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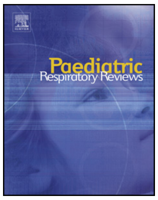

Mini-Symposium: Research Methodology

Comparative effectiveness research – what is it and how does one do it?

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SUMMARY

Recent initiatives have increased focus on medical research that explores robust comparisons of clinical approaches broadly defined as comparative effectiveness research (CER). Federal mandates have generated definitions, established priorities, and offered organizational approaches for coordinating and conducting CER. This review will summarize the various definitions of CER, the role of cost assessment, and key study components of CER including study populations, study design, the use of secondary data, comparators employed in studies, outcome measures, and how results of CER should be disseminated.

INTRODUCTION

Recent initiatives have increased focus on medical research that explores robust comparisons of clinical approaches broadly defined as comparative effectiveness research (CER). Federal mandates have generated definitions, established priorities, and offered organizational approaches for coordinating and conducting CER.

DEFINITION

A number of proposals have been put forth regarding how we define CER. Some of the similarities and differences are illustrated in Table 1. Based on some of these proposals, some have argued that CER is merely defining what in the past was called clinical outcomes research,[1] while others have argued that it represents a paradigm shift in how we conduct clinical research.[2] A number of the most common definitions share key themes that include assessing how different treatments and approaches to specific diseases perform in the real world and incorporating a broad source of evidence as part of this assessment (administrative data, systematic reviews, cohort studies and randomized clinical trials). The most commonly cited definitions all note that broad dissemination of the results is key. The three most common are from the Institute of Medicine, the U.S. Department of Health and Human Services and the Agency for Healthcare Research and Quality.

CER has been defined most broadly by the Institute of Medicine (IOM) as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat and monitor a clinical condition or to improve the delivery of care. . ..to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care..."[3] The U.S. Department of Health and Human Services (DHHS) and the Patient Protection and Affordable Care Act of 2010 established the Patient Centered Outcomes Research Institute (PCORI) to define methodological standards for CER and to establish policies regarding research funding. DHHS has defined CER as the "conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in 'real world' settings. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances."[4] This definition offers practical strategies that can be employed in pediatric research. The AHRQ definition is very similar but emphasizes the use of systematic reviews and makes specific mention of stakeholders. These varied CER definitions suggest a shift from investigator-driven research to a responsive and priority-driven infrastructure that identifies and coordinates research topics, priorities, methodologies, and data syntheses.[5–8] Implied in all the definitions is that CER responds to the expressed needs of patients, clinicians, and other decision-makers and recognizes a role for stakeholder involvement in research and its subsequent application. As part of PCORI, a methods core has begun work on synthesizing and developing the research

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Table 1
Definitions of comparative effectiveness research.

	Institute of Medicine (IOM)	Department of Health and Human Services (DHHS)	Agency for Healthcare Research and Quality (AHRQ)
Research Defined	Direct comparison of effective interventions, the study of patients in typical day-to-day clinical care, and the aim of tailoring decisions to the needs of individual patients. Primary interests are interventions such as disease prevention, systems of care, drug therapies, devices, surgery, and monitoring of disease. Synthesis of existing data and delivery of care aspects endorses CER.	Research that “provides information on the relative strengths and weaknesses of various medical interventions. Such research will give clinicians and patients valid information to make decisions that will improve the performance of the U.S. health care system.” CER is the “Conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in “real world” settings.	Comparative effectiveness research is designed to inform health-care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options. The evidence is generated from research studies that compare drugs, medical devices, tests, surgeries, or ways to deliver health care.
Study Description	IOM Researchers must choose among these methodologies and must inform the public about their methodological advantages and shortcomings. These include: (1) Systematic reviews guiding development of guidelines, established data set (2) Prospective registries and cohorts (3) Randomized controlled trials (4) Pragmatic randomized trials	DHHS Conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in “real world” settings. Requires the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness.	AHRQ (1) Existing data (systematic reviews of existing evidence). (2) Create new data: Researchers conduct studies that generate new evidence of effectiveness or comparative effectiveness of a test, treatment, procedure, or health-care service.
Stakeholder Description	IOM Made solicitations, created criteria that included: condition-level criteria, priority topic-level criteria, likelihood that the results would improve health Perspective is one of Overall Societal Good. However, consumers, patients, and caregivers as well as their health care providers must be involved in all aspects of CER.	DHHS Patients, clinicians, and other decision-makers. Generation of knowledge for the research community is specifically noted.	AHRQ Clinicians, consumers (payer, purchaser), and policymakers. Have a community forum to address different stake holders. Also uses the Healthcare Horizon Scanning System to identify new and emerging issues for comparative effectiveness review investment.
Definition of Value	IOM Not formally addressed	DHHS Not formally addressed	AHRQ Not formally addressed
Role in Dissemination of Information	IOM The nation will need effective strategies for disseminating CER findings and promoting their adoption by clinical practice.	DHHS Actively disseminate the results. Create the CER inventory.	AHRQ Dissemination of the results in a form that is quickly usable by clinicians, patients, policymakers, and health plans and other payers
Addresses Cost as Outcome	IOM Mentioned but not a focus of recommendations	DHHS Not mentioned	AHRQ Not mentioned. Goal is to support health services research that will improve the quality of health care and promote evidence-based decision making.
Resources and Workforce	IOM Requires increasing the need for trained experts in biostatistics, epidemiology, systematic reviews, observational and clinical trials, and more refined research methods for CER.	DHHS Development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness.	AHRQ Requires the development, expansion, and use of a variety of data sources and methods to conduct timely and relevant research
Specified Outcomes	IOM Not specified	DHHS Comprehensive array of health-related outcomes for diverse patient populations and subgroups	AHRQ Not specified

approaches that will be needed to conduct CER and existing Federal bodies such as the Agency for Healthcare Research and Quality (AHRQ) and the Clinical and Translational Science Award (CTSA) consortium are developing approaches to integrate and facilitate CER into strategic goals.[6–8]

EXCLUSION OF COST EFFECTIVENESS ANALYSIS

An important exclusion from CER is any explicit incorporation or consideration of cost effectiveness analysis (CEA). CEA is an integral component in the development of clinical guidelines in other countries including Australia, England, and Canada.[9] England’s National Institute for Health and Clinical Excellence (NICE) states that “guidelines should be based on the estimated costs of the interventions or services in relation to their expected health benefit (that is, their ‘cost effectiveness’), rather than on the total cost or resource impact of implementing them.”[10] Implicit in this statement is an understanding that all medical care, as with all other economic activity, draws on limited resources, and alternative uses of those resources should therefore be considered