Cost-Effectiveness Analysis

Before any attempt to address the issues implied in the article by Mohan and Miles (*1*) in this issue of *The Journal of Nuclear Medicine*, a brief and deliberately simplistic review of methodologic basics may facilitate understanding by nonexpert readers of that article (*1*).

Cost-effectiveness analysis (CEA) is a method that selects among competing wants when resources are limited (*2*). First applied to health care in the mid-1960s, CEA can indeed serve as a tool for the optimization of resource allocation to programs competing for the same limited funds. More generally, CEA evaluates the relative costs and benefits of different medical technologies, procedures, or clinical strategies (*3*). Typically, a new clinical strategy that includes, for example, a particular imaging study is compared with the most widely used current practice alternative. CEA helps to determine whether the health benefits (also designated as effectiveness) of the new strategy (commonly measured in terms of life expectancy or survival rates, such as the number of life years saved) are worth the additional costs generated. CEA therefore deals with marginal or "incremental" costs and benefits; the incremental cost-effectiveness ratio is the ratio of marginal cost to marginal effectiveness, a commonly accepted way of measuring the comparison of 2 strategies or, in other terms, a way of evaluating the "price" of the additional outcome. The incremental cost-effectiveness ratio can be expressed as the cost (in euros, dollars, or pounds sterling) per life years saved by adoption of the new strategy.

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The reality is, of course, more complex, and 2 issues, among others, exemplify it. First, the measure of effectiveness can also be based on the quality of life which, however, is not always simple to estimate (*4*). Even more basic and no less significant, the very notion of cost-effectiveness implies a value judgment: How low should the "price" be, so that the new strategy can be considered cost-effective? Mohan and Miles (*1*) adopted a threshold cost of, at most, £30,000 (~$42,900) per life years saved. Above that threshold, a strategy would not be considered cost-effective (*1*). Strategies with lower cost-effectiveness ratios are thought to be more cost-effective than those with higher ratios (*3*).

CEA is considered to be the most appropriate method for the evaluation of health economics when at least 2 alternatives are being compared and when outcomes can be expressed in a common unit, such as cost per life years saved (*5*). Decision analysis must be applied when the health effects of a medical intervention are major, thereby requiring the use of decision trees, a situation that is often encountered (*3*). These trees represent logical sequences structuring a problem related to a clinical decision. Decision analysis is used when conditions of uncertainty exist in both economic and clinical issues and allows the uncertainties to be taken into account by integrating all available information. The data required for decision trees can be provided by randomized controlled clinical trials, observational studies, or meta-analyses combining the results of multiple scientific studies (*1*). Because clinical studies do not always include economic data or do not always monitor patients for a long enough time after a medical intervention, such data are often insufficient. They must be enriched through the use of modeling techniques that enable extension of the economic analysis beyond the observed, for example, by extrapolating clinical outcomes such as survival (*5*) or by using a combination of data from different sources. Decision tree models are based on the strategies compared (see Fig. 1 in the study of Mohan and Miles (*1*)). Software packages for use in decision tree analysis are available (*1,6*); some of them were developed at the Crump Institute, University of California at Los Angeles.

CEA generally proceeds by first determining the best estimates of the parameters of interest, such as the sensitivity and specificity of a test or the prevalence of a disease in a target patient group, for performing a baseline analysis. Next, decision tree sensitivity analyses are used to determine the uncertainties of the parameter estimates used in decision tree modeling; models are reanalyzed as certain key parameters, such as diagnostic accuracy, cost, or life expectancy, are varied across a range of values spanning the range of uncertainties (see Table 1 in the study of Mohan and Miles (*1*)). For ^{99m}Tc-methoxyisobutylisonitrile SPECT aimed at selecting patients with lung cancer for chemotherapy (*1*), the prevalence of responders and the sensitivity and specificity of the test were varied over 95% confidence intervals derived from the meta-analysis (see Table 2 in the study of Mohan and Miles (*1*)). These sensitivity analyses evaluated the robustness of the results for the ranges of the model variables in terms of incremental costs, benefits, and cost-effectiveness (see Table 2 in the study of

Received Nov. 25, 2008; revision accepted Dec. 2, 2008.
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DOI: 10.2967/jnumed.108.057489

Mohan and Miles (*1*)). A robust strategy would not be influenced by such variations in baseline study parameters. A worst-case scenario with the SPECT cost doubled was also considered (*1*) to further test robustness.

The information provided by CEAs in nuclear medicine can be used for many purposes. In particular, it can help nuclear medicine physicians understand the impact of a procedure on overall patient care and guide policy-making and purchasing decisions at the societal, hospital, or health system level. Last, but not least, CEAs can provide data, and not just opinions, to nuclear medicine physicians trying to convince third-party payers to make coverage decisions (*3*).

