

Curricular considerations for pharmaceutical comparative effectiveness research

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ABSTRACT

In the U.S., pharmacoepidemiology and related health professions can potentially flourish with the congressional appropriation of \$1.1 billion of federal funding for comparative effectiveness research (CER). A direct result of this legislation will be the need for sufficient numbers of trained scientists and decision-makers to address the research and implementation associated with CER. An interdisciplinary expert panel comprised mostly of professionals with pharmaceutical interests was convened to examine the knowledge, skills, and abilities to be considered in the development of a CER curriculum for the health professions focusing predominantly on pharmaceuticals. A limitation of the panel's composition was that it did not represent the breadth of comparative effectiveness research, which additionally includes devices, services, diagnostics, behavioral treatments, and delivery system changes. This bias affects the generalizability of these findings. Notwithstanding, important components of the curriculum identified by the panel included study design considerations and understanding the strengths and limitations of data sources. Important skills and abilities included methods for adjustment of differences in comparator group characteristics to control confounding and bias, data management skills, and clinical skills and insights into the relevance of comparisons. Most of the knowledge, skills, and abilities identified by the panel were consistent with the training of pharmacoepidemiologists. While comparative effectiveness is broader than the pharmaceutical sciences, pharmacoepidemiologists have much to offer academic and professional CER training programs. As such, pharmacoepidemiologists should have a central role in curricular design and provision of the necessary training for needed comparative effectiveness researchers within the realm of pharmaceutical sciences. Copyright © 2011 John Wiley & Sons, Ltd.

KEY WORDS — comparative effectiveness research; curriculum; training

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The Patient Protection and Affordable Care Act (H.R. 3590) provides funding for comparative clinical effectiveness research (CER). CER is defined in the Patient Protection and Affordable Care Act as meaning 'research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of two or more medical treatments, services...'. Its scope includes 'health care interventions, protocols for treatment, care management and delivery, procedures, medical devices, diagnostic tools, pharmaceuticals (including drugs and biologics)', and other strategies.¹ CER is aimed at addressing gaps in information on the appropriate use of health services and technology

to prevent, diagnose, and treat illness. These components of real world treatment and care resonate loudly among pharmacoepidemiologists, drug safety scientists, health services researchers, and healthcare professionals.

An Institute of Medicine (IOM) consensus committee charged and funded by the American Recovery and Reinvestment Act (ARRA) identified a list of diverse priorities for CER and recommendations pertaining to structural needs to support a national program in CER.² The sudden influx of ARRA funding for comparative effectiveness and the rapid implementation of projects aimed at the priority areas identified by the IOM called attention to the need for comparative information on alternative treatments and the inadequate numbers of individuals capable of conducting CER and implementing the findings of such research.^{3,4} Because of the diversity in the

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definitions of CER, two primary groups could be targeted for training, namely researchers and decision-makers (i.e., those at the front-lines of the implementation of research in practice settings such as members of Pharmacy and Therapeutics committees and administrators). Therefore, universities and centers with healthcare professional training programs must consider updating their existing training and educational programs or developing new programs to meet the urgent need for CER researchers and decision-makers.

The diversity of CER creates broad needs for curricular content in graduate training programs. However, also needed are certificate training programs and various forms of continuing education for the existing workforce. Target groups for training include (1) researchers to conduct CER and advance methods, and (2) decision-makers to translate and implement CER findings into practice. The purpose of this report is to provide an expert panel's considerations on the creation of a model curriculum for use by academic training programs to educate healthcare professionals to conduct and implement CER with a focus on the pharmaceutical sciences. Nominal group process was used to evaluate the knowledge, skills and abilities required to competently conduct or expertly utilize CER and then develop a framework for a curriculum for CER training.⁵ Consensus development involved a panel survey, a meeting, and a written consensus report. An interdisciplinary panel convened at the Pharmaceutical Research Manufacturers Association Foundation, Washington, DC, for a moderated discussion of the core components of a curriculum to facilitate research and implementation of CER. The 17-member panel comprised academic researchers ($n=9$), pharmaceutical industry scientists ($n=5$), leaders in associations for health professions education ($n=2$), and a federal agency program officer ($n=1$). Panel members were predominantly those with interests in the pharmaceutical sciences (A listing of panel members appears at the end of this manuscript). Disciplines represented among the panel members included medicine, pharmacy, clinical epidemiology, pharmacoepidemiology, pharmacoconomics, informatics, information sciences, and health services research. Following discussion of the survey results and curricular design concepts, three groups of 5 or 6 panel members divided into pre-assigned groups, two for knowledge of CER, and one for skills and abilities.

