes that genetics can help us understand the fundamental basis of disease, stratify patients based on their predisposed genetic risk for preclinical intervention, and tailor treatment to individual risk and response. He reminded the roundtable, however, that genetics is not a magic bullet. It has been very successful in explaining disease caused by a single gene, but most common diseases are caused by a combination of multiple genes and the environment. He described how genetic research on disease is done with linkage and association studies to identify single DNA variants called single nucleotide polymorphisms (SNPs). He went on to describe the SNP Consortium, which is working to create a collaborative, real-time, web-based, public catalogue of SNPs. Challenges for the future include finding ways to facilitate multidisciplinary, multicentered research, fund capital and infrastructure intensive research, and reward collaborative research in academia.

Roundtable member William Crowley, M.D., Director of Clinical Research and Chief of the Reproductive Endocrine Unit at Massachusetts General Hospital, Director of the National Center for Infertility Research, and Professor of Medicine at Harvard University, discussed the future of clinical research from the perspective of the academic health center (AHC). He stated that funding constraints, such as those imposed by managed care, have reduced AHCs' ability to subsidize clinical research. In addition, federal funding cuts from the Balanced Budget Amendment limit AHCs' ability to conduct clinical research. AHC have had to look for new funding sources to support clinical research including partnerships with the private sector. He discussed his institution's collaborative research efforts with Millennium Pharmaceuticals and

Decode Genetics. The institution's goals are to learn management skills from the private sector, take advantage of industries' innovative technology, maintain some freedom regarding intellectual property, use industry money to build a lasting research infrastructure, and gain access to the Icelandic DNA database. Millennium Pharmaceuticals gets access to clinical researchers and a research population. Decode Genetics gets access to data on a comparison population and the opportunity to conduct joint research with Harvard faculty. Discussion centered around how the institution would deal with property rights, how it would train staff about the new research opportunities, and the adequacy of IRB review as a means of protecting participants in Iceland who contributed their DNA samples to the genetics database.

Panel 2: The Role of Clinical Information Systems in Clinical Research

The second panel focused on the role of medical informatics in the future of clinical research and the potential value of clinical information collected at the bedside and from medical records. William Stead, M.D., Professor of Medicine and Biomedical Informatics at Vanderbilt University, gave a presentation entitled "The Holy Grail: Data Management as a By-Product of Practice." He envisions a time in the future when "we should be able to get the advantages of data management that we need for clinical research as a simple by-product of managing the practice." He also looks forward to a time when information systems will streamline practice management, automate protocols, and allow us to aggregate national data. Barriers to achieving this vision include inconsistencies in the way data is collected, the need to have extremely large sample to "scrub" the data, the difficulty in drawing out discrete data to study from continuous data that has been captured, and the lack of decision rules that typically control a clinical trial. Next, he described numerous opportunities to leverage informatics in clinical research, such as through surveillance of populations, through targeted trials, by relating distant health outcomes to health care processes, and by translating research into customized patient care. He believes that we must start delivering on the promise of informatics-assisted research using systems that are currently available. We must also begin building for the future by investing in informatics research, standardizing information technology and vocabulary, and creating incentives to use "certified tools" that meet compliance standards in clinical practice.

Christopher Chute, M.D., Dr.P.H., Professor of Medical Informatics and Associate Professor of Epidemiology at the Mayo Clinic, discussed the use of patient data for research purposes. He stressed that one of the key barriers is a lack of consistent terminology or vocabulary. One of the most common coding systems, the *International Classification of Diseases, Ninth Revision* (ICD-9) was designed primarily for billing purposes. It was never designed to describe disease, to capture clinical data, or to be used for health research. Another problem is that the coding system keeps changing, so it is difficult to use it in longitudinal research. He suggested that a system called SNOMED III, (a comprehensive, multiaxial nomenclature classification for indexing the entire medical vocabulary, including signs, symptoms, diagnoses, and procedures) due to be released in December 2001, is more appropriate for clinical research. Although there are negotiations in place to purchase a US government site license, Dr. Chute is not sure whether it will go through. The advent of genomics will only confound our terminology and what we define as a disease. Additional challenges include training the people who input data to use the vocabulary correctly and developing business and research data systems that work synergistically. Finally, we will need to find ways to maintain patient confidentiality.

