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Theoretical Foundations of Medical Cost-Effectiveness Analysis

Implications for the Measurement of Benefits and Costs of Medical Interventions

David Meltzer

2.1 Introduction

Increasingly, both private and public health care institutions in the United States are looking toward medical cost-effectiveness analysis as they consider complex resource allocation decisions concerning medical technologies. Though many of its key ideas originated in the United States, medical cost-effectiveness analysis has, until recently, been more widely accepted and used in a number of European countries, as well as in Canada, Australia, and New Zealand. These countries share with the United States a significant concern about the role of new technology in increasing health care costs, but also have national health systems that are well positioned with strong incentives to engage in formal technology assessment. The recent increase in interest in medical cost-effectiveness analysis in the United States differs from the experience with cost-effectiveness analysis in other countries in that the private sector has played a much larger role in the United States. In particular, the demand for cost-effectiveness analyses in the United States appears to have been significantly influenced by the desire of pharmaceutical companies to collect evidence concerning the cost-effectiveness of their products in order to encourage managed care organizations to include their products on formularies. This is evident in both the recent establishment of the Association for Pharmaceutical Outcomes Research with the heavy involvement of the pharmaceutical industry and the tremendous increase in interest in pharmacoeconomics in the

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industry. This demand is also evident in the recent upsurge in interest in attempting to inform and even standardize methods for cost-effectiveness analysis in order to establish comparability among studies and minimize the chance for investigators with vested interests to use areas of methodological ambiguity to obtain desired results. This is most prominently evidenced by the report of the Panel on Cost-Effectiveness in Health and Medicine (Gold et al. 1996), but it is also shown by the work of Sloan (1995), the Task Force on Principles for Economic Analysis of Health Care Technology (1996), and others.

While attempting to enhance the comparability and validity of medical cost-effectiveness analyses, these recent efforts have also heightened the expectations for cost-effectiveness analyses and the scrutiny with which its methods are examined. This is perhaps particularly true of the report of the Panel on Cost-Effectiveness in Health and Medicine, which explicitly advocates that cost-effectiveness analyses adopt a “societal” perspective and asserts that the methods of cost-effectiveness analysis that adopt such a perspective have their roots in classical welfare economics.

This paper summarizes some recent and ongoing work in which I and others have been engaged that attempts to address the connection between the methods used in the most common form of medical cost-effectiveness analysis—that which utilizes quality-adjusted life years (QALYs)—and principles of welfare economics. While this paper is not intended to be a systematic review of this important topic, it aims to address two key issues concerning the connection between welfare economics and cost-effectiveness analysis: the measurement of benefits and the measurement of costs, especially future costs. In both of these cases, the application of basic principles of economic analysis provides unique insights into areas of ongoing controversy that are not apparent from other approaches. For example, by relying upon the economic principle of revealed preference, it is possible to learn about the validity of QALYs as a measure of patient preferences. Similarly, by defining a lifetime utility maximization model and deriving conditions for constrained maximization, formal models of utility maximization provide a framework for resolving methodological issues about the inclusion of costs in medical cost-effectiveness analysis. Though formal economic analysis could also be used to address other methodological issues in medical cost-effectiveness analysis, such as techniques for sensitivity analysis (Meltzer 1998) and challenges in incorporating distributional concerns into cost-effectiveness analyses (Wagstaff 1991), these will not be discussed in order to focus attention on the issues of the measurement of benefits and costs.

The paper proceeds as follows. Section 2.2 reviews the historical origins and development of cost-effectiveness analysis based on QALYs. Section 2.3 addresses the use of revealed preference measures to assess to what

extent QALYs reflect patient preferences. Section 2.4 addresses the inclusion of future costs. Section 2.5 concludes.

2.2 Historical Origins and Development of Cost-Effectiveness Analysis Using QALYs

Though medical cost-effectiveness analysis using QALYs appears to have originated with the work of Fanshel and Bush (1970), its growth seems to have begun with the work of Milton Weinstein and William Stason (1976) on the cost-effectiveness of the treatment of hypertension. Published both as a substantial and detailed book (Weinstein and Stason 1976) and in abbreviated form as an article in the *New England Journal of Medicine* (Stason and Weinstein 1977), their work first brought into prominence the idea that the benefits of medical intervention be quantified in terms of life years weighted by quality adjustment factors between zero and one, in which zero is equivalent to death, and one to perfect health. Unlike analyses of the costs of achieving some fixed objective (often called cost-minimization analysis), this approach aimed to permit comparison of the value of expending resources to achieve alternative health-related objectives. The QALY framework was thus designed to serve as a general one under which the costs and benefits of interventions aimed at vastly different diseases might be compared. In the context of an increasing acceptance within medicine of the idea that health care should attempt not only to minimize mortality but also to minimize morbidity, the concept of quality adjustment was key to the attraction to the concept of quality-adjusted life expectancy.

