The Patient-Centered Outcomes Research Institute: Methodology Committee Resource Guide
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Developed by the National Pharmaceutical Council
February 2011.

The National Pharmaceutical Council is a policy research organization dedicated to the advancement of good evidence and science, and to fostering an environment in the United States that supports medical innovation. Founded in 1953 and supported by the nation’s major research-based pharmaceutical companies, NPC focuses on research development, information dissemination, education and promotion of the critical issues of evidence, innovation and the value of medicines for patients.

To order reprints, contact NPC at info@npcnow.org or 703-620-6390. This guide is also available online at www.npcnow.org/methodsguide.
The Patient-Centered Outcomes Research Institute: Methodology Committee Resource Guide

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Letter From the National Pharmaceutical Council</td>
<td>4</td>
</tr>
<tr>
<td>About the PCORI Methodology Committee</td>
<td>5</td>
</tr>
<tr>
<td>Methodology Committee Member Biographies</td>
<td>7</td>
</tr>
<tr>
<td>Why Methods Are Important</td>
<td>42</td>
</tr>
<tr>
<td>Existing Methodological Standards and Good Practices</td>
<td>45</td>
</tr>
<tr>
<td>Additional Resources</td>
<td>47</td>
</tr>
<tr>
<td>Appendix</td>
<td>48</td>
</tr>
</tbody>
</table>
A Letter From the National Pharmaceutical Council

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, broad health reform legislation that established the Patient-Centered Outcomes Research Institute (PCORI). Since that time, a number of important steps have been taken to implement PCORI, starting with the September 2010 appointment of a Board of Governors and continuing with the January 2011 announcement of the members of the Methodology Committee. Among its many responsibilities, the PCORI Board of Governors is tasked with setting the research agenda, while the Methodology Committee members are tasked with the development of sound research methods and will have a large role in the type of research that is undertaken to answer specific research questions.

As the Methodology Committee begins its work, it will focus first on the vitally important job of developing and choosing the right research methods for conducting a comparative effectiveness study. Done well, the resulting research will be sound, credible and able to inform treatment options. Even with good research, however, the challenge remains in how to consider the rapidly evolving science related to subpopulations or personalized medicine. As the science continues to evolve, we will need the flexibility for methods to evolve as well, and it will be important for all stakeholders to remain engaged in those efforts and share new methodologies with researchers.

To provide a better understanding of this new committee and its role, the National Pharmaceutical Council has developed the PCORI Methodology Committee Resource Guide, which is a companion booklet to the Patient-Centered Outcomes Research Institute Resource Guide (available online at www.npcnow.org/pcoriguide). This new resource guide will assist you in understanding the most common types of comparative effectiveness research (CER); introduce you to the members of the Methodology Committee; and offer a variety of resources for additional information.

Both of these guides, along with the CER Daily Newsfeed, NPC’s source for the latest CER news and activities, and Demystifying Comparative Effectiveness Research: A Case Study Learning Guide, which aids in the basic understanding of the common types of CER, are available on NPC’s Web site at www.npcnow.org. We encourage you to check out these resources to help you stay abreast of ongoing CER developments.

Sincerely,

Robert W. Dubois, MD, PhD
Chief Science Officer
About the PCORI Methodology Committee

The Patient Protection and Affordable Care Act (PL 111-148) established the non-profit entity, the Patient-Centered Outcomes Research Institute (PCORI), which is charged with the oversight of comparative effectiveness research (CER). To assist PCORI with developing and improving the scientific methods of comparative clinical research, the law established a standing methodology committee composed of 17 members. These members, including the directors of the National Institutes of Health and the Agency for Healthcare Research and Quality (AHRQ) or their designees, “shall be experts in their scientific field, such as health services research, clinical research, comparative clinical effectiveness research, biostatistics, genomics, and research methodologies.” The methodology committee is appointed by the Government Accountability Office Comptroller General.

Tasks

The purpose of this committee is to ensure that the comparative effectiveness research developed under PCORI’s watch is of high quality, which is why this group is charged with the development of methodological standards for research. The types of research include not only new or primary research such as randomized clinical trials, molecularly informed trials, and observational studies, but also systematic reviews or synthesis of existing research, and any other methodologies recommended by the methodology committee. The law states that, “such methodological standards shall provide specific criteria for internal validity, generalizability, feasibility, and timeliness of research and for health outcomes measures, risk adjustment, and other relevant aspects of research and assessment with respect to the design of research.” In addition, the law allows for the flexibility to include new information, data and advances in technology in ongoing research projects; calls for public input as methods are developed and updated; and ensures that patient subpopulations are considered in different kinds of research.

Another important task for the committee is the development of a translation table, which would serve as a reference tool to assist the PCORI Board of Governors in determining which research methods are best suited for a specific research question. A translation table helps to lay out the framework for developing research by first looking at the questions that decision makers need answered, and then determining what kinds of research can best address those questions. This places the decision makers at the center of the development of CER, rather than as simply a recipient of research results.

Reports and Deadlines

The committee has a short amount of time in which to complete its work—merely 18 months after establishment—so it is permitted to rely on outside assistance. The methodology committee “may consult and contract with the Institute of Medicine of the National Academies and academic, non-profit, or other private and governmental entities with relevant expertise to carry out” its activities.

As the methodology committee moves forward with its tasks, it must submit reports to the PCORI Board of Governors. The reports should include “recommendations for the Institute to adopt methodological standards developed and updated by the methodology committee as well as other actions deemed necessary to comply with such methodological standards.”
Ongoing Methodology Development

A number of public and private sector organizations, such as AHRQ, the National Institutes of Health, the Cochrane Collaboration, the International Society for Pharmacoconomics and Outcomes Research (ISPOR), the Center for Medical Technology Policy (CMTP), and NPC, among others, are actively engaged in work to advance the methodology for conducting comparative effectiveness research. This work includes developing new methods, garnering agreement on good research practices, and exploring the types of questions facing researchers, providers, health systems and patients.

To date, there have been several initiatives resulting from those efforts, some of which were supported by NPC’s funding and participation. Those include the GRACE Principles (Good ReseArch for Comparative Effectiveness), which focus on observational studies; the PACE Initiative (Pragmatic Approaches to Comparative Effectiveness) for Bayesian and pragmatic trials; and guidance documents developed by CMTP. AHRQ, as well as ISPOR, also has developed key methodological documents. (See existing methodological standards and practices on page 47.) In the future, NPC will continue to engage in thoughtful research and partnerships to help inform the advancement of CER.

While much work is ongoing, it will require the research community to engage in dialogue with the decision makers who will need credible, reliable, and relevant CER in making treatment decisions. In the coming months, the members of the methodology committee will be certain to play a key role in this ongoing discussion.

