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

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The goal of this panel was to identify key issues with regard to addressing bias, credibility, and the quality of pharmacoeconomic evaluations. Its specific objectives were to:

- identify and prioritize the key issues associated with reducing bias and increasing credibility and quality of pharmacoeconomic evaluations;
- identify a plan of action to resolve these issues;
- recommend next steps.

Background and Context

Bias, quality, and credibility are long-term research issues addressed by experts in many fields. Like other disciplines, the field of health economics continues to evolve and challenge itself in this regard. Improvements in this field of research necessitate support and adhesion to the highest quality work and integrity, promotion of continuous quality enhancement, and open dialogue.

Definition of bias in the field of health economic research refers to a meaning beyond the Stanley and Campbell [1,2] statistical concept (i.e., as a threat to validity). Bias is also an ethical issue dealing with disclosure and conflict of interest. The following definition of bias was proposed by the Task Force on Principles for Economic Analysis of Healthcare Technology in 1995 [3]: “A range of factors that systematically influence the measures undertaken independent of the studied intervention; a tendency, intentional or unintentional, to inappropriately or unfairly favor one or more of the interventions being evaluated.”

Resolution of bias, quality, and credibility issues in health economics is complicated by a host of factors, especially the variety of stakeholders and their unique perspectives and information needs. These stakeholders include users of research (managed care organizations, governments, payers, and providers) and the producers of research (government agencies, pharmaceutical firms, payers and providers, academics, consultants, and foundations).

The objectives of this panel were to address the issues of bias, quality, and credibility of health economic research from the perspective of both producers and users of these data, with patient care as the underlying concern. The scope of the panel’s deliberation included public dissemination of research data, methods to improve quality, minimize bias, and thus enhance credibility of health economic studies. Methodology issues are elsewhere. The panel anticipates that as advances are made over time, concerns over bias, quality, and credibility of health economic research will diminish.

Problem Statement

Multiple published studies have criticized the rigor, relevance, objectivity, methods, and reports produced within the health economic research domain [4–12]. 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.

Issues

The panel identified the following 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?

Quality
Health economics is a relatively new science without strong consensus on all methods. There is a need to develop consensus on methodology for quality issues to be resolved. The multidisciplinary nature of this field of research makes peer identification for manuscript review difficult. In addition, there is a lack of consensus on evaluation criteria, rendering the peer review process difficult.

Bias
Bias can be divided into “intentional” bias and “unintentional” or “subtle” bias, which includes design flaws and inappropriate conclusions irrespective of the medical interventions under study. Bias can be related to the underpowered nature of many clinical and database studies, which would require much larger samples. There is a perception that financial sponsorship will bias study results. However, despite objectivity problems, industry is still the major funding body for healthcare economic information. Withholding negative findings and failure to submit data to public scrutiny can bias the literature and applications of research data that are disseminated. There are few occasions when circumstances would make the withholding of results acceptable [13].

Credibility
The relevance of health economic research data is questioned by decision-makers with respect to populations studied and the disconnect between decision-maker’s criteria (business decisions under risk or uncertainty where majority rules) and methodologist’s concerns (scientific standards seeking statistical significance). Stakeholders have different objectives. Methods are geared to societal decision-making, but practical applications are at a different level. In addition, decisions have to be made right away and cannot wait for the development of better methods. Some groups and journals such as the New England Journal of Medicine [14] have questioned the credibility of health economic analyses and restricted the dissemination of data. The ownership of health economic data must be defined, as well as access to this information. Health economic tools are expected to be employed to optimize use of the resources of society, but few decision-makers use them that way.

Recommendations and Next Steps
The following recommendations will improve the quality and credibility of health economic research. These recommendations pertain to these domains:

- design and research practices;
- sponsorship;
- publication and dissemination;
- role of professional societies and organizations;
- development of study methods and ethics standards;
- follow-up conference.

Design and Research Practices
Researchers should design and conduct studies using the best available practices consistent with the study objectives. Methods should be specified in advance and should be reported explicitly and transparently. Health economic studies should generally follow ethical Good Clinical Practices provisions such as those described by the American Federation of Clinical Research (AFCR, Good Clinical Practices) or other authoritative bodies. Prospectively designed pilot studies are essential for the evaluation of feasibility and the planning of future research. In addition, studies should not be terminated early in an attempt to hide unwanted health economic results of potential interest. Base case assumptions should be clear, and the sensitivity analyses should include conservative assumptions for the new technology being assessed.