Weinstein and Stason in turn refer to earlier work by Weinstein and Zeckhauser (1972) as providing the link between cost-effectiveness and welfare maximization. In essence, the argument is that the condition implied by utility maximization (that marginal utility be proportional to marginal cost for all goods purchased) implies that the ratio of marginal cost to marginal utility should be a constant. Interventions for which the ratio of costs to benefits exceeds that constant should be avoided, whereas interventions for which that ratio is smaller should be adopted. Coming out of utility maximization, decisions guided by these cost-effectiveness or cost-utility ratios are intended to direct resources toward efficient allocations generated by utility maximization under classical conditions. Findings such as these motivate the connection of cost-effectiveness analyses performed from a societal perspective to the realization of efficient allocations based on criteria of welfare economics (Weinstein 1995; Gold et al. 1996).

The methods of cost-effectiveness analysis and to what extent, if any, they provide a valid approach to resource allocation have long been subject to debate. Some of this debate relates to dissatisfaction with utilitarian

models as a basis for resource allocation (e.g., La Puma and Lawlor 1990). A much larger portion of this literature, however, accepts these utilitarian underpinnings and asks whether the methods of cost-effectiveness analysis are up to the task of identifying utility-maximizing choices. While by no means intending to dismiss the concerns of this former group, the methodological critiques of cost-effectiveness described later in this chapter fall into the latter group. As such, they may be viewed by some people as trying to fix a fundamentally flawed approach. This may be a valid criticism, but the importance of the issues addressed by cost-effectiveness analysis, its influence, and the lack of strong competitors to replace it suggest the need to probe into these issues even in the presence of concerns about whether the approach could ever be fully adequate to its task.

2.3 Measurement of Benefits

The attractiveness of quality-adjusted life years stems from its claim to be able to act as a global measure of preference for health-related decisions, allowing comparison of interventions that may have effects on length of life or quality of life for any intervention, regardless of the disease to which it is applied. This is essential if comparisons are to be made across interventions affecting disparate diseases, as is required for resource allocation decisions in practice.

However, the key concern about QALYs is their validity as measures of patient preferences. It is not an obvious proposition that people will prefer whichever lifestyle option that, when weighted between zero and one, will result in the highest number of quality-adjusted life years. Issues of risk aversion and the distribution of QALYs in a population are clearly crucial issues in this regard. Beyond this, however, there are more basic questions about the validity of QALYs even in the context of certainty. Are people truly indifferent between living two years with a quality of life weight equal to 0.5 or one year with a quality of life weight equal to 1? When quality weights are derived from linear analog ("Please rate health state X between zero and one where zero is death and one is perfect health") or ratio scalings ("How much better/worse is health state X than health state Y?"), there is no reason to suspect that this restriction should hold. When quality weights are derived from either standard gamble or time trade-off methods, there is at least some theoretical structure that suggests that people who prefer the options described in the questions used to elicit quality of life weights should prefer options that maximize quality-adjusted life expectancy. For example, in the time trade-off method, people are asked whether they would prefer a longer life in less-than-perfect health or a shorter life in perfect health. Quality weights derived by this method could be consistent with utility maximization if utility is the product of quality factor Q

and time t and there is no discounting (i.e., $U = Q \times t$). In the standard gamble method, people are asked to choose between continuation of a less-than-perfect health state or a gamble in which they are returned to full health with probability p and die immediately with probability $(1 - p)$. If people maximize expected utility and there is no discounting, resource allocations based on quality of life estimates derived from this method may be consistent with utility maximization.

Under these conditions, the validity of QALYs as an outcome measure comes down to an empirical question concerning whether the assumptions required for the logical consistency of QALYs are an adequate reflection of people's preferences. The problem in determining this, however, has been the absence of a "gold standard" by which to measure people's actual preferences. In the absence of such a "gold standard," the most common approach in the psychometric literature has been to elicit quality of life weights using multiple methods such as linear analog, standard gamble, and time trade-off, and then determine to what extent these measures are correlated (e.g., Blumenschein and Johannesson 1998). Studies of this type have often (though not universally) found substantial correlation among these measures. Nevertheless, this may suggest more that these measures are quantifying the same or similar concepts than representing patients' actual preferences.

An alternative approach to assess the validity of QALYs, which I am using in some ongoing work, relies instead on the idea of revealed preference—that one can learn about people's preferences based on the choices they are observed to make. Though the term "revealed preference" is drawn from economics, the concept of revealed preference is indeed a—if not the—central tenet of the practice of medicine: that the best therapy for a patient is identified by informing the patient about her options and allowing her to choose. This naturally suggests an alternative approach to determine whether QALYs reflect patient preferences—to test whether the gain in QALYs from a medical intervention predicts whether patients choose that intervention.