Source: Subtitle D–Patient-Centered Outcomes Research, SEC. 6301. PATIENT-CENTERED OUTCOMES RESEARCH, PL 111-148

Biographies of the Methodology Committee members follow:*

*Members of the Methodology Committee are widely published authors. Due to publication constraints, selected publications listed are from the last two years or are publications highlighted on members’ webpages.
Naomi Aronson, PhD

Executive Director, Blue Cross and Blue Shield Association Technology Evaluation Center

Biography:
Naomi Aronson, PhD, is the executive director of the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Dr. Aronson has overseen TEC’s development as a nationally recognized technology assessment program and an Evidence-based Practice Center (EPC) of the Agency for Healthcare Research and Quality (AHRQ). She has directed over 300 technology assessments and 13 evidence reports for AHRQ. She represented the private sector on a US Agency for International Development Team providing technical assistance to the Hungarian government on building evidence-based medicine capacity in the national health insurance system. She was a member of the 2007 Ontario Health Technology Assessment Evaluation Review Team. Dr. Aronson is a member of the Institute of Medicine Forum on Drug Discovery Translation and Development, the Institute of Medicine Genomics Roundtable, the Steering Committee of the Chicago-Area DEcIDE Research Center, the National Business Group on Health Committee on Evidence-Based Benefit Design, and a review committee co-chair for the International Society for Pharmacoeconomics and Outcomes Research 14th Annual International Meeting. Previously, Dr. Aronson was a member of the Northwestern University faculty, specializing in the sociology of science and medicine. She also was a post-doctoral fellow in the Science, Technology and Society Program at the Massachusetts Institute of Technology and received research awards from the National Science Foundation and the American Council of Learned Societies. Dr. Aronson’s academic research focused on how the organization of scientific specialties in biomedical and clinical research affects the process of scientific discovery.

Selected Publications:


**About the Blue Cross and Blue Shield Association Technology Evaluation Center:**

Founded in 1985 by the Blue Cross and Blue Shield Association, the Technology Evaluation Center (TEC) pioneered the development of scientific criteria for assessing medical technologies through comprehensive reviews of clinical evidence. TEC operates as part of the Association’s Office of Clinical Affairs.

Since its inception, TEC has been recognized for leadership in producing evidence-based technology assessments. Each TEC Assessment is a comprehensive evaluation of the clinical effectiveness and appropriateness of a given medical procedure, device or drug. Averaging 20 to 25 assessments a year, TEC provides health care decision makers with timely, rigorous and credible information on clinical effectiveness. TEC serves a wide range of clients in both the private and public sectors, including Kaiser Permanente and the Centers for Medicare and Medicaid Services (CMS).

**Additional Information:**

- Blue Cross and Blue Shield Association Technology Evaluation Center. [www.bcbs.com/blueresources/tec/](http://www.bcbs.com/blueresources/tec/)

**Sources:**


Ethan Basch, MD, MSc

Medical Oncologist and Health Services Researcher, Department of Medicine and Department of Epidemiology, Memorial Sloan-Kettering Cancer Center

Biography:
Ethan Basch, MD, MSc, is a practicing medical oncologist and health services researcher at Memorial Sloan-Kettering Cancer Center, with appointments in the Department of Medicine and in the Department of Epidemiology and Biostatistics. His research focuses on methods for using patient-reported data to evaluate the comparative effectiveness and safety of interventions. Dr. Basch is chair of the Health Outcomes Committee of the Cancer and Leukemia Group B of the National Cancer Institute (NCI), chair of the Clinical Practice Guidelines Committee of the American Society of Clinical Oncology (ASCO), and a member of ASCO's Comparative Effectiveness Task Force. He leads the NCI's PRO-CTCAE initiative to develop a standard system for patient-reporting of safety data in clinical trials. Dr. Basch received a BA from Brown University, an MD from Harvard Medical School, an MSc in epidemiology from Harvard School of Public Health, and an MPhil in literature from Oxford University.

Selected Publications:

About the Memorial Sloan-Kettering Cancer Center:
The world's oldest and largest private cancer center, Memorial Sloan-Kettering Cancer Center (MSKCC) has devoted more than a century to patient care as well as to innovative research, making significant contributions to new and better therapies for the treatment of cancer.

Today, the Center has more than 11,000 employees including 768 Memorial Hospital attending staff and 140 Sloan-Kettering Institute members. In 2009, more than 23,000 patients were admitted to Memorial Hospital, and Memorial Sloan-Kettering accommodated 500,317 outpatient visits at its Manhattan and regional sites combined.
Additional Information:

- Memorial Sloan-Kettering Cancer Center. http://www.mskcc.org
- Twitter: http://twitter.com/sloan_kettering

Sources:


Alfred O. Berg, MD, MPH
Professor, Department of Family Medicine, University of Washington

Biography:
Alfred O. Berg, MD, MPH, is a professor in the Department of Family Medicine at the University of Washington. He is chair of the Institute of Medicine's Committee on Standards for Systematic Reviews of Clinical Effectiveness Research and chair of the Panel on Evaluation of Genomic Applications in Practice and Prevention at the Centers for Disease Control and Prevention (CDC). He has served on numerous national expert panels using evidence-based medicine to develop clinical guidelines, including serving as chairman of the US Preventive Services Task Force. Dr. Berg also has served as chair of the CDC Sexually Transmitted Disease Treatment Guidelines Panel, co-chair of the Agency for Healthcare Research and Quality's otitis media panel, and as a member of the American Medical Association/CDC panel that produced Guidelines for Adolescent Preventive Services. Dr. Berg received a BA from Tabor College, an MD from Washington University School of Medicine, and an MPH in epidemiology from the University of Washington School of Public Health and Community Medicine.

Selected Publications:

About the Department of Family Medicine at the University of Washington:
The Department of Family Medicine at the University of Washington provides leadership for core curriculum in the School of Medicine and is recognized for its research and academic programs in rural communities. With over 800 clinical faculty members located throughout Washington, Wyoming, Alaska, Montana, and Idaho, and approximately 40 regular faculty located at the university site in Seattle, the department is one of the largest of its kind in the country. The research section is one of the largest family medicine research enterprises in the country.
Additional Information:


Sources:


Biography:
Carolyn M. Clancy, MD, was appointed director of the Agency for Healthcare Research and Quality (AHRQ) on February 5, 2003, and reappointed on October 9, 2009. Prior to her appointment, Dr. Clancy was director of AHRQ’s Center for Outcomes and Effectiveness Research.

Dr. Clancy, a general internist and health services researcher, is a graduate of Boston College and the University of Massachusetts Medical School. Following clinical training in internal medicine, Dr. Clancy was a Henry J. Kaiser Family Foundation fellow at the University of Pennsylvania. Before joining AHRQ in 1990, she was also an assistant professor in the Department of Internal Medicine at the Medical College of Virginia.

Dr. Clancy holds an academic appointment at the George Washington University School of Medicine (clinical associate professor, Department of Medicine) and serves as senior associate editor for the journal *Health Services Research*. She serves on multiple editorial boards, including *Annals of Internal Medicine*, *Annals of Family Medicine*, *American Journal of Medical Quality*, and *Medical Care Research and Review*.

Dr. Clancy is a member of the Institute of Medicine and was elected a Master of the American College of Physicians in 2004. In 2009, she was awarded the William B. Graham Prize for Health Services Research. Dr. Clancy’s major research interests include improving health care quality and patient safety and reducing disparities in care associated with patient race, ethnicity, gender, income, and education. As director of AHRQ, she launched the first annual report to Congress on health care disparities and health care quality.

Selected Publications:


Clancy CM. Getting to “smart” health care, comparative effectiveness research is a key component of, but tightly linked with, health care delivery in the information age. *Health Aff.* November/December 2006;25(6):w589-w592.


Clancy CM, Cronin K. Evidence-based decision making: global evidence, local decisions, the challenge now is to further develop and translate the worldwide evidence base for local application. *Health Aff.* January/February 2005;24(1):151-162.


