Pharmacoeconomics: Identifying the Issues Overview and Advisory Panel Report Summary

Jean Paul Gagnon, PhD,1 Conference Chair
Marilyn Dix Smith, PhD,2 Principal Investigator and Reports Editor
Donna Rindress, PhD,3 Report Director
Co-chairs: Margaret Healey, PhD,4 Patricia Deverka, MD, MS,5 Joel Hay, PhD,6 Joseph Jackson, PhD,7 Renee Goldberg Arnold, PharmD,8 James G. Kotsanos, MD, MS,9 Katie Copley-Merriman, MS, MBA,10 Gordon Vanscoy, PharmD, MBA,11 Jon Clouse, RPh, MS,12 Rod Barnes, MBA,13 Alan Heaton, PharmD,14 Alan Bakst, RPh, MS, PharmD,15 Elaine Power, MPP16

1Hoechst Marion Roussel, Inc., Kansas City, MO, 2International Society for Pharmacoeconomics and Outcomes Research, Princeton, NJ, 3BioMedCom Consultants inc., Montréal, Canada, 4The Institute for Research & Education, HealthSystems Minnesota, Minneapolis, MN, 5Merck Medco Managed Care, LLC, Montvale, NJ, 6University of Southern California, Los Angeles, CA, 7Bristol-Myers Squibb, Princeton, NJ, 8Pharmacon International, New York, NY, 9Eli Lilly and Company, Indianapolis, IN, 10Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 11Stadtlander Drug Company, Inc. and University of Pittsburgh, Pittsburgh, PA, 12Ingenix, Eden Prairie, MN, 13Alcon Laboratories, Inc., Fort Worth, TX, 14Prime Therapeutics, Eagan, MN, 15SmithKline Beecham, Collegeville, PA, 16Agency for Health Care Policy and Research, Rockville, MD

Healthcare administrators, policy-makers, and practitioners must balance the needs and desires of individual patients with those of society at large, recognizing that not all needs and desires can be met. Information comparing the expected gains of a medical intervention against the expected costs of that intervention versus other healthcare interventions is often difficult to interpret or compare.

The mission of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) is to translate pharmacoeconomics and outcomes research into practice to ensure that society allocates scarce healthcare resources wisely, fairly, and efficiently. Toward this mission, ISPOR, supported by grants from the US Department of Health and Human Services, Agency for Healthcare Policy and Research (grant number R13 HS09806), and the Health Outcomes Work Group of the Pharmaceutical Research Manufacturer’s Association, convened an Advisory Panel Meeting and Conference on Pharmacoeconomic Issues in February 1998. This conference provided a forum for researchers and practitioners to communicate needs and concerns as consensus is being developed on methodology, interpretation, and use of pharmacoeconomic information.

The objective of this interdisciplinary conference was to identify the issues in conducting pharmacoeconomic studies, interpreting the results of these studies, and using pharmacoeconomic information in healthcare decisions. The specific goals of the conference were to:

- identify key contentious methodology issues in conducting healthcare economic evaluations with clinical studies;
- identify key contentious methodology issues in conducting healthcare economic evaluations using modeling studies;
- identify key contentious methodology issues in conducting healthcare economic evaluations using databases;
- determine the education and skills needed for conducting and/or using pharmacoeconomic evaluations in healthcare decisions;
- identify the issues in application of economic evaluations in healthcare intervention protocol development, formulary decisions, and practice guideline development and use;
- identify the issues in addressing bias, credibility, and quality of pharmacoeconomic evaluations;
- identify the issues in communicating and reporting healthcare economic evaluation information.

During this conference, 61 pharmacoeconomics and outcomes researchers, clinical practitioners, and healthcare decision-makers in the United States met to develop consensus on issues relating to pharmacoeconomic and outcomes research evaluations and the use of these evaluations in healthcare deci-
sions. The seven advisory panels, in closed individual panel sessions followed by open sessions including all advisory panelists, discussed and debated the issues.

The specific objectives of each advisory panel and a report of each panel’s deliberations follow. Each of the seven advisory panel papers that follow summarizes the scientific and historical context for the issues discussed, the numerous points of view expressed, and the recommendations of each advisory panel for future directions of research and policy in the field of pharmacoeconomics. These papers are working documents presented as a basis for standardization of the science of outcomes research and healthcare economics, the development of generally accepted pharmacoeconomic policies, and an agenda for future research activities. A summary of the results of the advisory panel deliberations follows.

Panel 1: Methodological Issues in Pharmacoeconomic Evaluations—Clinical Studies

Pharmacoeconomic methods used to assess cost alone or other measures of value often fall short of regulatory standards. Conversely, study methods used to demonstrate drug efficacy, such as randomized clinical studies, are insufficient for addressing the question of value in applied settings. To overcome the limitations of using clinical studies data for health economic evaluations, researchers, decision-makers, policy-makers, and consumers should be well versed in the appropriate use of clinical studies.

