International Journal of Technology Assessment in Health Care, **17:1** (2001), 1–5.

INTRODUCTION

Bayesian Approaches to Technology Assessment and Decision Making

Bryan R. Luce
Ya-Chen Tina Shih
MEDTAP International Inc.

Karl Claxton
University of York

Until the mid-1980s, most economic analyses of healthcare technologies were based on decision theory and used decision-analytic models. The goal was to synthesize all relevant clinical and economic evidence for the purpose of assisting decision makers to efficiently allocate society's scarce resources. This was true of virtually all the early cost-effectiveness evaluations sponsored and/or published by the U.S. Congressional Office of Technology Assessment (OTA) (15), Centers of Disease Control and Prevention (CDC), the National Cancer Institute, other elements of the U.S. Public Health Service, and of healthcare technology assessors in Europe and elsewhere around the world. Methodologists routinely espoused, or at minimum assumed, that these economic analyses were based on decision theory (8;24;25). Since decision theory is rooted in—in fact, an informal application of—Bayesian statistical theory, these analysts were conducting studies to assist healthcare decision making by appealing to a Bayesian rather than a classical, or frequentist, inference approach. But their efforts were not so labeled. Oddly, the statistical training of these decision analysts was invariably classical, not Bayesian. Many were not—and still are not—conversant with Bayesian statistical approaches.

Thus, it should not come as a surprise that, when the pharmaceutical industry began to generate empirical, experimentally-based economic data alongside the empirical, experimentally-based efficacy data, these analysts appealed to the only statistical training they knew: classical, frequentist statistics. But they immediately ran into difficulties. For instance, the clinical trials that generated the empirical data were always powered for clinical, not economic endpoints. Thus, using frequentist rules, statements of "no difference" were commonplace even when economic differences were observed but did not reach statistical significance and when accompanied by clinical differences that were expected to

Reviewers for this special section include Andrew H. Briggs (Oxford University, UK); Byron W. Brown, Jr. (Stanford University, USA); James Burgess (VA Medical Center, USA); Mike Chamber (MEDTAP International, UK); Dennis G. Fryback (University of Wisconsin–Madison, USA); Frank E. Harrell, Jr. (University of Virginia, USA); Cristian P. Herrera-Salas (University of Birmingham, UK); John Hornberger (Roche, USA); Harold Lehmann (Johns Hopkins University, USA); Anthony O'Hagan (University of Sheffield, UK); John W. Stevens (AstraZeneca, UK); Natasha K. Stout (University Wisconsin–Madison, USA); Robert L. Winkler (Duke University, USA); and Marc Zodet (MEDTAP International, USA).

lead to economic efficiencies. Perhaps more problematic was the fact that the vehicle that generated the data, the clinical trial, was a highly constrained, if not inappropriate, vehicle to demonstrate economic consequences directly. Often the protocol itself induced healthcare utilization, in effect distorting the very evidence the researcher was trying to gather experimentally. Furthermore, these analyses are limited to the empirical data from the study at hand, and conversely do not take into account the full complement of knowledge and beliefs surrounding the problem being addressed. All in all, the resulting evaluations have not been shown to be of a great deal of use to healthcare decision makers. But this may be changing.

There is a gathering movement in Western countries to more formally incorporate economic evaluation with clinical evidence-based decision making. Virtually all of these efforts presume, encourage, and sometimes even require modeling to accompany systematic reviews of clinical evidence (10). Such is true of the Canadian Coordinating Office of Technology Assessment (CCOHTA), the U.K. National Institute for Clinical Excellence (NICE), the Australian Pharmacy Benefits Advisory Committee (PBAC), the U.S. Blue Cross/Blue Shield Technology Evaluation Center (TEC), and U.S. managed care organizations that are adopting pharmacoeconomic guidelines. All the above efforts to formally synthesize knowledge for decision making are quintessentially Bayesian in nature. The question is the degree to which a more formal application of Bayesian statistics can and will be used and how.