About the Agency for Healthcare Research and Quality:

AHRQ is the lead federal agency charged with improving the quality, safety, efficiency, and effectiveness of health care for all Americans. As one of 12 agencies within the Department of Health and Human Services, AHRQ supports health services research that will improve the quality of health care and promote evidence-based decision making.

Additional Information:

- Agency for Healthcare Research and Quality. [www.ahrq.gov](http://www.ahrq.gov)

Sources:


David Flum, MD, MPH

Biography:

David Flum, MD, MPH, is a professor in the Department of Surgery and an adjunct professor in the Department of Health Services at the University of Washington (UW) Schools of Medicine and Public Health. He is an attending physician in general surgery at the University of Washington Medical Center. He is a co-founder and member of the Leadership Council of the UW Centers for Comparative and Health Systems Effectiveness Alliance (CHASE) and directs UW's Surgical Outcomes Research Center. Dr. Flum's investigations have compared interventional and non-interventional approaches for common clinical conditions such as appendicitis, peripheral vascular disease, obesity, and multiple types of cancer. He received his BA and MD from the University of Miami School of Medicine and his MPH from the University of Washington School of Public Health.

Selected Publications:


About the University of Washington Medicine:

University of Washington Medicine's mission is to improve the health of the public by advancing medical knowledge, providing outstanding primary and specialty care to the people of the region, and preparing tomorrow's physicians, scientists and other health professionals. UW Medicine owns or operates Harborview Medical Center, the University of Washington Medical Center, Northwest Hospital and Medical Center, a network of seven UW Medicine Neighborhood Clinics that provide primary care, the UW School of Medicine, the physician practice UW Physicians, and Airlift Northwest. In addition, UW Medicine shares in the ownership and governance of Children’s University Medical Group and Seattle Cancer Care Alliance, a partnership composed of UW Medicine, Fred Hutchinson Cancer Research Center and Seattle Children's. UW Medicine faculty includes four Nobel Prize winners, 33 Institute of Medicine members, 32 National Academy of Sciences members and 16 Howard Hughes Medical Institute investigators.

Additional Information:

- University of Washington Department of Surgery. [http://depts.washington.edu/surgery](http://depts.washington.edu/surgery)
Sources:


David R. Flum, M.D., M.P.H., F.A.C.S. University of Washington Department of Surgery Faculty Web site.

Sherine Gabriel, MD, MSc

Methodology Committee Chair

Professor of Medicine and of Epidemiology, and the William J. and Charles H. Mayo Professor, Mayo Clinic

Biography:

Sherine Gabriel, MD, MSc, is a professor of medicine and of epidemiology and the William J. and Charles H. Mayo Professor at Mayo Clinic. She has served as chair of the Department of Health Sciences Research at Mayo Clinic, which includes the divisions of Epidemiology, Health Care Policy and Research, Biomedical Informatics, and Biostatistics. Dr. Gabriel also has served as vice-chair of Mayo Clinic’s Research Committee and as a member of the Mayo Clinic Executive Board. She founded Mayo Clinic’s Center for Patient Oriented Research as well as clinical research training programs that later transitioned into the Mayo Clinic’s Center for Translational Sciences Activities, where she serves as co-principal investigator. She has been president of the American College of Rheumatology (ACR) and is the founding chair of the ACR Quality Measures Committee. Dr. Gabriel received an MD, with distinction, from the University of Saskatchewan and an MSc in clinical epidemiology and biostatistics from McMaster University, Canada.

Selected Publications:


Singh JA, Gabriel SE, Lewallen DG. Higher body mass index is not associated with worse pain outcomes after primary or revision total knee arthroplasty. *J Arthroplasty*. April 2010.


About Mayo Clinic:

Mayo Clinic is a non-profit worldwide leader in medical care, research and education for people from all walks of life. More than 55,000 doctors, scientists, students and allied health staff work and study at Mayo Clinic campuses in Rochester, Minnesota; Jacksonville, Florida; and Scottsdale/Phoenix, Arizona. Collectively, Mayo Clinic cares for more than half a million people each year. Mayo Clinic also serves more than 70 communities in the upper Midwest through the Mayo Health System.

Additional Information:

- Mayo Clinic. [http://www.mayoclinic.org](http://www.mayoclinic.org)

Sources:


Biography:

Steven Goodman, MD, MHS, PhD, is professor of oncology in the Division of Biostatistics of the Johns Hopkins Kimmel Cancer Center, with appointments in the Departments of Pediatrics, Biostatistics, and Epidemiology in the Johns Hopkins Schools of Medicine and Public Health. He is also a core faculty member in the Johns Hopkins Bloomberg School of Public Health’s Center for Clinical Trials and the Johns Hopkins Berman Institute of Bioethics.

Since 2004 he has been the editor of Clinical Trials: Journal of the Society for Clinical Trials, and has served as senior statistical editor of the Annals of Internal Medicine since 1987.

He has served on the Institute of Medicine’s (IOM) Committees on Immunization Safety Review, Health Effects in Vietnam Veterans of Exposure to Herbicides: Second Biennial Update, Agent Orange and Diabetes, and the Committee on Alternative Models to Daubert Standards. He serves as co-chair of the IOM Ethical and Scientific Issues in Studying the Safety of Approved Drugs, as a member and scientific advisor to the Medical Advisory Panel of the National Blue Cross Blue Shield Technology Evaluation program, and served as a consultant to the President’s Advisory Commission on Human Radiation Experiments. He was the lead author of the chapter on causal assessment in the Surgeon General’s 2004 report on Smoking and Health.

He was co-director of the Johns Hopkins Evidence-based Practice Center from 2000-2004, and served for three years on the Medical Coverage Advisory Commission. He teaches and writes extensively on evidence evaluation and inferential, methodological, and ethical issues in epidemiology and clinical research.

Dr. Goodman received an AB from Harvard, an MD from New York University, trained in pediatrics at Washington University in St. Louis, and received his MHS in biostatistics and his PhD in epidemiology from Johns Hopkins Bloomberg School of Public Health.

Selected Publications:


About the Johns Hopkins University School of Medicine and Bloomberg School of Public Health:

From the 1889 opening of the Johns Hopkins Hospital, to the opening of the School of Medicine four years later, there emerged the concept of combining research, teaching and patient care. This model, the first of its kind, would lead to a national and international reputation for excellence and discovery.

Today, Johns Hopkins uses one overarching name—Johns Hopkins Medicine—to identify its entire medical enterprise. This $5 billion system unites the physicians and scientists of the Johns Hopkins University School of Medicine with the health professionals and facilities that make up the broad, integrated Johns Hopkins Health System.

The Johns Hopkins Bloomberg School of Public Health is dedicated to the education of a diverse group of research scientists and public health professionals, a process inseparably linked to the discovery and application of new knowledge, and through these activities, to the improvement of health and prevention of disease and disability around the world.

Additional Information:


Sources:


Mark Helfand, MD, MS, MPH

Professor of Medicine and of Medical Informatics and Clinical Epidemiology, Oregon Health and Science University; Staff Physician, Portland VA Medical Center

Biography:
Mark Helfand, MD, MS, MPH, is the founder and director of the Oregon Evidence-based Practice Center, and also directs the Veterans Affairs Evidence-based Synthesis Program and the Scientific Resource Center for the Agency for Healthcare Research and Quality (AHRQ) Effective Healthcare Program. Dr. Helfand has been a member of the Institute of Medicine Committee on Standards for Systematic Reviews of Comparative Effectiveness Research and the IOM Committee on Comparative Effectiveness Research Prioritization. From 1998-2002, he led a team that helped the US Preventive Services Task Force prioritize topics and develop evidence-based guidelines. Dr. Helfand is certified by the American Board of Internal Medicine and the American Board of Critical Care Medicine. He is a health and medical consultant with Consumers Union Reports’ Best Buy Drugs Project and is editor-in-chief of Medical Decision Making. Dr. Helfand received an AB and BS from Stanford University, an MD and MPH from the University of Illinois Medical School, and an MS in health services research from Stanford University.