The four key issues identified are:

1. Under what circumstances should randomized controlled trials (RCTs) be the primary approach for assessing questions of value?
2. How can RCTs be modified to improve their usefulness to inform economic decision-making?
3. Under what circumstances can observational studies be used to assess questions of value?
4. How can observational studies be modified to improve their usefulness to inform economic decision-making?

The panel’s recommendations are:

• Develop new methods to account for protocol-related costs (particularly in studies where these costs cannot be equated across study groups).
• Develop consensus on the definition of usual care. With the recommendation that trials should adopt more naturalistic designs, it is anticipated that the use of “usual care” as a comparator will continue to increase.

• Explore methods to supplement intent-to-treat analyses in usual care trials to address research questions important to decision-makers that may require alternate or additional analysis.
• Address problems of pooling economic data from multiple study sites. This problem is exacerbated in international studies where data are collected across countries.
• Improve statistical methods for adjusting for selection bias, which is a major drawback of observational studies.
• Use better methods for estimating variance around resource utilization and cost.
• Conduct systematic comparisons of RCTs and observational studies of the same interventions.
• Explore approaches from other disciplines (e.g., psychology, sociology, marketing research) to enhance current methods, particularly in the areas of data collection, instrumentation, and analytic techniques.
• Measure resource utilization in large simple trials. Resources currently dedicated to marketing studies could be reallocated for the identification and collection of relevant economic data.
• Create better methods of measuring direct medical costs that are not routinely captured (e.g., nursing time, telephone care).
• Create better methods of measuring relevant indirect costs (e.g., caregiver, lost productivity). There needs to be a greater appreciation of these cost drivers, and simple, easy methods to measure and document them.
• Encourage inclusion of standardized outcome measures in the evolving electronic medical record.

Panel 2: Methodological Issues in Conducting Pharmacoeconomic Evaluations—Modeling Studies

The primary purpose of modeling is to inform the decision-making process. One considerable benefit of model formalization is that the uncertainties and assumptions in this process are made explicit and transparent. Currently two major obstacles confronting modeling methodology are: (1) How do we optimize the production of useful information for health economic decision-makers? (2) How do we encourage its acceptance and use?

Seven key areas of controversy in modeling methodology are:
1. standardization;
2. making choices;
3. methodological development;
4. extending clinical studies and data issues;
5. effectiveness measures;
6. model validation;
7. peer review.

The panel’s recommendations are:

• Work towards general acceptance that modeling of both costs and effectiveness is a valid and often essential method to inform healthcare decision-making.
• Assemble a consensus of opinion on standardized practices and policies.
• Prepare and disseminate a reference text of these practices once standardization has been achieved.
• Permit pharmacoeconomic claims based on these generally accepted modeling approaches by regulatory agencies; always be transparent and include appropriate disclaimers.
• Initiate and assemble a balanced international panel of thought-leaders and end-users in the field of modeling to develop a package of generally accepted modeling practices.
• Encourage all stakeholders (professional societies, manufacturing associations, journals, government agencies, regulatory agencies, payers, and healthcare providers) to accept these standards and to endorse their use once these practices have been documented.

Panel 3: Methodological Issues in Conducting Pharmacoeconomic Evaluations—Retrospective and Claims Database Studies

Healthcare decision-makers require rapid access to information. Often the evidence to assist decision-makers in drawing conclusions has not been available. Both RCTs and retrospective methods using existing databases provide such information, and they typically answer different questions. Most RCTs are designed to measure efficacy, not effectiveness. “Real-world” data can be provided by database studies.

Eight key issues are identified:

1. What research questions can be answered by retrospective analyses?
2. What data sources are available to answer these questions?
3. How is cost-effectiveness measured using automated databases?
4. How can data quality within a database be evaluated?
5. What types of statistical methods can be utilized to control for treatment effects?
6. What potential types of bias exist in retrospective database analyses?
7. What alternative methods for assessing selection bias are available?
8. How can transparency be ensured in retrospective database analyses?

The panel’s recommendations are:

• Begin retrospective database analysis studies with a clear question and design, based on guidelines for good epidemiological practices.
• Ensure privacy of individuals at all times in retrospective database analyses.
• Use techniques that exist to address shortcomings of retrospective data sets.
• Subject multivariate models to extensive specification testing.
• Examine age- or gender-adjusted utilization rates and annual per capita expense by payer, health plan, geographic region, and country.
• Augment administrative databases, frequently used for retrospective pharmacoeconomic studies, to include more clinical information.
• Establish standard measures to deal with all areas of potential bias.