We have been examining this question in the context of patient preferences for intensive therapy for type I diabetes mellitus (Meltzer, Polonsky, and Tobian 1998). From the Diabetes Control and Complications Trial (DCCT; DCCT Research Group 1993), it is now known that the frequent glucose checks and increased insulin dosing required under intensive therapy for diabetes can help prevent the early changes that may eventually result in the major complications of diabetes such as blindness, kidney failure, and neuropathy that can often result in amputation. On the other hand, the frequent glucose checks and insulin doses required for intensive therapy may be burdensome for many individuals and result in more frequent hypoglycemic symptoms. The decision to follow intensive therapy can be viewed as a trade-off involving quality and length of life now and

quality and length of life in the future; thus, the choice between intensive and conventional therapy is a natural application of QALYs. Indeed, the DCCT investigators developed and published a cost-effectiveness analysis of intensive therapy based on the DCCT data. This suggests that intensive therapy is highly cost-effective, with an average cost of \$19,987/QALY (DCCT Research Group 1996). It is perhaps revealing about the ability of QALYs to reflect patient preferences that, despite this finding, many patients who are aware of the DCCT results, and even many who bear no out-of-pocket expenses for their care, have not elected to pursue intensive therapy.

In our work, my colleagues and I have surveyed approximately 130 patients with diabetes on either intensive or conventional therapy who are similar to the population examined in the DCCT to ask them all the questions necessary to calculate their quality-adjusted life expectancy with and without intensive therapy. The predicted gain in quality-adjusted life expectancy from intensive therapy is then compared to their actual choice of therapy to see if those people with the greatest gain in QALYs from intensive therapy are in fact those who choose intensive therapy. Because factors other than patient preferences, such as cost and the preferences of physicians, may also affect choice, we have also collected information on these factors, although our initial analyses do not suggest any substantial role for these factors in the choice of therapy in our study population.

While we have not yet completed our calculation of the gain in QALYs resulting from intensive or conventional treatment for each patient, preliminary analyses using logistic regression demonstrate that the elements used to calculate QALYs do predict choice. Specifically, we find that patients are more likely to report themselves as having chosen intensive therapy when they report the beliefs that (1) quality of life would be relatively lower with complications of diabetes, (2) quality of life is little affected by the demands of intensive therapy, (3) intensive therapy will reduce the likelihood of complications, and (4) the future is more important than the present (a positive rate of time preference). Combining these elements in a logistic regression, it is possible to plot a receiver operating characteristic (ROC) curve (figure 2.1), which has what to many may seem a surprisingly high area under the curve (0.84). This seems to suggest that the gain in QALYs has a substantial ability to predict a patient's reported choice of therapy. For example, an appropriately chosen cutoff for this regression would correctly classify about 80 percent of patients as preferring intensive or conventional therapy. This may surprise many in the economics community who have tended to view QALYs as having little connection to the actual preferences of patients, and who strongly preferred willingness-to-pay approaches. The ability of the predicted gain in QALYs based on the decision model (as opposed to the rather less restrictive logistic regression

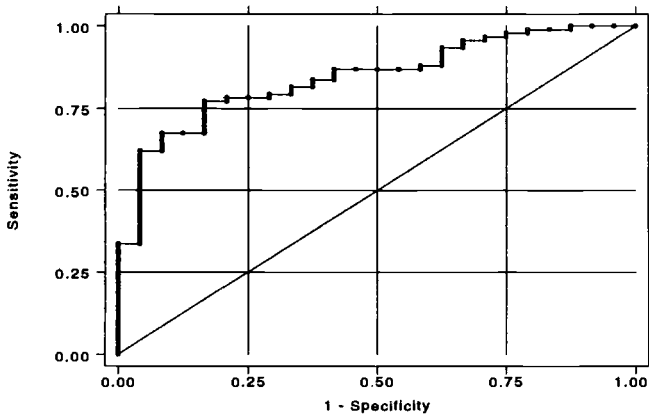


Fig. 2.1 ROC curve for logistic regression of QALY elements on reported therapy
Note: Area under ROC curve = 0.8442.

form) to predict choice may be somewhat less than this, but need not necessarily be.

Putting aside these issues of functional form, an important argument favoring the critics of the QALY approach is the possibility that any correspondence between choices and a gain in QALYs may reflect attempts of respondents to minimize cognitive dissonance. Cognitive dissonance is the idea that individuals experience an aversive state whenever their beliefs are inconsistent with their actions and may respond to minimize this discordance by changing either their actions or their beliefs (Festinger 1957). One piece of evidence supporting the potential importance of cognitive dissonance in determining how people respond to the questions used to calculate quality-adjusted life expectancy is a paper by Kruminis, Fihn, and Kent (1988) that reports a very strong correspondence between patients' predicted gains in quality-adjusted life expectancy from surgery for benign prostatic hypertrophy and the incidence of patients' selecting surgery. The irreversible nature of prostate surgery is probably particularly likely to generate responses designed to minimize cognitive dissonance. Intensive therapy may be somewhat less affected by cognitive dissonance than prostate surgery. The reversible nature of the decision to follow intensive therapy presumably places an upper bound on the degree of cognitive dissonance, because people for whom that dissonance was sufficiently large would presumably alter their decision. Nevertheless, we find in our study that about one-third of patients who report themselves as following intensive therapy are actually on conventional therapy according to the strict definition of the DCCT, suggesting that patients may hold a belief that intensive therapy is the right thing to do and therefore report following