Selected Publications:


About the Oregon Evidence-based Practice Center:
The Oregon Evidence-based Practice Center (Oregon EPC) conducts systematic reviews of health care topics for federal and state agencies and private foundations. These reviews report the evidence from clinical research studies and the quality of that evidence for use by policymakers in decisions on guidelines and coverage. The Center is one of 14 EPCs sponsored by the Agency for Healthcare Research and Quality.

Investigators with the Evidence-based Practice Center have a particular interest in diagnostic technology assessment, prevention effectiveness, evidence-based informatics, research in managed care, and critical appraisal of cost-effectiveness analysis and decision analysis. In the past, faculty affiliated with the center have investigated areas such as acute head injury, pain management, drug effectiveness, thyroid function tests, cancer screening, diagnostic use of upper gastrointestinal endoscopy, asthma diagnosis and management, telemedicine, menopausal symptoms, osteoporosis, vaginal birth after cesarean section, and statewide trauma systems.

Additional Information:

Sources:


John Ioannidis, MD, DSc

C.F. Rehnborg Professor in Disease Prevention, Professor of Medicine and Director, Stanford Prevention Research Center, Stanford University School of Medicine

Biography:

John Ioannidis, MD, DSc, is the C.F. Rehnborg Professor in Disease Prevention, professor of medicine and director of the Stanford Prevention Research Center at the Stanford University School of Medicine. He is an adjunct professor at the Harvard School of Public Health and Tufts University School of Medicine and a visiting professor at Imperial College London. He previously chaired the Department of Hygiene and Epidemiology at the University of Ioannina School of Medicine in Greece. Since 2008, Dr. Ioannidis has led the Genetics/Genomics component of the Tufts Clinical and Translational Science Institute (CTSI) and the Center for Genetic Epidemiology and Modeling of the Tufts Institute for Clinical Research and Health Policy Studies at Tufts Medical Center. Dr. Ioannidis serves on the executive board of the Human Genome Epidemiology Network and has served as president of the Society for Research Synthesis Methodology. He has been a member of the editorial boards of 26 international journals, including *Lancet, Annals of Internal Medicine, PLoS Medicine, Journal of the National Cancer Institute, Journal of Clinical Epidemiology*, and *Clinical Trials*, and is editor-in-chief of the *European Journal of Clinical Investigation*. Much of Dr. Ioannidis’ own work involves strengthening the way that research is planned, carried out and reported. Dr. Ioannidis graduated from Athens College and received an MD and DSc in biopathology from the University of Athens School of Medicine.

Selected Publications:


Ioannidis JP, Karassa FB. The need to consider the wider agenda in systematic reviews and meta-analyses: breadth, timing, and depth of the evidence. *BMJ.* September 13, 2010:341:c4875.


**About Stanford Medicine:**
Vast in both its physical scale and its impact on human health—locally, nationally, and globally—Stanford Medicine is composed of three main components:

- Stanford School of Medicine, a premier research-intensive medical school that improves health through leadership and collaborative discoveries and innovation in patient care, education, and research.
- Stanford Hospital and Clinics, consistently ranked among the top hospitals in the nation for advanced care in such areas as cancer treatment, cardiac care, neurology, orthopedic surgery, and organ transplantation.
- Lucile Packard Children’s Hospital, internationally recognized for advancing family-centered care of children and expectant mothers.

The Medical Center is located on the main Stanford University campus, adjacent to top-ranked programs in engineering, physical and biological sciences, computer science, ethics, and other disciplines. This close proximity—coupled with Stanford’s long tradition of encouraging collaboration—fosters multidisciplinary research and ultimately accelerates the pace at which new knowledge can be translated into new ways to prevent, diagnose, and treat disease.

**Additional Information:**
- Stanford Medicine. [http://stanfordmedicine.org](http://stanfordmedicine.org)

**Sources:**
Michael Lauer, MD
NIH Designee to the Methodology Committee
Director, Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health

Biography:

Michael Lauer, MD, is the director of the Division of Cardiovascular Sciences at the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH). In this position, Dr. Lauer provides leadership for the Institute’s national program for research on the causes, prevention, and treatment of cardiovascular (basic, clinical, population, and health sciences) diseases. Dr. Lauer joined the NHLBI in July 2007.

Dr. Lauer’s primary research interests include cardiovascular clinical epidemiology and comparative effectiveness, with a focus on diagnostic testing. He also has a strong background in leadership of the cardiovascular community and longstanding interests in medical editing—for seven years he was a contributing editor for *Journal of the American Medical Association*—and human subjects protection.

Prior to joining the NHLBI, Dr. Lauer served as the director of the Cleveland Clinic Foundation Exercise Laboratory and vice chair of the clinic’s Institutional Review Board. He also served as co-director of the Coronary Intensive Care Unit and director of clinical research in the clinic’s department of cardiology.

Dr. Lauer earned his Bachelor of Science degree in biology, summa cum laude, from Rensselaer Polytechnic Institute in 1983 and his Doctor of Medicine, magna cum laude, from Albany Medical College in 1985. Following internal medical training at the Massachusetts General Hospital, Harvard Medical School, he completed a clinical fellowship in cardiology at the Boston Beth Israel Hospital, Harvard Medical School. His further training in epidemiology included a research fellowship at the NHLBI’s Framingham Heart Study, Boston University; the program in clinical effectiveness, Harvard School of Public Health, Harvard University; and the Program for Physician Educators, Harvard Macy Institute.

Dr. Lauer is an elected fellow of the American College of Cardiology and American Heart Association, and has been elected to membership in the American Society for Clinical Investigation. He also served as chairman of the Exercise, Cardiac Rehabilitation, and Prevention Committee of the American Heart Association’s Council of Clinical Cardiology, and has received numerous awards in recognition of his scientific and teaching accomplishments.

Selected Publications:


**About the National Heart, Lung and Blood Institute:**

The National Heart, Lung, and Blood Institute (NHLBI) provides global leadership for a research, training, and education program to promote the prevention and treatment of heart, lung, and blood diseases and enhance the health of all individuals so that they can live longer and more fulfilling lives.

The NHLBI stimulates basic discoveries about the causes of disease, enables the translation of basic discoveries into clinical practice, fosters training and mentoring of emerging scientists and physicians, and communicates research advances to the public. It creates and supports a robust, collaborative research infrastructure in partnership with private and public organizations, including academic institutions, industry, and other government agencies. The Institute collaborates with patients, families, health care professionals, scientists, professional societies, patient advocacy groups, community organizations, and the media to promote the application of research results and leverage resources to address public health needs. The NHLBI also collaborates with international organizations to help reduce the burden of heart, lung, and blood diseases worldwide.