Panel 4: Education and Skills Needed to Conduct, Interpret, and Use Economic Evaluations in Healthcare

Like other disciplines, to expand and grow as a mature area of research and application, the field of health economics requires experts and skilled professionals. Unlike many other scientific fields, there is no single background or training to prepare the researcher or the user of health economic information, who currently come from a diversity of educational and experiential backgrounds.

The key issues related to education and skills in the field of health economics are as follows:

1. The structuring of multidisciplinary programs needs to be defined for people coming from a variety of backgrounds.
2. Training must include “real-world” applications.
3. It is unlikely that an “ideal program” can be created within one institution or group without collaboration with others.
4. The usefulness of defined “minimal competencies” in the field has to be determined. Minimal competencies will differ for current and future practitioners, and by depth of involvement.

5. Questions need to be answered pertaining to who should be trained, how training should be performed, and what level of training is required.

6. The necessity for “credentialing” needs to be assessed.

7. There is a need to improve the way information concerning training opportunities is disseminated.

The panel’s recommendations are:

• Develop three levels of expertise: awareness, application, and conceptualization.

• Develop access to detailed information about available educational programs in the field of health economics.

• Utilize relevant educational resources outside of health economics to enhance the educational infrastructure.

• Accommodate multidisciplinary participants through the availability of prerequisite trainings and flexible core course offerings for degree programs.

• Balance didactic and experiential education.

• Develop a credentialing process to establish standards for the field.

• Standardize training and certification through a three-step process: (1) develop guidelines for postprofessional degree training; (2) accredit pharmacoeconomic residencies and fellowships; and (3) establish collaborations with other organizations to expand accreditation to other relevant residencies.

Panel 5: Application of Healthcare Intervention Economic Evaluations in Healthcare Decision-Making

Information about the impact of new therapies on costs within a healthcare system should be essential for making better healthcare decisions. However, the relevance of health economic information to decision-makers has not been demonstrated. There is little user-friendliness in health economic data. There is a lack of consistency of approach and format that would facilitate comparison, and much of the information presented lacks the transparency necessary for the user to determine the appropriateness of methods or the soundness of assumptions. A fundamental disconnect exists between (1) the way decisions are made by healthcare decision-makers, (2) the type of information presented to healthcare decision-makers, and (3) the type of information produced by health economic and outcomes researchers.

There are 11 key issues:

1. Evaluative criteria are often weighed differently by potential users of health economic research data for decision-making purposes, such as formulary committees, providers, health plan managers, patients, and employers.

2. Language and definitional barriers hinder effective communication between potential users and producers of the information.

3. There is little of the direct treatment comparison done that would be of greatest interest to users.

4. Insufficient dialogue exists between potential users and producers of information on relevance and availability of information generated by health economic research.

5. Potential users of health economic research data may be hesitant to include health economic information in their decision-making process because it is unfamiliar.

6. There may be conflict between studies designed to provide health economic and outcomes information that meets user’s needs and those of clinical design, causing regulatory and liability concerns.

7. Some sources of research funding may present a barrier to the credibility and application of study results.

8. A conflict may exist between recommendations based on population data and the care of individual patients.

9. When health economic research data are used in the decision-making process, there is no recognized approach for measuring the quality of the decision or the net result.

10. There are few skilled opinion leaders or other resources from which potential users can seek advice and assistance.

11. Decision-maker organizations segregate budgetary decisions for pharmaceuticals from those related to other medical technologies and services.

The panel’s recommendations are:

• A central organization should coordinate the development of application of healthcare intervention economic evaluations in healthcare decision-making.

• Create focus groups to provide a forum for dialogue between potential users, producers, and
Pharmacoeconomics: Identifying the Issues

regulators of information. Researchers and suppliers of health economic data must actively engage with decision-makers to determine key health economic evaluation criteria for decision-making purposes and to formulate ways to supply information consistently.

- Determine a set of variables that researchers can supply. Decisions are seldom made using a single variable.
- Develop a set of simple criteria for evaluation of these studies. They should be agreed upon by consensus of all parties involved and designed to recognize different types of perspectives and research design so that specified research questions and business needs are met.
- Seek to bolster the objectivity, reliability, and credibility of the health economic studies through various mechanisms, including working with sponsors, researchers, and journal editors, to adopt protocols that will establish the independence of research and statements for the disclosure of funding sources.
- Offer training for decision-makers in using health economic research information. A consortium of managed care and other purchasing organizations, academic researchers, and one or more health economic research organizations should be formed to execute this recommendation.
- Develop a standard reporting format to allow flexible weighting of factors based on individual decision-making preferences. The presentation of the results of health economic analyses should show the various components of effectiveness measures, service utilization measures, and costs.
- Form a committee to produce a standard format for Data Element Shells (DES). ISPOR, in collaboration with potential users and producers of information, could be responsible for creation and updating of a DES form. The ISPOR committee would decide on the level of specificity of the DES, perhaps either a general format for all drugs or a specific format for individual drug classes.
- Support an information clearinghouse of available thought-leaders and experts in the field. This could include development and maintenance of an Internet Web site with links to expert's homepages and email addresses. ISPOR as an organization brings together many of the researchers qualified to evaluate health economic research and interpret findings.
- Develop rosters of persons qualified to review studies, similar to editorial boards for journals, where the reviewers would agree to participate in reviewing documents or addressing queries to promote a better understanding of the field of healthcare economics.