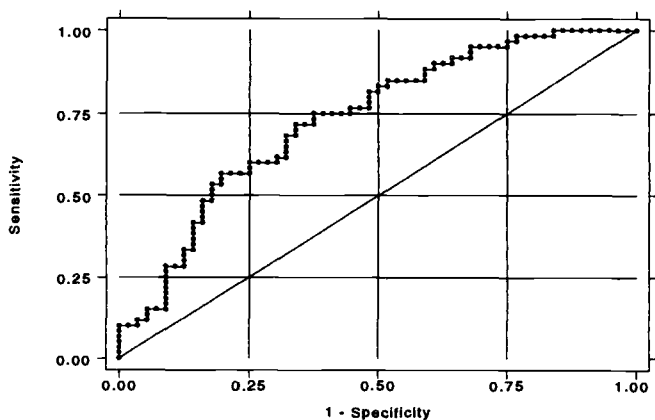


Fig. 2.2 ROC curve for logistic regression of QALY elements on actual therapy

Note: Area under ROC curve = 0.7318.

intensive therapy even when their therapy is not fully intensive. Interestingly, the area under the ROC curve for the regression of patients' answers to the QALY questions on actual choice of intensive therapy according to the DCCT definition is only 0.73 (fig. 2.2). This corresponds, for instance, to correctly classifying only two-thirds of patients as preferring intensive or conventional therapy. Thus the relationship between the psychometrically measured preferences used to calculate QALYs and stated therapeutic choices may be partially inflated by attempts to minimize cognitive dissonance. Validation of QALYs that would not be contaminated by cognitive dissonance would presumably require elicitation of preferences in a prospective setting before patients had even considered the choice they might face.

Given the diminution of the predictive power of QALYs for actual as opposed to reported therapeutic choice, it seems likely that a prospective analysis of the validity of QALYs that would presumably not be affected by attempts to minimize cognitive dissonance would suggest that QALYs are far less able to predict choice than is desirable. However, this has not yet been demonstrated, and even if it were shown to be the case, the revealed preference approach suggests that QALY measures might in time be improved by seeking methods to develop QALY measures that better predict choices. Thus, rigorous application of the principle of revealed preference offers the opportunity both to assess the validity of QALYs and potentially to improve their validity. Moreover, the principle of revealed preference could be used to compare the preference measures based on QALYs to the preference measure that most economists have favored: willingness to pay (Pauly 1995). If the prior beliefs of most economists are

correct, the willingness-to-pay measure should outperform QALYs in predicting choice. Though willingness to pay has been shown to predict choice in some cases (Brookshire, Coursey, and Schulze 1987), many results of willingness-to-pay studies are clearly incompatible with observed choices (e.g., Fisher, Chestnut, and Violette 1989). A healthy competition between willingness-to-pay measures and QALY measures of health outcomes to predict behavior is likely to advance the quality of both measures. In the meantime, prudent investigators must be cautious in interpreting the results of any cost-effectiveness study that depends on the accurate measurement of the value of improvements in outcomes using any unitary scale of outcomes, whether QALYs or willingness to pay.

2.4 Measurement of Future Costs

Formal economic models of utility maximization also provide a valuable framework for considering the measurement of costs in medical cost-effectiveness analysis. Though it is not controversial, justification for the insistence of cost-effectiveness analysts on the measurement of marginal as opposed to average costs, for instance, comes directly out of the marginal conditions for utility maximization. Similar reasoning about marginal changes in expenditures can be applied to address the question of when marginal adjustments in other medical expenditures that take place when a medical intervention is undertaken need to be considered in a cost-effectiveness analysis (Meltzer 1997).