**Additional Information:**


**Sources:**


David Meltzer, MD, PhD

Director, Center for Health and the Social Sciences, Chief of the Section of Hospital Medicine, and Associate Professor, Department of Medicine, Department of Economics, and Graduate School of Public Policy Studies, University of Chicago

Biography:

David Meltzer, MD, PhD, is director of the Center for Health and the Social Sciences and chief of the Section of Hospital Medicine at the University of Chicago. He is also an associate professor in the Department of Medicine, Department of Economics, and Graduate School of Public Policy Studies at the University of Chicago. Dr. Meltzer also serves as co-director of the Program on Outcomes Research Training and the MD/PhD program in the social sciences. In addition, he is on the faculty of the Graduate Program in Health Administration and Policy, the Population Research Center, the Center on Aging, and the Hospital Medicine and Economic Center for Education and Research in Therapeutics, which is funded by the Agency for Healthcare Research and Quality.

Dr. Meltzer’s research explores problems in health economics and public policy with a focus on the theoretical foundations of medical cost-effectiveness analysis and the determinants of the cost and quality of care, especially in teaching hospitals. He is currently completing a randomized trial comparing the use of doctors who specialize in inpatient care (“hospitalists”) with traditional physicians in six academic medical centers.

Dr. Meltzer is the recipient of numerous awards, including the National Institute of Health Medical Scientist Training Program Fellowship, the National Science Foundation Graduate Fellowship in Economics, the University of Chicago Searle Fellowship, the Lee Lusted Prize of the Society for Medical Decision Making, the Health Care Research Award of the National Institute for Health Care Management, the Eugene Garfield Award from Research!America, and the Robert Wood Johnson Generalist Physician Award. Dr. Meltzer is a research associate of the National Bureau of Economic Research, an elected member of the American Society for Clinical Investigation, and past president of the Society for Medical Decision Making. He has served on panels examining the future of Medicare for the National Academy of Social Insurance and the Department of Health and Human Services (HHS), and US organ allocation policy for the Institute of Medicine (IOM). He recently served on an IOM panel examining the effectiveness of the US drug safety system and currently serves on the HHS Secretary’s Advisory Committee on Healthy People 2020, which aims to establish health objectives for the US population.

Selected Publications:


About the University of Chicago Center for Health and the Social Sciences:
The University of Chicago Center for Health and the Social Sciences provides needed infrastructure to support and encourage new research initiatives at the interface of health and the social sciences. Such infrastructure includes: coordination of collaborative efforts in research and training; shared space; grant support and fundraising; and computer, data, and focused methodological support.
The center also provides a venue to promote interdisciplinary collaboration for research and training at the university. The center complements the resources of existing centers, functioning not only as an independent center in the usual sense, but also as a collaborator with existing centers. The center aims to facilitate the development of additional new centers in focused related areas as faculty interest and funding opportunities arise. This is to be accomplished partially through the creation of program areas that organize faculty interested in specific topic areas. Ultimately, this arrangement will allow the center to act as an incubator to facilitate the further growth of innovative research in health and the social sciences both within and across the units of the university.

Additional Information:
- Centers for Education and Research on Therapeutics (CERTs), University of Chicago. http://chess.uchicago.edu/cert/cert.html
- The Harris School of Public Policy Studies, University of Chicago. http://harrisschool.uchicago.edu/

Sources:
Brian Mittman, PhD

Director, VA Center for Implementation Practice and Research Support, Department of Veterans Affairs Greater Los Angeles Healthcare System

Biography:

Brian Mittman, PhD, is the director of the Veterans Affairs (VA) Center for Implementation Practice and Research Support and senior social scientist at the VA/UCLA/RAND Center for the Study of Healthcare Provider Behavior, both at the VA Greater Los Angeles Healthcare System. From 2002 to 2004 he served as interim associate director of the VA’s Health Services Research and Development Service, directing the VA Quality Enhancement Research Initiative (QUERI). Dr. Mittman served as a visiting professor in the Department of Health Services, UCLA School of Public Health, from 2003 to 2006, and taught at the UCLA Anderson Graduate School of Management (visiting lecturer to visiting associate professor) from 1986 to 1993.

Dr. Mittman’s research interests include implementation science, health care quality improvement, and health care management. He convened and chaired the planning committee that launched the journal Implementation Science and serves as co-editor-in-chief of the journal. He was a founding member of the Institute of Medicine Forum on the Science of Quality Improvement and Implementation (2006–2008) and is a consultant and member of the editorial board for the Agency for Healthcare Research and Quality (AHRQ) Health Care Innovations Exchange. This initiative classifies innovative strategies to increase implementation of evidence-based clinical practices and enhance the efficiency and effectiveness of health care delivery.

Dr. Mittman served on the National Institutes of Health (NIH) review committee (Special Emphasis Panel) on Dissemination and Implementation Research in Health in 2006 and chaired the panel in March and October of 2007. His published research appears in the Journal of the American Medical Association, Annals of Internal Medicine, Medical Care, Health Services Research, and other journals. He is a frequent speaker on implementation research.

Selected Publications:


**About the VA Greater Los Angeles Healthcare System:**

The VA Greater Los Angeles (GLA) Healthcare System is the largest, most complex health care system within the Department of Veterans Affairs. It is one component of the VA Desert Pacific Healthcare Network (VISN22) offering services to veterans residing in Southern California and Southern Nevada. GLA consists of three ambulatory care centers, a tertiary care facility and 10 community based outpatient clinics. GLA serves veterans residing throughout five counties: Los Angeles, Ventura, Kern, Santa Barbara, and San Luis Obispo. There are 1.4 million veterans in the GLA service area. GLA is affiliated with both UCLA School of Medicine and University of Southern California School of Medicine, as well as more than 45 colleges, universities and vocational schools in 17 different medical, nursing, paramedical and administrative programs.

**Additional Information:**

- US Department of Veterans Affairs. [http://www.va.gov/landing2_about.htm](http://www.va.gov/landing2_about.htm)

**Sources:**


Robin Newhouse, PhD, RN

Assistant Dean, Doctor of Nursing Practice Program and Associate Professor, Organizational Systems and Adult Health, University of Maryland School of Nursing

Biography:
Robin Newhouse, PhD, RN, is assistant dean for the Doctor of Nursing Practice Program and an associate professor for organizational systems and adult health at the University of Maryland School of Nursing. She conducts randomized controlled trials and systematic reviews with research focusing on quality of care, evidence-based practice among clinicians, and outcomes research in health care delivery systems. Dr. Newhouse has served as chair of the Johns Hopkins Nursing Evidence Based Practice Model and implemented a strategic plan for evidence-based practice and research at the Johns Hopkins Hospital. She is a peer reviewer for the *Journal of Nursing Administration* and for the *Journal of Nursing Scholarship*. Dr. Newhouse received her BS and her PhD in nursing from the University of Maryland School of Nursing.

Selected Publications:


About the University of Maryland School of Nursing:
The University of Maryland School of Nursing shares a 61-acre campus in downtown Baltimore with the University of Maryland, Baltimore’s (UMB) six other professional schools—Dentistry, Law, Medicine, Pharmacy, Social Work, and the Graduate School—and is in close proximity to the University of Maryland Medical Center, University of Maryland Biotechnology Institute, University of Maryland Biopark, and the Baltimore VA Medical Center. The School of Nursing also maintains facilities and conducts classes at the University System of Maryland regional center at Shady Grove in Rockville, Maryland. The School is dedicated to creating a research-intensive environment that will advance the science of nursing through research and scholarship of the highest quality.