Sponsorship
Full disclosure of any financial relationships that authors and speakers have linking them directly or indirectly to the interventions under study should be listed. Sponsored research should have a written protocol agreed to by researchers and sponsors in advance. Unanticipated issues should be handled by mutually agreed protocol amendments. Access to relevant documents and data, project control, presentation, and publication rights should be defined in advance in the contract [15]. The contract would reflect the code of ethics recommended by this panel.

Publication and Dissemination
Authorship should conform to generally recognized practices among the peer research community. Research data, given full disclosure, transparency, and sufficient information to replicate the study, should be judged on the merits of its
content. One or more authors should be receptive to and available for reader inquiries in those cases where it is clearly not practical or possible to provide all information necessary for replication of the study within a manuscript. Publication decisions by journals should use the same criteria for evaluating merit of health economic studies that are used for other types of manuscripts, and should not preclude publication of health economic work due solely to funding arrangements or author affiliations. Published reports should address the criteria established by experts and be completely transparent to facilitate evaluation, comparison, or reproduction.

Mandating full publication rights in a code of ethics for health economic research remains an area of debate among panel members. Certain members believe that this issue is at the heart of bias and credibility problems, and they advocate full publication rights for contractors performing health economic research. Other panel members anticipate that mandatory rights in certain health economic studies could be problematic. Organizations, industries, or government bodies using contractors to perform studies are not likely to allow full publication rights for their services.

**Role of Professional Societies and Organizations**

A professional society such as the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), the Association for Health Services Research (AHSR), or the Society for Medical Decision-Making (SMDM) should consider developing a code of ethics for health economic researchers. Those professional societies need to collaborate on education and best practices for the benefit of association members, the journal community, and research users, and to improve quality, reduce bias, and enhance credibility of health economic research. Professional societies should also help journal editors identify peer reviewers and advise on their review procedures. A foundation to address these ideas may be in order. ISPOR and similar bodies should also publicize awards for high-quality research, including student or fellowship awards.

The concept of an independent body that would provide confidential advice and would certify voluntarily submitted health economic study designs and reports deserves further discussion. This body could be a quasi-public organization that discloses all its financial relationships. Importantly, a similar body might also investigate means of evaluating health economic research for continuous quality improvement and development of the field.

**Development of Study Methods and Ethics Standards**

In the near future, clear best methodological and ethical practice statements should be developed and disseminated. Meetings with journal editors and users should be organized to educate and offer assistance to stakeholders. Specific recommendations are:

- Researchers should design and conduct studies using the best practices consistent with the study objectives. Methods should be specified in advance, explicitly and transparently reported.
- Health economic studies should generally follow the ethical Good Clinical Practices provisions described by authoritative organizations such as the American Federation of Clinical Research.
- Authorship should conform to generally recognized practices among the peer research community.
- Full disclosure of financial relationships of authors and speakers should be listed.

**Follow-Up Conference**

A conference similar to this one should be convened in 2 years to review progress made as a result of these deliberations. ISPOR should work with other societies and organizations to further explore all the other recommendations made by the panel that require additional thought.

In addition to the above recommendations, ISPOR should develop the following activities:

- Establish a code of ethics addressing among other issues the use of appropriate methodology, reproducibility, publication rights, and disclosure of potential conflicts of interest. Internal distribution and acceptance should be sought in the coming year, with subsequent external promotion.
- Create an office to continue work on the issues raised by the panel, to coordinate collaborative efforts with other organizations, to provide regular commentary and input, and to facilitate the exchange of ideas in the ISPOR journal, *Value in Health*.
- Disseminate and increase exposure of information related to awards obtained for high-quality research including annual meeting presentations, journal articles, and student fellowships.
• Establish a working relationship and coordinate regular meetings with the Food and Drug Administration (FDA) to develop health economic guidelines to address concerns related to bias, quality, credibility, and ethics.

Summary
Criticism of health economic research has resulted in limited utilization of this data by decision-makers and end-users, potentially affecting care for populations. A number of recommendations were proposed by the panel to address the issues of bias, quality, and credibility of health economic research from the perspective of both producers and users of these data with patient care as the underlying concern. Suggestions include design and research practice, sponsorship, publication and dissemination of research data, and the role of professional associations and organizations.

References