Panel 6: Addressing Questions of Bias, Credibility, and Quality in Health Economic Evaluations

Multiple published studies have criticized the rigor, relevance, objectivity, methods, and reports produced within the health economic research domain. Consequently, health economic research findings are not used as extensively as they could be, and rational decision processes about the efficient use of healthcare resources may not be fully informed. Ultimately, care for patients and populations may be adversely affected. In this context, there is a need for continued improvement in the quality of economic research conducted.

There are three key issues:

1. Quality: Are the best methods being used?
2. Bias: Whether it is real or perceived, how do we deal with it?
3. Credibility: Do we have a problem with believability or with relevance?

The panel’s recommendations are:

- Design and conduct studies using the best available practices consistent with the study objectives.
- Disclose all financial relationships.
- Authorship should conform to generally recognized practices among the peer research community.
- Research data should be transparent, including full disclosure and sufficient information to allow replication. Given this, it should be judged solely on the merits of its content.
- Develop a code of ethics for health economic researchers.
- Develop study methodology practice standards.
- Convene a conference similar to this conference in 2 years to evaluate progress and recommend next steps.

Panel 7: Communication and Reporting Health Economic Information

Users of health economic information represent many different perspectives with various levels of expertise and information needs. To obtain most
value from the resources invested in health economic research, how do we optimize the effectiveness of communication of health economic information?

There are three key issues:

1. Relevance: Is it needed?
2. Usefulness: Will the intended audience be able to make use of it?
3. Credibility: Is it believable?

The panel’s recommendations are:

- Identify the needs of users of health economic information. A survey of all users of health economic information will provide a basis for standardization of communications.
- Establish standard communication formats based on predetermined relevance, information, and credibility needs of users and on standard health economic performance standards that should be under development elsewhere. These should eventually include uniform presentation, standard terminology, and adequate disclosure, and should have a basis in previously published guidelines.
- Adopt reporting guidances (RGs) and apply these to all publicly presented communications, as standardized formats are established.
- Evaluate the use of RGs and the quality of reporting on a biannual basis.
- Establish a principle of publicly accessible reports that adhere to ISPOR RGs. This would allow access to research reports not directly controlled by the researcher or the research organization. Once a report has been “filed” for public accessibility, all subsequent communications could refer to that report.
- Institute an enhanced mode of peer review for all forms of health economic communications. This type of review would assure that there was compliance with ISPOR RGs, as well as fair, full, and adequate disclosure, allow for review of the underlying data and any model used, and confirm that all other ISPOR standards for the conduct of health economic studies have been met.

Expected Outcomes of the Conference

The expected products of this conference are:

1. Publication: These papers are to be published in *Value in Health*, the Journal of the International Society for Pharmacoeconomics and Outcomes Research.
2. Follow-up activities: Conferences are planned based on the recommendations given in this report.
3. ISPOR policy statements: Specific policies of the International Society for Pharmacoeconomics and Outcomes Research will be developed from these recommendations. ISPOR, in cooperation with other scientific, practitioner, and institutional organizations, will work to implement these policies. These organizations include the Health Outcomes Work Group of the Pharmaceutical Research Manufacturers of America and the Pharmaceutical Research Standards Committee of the American Managed Care Pharmacy Association.
4. Agenda for future research activities. The recommendations included in these reports are proposed as the agenda for future research activities by the Agency for Health Care Policy and Research.

In addition to the advisory panel co-chairs and panelists, the following pharmacoeconomic researchers participated in the meeting: Daniel Mullins, PhD, University of Maryland, Baltimore, MD, Tom Einarson, PhD, University of Toronto, Canada, William McGhan, PharmD, PhD, University of the Sciences in Philadelphia, Philadelphia, PA, James Smeding, RPh, MBA, University of Texas, Austin, TX, Hugh Tilson, MD, DrPH, Glaxo Welcome, Research Triangle Park, NC, and Yen-Pin Chiang, PhD (observer), Agency for Health Care Policy and Research, Rockville, MD.

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The views expressed herein are those of the panelists and do not necessarily represent the position of the organizations for which they work.