Additional Information:
- University of Maryland School of Nursing, [http://nursing.umaryland.edu/](http://nursing.umaryland.edu/)
Sources:


Sharon-Lise T. Normand, PhD
Methodology Committee Vice Chair
Professor of Health Care Policy, Harvard Medical School; Professor of Biostatistics, Harvard School of Public Health

Biography:
Sharon-Lise Normand, PhD, is a professor of health care policy (biostatistics) in the Department of Health Care Policy at Harvard Medical School and in the Department of Biostatistics at the Harvard School of Public Health. Dr. Normand’s research focuses on the development of statistical methods for health services research, primarily using Bayesian approaches to problem solving, including assessment of quality of care, methods for causal inference, provider profiling, meta-analysis, and latent variable modeling. She has developed a long line of research on methods for the analysis of patterns of treatment and quality of care for patients with cardiovascular disease and with mental disorders in particular.

Dr. Normand earned her BSc and MSc degrees in statistics from the University of Western Ontario and her PhD in biostatistics from the University of Toronto. She is a fellow of the American Statistical Association, a fellow of the American College of Cardiology, and an associate member of the Society of Thoracic Surgeons. She was president of the Eastern North American Region of the International Biometrics Society in 2010; serves on task forces for the American Heart Association, the American College of Cardiology, and the Society of Thoracic Surgeons; and is currently a member of two Institute of Medicine Committees: the Committee on Aerospace Medicine and the Medicine of Extreme Environments; and the Committee on Future Directions for the National Healthcare Quality and Disparities Reports.

Selected Publications:


**About the Department of Health Care Policy at Harvard Medical School:**
The Department of Health Care Policy at Harvard Medical School is one of only a few academic departments of health policy nationwide located in a medical school. Research includes broad topics on financing and delivery of health care, quality of care, studies on special and disadvantaged populations (including those with mental disorders), and access to care.

**About the Harvard School of Public Health:**
The Harvard School of Public Health is dedicated to advancing the public’s health through learning, discovery, and communication. More than 400 faculty members are engaged in teaching and training the 1,000-plus student body in a broad spectrum of disciplines crucial to the health and well being of individuals and populations around the world. Programs and projects range from the molecular biology of AIDS vaccines to the epidemiology of cancer; from risk analysis to violence prevention; from maternal and children’s health to quality of care measurement; and from health care management to international health and human rights.

**Additional Information:**
- Department of Health Care Policy, Harvard Medical School. [http://www.hcp.med.harvard.edu/about](http://www.hcp.med.harvard.edu/about)

**Sources:**


Sebastian Schneeweiss, MD, ScD

Associate Professor, Department of Medicine, Harvard Medical School; Associate Professor, Department of Epidemiology, Harvard School of Public Health; Vice Chief and Director, Drug Evaluation and Outcomes Research, Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women’s Hospital

Biography:

Sebastian Schneeweiss, MD, ScD, is an associate professor in the Department of Medicine at Harvard Medical School and in the Department of Epidemiology at the Harvard School of Public Health. He also serves as vice chief and director of drug evaluation and outcomes research for the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women’s Hospital (BWH). In addition, Dr. Schneeweiss is the director and chair of the Executive Board of the DEcIDE Research Center (Developing Evidence to Inform Decisions about Effectiveness) at Brigham and Women’s Hospital and of the DEcIDE Methods Center. His research interests include pharmacoepidemiology and pharmaceutical outcomes research, with particular interest in the comparative safety and effectiveness of pharmaceuticals and biotech products, drug policy and risk management program evaluation, and epidemiologic methods using electronic health care databases. An important part of Dr. Schneeweiss’s teaching is the development and testing of new pharmacoepidemiologic methods that rely on large computerized claims databases. Dr. Schneeweiss received a BA from Gymnasium Icking in Germany, an MD from Ludwig-Maximilians-University Medical School, and an ScD in Epidemiology from Harvard School of Public Health.

Selected Publications:


About the Harvard School of Public Health:
The Harvard School of Public Health is dedicated to advancing the public’s health through learning, discovery, and communication. More than 400 faculty members are engaged in teaching and training the 1,000-plus student body in a broad spectrum of disciplines crucial to the health and well being of individuals and populations around the world. Programs and projects range from the molecular biology of AIDS vaccines to the epidemiology of cancer; from risk analysis to violence prevention; from maternal and children’s health to quality of care measurement; and from health care management to international health and human rights.

About Brigham and Women’s Hospital:
Recognized internationally for its excellence in patient care, its outstanding reputation in biomedical research, and its commitment to educating and training physicians, research scientists and other health care professionals, Brigham and Women’s Hospital (BWH) is a 793-bed teaching affiliate of Harvard Medical School located in the heart of Boston’s renowned Longwood Medical Area. Along with its modern inpatient facilities, BWH boasts extensive outpatient services and clinics, neighborhood primary care health centers, state-of-the-art diagnostic and treatment technologies and research laboratories.

Additional Information:
- Harvard School of Public Health. [http://www.hsph.harvard.edu](http://www.hsph.harvard.edu)
- Brigham and Women’s Hospital. [http://www.brighamandwomens.org](http://www.brighamandwomens.org)

Sources:


Mary Tinetti, MD

Professor of Medicine, Epidemiology, and Public Health, Division of Geriatrics, Yale University School of Medicine; Director, Program on Aging, Yale University School of Medicine

Biography:

Mary Tinetti, MD, is a professor of medicine, epidemiology and public health in the Division of Geriatrics at Yale University School of Medicine. She also serves as director for both the Program on Aging and the Hartford Center of Excellence in Aging at Yale University School of Medicine.

Dr. Tinetti has conducted extensive research in the field of aging and geriatrics and served as chair of the National Institute on Aging (NIA) Advisory Council review of the NIA Gerontology and Clinical Geriatrics Program. Dr. Tinetti has been elected to the Institute of Medicine and was named a 2009 MacArthur Foundation Fellow for her work in the area of morbidity due to falls by elderly people.

Dr. Tinetti's research focus includes the health effects of multiple chronic conditions, the relative and absolute benefits versus risks of comparative treatments, morbidity due to falling, and cross-disease health outcomes and measurement for older adults. She has conducted pioneering work in diagnosis, treatment and outcomes of elderly patients.

Dr. Tinetti received a BA from the University of Michigan at Ann Arbor and an MD from the University of Michigan Medical School.

Selected Publications:


About the Yale University School of Medicine:
Located in New Haven, Connecticut, the Yale School of Medicine is a world-renowned leader in biomedical research, education and advanced health care and is one of the nation’s oldest and largest schools of medicine and public health. It is preeminent in medical studies and has long been regarded as one of the world’s foremost medical institutions.

Yale School of Medicine consists of 28 departments, is one of 41 comprehensive cancer centers designated by the National Cancer Institute, and is a member of the Association of American Medical Colleges (AAMC) and the Association of Academic Health Centers (AAHC). Yale is a leading recipient of research funding from the National Institutes of Health.

Additional Information:
- Yale University School of Medicine. http://medicine.yale.edu
- Yale University School of Medicine Program on Aging. http://medicine.yale.edu/intmed/geriatrics/research/index.aspx

Sources:


Clyde Yancy, MD, MSc

Chief, Cardiology, Northwestern University Feinberg School of Medicine; Associate Director, The Bluhm Cardiovascular Institute, Northwestern Memorial Hospital

Biography:

Clyde Yancy, MD, MSc, was recently appointed Magerstadt professor and chief of cardiology at the Northwestern University Feinberg School of Medicine. He is also currently serving as the associate director of the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital.