The pre-meeting survey categories for analysis described knowledge, skills, and abilities to consider for individuals conducting or implementing CER competently. Knowledge concepts for CER are shown

in Figure 1. The top knowledge content areas included: (1) understanding methods used to control for comparator group differences such as confounding and channeling bias; (2) methods of exposure validation; and (3) interpretation of the results of CER studies, both scientifically and in terms of clinical implications.

Skills and abilities that would facilitate the conduct of CER are found in Figures 2 and 3. The top skills for CER found in Figure 2 included: (1) critical review and appraisal of studies; (2) interpreting results of CER studies; and (3) developing analytic plans to test for CER. Abilities identified (Figure 3) as requisites for competent comparative effectiveness researchers included: (1) understanding methods to compare treatment groups on effectiveness (including both benefits and harms); (2) evaluating analytic plans and designing study analyses; and (3) performing formal statistical comparisons, including estimating effects and possibly testing statistical significance of study results.

The ranked listings of knowledge concepts produced by breakout groups had excellent agreement and were merged into a single list (Table 1). Groups identified key areas for researchers including study design, statistical procedures for adjustment for differences in background characteristics of comparator groups, critical appraisal, decision analysis, and synthesis of study results for systematic reviews. Recurring themes involved the importance of understanding the relationships among the study question and the elements available within accessible data sources, medical informatics, medication safety, the importance of privacy and confidentiality, accelerating the translation of evidence into practice, and general comprehension of the health care and regulatory systems for drugs, and health services.

There was considerable overlap between the skills and abilities identified (Table 2). The group discussed the importance of analytical skills involving methods for adjustment for differences in comparator group characteristics to control confounding and bias, data management skills to handle, organize, and merge potentially large datasets, clinical skills and insights into the relevance of comparisons made, and the influence of CER on insurance benefit design.

The panel recognized the need for didactic and experiential components ultimately for a wide range of audiences involving both researchers and decision-makers. On this note, two especially relevant issues were discussed. First, was CER really something new? Several panel members felt that it was not new and that components of the existing curricula in many institutions could be reorganized to teach CER. Modest reorganization would be likely at universities and

other training settings where pharmacoepidemiology and health services research are prominent. New aspects of CER might include a greater emphasis on real world decision-making, the emphasis on effectiveness instead of efficacy (e.g., head to head comparisons of commonly prescribed drugs as opposed to drug comparisons to placebo), interest in greater interdisciplinary collaboration, use of health information technology that will generate large electronic health care data bases, and focus on new experimental and quasi-experimental methods development in CER.

Second, what types of experiences would be most relevant to researchers and decision-makers for the

competent conduct of CER? Most of the discussion involved training of researchers in graduate and post-graduate programs. Active learning experiences would be the most relevant such as case-based (both live and written) learning, rigorous and well-organized journal clubs, mentored projects, research practica and dissertations for pre-doctoral graduate students, internships, and fellowship research projects. Projects could involve systematic reviews; comparisons of marketed pharmaceuticals, diagnostics, and devices using observational data; and methods development targeting CER, and studies tapping multiple methodologies to address a relevant question. Each of these project types would require strong mentoring within well-estab-