The purpose of this special issue is to provide an overview of selected aspects of the Bayesian approach that are most useful in healthcare technology assessment. Nine articles are included in this issue to either present the theoretical framework of the Bayesian methods (part I) or their empirical applications (part II), providing a foundation to understanding the Bayesian approaches to technology assessment and decision making.

Applications of the Bayesian approach in healthcare technology assessment can be as straightforward as calculating a posterior distribution from Bayes formula or as sophisticated as finding optimal stopping rules for clinical trials (4;7) or reporting a cost-effectiveness acceptability curve (16). The introductory article by Dr. John Hornberger reviews the fundamental concepts of Bayesian reasoning and illustrates the Bayesian concept through a simplified example and a more complicated study estimating treatment effects on a population.

The field of healthcare technology assessment employs a variety of statistical tools to quantify clinical and economic evidence. Drs. Frank Harrell and Ya-Chen Tina Shih summarize the above statistical methods and demonstrate the advantages of the Bayesian approach in quantifying and reporting scientific evidence and in assisting decision making. As illustrated in this paper, one of the most attractive features of the Bayesian approach lies in its ability to report multiple endpoints such as cost-effectiveness ratios simultaneously.

Loss function is a useful tool to explicitly express the decision maker's objective. Optimal decision making is then achieved through either maximizing expected utility or minimizing expected loss. The paper by Drs. Mohan Bala and Josephine Mauskopf incorporates the conjoint analysis technique in the estimation of the Bayesian loss function, which is then used to guide decision making by choosing the "action" that minimizes the "loss." Through a simplified example, the authors introduce an innovative way to conduct cost-benefit analyses using a Bayesian approach.

Another important Bayesian concept is value of information analysis. A Bayesian decision theoretic approach utilizing the concept of "expected value of perfect information" is presented by Dr. Karl Claxton and his co-authors. Through a policy model of Alzheimer's disease, the authors demonstrate how to use the Bayesian value of information analysis to establish a technically efficient research design and to provide guidance to allocate research and development resources optimally.

In the concluding article for part I, Dr. Robert Winkler discusses the strength of the Bayesian methods and weakness of the frequentist methods, explores the obstacles of using the Bayesian approach in the current research environment from the philosophical and practical aspects, and recommends strategies to increase the popularity of this approach. Rather than seeking reconciliation, the author urges the Bayesian researchers to put extra efforts in communicating with end-users at all levels and make this approach more user-friendly.

A recent development in the methodologies of economic evaluation is the introduction of the net health benefits approach (21) and the concept of cost-effectiveness acceptability curve (23). In the empirical article by Dr. Andrew Briggs, an example of blood pressure control among hypertensive type II diabetic patients is used to discuss the common ground between Bayesian and frequentist approaches to stochastic cost-effectiveness analysis, to demonstrate the Bayesian applications to the net health benefits approach, and to explore the use and advantage of the cost-effectiveness acceptability curve. This article is an excellent source for readers who are interested in learning both the classical and Bayesian applications and interpretations of stochastic cost-effectiveness analysis.

Growing interests in the Bayesian approach among health researchers emerged upon the publication of a Bayesian article by Brophy and Joseph (3). A Bayesian interpretation challenging previous findings using the classical approach was presented in that paper, after reanalyzing data in the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) trial. Following the same effort, Dr. Dennis Fryback and his co-authors conducted a Bayesian cost-effectiveness analysis reexamining the GUSTO cardiovascular trial. This empirical paper provides a superb pedagogic example; it gives a comprehensive demonstration of the Bayesian cost-effectiveness analysis, from the formation and parameterization of treatment alternatives to the computation and interpretation of cost-effectiveness analysis results.

Several authors have pointed out that the advance in computing capability has greatly eased the analytical burden experienced earlier by researchers using or wishing to use the Bayesian techniques. The development of the Bayesian Inference Using Gibbs Sampling (BUGS) program, which is a Bayesian statistical software based on the Markov Chain Monte Carlo simulation technique, has made the Bayesian approach a lot more user-friendly for researchers interested in applying this approach. In their software tutorial, Dr. Fryback and his co-authors provide two teaching examples to demonstrate step by step how to structure and analyze health economic studies using WinBUGS (Windows-based Bayesian Inference Using Gibbs Sample). Readers who are interested in the Bayesian approach and want to familiarize themselves with the BUGS software will benefit greatly from this introductory tutorial.