During the 2009-2010 fiscal year, Dr. Yancy served as president of the American Heart Association (AHA), and prior to his position at Northwestern he was the medical director of the Baylor Heart and Vascular Institute and chief of cardiothoracic transplantation at Baylor University Medical Center.

Dr. Yancy is a fellow of the American College of Cardiology (ACC) and the American College of Physicians and is a member of the ACC/AHA guideline writing committee for chronic heart failure. Dr. Yancy has served on the executive committee for the Heart Failure Society of America and has also served as the chair of the Food and Drug Administration's cardiovascular device panel.

Dr. Yancy’s work has focused on areas including hypertension, heart failure and heart transplantation, and ethnic and racial disparities in cardiovascular disease. He has authored or co-authored more than 200 papers and has been honored by his colleagues through multiple awards including the “Cardiologists-In-Training” hero award from the National Association of Black Cardiologists, Inc, in 2006 and American Heart Association’s “Physician of the Year” award in 2003.

Dr. Yancy earned his medical degree from Tulane University School of Medicine in 1982 and completed an internship and residency in internal medicine at Parkland Memorial Hospital in Dallas, Texas in 1985. He completed a fellowship in cardiology at the University of Texas Southwestern Medical Center and subsequently led the institution’s heart-transplant and heart-failure programs.

Selected Publications:


- Albert NM, Fonarow GC, Yancy CW, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, McBride M, Mehra MR, O’Connor CM, Reynolds D, Walsh MN. Influence of dedicated heart failure clinics on delivery of recommended therapies in outpatient cardiology practices: findings from the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). Am Heart J. February 2010;159(2):238-244.


About the Northwestern University Feinberg School of Medicine:
Northwestern University Feinberg School of Medicine was founded in 1859 and initially led by Nathan Smith Davis, who was instrumental in the founding of the American Medical Association. Part of Northwestern University, an independent private institution founded in 1851, Feinberg School of Medicine is widely considered one of the world’s premier medical research and educational institutions.

Located on a 20-acre campus in Chicago, Illinois, Feinberg School of Medicine retains more than 4,000 leading research and educational faculty members. With over 2,000 students from all over the world currently enrolled, Feinberg School of Medicine seeks to prepare the next generation of doctors while conducting groundbreaking research in a variety of fields.

About the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital:
The Bluhm Cardiovascular Institute is Northwestern Memorial Hospital's heart and vascular division. The Bluhm Institute is a teaching clinic, offering world-class treatment to patients and a hands-on learning environment for Northwestern University medical students.

The Bluhm Institute is separated into six centers: the Center for Atrial Fibrillation, the Center for Coronary Disease, the Center for Heart Failure, the Center for Heart Valve Disease, the Center for Vascular Disease, and the Center for Women's Cardiovascular Health.

Additional Information:
- Northwestern University Feinberg School of Medicine. [http://www.feinberg.northwestern.edu/](http://www.feinberg.northwestern.edu/)
- The Bluhm Cardiovascular Institute at Northwestern Memorial Hospital, Chicago. [http://www.nmh.org/nm/bluhm+cardiovascular+institute](http://www.nmh.org/nm/bluhm+cardiovascular+institute)

Sources:
Decisions made by patients and providers about the care that the patient will receive frequently involve choices among available therapies. Commonly, there are few research studies that compare alternative treatments or treatment strategies in a “head-to-head” fashion. For this reason, it can be challenging for clinicians and patients to make care decisions. Even less plentiful are studies that compare treatment options in real-world settings, where results may differ from those observed in the well-controlled experimental clinical trials. As the realization of this need for enhanced comparative information to achieve best outcomes has grown, attention has focused on comparative effectiveness research (CER).

Although there are many types of biomedical research that are very useful in understanding disease and developing new treatments, the three most commonly utilized types of CER are 1) randomized controlled trials (RCTs) which directly compare two (or more) approaches to diagnosing or treating patients, 2) meta-analysis, or systematic reviews, and 3) observational or "non-experimental" studies. If conducted and interpreted correctly, these types of research can help to inform health care decision making. If, however, such studies are conducted or interpreted incorrectly, the comparative answers from these studies may be inaccurate, or worse, misleading.

**Why Methods Are Important**

Decisions made by patients and providers about the care that the patient will receive frequently involve choices among available therapies. Commonly, there are few research studies that compare alternative treatments or treatment strategies in a “head-to-head” fashion. For this reason, it can be challenging for clinicians and patients to make care decisions. Even less plentiful are studies that compare treatment options in real-world settings, where results may differ from those observed in the well-controlled experimental clinical trials. As the realization of this need for enhanced comparative information to achieve best outcomes has grown, attention has focused on comparative effectiveness research (CER).

Although there are many types of biomedical research that are very useful in understanding disease and developing new treatments, the three most commonly utilized types of CER are 1) randomized controlled trials (RCTs) which directly compare two (or more) approaches to diagnosing or treating patients, 2) meta-analysis, or systematic reviews, and 3) observational or "non-experimental" studies. If conducted and interpreted correctly, these types of research can help to inform health care decision making. If, however, such studies are conducted or interpreted incorrectly, the comparative answers from these studies may be inaccurate, or worse, misleading.
Randomized Controlled Trials

- RCTs can determine whether an intervention provides benefit in a very controlled environment.
- The controlled nature of an RCT may limit its generalizability to a broader population.
- Targeted therapy illuminated by carefully thought out subgroup analyses can improve the efficacious and safe use of an intervention.

There are several kinds of randomized controlled trials that can be matched to potential research questions. These include:

- Pragmatic clinical trials, which are designed to demonstrate how a medical intervention works in a typical, real-world setting;
- Cluster RCTs, in which groups are randomized to an intervention instead of randomizing individuals;
- Bayesian, or adaptive trials, which makes use of prior information on a medical intervention to estimate a prior distribution. This prior information is then combined with trial data to create a posterior distribution;
- N-of-1 trials, which are single event case studies to look at the effect of an intervention in an individual;
- Delayed-design or "advance coverage" trials, which have many variations, but the most common version of this design randomizes participants to either receive the intervention from the start of the trial, or have the intervention withheld for a pre-specified amount of time. By the end of the trial, both study groups have received the intervention.

Meta-Analyses

Meta-analyses synthesize existing data across a series of similar studies, generally RCTs. This study design requires careful selection of which studies to include and which statistical methods to employ. Publication bias, which occurs when positive studies are more abundantly available on a topic due to negative studies not being published, can significantly impair the validity of this study type. However, a balanced meta-analysis can produce a summary estimate of the medical literature that underpins benchmarks of clinical decision making.

Meta-Analyses

- The results of a meta-analysis are highly dependent on the studies included (and excluded). Are these criteria properly defined and relevant to the purposes of the meta-analysis? Were the combined studies sufficiently similar?
- The statistical methodology can impact study results. Have there been reviews critiquing the methods used in the meta-analysis? The statistical methodology can impact study results. Have there been reviews critiquing the methods used in the meta-analysis?
- Nothing is permanent. Emerging data may change the playing field, and meta-analysis results are only as good as the data and statistics from which they are derived.
**Observational Studies**

Observational studies follow participants over a period of time to examine the potential associations between patients' exposure to treatment and health outcomes. These studies can be performed prospectively, observing patients in real time, or they can be retrospective analyses of existing databases. Given the abundance of billing or administrative databases, comparisons of therapies and their outcomes will frequently use these databases, as they embody the experience of patients in real-world settings. While results from observational studies tend to generate hypotheses and may require the more rigorous RCT for confirmation, long-term observational studies have provided substantial medical knowledge (e.g., demonstrating the link between elevated blood cholesterol and the development of heart disease).