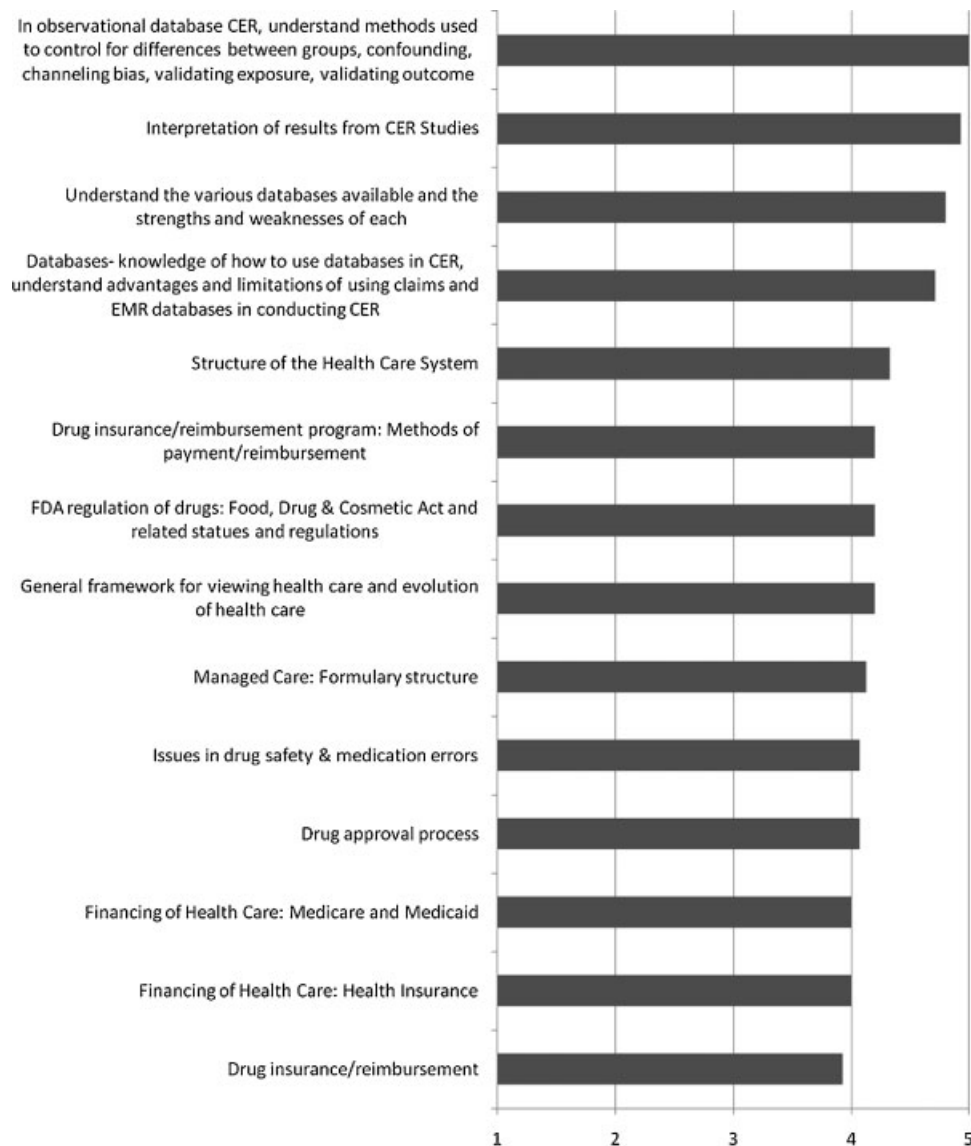


Figure 1. Knowledge rankings from the pre-panel meeting survey (1 = least important; 5 = most important)

