COMPARATIVE EFFECTIVENESS NEWS

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Building the Foundation: Research Methods for Patient-Centered Outcomes Research

THIS ISSUE OF *COMPARATIVE EFFECTIVENESS NEWS* demonstrates AHRQ's commitment to the development and dissemination of quality research methods.

Research methods serve as the foundation of AHRQ's Effective Health Care (EHC) Program. Behind each of the many reports and systematic reviews created by the Program are hundreds of critical decisions that AHRQ-funded researchers must make about how to consider and coordinate disparate sets of data so that valid and useable conclusions can be drawn. Well-developed methods enable EHC Program reports to become trustworthy and actionable assessments of benefits and harms across multiple subpopulations for a wide variety of conditions.

The research methods are constantly being refined and broadly disseminated through a variety of channels. The various methods projects are intended to ensure a high level of transparency, consistency, and scientific rigor across the findings reported by the EHC Program.

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New Methods Guide Chapter Focuses on Observational Studies for Systematic Reviews

A NEWLY PUBLISHED CHAPTER of the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* offers a conceptual framework for Agency for Healthcare Research and Quality (AHRQ) researchers who are considering observational studies to determine the benefits of pharmacotherapeutic, device, or procedural interventions. Posted to the Effective Health Care (EHC) Program Web site on June 14, 2010, the chapter offers researchers a clear set of decision criteria for whether to include or exclude observational studies when conducting systematic reviews.

While most researchers agree that observational studies are appropriate for identifying and quantifying adverse events, the use of data from observational studies to answer questions about intended effects or benefits is more controversial. Some researchers believe that observational studies cannot provide valid or useful evidence of benefit.

The framework focuses on two questions: (1) Are there gaps in the evidence from randomized controlled trials (RCTs)? (2) Will observational studies provide valid and useful information? The chapter then describes in detail how to answer these questions in order to make a final determination about the inclusion of observational studies, such as refocusing the review questions on the gaps in the evidence from RCTs, and assessing the

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New Methods Guide Chapter Focuses on Observational Studies for Systematic Reviews

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risk of bias in the observational studies. A set of criteria are provided to assist researchers in making an assessment of the data in an RCT to determine if gaps exist. The chapter also includes scenarios where decisions to include or exclude observational studies were made, as well as a flow diagram for considering observational studies for answering comparative effectiveness questions.

The authors—a team of scientists from seven of the Evidence-based Practice Centers (EPCs), AHRQ, and the VA Quality Enhancement Research Initiative (QUERI)—remind readers that the framework of comparative effectiveness reviews (CERs) differs from traditional systematic reviews. As they state, CERs "more closely parallel the decisions facing clinicians, patients, and policymakers, who must choose among a variety of alternatives in making diagnostic, treatment, and health care delivery decisions." The authors suggest, however, that comparative effectiveness reviewers should routinely assess whether the inclusion of observational studies is appropriate for questions of benefit, and that reviewers should explicitly state their rationale for including or excluding observational studies in the reviews. ◄

Methods Symposium Papers Published

PAPERS ORIGINALLY PRESENTED at the June 2009 invitational symposium on research methods for clinical and comparative effectiveness studies have now been published in the June 2010 supplemental issue of the journal *Medical Care*. The collection is available free online or through PubMed.

The symposium brought together an international group of scientists to continue the ongoing discussion and subsequent development of research methods for comparative effectiveness research, a timely endeavor in light of the additional funding provided by the American Recovery and Reinvestment Act (ARRA) of 2009. Symposium speakers and authors addressed two main themes: (1) including more data from clinically heterogeneous populations into comparative effectiveness research projects, and (2) employing longitudinal investigative methods intended to capture patient-reported outcomes over a longer term.

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>
> Kathleen N. Lohr, Ph.D.
> RTI International

More than 75 abstracts were reviewed by a planning committee of experts from academia, the private sector, and the Federal Government. Authors of chosen abstracts were also invited to submit a manuscript for publication in the *Medical Care* supplement. Submitted manuscripts went through a blind editorial review, and the final collection of accepted articles was published in record time. "We were able to get the papers published in a short time by academic journal standards," said Kathleen N. Lohr, Ph.D., of RTI International, who led the staff of the RTI DEcIDE (Developing Evidence to Inform Decisions about Effectiveness) Center in organizing the event and supplemental publication. "As this field is relatively new, continuing to pave the road of improved methods through publications of peer-reviewed literature that are reachable around the globe is critically important."

The collection includes an editorial from AHRQ Program Director Scott R. Smith, Ph.D., that provides an overview of the crucial role of AHRQ and its Effective Health Care Program in advancing methods for comparative effectiveness research, an overview of the original symposium by Dr. Lohr; and an introduction by Harold C. Sox, M.D., who served as the chair of the Committee on Comparative Effectiveness Research Priorities convened by the Institute of Medicine and is a past president of the American College of Physicians.