Unlike the question of whether to calculate average or marginal cost-effectiveness ratios, the question of whether to include future costs for “unrelated” illnesses and future nonmedical costs has been highly controversial. Nevertheless, it is equally amenable to analysis in a utility maximization model. Indeed, it is likely that one reason that the controversy about future costs has persisted so long is that the question has been subject to little formal analysis. For instance, while analysts have consistently argued the need to include future costs for related illnesses, analysts have come to dramatically divergent conclusions about whether future unrelated and future nonmedical costs should be included. For example, early work in cost-effectiveness analysis by Weinstein (1980) supported the inclusion of future costs for unrelated illnesses, arguing that “the cost of treating disease that would not otherwise have arisen must be considered” (p. 240). Though a few studies, such as the Office of Technology Assessment evaluation of influenza vaccination (U.S. Congress 1981), did at least consider this approach, the vast majority of studies have not included future costs for unrelated illnesses. Typical in justifying this approach is the argument of Louise Russell (1986) in “Is Prevention Better Than Cure?” where she argues, “Added years of life involve added expenditures for food, clothes, and housing as well as medical care. None of these is relevant for deciding

whether the program is a good investment" (p. 36). Interestingly, Weinstein (1986) concurs about the exclusion of future nonmedical costs, but does so on the grounds that "the explicitly constrained resource is health care cost, and other costs are the price we all willingly pay to live" (p. 196). Thus there is a sense from the literature that it is reasonable to count certain costs while excluding others, though researchers disagree on which costs should fall into the two categories.

The persistence of the controversy concerning the measurement of future costs probably is related to the lack of formal analysis of the issue. However, two papers recently published in the *Journal of Health Economics*, one by Alan Garber and Charles Phelps (1997) and another by myself (Meltzer 1997), have applied formal economic analysis to this question. Unfortunately, the papers come to somewhat different conclusions. The Garber and Phelps paper concludes that under a rather restrictive set of assumptions, a set of rankings that excludes future costs will be the same as a set of rankings that includes future costs. My paper uses a more general model to show that, in the general case, a cost-effectiveness analysis should include all future costs, whether medical or nonmedical. Moreover, the set of restrictions under which the rankings would be preserved when future unrelated and nonmedical costs are excluded is shown to be far more restrictive than is recognized in the paper by Garber and Phelps. The restrictions turn out to make cost-effectiveness analyses that exclude future costs incompatible with important goals of cost-effectiveness analysis, such as comparing interventions at different ages and comparing interventions that have different effects on length of life and quality of life. Thus, the clear theoretical implication from a model of lifetime utility maximization is that cost-effectiveness analyses should include all future costs, whether medical or nonmedical. A corollary to this is that resource allocation decisions for medical spending cannot be made efficiently in isolation from the nonmedical cost implications of those decisions, as is implicit in the approach advocated by Weinstein (1986) that views health care spending as coming from a "health care budget."

A second critical result that comes out of the analysis in the Meltzer (1997) paper is that analyses that fail to include future costs will be biased in favor of interventions that extend life over interventions that improve the quality of life, especially among the elderly. These effects of future costs are most precisely described in the context of lifetime utility maximization models, such as those described in Meltzer (1997). However, the essence of the effects of including future costs in medical cost-effectiveness analysis can be described by breaking total costs into the sum of current costs and future costs and then assuming that future net resource use is equal to a constant amount C per life year multiplied by the number of life years saved (ΔLE). In that case, the cost-effectiveness ratio (cost per QALY) can be written

$$\begin{aligned}
 CE &= \frac{\Delta \text{cost}}{\Delta \text{QALY}} \\
 &= \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + \frac{\Delta \text{future cost}}{\Delta \text{QALY}} \\
 &= \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + C \times \frac{\Delta LE}{\Delta \text{QALY}}.
 \end{aligned}$$

The first term in this equation describes the cost-effectiveness ratio that only includes current costs. The second term in the equation describes the future costs that have traditionally been omitted from cost-effectiveness analyses. The equation implies that these costs will be largest when future costs per year of life lived (C) are large and when the ratio of the change in life expectancy to the change in quality-adjusted life expectancy is large.

Meltzer (1997) develops some rough but useful estimates of C based on population average data for consumption plus medical expenditures plus earnings by age the United States, suggesting that C varies from about $-\$10,000$ at age twenty to about $+\$20,000$ at age seventy and above. These numbers go gradually from negative to positive because young people on average produce more than they consume over their lifetime, whereas people who are older and have already passed through their working years on average consume more than they produce after that age. Table 2.1, reproduced from Meltzer (1997), uses these estimates and the approximation described above, based on the ratio of effects on length of life and quality of life, to estimate the effects of including future costs on the cost-effectiveness of a number of common medical interventions. The interventions are listed in the table in order of diminishing cost-effectiveness based on traditional estimates that exclude future costs for unrelated and non-medical expenditures. The last column then reports the cost-effectiveness ratio that includes these future costs. The results clearly show that the relative rankings of interventions can change—rising or falling based on the effects on length of life and quality of life and on the age of the patient at the time of the intervention, which can imply positive or negative annual costs. Many of the changes in rankings appear at the top of the table and may be considered substantively important by some analysts, though perhaps not by others because even the ratios that include future costs suggest that the interventions remain relatively cost-effective by most standards (i.e., $< \$50,000 - \$100,000/\text{QALY}$; Goldman et al. 1991).