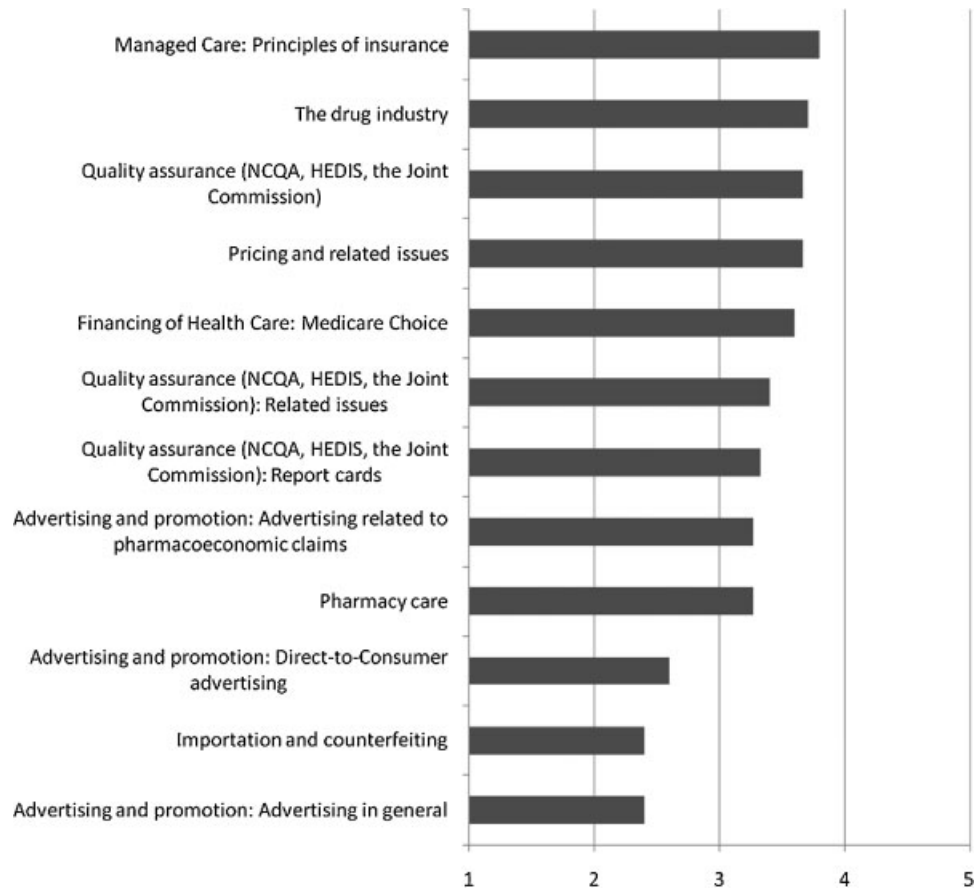


Figure 1. (Continues)

lished training programs. Assignments for trainees should be important (relevant to a real-world or public health challenge), reasonable, and feasible in terms of completion within the time of the training program and available resources. A major goal is to provide actionable evidence for stakeholders including patients, clinicians, purchasers of health care, and regulators.

Panel members felt that comparative effectiveness researchers typically would have prior training in a health profession or some training in a key area relevant to CER such as clinical epidemiology, biostatistics, or health economics, or a combination of training. Decision-makers may have clinical training but might also come from varied professional backgrounds such as health care administration or business and finance. Beyond formal training, specific topics for consideration in the CER curriculum would include those found in Table 3. The panel felt that the advanced knowledge and skills should be part of a rigorous graduate program, independent of whether that program teaches/focuses on CER.

A limitation of the panel's composition was that it did not represent the breadth of comparative effectiveness research, which additionally includes devices, services, diagnostics, behavioral treatments, and delivery system changes. This bias affects the generalizability of these findings. Notwithstanding, the limited generalizability of these results, they derive from an interdisciplinary panel to provide preliminary considerations for a curriculum for CER emphasizing this key area of CER. The participants discussed training for both research and implementation of CER but emphasized programs for researchers. Faculty at universities and institutes, professional associations, and others planning or modifying formal training curricula for CER are now considering what adjustments might be needed to address the need for more CER personnel. This is not new. Curricula are constantly changing, as they should. The health professions have seen recent changes to their curricula from the growing interests in genomics, informatics, and health services research. Such remodeling of the curriculum is normal and important for the quality of