In his introduction, Dr. Sox focused on the importance of having a clear definition of comparative effectiveness research to guide the methods process. In his article based on the Symposium's keynote address, he states: "Defining CER [comparative effectiveness research] forces decisionmakers—health professionals and patients—to identify the information that they need. The definitions of CER all focus on making head-to-head comparisons in study populations that are typical of clinical practice. That health professionals seem to agree on these attributes of the inputs to decisionmaking is reason to celebrate."

An additional 20 articles round out the collection and fall under one of four major content areas: (1) study design, (2) data collection, (3) statistics and analytic methods, and (4) policy issues and applications. Several of the articles address specific methodological approaches such as prediction modeling and Bayesian meta-analysis; others focus on particular patient populations such as the elderly or cancer patients.

The 2009 event marks the second time that an AHRQ-supported effort to advance methods was developed by members of the DEcIDE Network, whose primary duty is to generate new comparative evidence for the Effective Health Care Program. Papers from the 2006 AHRQ Conference on Emerging Methods in Comparative Effectiveness and Safety, which was also published as a supplement in *Medical Care*, focused primarily on methods for generating data on the benefits and safety of pharmaceutical interventions.

Dr. Lohr believes that both publications represent an ongoing conversation that will continue for many years. "Nothing in these articles puts an end to the issues, but certainly they add materially to the literature and to the knowledge base. I give great credit to AHRQ for recognizing and supporting the importance of developing methods for DEcIDE researchers and others, and I hope we'll see more symposiums and publications in the future," she said.

A printed copy of the supplement, AHRQ Publication No. OM10-0067, is available free of charge through the AHRQ Publications Clearinghouse. To order the supplement, call 800-358-9295 or send an e-mail to AHRQpubs@ahrq.hhs.gov. ◄

Education Modules Provide Instruction to New Researchers on Reviewing Evidence

INCREASING INTEREST FOR comparative effectiveness research has created the need to expand the Nation's capacity to conduct systematic reviews. To help train new generations of researchers in the methods used to conduct these reviews, the Effective Health Care (EHC) Program recently contracted with four Evidence-based Practice Centers (EPCs) to create training modules based on chapters from the EHC Program *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Composed of PowerPoint® presentations, case examples, and linkages to other references and tools, the modules have now been posted on the EHC Program Web site for use free of charge.

In addition to their use by faculty within the EPCs to mentor and teach new investigators, the training modules are also available to (1) investigators interested in the self-study of systematic review methods for *AMA PRA Category 1 Credit*™, and (2) instructors who teach clinical researchers and students about the systematic review process in graduate training programs around the globe. A slide library allows faculty to select a complete set of lecture slides by topic or to create their own presentation by mixing and matching slides.

Thirteen education modules, along with an introductory slide set written by AHRQ officers Stephanie Chang, M.D., M.P.H., and Elizabeth Kato, M.D., M.R.P., take researchers who are unfamiliar with the systematic review process through a series of steps from topic refinement to reporting review results. The introductory module introduces future researchers to the goals of the EHC Program, the many partners and stakeholders involved in the Program, and the key terms and concepts of the Program. Most importantly, a conceptual model of the EHC systematic review process is presented for the AHRQ systematic review process. The slides and lecture notes in the introductory module explain confusing terminology such as subtle differences between "systematic review," "effectiveness review," and "comparative effectiveness review," as well as the role of the PICO typology (or framework) used in systematic reviews. PICO stands for the four elements to be considered when developing the overarching questions of the review: Population, Intervention, Comparison, and Outcome. Two other elements—Timing and Setting (or Study Design)—are sometimes added, with the term PICOTS used instead.

The five EPCs responsible for the modules—RT International–University of North Carolina, Tufts–New England Medical Center, Vanderbilt University, the University of Connecticut–Hartford Hospital, and the University of Ottawa—developed a research protocol and conceptual model of the EHC Program systematic review process to guide the creation of the modules. Each module was then peer-reviewed by five experts in the field to ensure quality and consistency with the *Methods Guide* and other relevant literature, and edited by staff at the John M. Eisenberg Center for Clinical Decisions and Communications Science.

National Action Plan on Health Literacy Launched

ACCORDING TO RESEARCH from the U.S. Department of Education, only 12 percent of English-speaking adults in the United States have proficient health-literacy skills. The overwhelming majority of adults have difficulty understanding and using everyday health information that comes from many sources, including the media, Web sites, nutrition and medicine labels, and health professionals. A 2004 AHRQ systematic research review of the impact of health literacy found associations between limited health literacy and adverse outcomes such as increased disease prevalence and severity, lower utilization of screening and preventative services, and higher hospitalization rates.

To help address these issues, the United States Department of Health and Human Services (HHS) launched a *National Action Plan to Improve Health Literacy.* According to the National Action Plan (NAP) document published in May, 2010, the national effort seeks to "engage organizations, professionals, policymakers, communities, individuals, and families in a linked, multisector effort to improve health literacy." The Institute of Medicine defines health literacy as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."