In contrast, some of the interventions at the bottom of the table imply larger changes that could alter whether an intervention is considered cost-effective. For example, the estimates that exclude future costs suggest that among sixty-year-old men, the treatment of hypertension and adjuvant chemotherapy for Duke's C colon cancer are both cost-effective compared to dialysis for end-stage renal disease that lies somewhat above the range

Table 2.1 **Effect of Future “Unrelated” Costs on the Cost per Quality-Adjusted Life Year**

Intervention	Change in Life Expectancy (LE)	Change in Quality-Adjusted Life Expectancy (QALE)	Change in LE/QALE	Annual Future Cost (C)	Bias Due to Future Cost	Reported Cost/QALY	Actual Cost/QALY
Adjuvant chemotherapy for Duke’s C colon cancer age 55 (Smith et al. 1993)	2.4 yr	0.4 yr	6.00	3,000	18,000	16,700	34,700
Treatment of severe hypertension men age 40 ^a (Stason and Weinstein 1977)	4 yr	3.9 yr	1.03	−5,000	−5,200	18,000	12,800
Adjuvant chemotherapy for node-negative breast cancer age 45 (Hillner and Smith 1991)	11 mo	5.1 mo	2.16	−4,000	−8,700	18,000	9,300
Adjuvant chemotherapy for node-negative breast cancer age 60 (Hillner and Smith 1991)	7.7 mo	4.0 mo	1.93	8,000	15,400	21,000	36,400
Treatment of severe hypertension, men age 50 ^a (Stason and Weinstein 1977)	2.6 yr	2.5 yr	1.04	0	0	25,000	25,000
Coronary artery bypass 3-vessel disease, mild angina age 55 (Wong et al. 1990)	0.6 yr	0.7 yr	0.86	3,000	2,600	31,000	33,600
Coronary artery bypass 3-vessel disease, severe angina age 55 (Wong et al. 1990)	1.4 yr	1.4 yr	1.00	3,000	3,300	45,000	48,300

Adjuvant chemotherapy for node-negative breast cancer age 75 (Desch et al. 1993)	2.9 mo	1.8 mo	1.61	20,000	32,200	54,000	86,200
Hormone replacement therapy ages 55–65 (Tosteson and Weinstein 1991)	0.0458 yr	0.0387 yr	1.18	8,000	9,400	54,200	63,600
Treatment of severe hypertension, men age 60 ^a (Stason and Weinstein 1977)	1.5 yr	1.4 yr	1.07	8,000	8,500	60,000	68,500
Adjuvant chemotherapy for Duke's C colon cancer age 60 (estimated based on Smith et al. 1993) ^b	1.8 yr	0.1 yr	18.00	8,000	144,000	67,000	211,000
Hemodialysis for end-stage renal disease (ESRD) men aged 30 (estimated based on Garner and Dardis 1987 and Hornberger, Redelmeier, and Peterson 1992) ^c	—	—	1.50	0	0	117,000	117,000
Hemodialysis for ESRD men aged 60 (estimated based on Garner and Dardis 1987 and Hornberger, Redelmeier, and Peterson 1992) ^c	—	—	1.50	8,000	12,000	117,000	129,000

Note: Costs converted to 1993 dollars using the medical CPI (U.S. Department of Labor 1994).

^aStason and Weinstein already include future unrelated medical costs, so the additional future costs here refer only to consumption net of earnings.

^bEstimates made for sixty-year-old assuming life expectancy of sixteen years at age sixty as opposed to twenty years at age fifty-five used to calculate the cost-effectiveness at age fifty-five.

^cCost-effectiveness estimates based on Garner and Dardis (1987) using quality of life estimates from Hornberger, Redelmeier, and Peterson (1992).

that people often cite as cost-effective. In contrast, when future costs are included, the cost-effectiveness of adjuvant chemotherapy deteriorates markedly, rising to over \$200,000/QALY. This large change in the cost-effectiveness ratio occurs because chemotherapy has large effects on length of life compared to quality of life. This illustrates the quantitative significance of the potential for excluding future costs to bias analyses to favor interventions that extend life over those that improve the quality of life.

Although these estimates of the effects of including future costs are based on the approximations described above, which may be inaccurate for a variety of reasons, other work that I have done with Magnus Johannesson and Richard O'Connor on the cost-effectiveness of treatment for hypertension suggests that the estimates based on this approximation correspond fairly well to estimates that directly incorporate future costs into the cost-effectiveness analysis (Johannesson, Meltzer, and O'Connor 1997). Other work I am involved in that directly incorporates future costs into a cost-effectiveness analysis of hip replacement among the elderly—which provides its benefit by improving quality of life—reinforces the finding that excluding future costs favors interventions that extend life over those that improve the quality of life (Meltzer et al. 1998). A contrasting example to the case of hip replacement is that of prostate cancer treatment, which may not offer any advantage in life expectancy—no less quality-adjusted life expectancy—because of the potentially substantial negative effects of treatment on quality of life. However, even if treatment does offer an advantage in life expectancy and quality-adjusted life expectancy, it is likely to have a small effect on quality-adjusted life expectancy compared to life expectancy. Indeed, the most optimistic cases considered by Fleming et al. (1993) concerning the value of radical prostatectomy for moderately differentiated prostate cancer in sixty-five-year-old men suggest an average gain in QALYs of 0.2 QALY compared to average gain in life expectancy of 0.7 life year. This suggests a ratio of $\Delta LE/\Delta QALY$ of 3.5, which, with a future cost C of \$16,000 per year at age sixty-five, implies a cost-effectiveness ratio of \$56,000 per year even if treatment of prostate cancer had no direct costs. Thus prostate cancer may be an excellent example of an intervention where the potential for negative effects on quality of life has important implications for cost-effectiveness.