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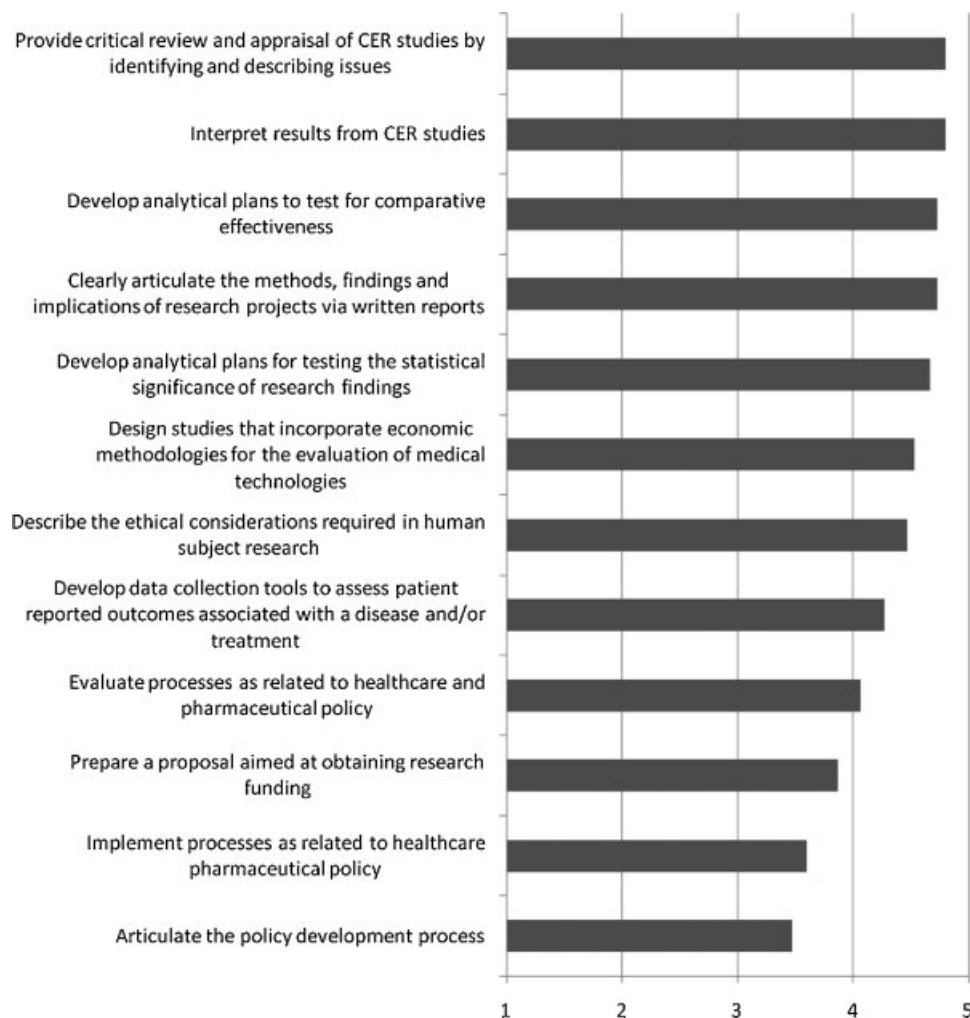


Figure 2. Skill rankings from the pre-panel meeting survey (1 = least important; 5 = most important)

the trainees. It is also important from the standpoint of academe's accountability to the public.⁶ What is different with CER in the U.S. is the pace of need precipitated by ARRA funds.

The panel used a broad definition of curriculum in its work. Kern and colleagues⁷ definition is applicable: 'A planned educational . . . encompassing a breadth of educational experiences, from one or more sessions on a particular subject, to a clinical rotation or clerkship, or an entire training program.' Kern and colleagues operationalized this definition into a six-step dynamic, iterative process in developing a curriculum for medical education including: (1) problem identification and general needs assessment, (2) needs assessment for targeted learners, (3) goals and objectives, (4) educational strategies, (5) implementation, and (6) evaluation and feedback. The work of our panel touched broadly on the first four of these steps in

hopes of stimulating further discussion and action on all six. It was also the hope of the panel that further work on CER curricula by academic and professional training programs would be shared and disseminated to facilitate future curricular refinements.

Current definitions of CER vary but have at their hearts the central concept of comparing existing, marketed technologies and health care services to promote prevention, diagnosis, and treatment of illness that are relevant to patients, clinicians, and other stakeholders in order to apply the best evidence to practice. Another aspect of CER is the need for quick access to, and analysis of, actionable and readily retrievable clinical data from existing data sources, which could derive from claims data, electronic medical records systems, registries, or systematic reviews. As such, observational research methods and synthesis of existing study results become relevant, in