Two principles guide the NAP: (1) everyone has the right to health information that helps them make informed decisions and (2) health services should be delivered in ways that are understandable and beneficial to health, longevity, and quality of life.

Organized into four sections and three appendixes, the NAP reviews the research on limited health literacy as a public health problem, discusses the development of a "health literate society" that "supports lifelong learning and skills to promote good health," and outlines seven goals for the improvement of health literacy, with several that are immediately relevant to the translation and dissemination of AHRQ research:

1. Develop and disseminate health and safety information that is accurate, accessible, and actionable.
2. Promote changes in the health care system that improve health information, communication, informed decision-making, and access to health services.

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3. Incorporate accurate, standards-based, and developmentally appropriate health and science information and curricula in child care and education through the university level.
4. Support and expand local efforts to provide adult education, English-language instruction, and culturally and linguistically appropriate health information services in the community.
5. Build partnerships, develop guidance, and change policies.
6. Increase basic research and the development, implementation, and evaluation of practices and interventions to improve health literacy.
7. Increase the dissemination and use of evidence-based health literacy practices and interventions.

The plan presents a set of strategies per goal that can be employed by particular organizations or professions to accomplish the seven goals. For example, in the section of the NAP that discusses goal 6—increase basic research and evaluation of practices and interventions—some of the suggestions for researchers, evaluators, and funders include:

- Identify and address gaps, such as numeracy and visual communication, in health literacy research.
- Collaborate to develop a national research agenda and include health literacy innovations and interventions in research plans and goals.
- Develop more rigorous and comprehensive methods to measure individual and population health-literacy skills that capture the full range of skills, including listening and speaking, writing, numeracy, and cultural and conceptual knowledge.
- Develop methods to measure the full range of health literacy skills of health professionals and organizations.
- Conduct studies of the economic impact of limited health literacy.
- Explore technology-based interventions to improve health literacy.
- Assess barriers and strategies to improve access to health information and navigation of the health care system.

The Effective Health Care Program is currently in the process of updating its 2004 systematic review of research on health literacy, with a draft available this month for public comment. In alignment with the NAP, the update, titled *Health Literacy Interventions and Outcomes: An Update of the Literacy and Health Outcomes Systematic Review of the Literature,* expands its synthesis beyond the outcomes of limited health literacy and also includes research findings on literacy assessment tools and interventions.

The NAP was led by the Health Literacy Workgroup of the U.S. Department of Health and Human Services. The information within the plan was based on the 2006 Surgeon General's Workshop on Improving Health Literacy, a series of town hall meetings held in 2007 and 2008, and feedback from stakeholder organizations in 2009. ◄

EHC PROGRAM SPOTLIGHT:
University of Connecticut–Hartford Hospital Evidence-based Practice Center

THE UNIVERSITY OF CONNECTICUT (UCONN) AND HARTFORD HOSPITAL (HH) were jointly selected as an Evidence-based Practice Center (EPC) by the Agency for Healthcare Research and Quality (AHRQ) in July 2007. The UCONN-HH EPC is part of the Health Outcomes Policy and Economics (HOPE) Collaborative, a multifaceted group interested in evidence-based medicine, health economics, and health care policy at the University of Connecticut School of Pharmacy and the Hartford Hospital.

EPCs are top-ranking institutions where research reviews are conducted on behalf of the Effective Health Care (EHC) Program. These centers review existing scientific research about important health care topics to help patients, physicians, and policymakers make better decisions about tests, treatments, or therapies. EPCs produce comparative effectiveness reviews or effectiveness reviews on medications, devices, and other health care services.

C. Michael White, Pharm.D., FCP, FCCP, Professor of Pharmacy Practice at the University of Connecticut School of Pharmacy, is the Director of the UCONN-HH EPC. He is a fellow of both the American College of Clinical Pharmacologists and the American College of Clinical Pharmacists. Working with Dr. White are Co-Director Craig I. Coleman, Pharm.D., Associate Director and Medical Chief Jeffrey Kluge, M.D., FACC, and Project Manager Diana Sobered, Pharm.D. Dr. White's group received the Drug Therapy Research Award, an annual award for the best research publications by a pharmacist, from the American Society for Health System Pharmacists in 2000, 2002, 2004–2006, and 2008.

In October of 2009, the UCONN-HH EPC published a systematic review entitled "Comparative Effectiveness of Angiotensin Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Added to Standard Medical Therapy for Treating Stable Ischemic Heart Disease" for the EHC Program. Members of the UCONN-HH EPC were also involved in writing a chapter entitled "Using Existing Systematic Reviews To Replace De Novo Processes in Comparative Effectiveness Reviews," which was published in the EHC Program's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Ongoing and future research projects will continue to utilize the UCONN-HH EPC's expertise in pharmacology and cardiac therapies. ◄