In his presentation entitled "Using Automated Data for Clinical Research. What to Do While We Wait for What We Really Want," Richard Platt, M.D., M.Sc., Professor of Ambulatory Care and Prevention, Harvard Pilgrim Health Care, pointed out that HMOs are optimal laboratories for conducting health services, epidemiological, and some clinical research. Advantages include access to a defined population and provider group, access to demographic, clinical, and resource use data, and the ability to intervene at the organizational level. HMOs are primarily interested in research that sheds light on the effectiveness of available tests and treatments, prevention and management strategies for common conditions, and new therapies. At least 14 different HMO systems have in-house research centers that are part of a national HMO research network with a combined budget of over \$100 million. Major funders include NIH, the Centers for Disease Control and Prevention, the Agency for Healthcare Research and Quality, the Food and Drug Administration, the Health Care Financing Administration, state and local health agencies, foundations, and industry. He echoed others in arguing that the major limitations, even within an HMO system, are conducting clinical research with databases that were designed for business rather than research purposes and a lack of common terminology. In addition, research needs often differ from clinical needs; thus, physicians may not include information that would be relevant for research purposes in the patient file.

Stan Huff, MD, Senior Medical Informaticist at Intermountain HealthCare, gave a presentation entitled "Integrating Clinical Research and Patient Care at Intermountain HealthCare Using Data Exchange and Terminology Standards." Intermountain HealthCare is a not-for-profit corporation of 22 hospitals, 24 clinics, 14 urgent care centers, health plans, and physicians' divisions. They are using their clinical information systems to monitor and assess quality assurance, patient outcomes, complication rates, and disease outbreaks. According to Dr. Huff, a good clinical information system puts the patients' needs first, integrates decision support with the patient care process, has comprehensive content, captures real-time, point-of-care data, and facilitates clinical and administrative research. He agreed with other speakers that the lack of a universal terminology as well as a lack of data exchange standards are major barriers to having an integrated information system. He believes HL-7, a format and vocabulary standard for sending data between two computer systems, should be the most widely used data exchange standard.

A lively discussion followed this panel. Dr. Huff stated that he did not understand why the National Cancer Institute is working to create its own data exchange standard when 80 to 90 percent of US hospitals as well as 100 percent of health care providers in a number of other countries have already adopted HL-7 as the standard. There was discussion about the level of standardization of data collection in clinical research vs. clinical practice. There was skepticism among the panel members that medical records will ever reach a level of standardization that would make clinical research from abstracted records simple. A discussion of regulatory efforts to ensure patient privacy followed. Panel members pointed out that in many cases in which data are not linked to identifiable individuals, patient consent should not be necessary, and requiring it will inhibit research. Another suggestion was to get a blanket consent from the patient, prior to treatment, to use their information for certain types of research, such as quality improvement. There was a concern expressed that the pending confidentiality rule stemming from the Health Insurance Portability and Accountability Act could create major barriers to quality and outcomes research by creating such onerous informed consent requirements that researchers would be

unable to do the research. There was also an acknowledgement that health care providers often do not take data privacy seriously enough, so there needs to be some balance in the type of protections that are established. A final point was that creating an electronic record for a patient is expensive and time consuming for health care providers. Dr. Platt stated that it would cost \$25 billion for the US to create a fully automated ambulatory medical record for every patient. His HMO also found a 15 to 20 percent cost in clinician efficiency when they were required to create electronic records. Several participants expressed support for incentives to encourage providers to make the investment. Dr. Huff described a process Intermountain uses where physicians set the standards, Intermountain measures those parameters and then feeds them back to the clinicians to improve their practice. Dr. Chute argued that physicians are highly motivated to accurately document information that is directly related to clinical care, so research needs must be directly linked to clinical care in order to get accurate data. Dr. Scheinberg disagreed and argued that the primary problem is that standards for information reporting (such as how to define "severity") do not exist, so it is next to impossible for physicians to record data that is useful for research purposes. Drs. Stead and Chute argued that there are ways, through consistent terminologies and input structures (ability to browse patient data and local and national guidelines combine with tools to write orders) to create patient records that are more compatible with clinical research.