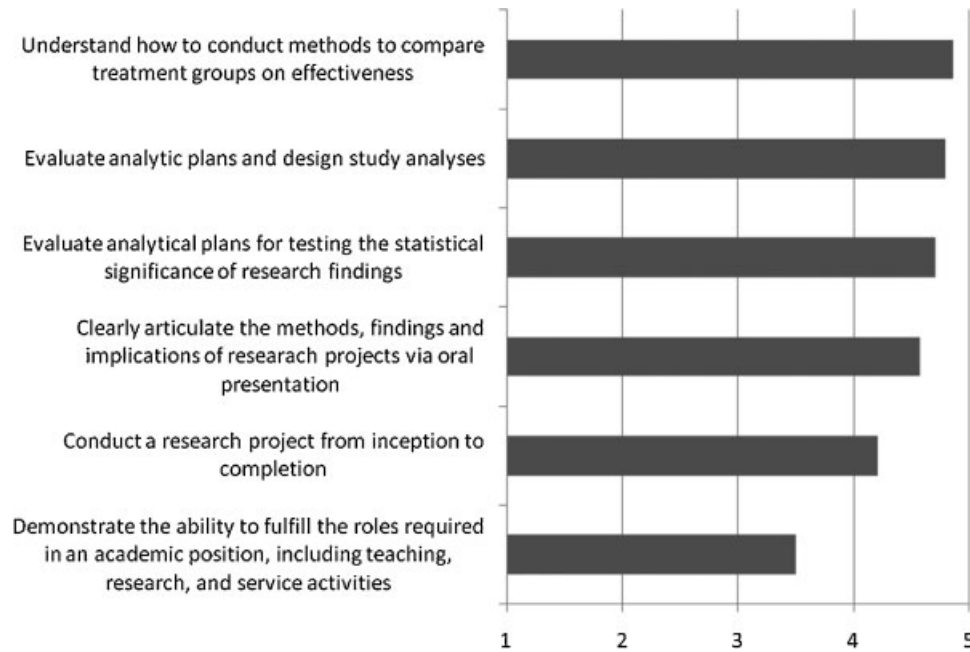


Figure 3. Ability rankings from the pre-panel meeting survey (1 = least important; 5 = most important)

addition to research involving long durations to results such as randomized trials or prospective cohort studies conducted *de novo*. Pragmatic clinical trials or cluster-randomized trials may also be considered appropriate to address some CER questions. Importantly, research involving observational and synthesis methodologies require special expertise that is still evolving. Hence, recent discussions pertaining to CER by the IOM² and AcademyHealth⁸ have recognized the need for a larger

pool of competent comparative effectiveness researchers. Likewise, health professions associations³ and the U.S. Chamber of Commerce⁹ are weighing in on the needs for trained decision-makers.

The curriculum for CER, like other forms of training in the health professions, should run the gamut of curricular development and consider the teacher's materials, methods, and evaluations in the classroom and clinical settings; the learner's experiences, knowl-

Table 1. Knowledge content areas ranked by panel members for inclusion in an interdisciplinary comparative effectiveness curriculum considered for training researchers and decision-makers

Content domain	Researcher	Decision-maker
Knowledge		
Methods to control between comparator group differences including confounding, channeling bias	●	
Interpretation of study results	●	●
Process for validation of exposure and outcomes	●	
Contents of various types of data sources and the strengths and weaknesses of data source types	●	●
Structure and function of the health care system	●	●
Evolution and framework of health care		●
Food and Drug Agency regulations on approval and monitoring of drugs, biologics, and devices	●	●
Medication safety	●	●
Managed care principles involving formulary structure, insurance, and reimbursement		●
Basic framework and functioning of the pharmaceutical industry		●
Financing of health care		●
Quality assurance parameters monitored by NCQA, HEDIS, and the Joint Commission		●
Pharmacy drug delivery and pharmaceutical care		●
Drug product advertising and promotion		●
Importation and counterfeiting		●

The knowledge concepts listed were from merging concepts identified by two separate breakout groups.

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Table 2. Skills and abilities ranked by panel members for inclusion in an interdisciplinary comparative effectiveness curriculum considered for training researchers and decision-makers

Content domain	Researcher	Decision-maker
Skills and abilities		
Methods to compare treatment groups for effectiveness	●	
Critical review and appraisal	●	●
Interpretation of study results	●	●
Evaluation of study designs and analytic plans	●	
Study design and its relation to statistical analysis	●	
Report study methods and results	●	
Evaluation of statistical procedures to test significance	●	
Statistical analysis plan	●	
Incorporation of economic methods to evaluate medical technology	●	
Ethical considerations in human subject research	●	
Develop data collection tools to assess patient reported outcomes of disease or treatments	●	
Conduct research from study inception to completion	●	
Evaluate processes related to health care and pharmaceutical policy		●
Write proposals to conduct research	●	
Implement pharmaceutical policy		●
Describe the health care policy development process		●
Fulfill roles common academic roles (teaching, research, and service)	●	

Skills and abilities were merged to form one ranked listing.

edge, skills and abilities, and attitudes; all to favorably affect current best practices and improve patient outcomes.¹⁰ Understanding the responsibilities relating to the costs of care for beneficial patient outcomes is also an important consideration of clinical decision-making and therefore clinical training.¹¹ Ultimately, we see the work of the panel running a course similar to the one around health services research wherein core competencies for doctoral training have been described.¹² We hope that such competencies will be

developed for both pharmacoepidemiologists and health services researchers conducting and proposing new methods for CER and those translating the results on the front lines of practice. While our primary focus was the pharmaceutical sciences, future guidance for the health professions should have greater breadth.