2.5 Conclusion

This review has focused on two methodological areas in cost-effectiveness analysis—the validity of the measurement of benefits as quality-adjusted life years and the appropriate treatment of future costs—in which reliance on economic theory can provide valuable methodological insights. On the benefits side, the concept of revealed preference provides evidence consistent with the hypothesis that patients value gains in

QALYs, though the results may also be consistent with cognitive dissonance. Ultimately, the results suggest the need for further work using revealed preference to evaluate and improve quality of life measures, whether based on QALYs or willingness-to-pay measures, and suggest the need for caution in the interim whenever a study relies on such measures. On the cost side, models of lifetime utility maximization point out the need to include all future medical and nonmedical costs and also point out the bias in favor of interventions that extend life over the improvement in quality of life that often occurs when such future costs are excluded.

An important interaction between these two results relates to the dependence of the future-cost term on the ratio of changes in life expectancy to changes in quality-adjusted life expectancy. The presence of the change in QALYs in the denominator of this ratio implies a high degree of sensitivity of cost-effectiveness estimates to quality of life assessment. Thus the problems in accurately measuring quality of life can have immense effects on cost-effectiveness, especially once future costs are considered.

Though the application of insights from economic theory to the measurement of benefits and costs in medical cost-effectiveness analysis is important, there are other controversial issues in which economic theory may provide valuable insights into the methods needed to improve cost-effectiveness analysis as well. These include methods for sensitivity analysis based on utility maximization (Meltzer 1998) and techniques to address distributional concerns (Wagstaff 1991). Though neither question is provided an unambiguous response by the application of utility maximization, the discussion generated by such models provides a key framework for understanding these problems. If the influence of cost-effectiveness analysis is to continue to increase as it appears to be doing currently, and if it is to do more good than harm, it is crucial that its methods continue to undergo rigorous scrutiny.

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Comment Douglas L. Cocks

This paper provides an extremely useful contribution to the field of health economics as it is applied to the economic evaluation of pharmaceutical medical interventions. In recent years the quasi-application of economics to the evaluation of pharmaceuticals has come under the scrutiny of many diverse disciplines (medicine, pharmacy administration, sociology, psychology, business administration, anthropology, statistics, and others), which in turn derived the new discipline known as pharmacoeconomics.

Dr. Meltzer's discussion of the relationship between the concept of

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quality-adjusted life years (QALYs) and the economic concept of revealed preference highlights the possible notion that the relationship between pharmacoeconomics and real health economic analysis is tenuous. The implication of the discussion is that the concept of QALYs confuses the basic microeconomic distinction between cardinal and ordinal utility. In essence, the QALY designation is founded as a cardinal representation of utility and therefore cannot be translated into the true concepts of classical welfare economics. As the paper points out, even the report of the Panel on Cost-Effectiveness in Health and Medicine “explicitly advocates that cost-effectiveness analyses adopt a ‘social’ perspective, and asserts that the methods of cost-effectiveness analysis that adopt such a perspective have their roots in classical welfare economics.” This cardinal orientation renders the use of QALYs very limited, especially in making economic comparisons of drugs that are similar in therapeutic activity and chemical makeup.

The empirical data presented on the limitations of QALYs indicate that these measures are not necessarily a reliable measure of the *economic* significance of a particular medical intervention. The application of traditional microeconomic welfare economics to questions of the economic significance of medical interventions may be the best guide to both public and private policy issues concerning these interventions.