However, CEAs do have limitations, such as uncertainties in both economic and medical evaluations. Critical readers (*2*) of CEAs should also carefully consider the generalizability of efficacy data, such as the medical results of a certain surgical procedure performed in experienced centers versus broad implementation of the strategy by community providers. Another basic question concerns the validity of effectiveness data, which ideally should come from randomized controlled clinical trials; however, these trials, particularly in diagnostic technology evaluations, have some disadvantages, such as their high costs in money and time. The following question should also be answered (*2*): "Was the use of the resource modeled or measured in real practice?" Despite these apparent contradictions, the importance of proper prospective clinical trials should be stressed, in particular, for new imaging technology. A careful assessment of cost-effectiveness evaluations should be performed with clinical studies whenever possible (*1,7–9*).

More than 30 y have elapsed since Weinstein and Stason enthusiastically introduced CEA to clinicians in 1977 (*10*), stating that if CEA approaches were to become accepted, important health benefits or cost savings might be realized. Some 20 y later, Gambhir (*6*) wrote that CEA is still underutilized by nuclear medicine researchers. Lately, Gazelle et al. (*3*) wondered why CEA is not yet universally used to make decisions on health care spending in an era when the growth of health care costs is or will be constrained. The authors concluded that cost-effectiveness ratios ignore, among others, issues such as distributive justice and equity. CEA may also not be the most appropriate metric for comparing interventions affecting young versus old people or wealthy versus poor people. Indeed, because CEA addresses fundamental human values of life and death, its application affects issues of justice and equality, which are not easy to evaluate. Physicians rarely calculate the costs and eventual benefits of new medical interventions or strategies at the societal level because medical decisions are usually made for an individual patient. CEA would only be helpful for decision making in clinical practice (*11*).

Despite all of these discouraging considerations, it can be affirmed that CEA and decision analysis "efficiently narrow the bounds of uncertainty surrounding those variables or assumptions that have the greatest effect on the ultimate (clinical) decision" (*3*). They thus provide a transparency tool that facilitates communication between nuclear medicine physicians and providers. As judiciously noted by Mohan and Miles (*1*), CEA can also help to prioritize clinical trials because of their likely effect on evidence-based medicine.

Notwithstanding limitations stemming mainly from the human "material" involved, economic and medical researchers should pursue careful attempts to evaluate the costs, benefits, and cost-effectiveness of medical interventions—a must in modern medical challenges. Optimally performed CEA requires a multidisciplinary effort involving clinicians, mathematicians, and statisticians, and, as early as possible in the planning of clinical trials, an economist, who should ensure adherence to minimum standards for economic analysis research (*12*). This methodologic recommendation is a powerful and practical way of strengthening research efforts. It is particularly true and vital in nuclear medicine.

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ACKNOWLEDGMENT

The author wishes to thank Jean Karger and Isabelle Stroweis for their help.

REFERENCES

1. Mohan HK, Miles KA. Cost-effectiveness of ^{99m}Tc-sestamibi in predicting response to chemotherapy in patients with lung cancer: systematic review and meta-analysis. *J Nucl Med.* 2009;50:376–381.
2. Primer on cost-effectiveness analysis. *Eff Clin Pract.* 2000;3:253–255. Available at: http://www.acponline.org/clinical_information/journals_publications/ecp/sepoct00/primer.pdf. Accessed February 3, 2009.
3. Gazelle GS, McMahon PM, Siebert U, Beinfeld MT. Cost-effectiveness analysis in the assessment of diagnostic imaging technologies. *Radiology.* 2005;235:361–370.
4. Atherly A, Culler SD, Becker ER. The role of cost effectiveness analysis in health care evaluation. *Q J Nucl Med.* 2000;44:112–120.
5. Brockhuis B, Lass P, Popowski P, Scheffer J. An introduction to economic analysis in medicine: the basics of methodology and chosen terms. *Nucl Med Rev.* 2002;5:55–59.
6. Gambhir SS. Cost-effectiveness analysis in nuclear medicine. *J Nucl Med.* 1998;39:17N–18N.
7. Gambhir SS, Hoh CK, Phelps ME, Madar I, Maddahi J. Decision tree sensitivity analysis for cost-effectiveness of FDG-PET in the staging and management of non-small-cell lung carcinoma. *J Nucl Med.* 1996;37:1428–1436.
8. Dietlein M, Weber K, Gandjour A, et al. Cost-effectiveness of FDG-PET for the management of potentially operable non-small cell lung cancer: priority for a PET-based strategy after nodal-negative CT results. *Eur J Nucl Med.* 2000;27:1598–1609.
9. Hernández R, Vale L. The value of myocardial perfusion scintigraphy in the diagnosis and management of angina and myocardial infarction: a probabilistic economic analysis. *Med Decis Making.* 2007;27:772–788.
10. Weinstein MC, Stason WB. Foundations of cost-effectiveness analysis for health and medical practices. *N Engl J Med.* 1977;296:716–721.
11. Luce BR, Simpson K. Methods of cost-effectiveness analysis: areas of consensus and debate. *Clin Ther.* 1995;17:109–125.
12. CES (College des economistes de la sante). Guide methodologique pour l'evaluation economique des strategies de la sante. 2003;1–89. Available at: http://www.cocof.irisnet.be/site/common/filesmanager/sante/resauxsante/doc_guide_methodologique/. Accessed February 3, 2009.