Panel Members: Kathryn Bennett, PhD, McMaster University; Jesse A. Berlin, ScD, Johnson & Johnson; Jean Paul Gagnon, PhD, Sanofi-Aventis; William Hersh, MD, Oregon Health & Science University;

Table 3. Topics for consideration for a curriculum in comparative effectiveness research to provide the needed knowledge, skills, and abilities researchers and decision-makers

Fundamentals for researchers and Decision-makers	Advanced for researchers
Basic clinical epidemiology	Advanced epidemiology and pharmacoepidemiology
Basic biostatistics	Methods for conducting and evaluating systematic reviews of published and unpublished research
Interpretation of systematic reviews and meta-analyses	Methods for prospective study designs, including distributed networks, adaptive designs, point of care data collection
Understanding clinical heterogeneity	Advanced statistical approaches such as general linear models (GLM) and general estimating equations (GEE)
Cost-effectiveness	Bayesian approaches to design and analysis
European, Canadian, and Australian approaches to comparative effectiveness research	Econometric modeling
Fundamentals of health services research	Data source strengths and limitations including data from claims databases and electronic medical records
FDA regulation of other medical products, particularly devices	Fundamentals of longitudinal analysis
Health technology assessment	Multi-methods research skills
Indirect treatment comparisons	Expecting value of perfect information
Issues related to biomedical informatics, e.g., standards, ARRA, privacy, etc.	Linking comparative effectiveness research to payment policy
Methods for registries	Evaluation of devices
Patient-centered team based care delivery	Evaluation of diagnostic tests
Risk adjustment methods	Propensity scores
Sociobehavioral research methods	Instrumental variables

KEY POINTS

- The sudden availability of U.S. federal funding creates a need for more scientists trained to conduct comparative effectiveness research in the pharmaceutical sciences and decision-makers to implement research findings.
- Universities with health professional programs and other academic training programs should begin to include training in comparative effectiveness in their curricula.
- Researchers will require advanced training in study design and statistical analyses related to comparative research.
- Decision-makers will need training on how to interpret comparative effectiveness research and how to appropriately implement comparative effectiveness findings.
- Because pharmacoepidemiologists are trained in many of the core aspects of comparative effectiveness research, they will be called upon to assist in curricular development for the health professions.
- An important limitation of this work is that, whereas comparative effectiveness research is broad in scope, panel members were largely from areas with pharmaceutical interests and the considerations of the panel largely pharmaceutical in nature.

Lucinda L. Maine, PhD, American Association of Colleges of Pharmacy; Daniel C Malone, PhD, University of Arizona; Ann McKibbin, MLS, PhD, McMaster University; C. Daniel Mullins, PhD, University of Maryland School of Pharmacy; Michael D. Murray, PharmD MPH, Purdue University College of Pharmacy and Regenstrief Institute; Eleanor Peretto, PhD MS, Pfizer, Inc.; Eugene C. Rich, MD FACP, Association of American Medical Colleges; Nancy C. Santanello, MD MS, Merck Research Laboratories; Karen Smith, MD PhD, MBA AstraZeneca; Scott R. Smith, PhD, Agency for Healthcare Research and Quality; Brian L. Strom, MD, University of Pennsylvania; Til Stürmer, MD, MPH, UNC Gillings School of Global Public Health; Dong-Churl Suh, MBA PhD, Rutgers University School of Pharmacy.

Moderator: Clifford Goodman, PhD, The Lewin Group.

Attendees: Eileen M. Cannon, PhRMA Foundation; Emily S. Reese, MPH, University of Maryland School of Pharmacy; Robert Beardsley, MS PhD, University of Maryland School of Pharmacy.

CONFLICT OF INTEREST

Most of the panel members received travel remuneration and an honorarium for their participation in the project. The representatives from industry and government were not reimbursed for their travel expenses and they did not receive an honorarium. The PhRMA Foundation played no role in the preparation of the final results or manuscript.

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