As a final remark to this special issue, Dr. Steven Sheingold shares his thoughts on Bayesian methods from a Medicare perspective and provides strategic advice for Bayesian researchers to overcome the resistance toward this approach among policy and/or decision makers. An analogy between the current development of the Bayesian approach and the development of cost-effectiveness analysis in the past was drawn in his concluding remarks, suggesting that with proper communications and educational promotions, greater understanding and acceptance of the Bayesian approach can be expected in the future.

As demonstrated by articles included in this special issue, there are clear advantages of taking a Bayesian view of probability to make useful inferences about both the effectiveness and cost-effectiveness of healthcare technologies when decisions about adoption must be made. However, Bayesian analysis can provide a much more comprehensive and explicit framework when combined with decision theory. The possibilities of taking this next logical step from Bayesian inference to a formal Bayesian decision theoretic approach

to health technology assessment has been debated for some time (2;11). In point of fact, until very recently the Bayesian decision theoretic approach has often been rejected within the Bayesian biostatistics literature both on the grounds that specification of utilities is rather speculative and due to the difficulty of combining resource use with a range of health outcomes (1;19). However, even those that have rejected Bayesian decision theory in the past accept that, at least in principle, this approach is more coherent than using inferential rules where adoption decisions are based on conventional benchmark error probabilities (levels of significance) such as 5% or 2.5%.

Recently there have been a number of developments in both the health economics (4;5) and the biostatistics literature (7;9;22) that suggest that Bayesian decision theory is both practical and useful, and a body of applied work in this area is starting to develop. This more recent attention to the possibilities of using formal Bayesian decision theory can provide tools to address some important policy issues such as the appropriate regulation of healthcare technologies, setting priorities in research and development, and establishing the efficient design of clinical research.

For example, the recent debate about the implementation of section 114 (Health Care Economic Information) of the FDA Modernization Act has highlighted the issue of balancing the benefits of a regulatory agency demanding more information to substantiate a claim about the cost-effectiveness of a new technology and the costs of acquiring that information both in terms of resources and delayed adoption of cost-effective technologies. The general debate has been taken up in the biostatistics literature (18), and a number of examples of the use of Bayesian analysis in FDA submissions and a general interest in Bayesian methods by the FDA can be identified (20). Others have also suggested that Bayesian decision theory and value of information analysis provides a framework where the benefits and costs of acquiring information before a claim can be made can be valued explicitly (6). Bayesian decision theory may also provide the tools to address the incentive problems that arise when agencies attempt to balance the efficient flow of pharmacoeconomic information with the potential adverse incentives to research and development (14).

Similar issues are now faced in the United Kingdom by the NICE. Clearly, issues such as combining data from a variety of sources in an explicit, transparent way and providing probability statements directly relevant to a decision to adopt a technology are central to the task that NICE faces. Although the primary question facing NICE is whether a technology should be adopted by the NHS (which itself benefits from a Bayesian view of probability and rejection of inferential rules), it can also issue guidance on the need for further investigation and adoption conditional on further evidence (for example, recent guidance on primary hip replacement) (12) or the results of pilot studies (for example, recent guidance on liquid-based cytology) (13). Although the methodologic guidance adopted by NICE does not promote a Bayesian inference or a Bayesian decision theoretical approach, NICE does not necessarily discourage it. Indeed, the evaluation report for the appraisal of liquid-based cytology presented an implicitly Bayesian value of information analysis based on a decision theoretic model of cervical cancer screening (17).

Before the mid-1980s most economic evaluations were based on some form of decision analytic modeling but without formal Bayesian statistical analysis. Until recently almost all economic analyses of clinical trial data have been based on frequentist inference. The general move toward evidence-based decision making provides an opportunity not simply to substitute Bayesian inference for a frequentist analysis of clinical trial data but to adopt formal Bayesian decision theory. Indeed, we believe that as the policy decisions and trade-offs in health care are being posed more explicitly, approaches that offer both an explicit and rigorous framework as well as that address directly the decisions themselves will likely become more widely accepted.