The second major part of the paper deals with the importance of dealing with future costs when analyzing the economic cost and benefits of medical interventions. This is an extremely important concept that is often misunderstood or forgotten in the field of pharmacoeconomics. This basic concept is related to an economic principle that is also misunderstood, the principle of the distinction between systems costs and component (sometimes known as line item) costs.¹ This distinction is important because much of the management of health care in the United States and in certain foreign health care systems relies on the use of component management, rather than addressing health care costs from a systems perspective. The major economic issue is centered around resource allocation decisions. Resource allocation decisions are grounded in production functions in classical economics, which require an answer to the question What allocation of inputs results in the greatest output at the lowest cost? The case for a systems approach, as opposed to a component/line item approach, has been analyzed empirically. Several studies have shown that focusing on one component of cost without considering interaction effects can cause the unintended effect of increasing total costs even as the cost of the single component is reduced.²

The concept of systems management can be framed analytically in a

1. This discussion is based on Cocks and Croghan (1996).

2. Soumerai et al. (1994); Sloan, Gordon, and Cocks (1993); Moore and Newman (1993); Dranove (1989); Horn et al. (1996).

methodology of economics known as economic growth accounting. This methodology, developed by Denison (1974), was first applied to health care by Klarman et al. (1970) followed by Virts (1977) and Virts and Wilson (1983, 1984).

The fundamental notion of economic growth accounting is that health care costs cannot be addressed until they have been broken down into their basic factors. From an economic perspective, these factors can be expressed in a simple identity,

$$\text{THE}_t = P_t \cdot U_t \cdot N_t,$$

where THE_t equals total health care expenditures in a given time period, t ; P_t is the price per unit of health care goods and services in time period t ; U_t is the utilization of health care goods and services—the number of units of health care goods and services consumed *per person* in time period t ; and N_t is the number of persons consuming health care goods and services in time period t . Historically, identities have been used in economic analysis to convey fundamental economic concepts algebraically and graphically. The most recognized identity is the equation for the quantity theory of money (Glahe 1973).

The simple model of health care expenditures can be applied to the many institutional forms that make up the total health care system. At the aggregate level, total U.S. health care expenditures represent the summation of the many THE_t equations emanating from the myriad of health care delivery systems. Thus, the analytic or managerial problem is to determine how the level of total health care expenditures (THE_t) changes over time and the relative contribution of each major element (P_t , U_t , and N_t) to the growth in health care costs/expenditures.

In applying the basic model, a fundamental issue highlights the importance of a systems approach to health care management. Many interaction effects exist among the individual factors as those factors change both in magnitude and over time. For example, as the price of a good or service rises, the number of units purchased of that good or service usually falls. The price rise also results in increased consumption of an alternative or substitute good. These interaction effects are difficult to understand and even more difficult to account for numerically.

The relationship among the factors can be observed by examining the simple mathematics of change derived from the expenditure/cost equation, $\text{THE}_t = P_t \cdot U_t \cdot N_t$. Therefore, the changes in spending can be expressed as

$$\Delta \text{THE} = \Delta P + \Delta U + \Delta N + (\Delta P \cdot \Delta U) + (\Delta P \cdot \Delta N) + (\Delta N \cdot \Delta U).$$

In this relationship, the terms are defined as follows:

- $\Delta \text{THE} = \text{THE}_t - \text{THE}_0$ —the change in total health care expenditures is the difference in total health care expenditures in the given year, t , and a beginning or base year, 0.

- $\Delta P = P_t - P_0$ —the change in health care prices is the difference in the price level in the given year, t , and the base year, 0.
- $\Delta U = U_t - U_0$ —the change in utilization is the difference in utilization in the given year, t , and the base year, 0.
- $\Delta N = N_t - N_0$ —the change in the number of persons consuming health care goods and services is the difference in the number of persons in the given year, t , and the base year, 0.
- $(\Delta P \cdot \Delta U)$, $(\Delta P \cdot \Delta N)$, $(\Delta N \cdot \Delta U)$ —represents the interaction effects that result from the individual factor changes that operate on each other.

This simple model as it is presented represents the aggregation of health care expenditures at a total level. Thus, the total health expenditures term, THE_t , represents the summation of expenditures for all the goods and services that constitute health care spending. In simple mathematical terms, this can be expressed accordingly:

$$THE_t = \Sigma SPE_{it},$$

where ΣSPE_{it} is the summation of spending on specific health care goods and services, i , for the time period, t . The term ΣSPE_{it} represents the crux of the problem of managing health care costs. The management problem this model exposes has four dimensions: (1) the complexity inherent in examining the number of items that make up health care spending, ΣSPE_{it} ; (2) the need to determine the contribution of each component of individual spending (P_t , U_t , and N_t) to total expenditures, THE_t ; (3) the need to specifically address the interaction effects among prices, utilization, and population ($\Delta P \cdot \Delta U$), $(\Delta P \cdot \Delta N)$, and $(\Delta N \cdot \Delta U)$; and (4) the need to examine substitutions among health care goods and services that take place with the summation of expenditures, ΣSPE_{it} . In economic terms, the last dimension represents the need to address the elasticity of substitution among the various inputs that constitute total health care spending.

The purpose of the preceding discussion is to emphasize the importance of Dr. Meltzer's point on the significance of addressing the issue of future costs in cost-effectiveness studies. The economic implications of the introduction and use of innovative medical interventions have many dimensions that must be addressed when considering the allocation of health resources.

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