- Observational studies provide an understanding of real-world care and its impact, but can be biased due to uncontrolled factors.
- Before accepting the findings from an observational study, consider whether confounding factors may have influenced the results.
- Observational studies can identify associations but cannot prove cause-and-effect relationships.
- The GRACE Principles (www.graceprinciples.org) are an excellent source of further information about observational studies and their application in CER.

**How Could These Designs Be Used?**

One of the PCORI Methodology Committee’s first tasks will be to prepare a translation table to assist in the development of research designs, which will help researchers match the research method to the question at hand. Certain methods are better suited for certain designs than others. For example, a translation table will indicate the types of studies (or methods) that might be appropriate to assess real-world patient adherence to medications, which likely differ from the study types appropriate to assess whether surgical or non-surgical therapy provides the best outcomes for low back pain. Other considerations for choosing a particular method include its strengths and limitations, such as the internal validity (strength of cause and effect), the generalizability (ability to extend research findings to other groups, patients, or settings), feasibility (to understand the conduct of the research or the costs to conduct), and the timeliness of research findings (how long it will take to conduct a study).

Sources:

Existing Methodological Standards and Good Practices

There are a number of existing methodological standards and good practices for randomized clinical trials, systematic reviews, meta-analyses and observational studies. The following list highlights some of the most widely recognized approaches.

For a broader listing, view the online library maintained by the Enhancing the Quality of Transparency of Health Research (EQUATOR) Network at www.equator-network.org.

**Bodies of Evidence**

**Systematic Reviews and Meta-Analysis**


Cochrane Collaboration Reviews. [www.cochrane.org](http://www.cochrane.org)


**Grading Systems and Tools for Studies**


Conference on Guideline Standardization (COGS). [gem.med.yale.edu/cogs](http://gem.med.yale.edu/cogs)

**Individual Study Types**

**Randomized Controlled Trials**

Consolidated Standards of Reporting Trials (CONSORT). [www.consort-statement.org](http://www.consort-statement.org)


**Observational Studies**

Good ReseArch for Comparative Effectiveness (GRACE) Principles. [www.graceprinciples.org](http://www.graceprinciples.org)


Other Applications

Sox, et al, Editorial Standards for the Conduct and Reporting of CER. www.ncbi.nlm.nih.gov/pmc/articles/PMC2860496

Standards for the Reporting of Diagnostic Accuracy Studies (STARD). www.stard-statement.org


Source:
Additional Resources

Many organizations—including, but not limited to those listed below—are taking an active role in examining research methods. There is also a wide variety of collaborative efforts among academic researchers, many of which are listed in the preceding section of this resource guide.

Agency for Healthcare Research and Quality Effective Healthcare Program. effectivehealthcare.ahrq.gov
Center for Medical Technology Policy (CMTP). www.cmtpnet.org
Cochrane Collaboration. www.cochrane.org
ECRI. www.ecri.org
European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). www.encepp.eu
Hayes, Inc. www.hayesinc.com
Institute of Medicine. www.iom.gov
International Network of Agencies for Health Technology Assessment. www.inahta.org
International Society for Pharmacoeconomics and Outcomes Research (ISPOR). www.ispor.org
International Society for Pharmacoepidemiology (ISPE). www.pharmacoepi.org
James Lind Library. www.jameslindlibrary.org
Patient-Centered Outcomes Research Institute (PCORI). www.pcori.org
Pragmatic Approaches to Comparative Effectiveness (PACE) Initiative. www.paceinitiative.org/index.html

The National Pharmaceutical Council plans to regularly update this list on its Web site. To be considered for inclusion, please send an email with the organization’s name and Web address to info@npcnow.org.
Appendix

Excerpted from The Patient Protection and Affordable Care Act, PL 111-148.

Subtitle D—Patient-Centered Outcomes Research, SEC. 6301. PATIENT-CENTERED OUTCOMES RESEARCH

CARRYING OUT RESEARCH PROJECT AGENDA.-

“(A) RESEARCH.-The Institute shall carry out the research project agenda established under paragraph (1)(B) in accordance with the methodological standards adopted under paragraph (9) using methods, including the following:

“(i) Systematic reviews and assessments of existing and future research and evidence including original research conducted subsequent to the date of the enactment of this section.

“(ii) Primary research, such as randomized clinical trials, molecularly informed trials, and observational studies.

“(iii) Any other methodologies recommended by the methodology committee established under paragraph (6) that are adopted by the Board under paragraph (9).

(6) ESTABLISHING METHODOLOGY COMMITTEE-

‘(A) IN GENERAL- The Institute shall establish a standing methodology committee to carry out the functions described in subparagraph (C).

‘(B) APPOINTMENT AND COMPOSITION- The methodology committee established under subparagraph (A) shall be composed of not more than 15 members appointed by the Comptroller General of the United States. Members appointed to the methodology committee shall be experts in their scientific field, such as health services research, clinical research, comparative clinical effectiveness research, biostatistics, genomics, and research methodologies. Stakeholders with such expertise may be appointed to the methodology committee. In addition to the members appointed under the first sentence, the Directors of the National Institutes of Health and the Agency for Healthcare Research and Quality (or their designees) shall each be included as members of the methodology committee.

‘(C) FUNCTIONS- Subject to subparagraph (D), the methodology committee shall work to develop and improve the science and methods of comparative clinical effectiveness research by, not later than 18 months after the establishment of the Institute, directly or through subcontract, developing and periodically updating the following:

‘(i) Methodological standards for research. Such methodological standards shall provide specific criteria for internal validity, generalizability, feasibility, and timeliness of research and for health outcomes measures, risk adjustment, and other relevant aspects of research and assessment with respect to the design of research. Any methodological standards developed and updated under this subclause shall be scientifically based and include methods by which new information, data, or advances in technology are considered and incorporated into ongoing research projects by the Institute, as appropriate. The process for developing and updating such standards shall include input from relevant experts, stakeholders, and decisionmakers, and shall provide opportunities for public comment. Such standards shall also include methods by which patient subpopulations can be accounted for and evaluated in different types of research. As appropriate, such standards shall build on existing work on methodological standards for defined categories of health interventions and for each of the major categories of comparative clinical effectiveness research methods (determined as of the date of enactment of the Patient Protection and Affordable Care Act).

‘(ii) A translation table that is designed to provide guidance and act as a reference for the Board to determine research methods that are most likely to address each specific research question.
‘(D) CONSULTATION AND CONDUCT OF EXAMINATIONS- The methodology committee may consult and contract with the Institute of Medicine of the National Academies and academic, nonprofit, or other private and governmental entities with relevant expertise to carry out activities described in subparagraph (C) and may consult with relevant stakeholders to carry out such activities.

‘(E) REPORTS- The methodology committee shall submit reports to the Board on the committee’s performance of the functions described in subparagraph (C). Reports shall contain recommendations for the Institute to adopt methodological standards developed and updated by the methodology committee as well as other actions deemed necessary to comply with such methodological standards.