REFERENCES

1. Armitage P. The search for optimality in clinical trials. *Int Stat Rev.* 1985;53:15-24.
2. Berry DA. Discussion of the paper by Spiegelhalter, Freedman and Parmar. *J R Stat Soc A*. 1994;157:399.
3. Brophy JM, Joseph L. Placing trials in context using Bayesian analysis. *JAMA*. 1995;273:871-875.
4. Claxton K, Posnett J. An economic approach to clinical trial design and research priority setting. *Health Econ.* 1996;5:513-524.
5. Claxton K. The irrelevance of inference: A decision making approach to the stochastic evaluation of health care technologies. *J Health Econ.* 1999;18:341-364.
6. Claxton K. Bayesian approaches to the value of information: Implications for the regulation of new pharmaceuticals. *Health Econ.* 1999;8:269-274.
7. Claxton K, Walker S, Lacey L. A utility based approach to decision making with multiple disease state process. *J R Stat Soc A.* 2000;163:211-225.
8. Eddy DM. *Screening for cancer: Theory, analysis, and design*. Englewood Cliffs, NJ: Prentice Hall; 1980.
9. Gittins J, Pezeshk H. How large should a clinical trial be? *J R Stat Soc D.* 2000;49:177-188.
10. Hutton J, Maynard A. A nice challenge for health economics [editorial]. *Health Econ.* 2000;9: 89-93.
11. Lindley DV. Discussion of the paper by Spiegelhalter, Freedman and Parmar. *J R Stat Soc A.* 1994;157:393.
12. National Institute for Clinical Excellence guidance: Prosthesis for primary hip replacement. Available at: www.nice.org.uk. 2000.
13. National Institute for Clinical Excellence guidance: Liquid–based cytology for cervical screening. Available at: www.nice.org.uk. 2000.
14. Neumann PJ, Claxton K, Weinstein MC. The FDA's regulation of health economic information: Issues and options for Section 114 of FDAMA. *Health Affairs*. 2000;19:129-137.
15. Office of Technology Assessment (OTA), U.S. Congress. *Review of selected federal vaccine and immunization policies based on case studies of penumonococcal vaccine*. Washington, DC: U.S. Government Printing Office; 1979.
16. O'Hagan A, Stevens JW, Montmartin J. Inference for the C/E acceptability curve and C/E ratio. *PharmacoEconomics*. 2000;17:339-349.
17. Payne N, Chilcott J, McGoogan E. Liquid based cytology for cervical cancer screening. Health Technology Assessment Report. Available at: www.nice.org.uk. January 2000.
18. Sen S. Consensus and controversy in pharmaceutical statistics (with discussion). *J R Stat Soc D*. 2000;49:135-176.
19. Spiegelhalter DJ, Freedman LS, Parmar MKB. Bayesian approaches to randomised trials. *J R Stat Soc A.* 1994;157:357-416.
20. Spiegelhalter DJ. Discussion of Sen S: Consensus and controversy in pharmaceutical statistics. *J R Stat Soc D.* 2000;49:157-159.
21. Stinnett AA, Jullahy J. Net health benefits: A new framework for the analysis of uncertainty in cost-effectiveness analysis. *Med Decis Making.* 1998;18(suppl):S65-80.
22. Tan SB, Smith AFM. Exploratory thoughts on clinical trials with utilities. *Stat Med*. 1998;17: 2771-2791.
23. van Hout BA, Al MJ, Gordon GS, Rutten FF. Costs, effects, and C/E-ratios alongside a clinical trial. *Health Econ.* 1994;3:309-319.
24. Warner KE, Luce BR. *Cost-benefit and cost-effectiveness analysis in health care: Principles, practice and potential*. University of Michigan: Health Administration Press; 1982.
25. Weinstein M, Stason W. Foundations of cost-effectiveness analysis for health and medical practices. *N Engl J Med.* 1977;296:716-721.