Panel 3: What Is Evidence-Based Medicine and How Do We Get There?

Using information to construct rational, evidence-based care was the subject of the third panel. The presentation given by John Wennberg, M.D., M.P.H., Director of the Center for Evaluative Clinical Sciences at Dartmouth Medical School entitled "Evidence-based Medicine and Outcomes Research: The Unfinished Agenda," began with a brief history of the growth in evidence-based research. Its development was largely a reaction to widely differing geographic practice patterns. Interest in it grew to the point that the federal Agency for Healthcare Research and Quality (AHRQ) was created to support evidence-based research. Dr. Wennberg assessed why this type of research has failed to have a major impact on practice variations: physicians resist evidence-based practice, outcomes research does not keep up with dynamic changes in medical theory, the central role of patient choice for elective treatment is neglected, and that outcomes research has yet to address "supply-sensitive" clinical practice styles (for instance, increased availability of health care services like laboratory testing may increase a physician's referral/prescribing behavior). He gave a number of examples to back up these assertions and argued that "increased spending does not result in more effective care." He believes that renewed enthusiasm and funding for evidence-based research needs to come from academic health centers and the federal government. The essential final step is to link evidence-based research to clinical practice through the development of practice guidelines.

The next speaker was, Francis Chesley, M.D., Director of the Office of Research Review, Education, and Policy at the Agency for Healthcare Research and Quality (AHRQ), the federal agency charged with funding and promoting evidence-based research, and a roundtable member. Dr. Chesley reviewed a number of definitions of evidence-based medicine and concluded that the best definition is "clinical decision making that integrates both individual clinical expertise and the best external evidence." Next, he discussed the critical features of good evidence-based research, which are: (1) it identifies answerable questions within clinical decisions; (2) it locates

best evidence that is valid and applicable; (3) it evaluates the evidence for its validity and usefulness; (4) it estimates benefits and harms for individuals; (5) it evaluates clinical performance; and (6) it identifies gaps in the science. He also discussed the advantages and disadvantages of promoting evidence-based clinical practice. Advantages of evidence-based medicine include (1) that it integrates medical education with clinical practice; (2) that it can be learned at any career stage; (3) that it reduces uncertainty; and (4) it may allow for better use of limited resources. Disadvantages include (1) it takes time to learn and practice; (2) the evidence is often lacking; (3) it exposes gaps in the evidences; (4) there is difficulty balancing harms and benefits; and (5) the systematic evaluation of evidence requires interpretation. Dr. Chesley discussed a number of methods for promoting evidence-based practice including the development of practice guidelines, AHRQ's translational projects, Evidence-Based Practice Centers, the National Guideline Clearinghouse, and opportunities for training in evidence-based medicine.

In his presentation on "Large Trials vs. Meta-Analysis of Smaller Trials: Implications to Evidence-Based Medicine," Joseph C. Cappelleri, Ph.D., M.P.H., an associate director supporting Global Outcomes Research and Medical Services, Pfizer, Inc., described the findings of an investigation he and his colleagues conducted evaluating the differences between mega trials and meta-analysis of smaller trials. Dr. Cappelleri wanted to understand how often these two types of research come to different conclusions and why such discrepancies occur. He found that conclusions drawn from mega trials and meta-analysis usually agree, but not always. Potential explanations for the discrepancies include possible publication bias (for instance, small studies demonstrating no effect are unlikely to be published), dissimilar patient populations, and protocol differences. As a summary measure of patient or study differences, the control rate in a study (i.e., the proportion of events in the control group) may also help to explain discrepancies between large trials and meta-analysis of smaller trials. He stressed that these research methods are complementary, each with benefits and drawbacks, and that meta-analysis should also be applied to examine study and population differences.

Larry Green, M.D., Director of the Center for Policy Studies in Family Practice and Primary Care of the American Academy of Family Physicians, gave a presentation entitled "Practice-Based Primary Care Research Networks: A Critical Clinical Research Infrastructure Able to Uncover Origins of Illness and Discover New Remedies for the Bulk of Medical Practice." Dr. Green's key message was that by focusing only on health-related problems that are present in academic health centers, researchers neglect the vast majority of health problems that people say affect their health and well-being. He used the Ecology of Medical Research Figure to illustrate his point. He argued that researchers must study people who receive their health care from family physicians and local hospitals in addition to people who do not have access to the health care system. His second point was that community-based physicians *are* willing to participate in clinical research, particularly if they can see that the findings of the study will improve their clinical practice. Research networks, supported by AHRQ, exist to facilitate practice-based recruiting; however, they need help establishing their infrastructure and establishing their linkages to other research entities. Finally, he stressed that investigators need to focus research questions on problems that confront local communities and shift from a framework of researcher/subject to a more collaborative approach with patients.

Panel 4: Should Purchasers of Health Care Be Concerned About Clinical Research?

Panel 4 included presentations from both public and private health care purchasers. They were asked to discuss what purchasers expect from clinical research and whether purchasers should care about clinical research. Jeffrey Kang, M.D., M.P.H., Director of the Health Care Financing Administration's (HCFA's) Office of Clinical Standards and Quality, presented a public purchaser's point of view. Dr. Kang stated that the Medicare program (administered by HCFA) only covers health care services that are "reasonable and necessary." In other words, HCFA is charged with spending Medicare funds wisely; therefore, it looks at clinical evidence to help make coverage decisions. Factors that affect coverage decisions include product or service effectiveness and effectiveness compared to other interventions, as well as the appropriateness of use in defined populations. Ideally, HCFA would like to base all its coverage decisions on clinical evidence; however, this evidence is limited. This would help the program eliminate coverage for ineffective therapies and invest instead in interventions proven to be more beneficial than current covered practice. Dr. Kang discussed the recent decision that the Medicare program would start financing routine costs associated with beneficiaries participating in clinical research. He believes this is appropriate, but cautioned the CRR against assuming that purchasers should finance clinical research through cost shifting.

Robert Galvin, M.D., Director, Corporate Health and Medical Programs for General Electric, presented his views on clinical research as a private purchaser. He argued that clinical research can contribute to improving health care by focusing on prevention, diagnosis, and treatment of disease, but this is not enough. Research also has a major role to play in assessing and determining how to improve quality of care. He does not believe that better quality care is necessarily more expensive, particularly if research is used to eliminate overuse and misuse of health care services. He predicts that a market-based, competitive approach will only work for health care if consumers become savvier about health care decisions. Health purchasers can facilitate this by supplying consumers with information on quality and cost-effectiveness of providers to help them make informed choices. He mentioned the Leap Frog Group, which is a group of private and public sector purchasers devoted to improving patient safety, which has identified certain advances in hospital systems that appear to improve safety, and used this information to rank hospitals. When asked about the purchaser's role in financing clinical research, Dr. Galvin stated that corporations finance clinical research through taxes, donations to foundations, and directly when it is in their direct interest to do so. For instance, GE funded a study looking at alcohol impairment in the workplace and they also fund the Leap Frog group through the National Business Roundtable.

Anthony Kotin, M.D., Senior Vice President of Operations for Internet Healthcare Group, commented on the profound impact that increasing commercialization has had on clinical research over the past decade. For instance, insurers are feeling intense pressure to finance clinical research, particularly because they must deal with demands from patient groups to pay for unproven therapies. One option is for insurers to develop a separate fund so employees can purchase additional coverage that covers the cost of clinical research. Southwest Bell tried this and found that it was very profitable for the insurer because employees purchased "but rarely used" the additional coverage. Dr. Kotin does not support this funding mechanism because he believes it will lead patients to select unproven treatments and increase the cost of health care. He also commented that one of the main challenges is to weed out the good data and information

from the bad regarding product and procedure outcomes. He believes there will be new opportunities for investigators to conduct research on large-scale datasets collected by payers in the near future.

Discussion followed about whether it is possible to make information on the Internet more reliable. Panel members did not have any solutions to this problem, but said the real challenge for employers and purchasers was in finding ways to funnel good health information to their employees.

Comments regarding this symposium or other CRR activities may be sent to clinical@nas.edu.