

**Office of Dietary Supplements
National Institutes of Health**

**Economic Analysis of Nutrition Interventions for Chronic
Disease Prevention: Methods, Research, and Policy**

**February 23–24, 2010
Bethesda North Marriott Hotel and Conference Center
Bethesda, MD**

The workshop was jointly sponsored by the Office of Dietary Supplements, the National Center for Complementary and Alternative Medicine, the National Cancer Institute, and the National Institute for Nursing Research, all of the National Institutes of Health.

Introduction

The Office of Dietary Supplements (ODS) of the National Institutes of Health (NIH) recently published its strategic plan for the next 5 years. In this plan, the Office commits itself to expanding its efforts to further research on the role of dietary supplements in health promotion and chronic disease prevention. As part of ODS's continued implementation of its strategic plan, the Office is assessing ways to enhance methodologies for evaluating the role of dietary supplements and other nutritional interventions in disease settings.

Health economic issues in the U.S. healthcare delivery have gained increased prominence with President Obama's expressed desire to "raise health care's quality and lower its costs." Despite the rapid escalation of healthcare costs, research into healthcare economic solutions has not taken center stage. Nutrition is a foundation of preventive and curative medicine in our healthcare system, and it is postulated that better health outcomes can be achieved for dollars spent by ensuring proper nutrition of the population. In light of increased interest in the potential societal benefit of incorporating health economics as a part of clinical translational science, ODS hosted the Economic Analysis of Nutrition Interventions for Chronic Disease Prevention: Methods, Research, and Policy workshop on February 23–24, 2010 in Bethesda, Maryland. This 1.5-day event brought together U.S. and international academicians, researchers, policy makers, and regulators to address the following key and questions with respect to nutrition interventions:

- *State of the science.* What health economic methods are currently used to judge the burden of illness, interventions, or health care policies? What new research methodologies are available or needed to address critical knowledge or methodological gaps or barriers?
- *Research applications.* What evidence-based health economic research activities in nutrition are ongoing or planned at the NIH, Centers for Disease Control and Prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), and Economic Research Service in the Department of Agriculture?
- *Regulatory, policy maker, and clinical practice perspectives.* Once these research goals have been met, how can the results help regulators and policy makers at the Government Accountability Office (GAO), Food and Drug Administration (FDA), Office of the Assistant Secretary for Planning and Evaluation in the Department of Health and Human Services (DHHS), and Centers for Medicare and Medicaid Services (CMS) make nutrition policy decisions? What health economic and policy activities are taking place in other countries? How does economics affect the development of clinical guidelines?

The workshop's goal was to enhance communication among health economic methodologists, researchers, reimbursement policy makers, and regulators about needs, capabilities, and future directions. The workshop's objectives were to inform policy decision making by:

- Improving the methodologies used for health economic research in nutrition.
- Identifying areas of congruence between health economic research aims and health policy and regulatory needs.
- Establishing a health economic research agenda to foster the use of health economics in clinical and translational health science.

Methods in Economic Analysis of Nutrition Interventions Session 1 Summary

Session 1 Moderator: Dr. John Wong, Tufts Medical Center

Making America Healthier and Its Medical Care Less Costly: Initial Reflections

Dr. Theodore Marmor, Yale Law School

The control of American health care costs must be costly to some group to save money. For example, national medical expenditures must equal the income of health care industry entities.¹ As a result, cost control must be controversial; the income of some component of the health care system will be less than it otherwise would have been and those whose income is threatened will try to protect their interests in the political process. Furthermore, if cost control must be costly to someone, no “costless” or benign form of cost control exists.

Three benign approaches to reduce costs have been extensively promulgated:

1. Increasing the prevention of illness, morbidity, and death.
2. Using health information technology and electronic medical records to reduce errors and adverse drug interactions.
3. Conducting comparative effectiveness research on the effects and costs of two or more interventions.

Although each of these may be beneficial, the presumption that they would each reduce costs has yet to be demonstrated.

Without doubt, research on health politics, policy, and economics suggests that efforts to make a population healthier do not make medical care less expensive. This is widely accepted in other countries, such as Canada but is not a central presumption of the health care reform discussion in the United States.

In 1970, the United States and Canada spent approximately the same proportion, about 7%, of their gross national product (GNP) on health care. By 2000, the United States was spending 14% of its GNP on health care compared with 10% in Canada. The best explanation for this difference is that Canadians spend less for the same medical care than Americans. For example, even though Canadians use more bed-days per 1,000 people and have more office visits per capita than Americans, overall medical costs are lower in Canada because the cost per bed-day and office visit is lower.

Economic analyses of nutritional interventions must not ignore the political climate. Nutritional reform should not be oversold in the same way as prevention, health information technology and electronic medical records, and comparative effectiveness research.

Discussion

Dr. Marmor explained that the lack of a realistic discussion of cost control relative to the health care system is hardly accidental because such a discussion would identify winners and losers. Because this discussion has not taken place, the population has been misled about sources of cost control in health care reform. The American public is being misled by those who state that costless cost control is possible and those who argue that health care reform involves “Medicare death squads” and the like. As a result, the public is no more illuminated about what health care reform is about in 2010 than it was in 2009 or 2008. Furthermore, no U.S. political leader has identified clearly what providing, sustaining, and financing affordable health care for all American families would require. As a result, the public is convinced that trouble exists in the health care world and that reducing fraud, waste, and abuse could largely pay for most bills in the future.

In response to a question about forces sustaining the current state of affairs in the U.S. health care system, Dr. Marmor suggested examining ways to prevent this predicted future. All over the globe, hospital administrators, physicians, nurses, consultants, professors, and others would like to be paid more (which is basic human nature). What does the United States lack that other countries have to concentrate the countervailing power to resist this omnipresent set of inflationary forces? If the overall expenditures for medical care increase disproportionately with no organized arrangement in which the “losers” are at the same table, medical care costs will rise. In Canada, this discussion occurs with all parties present so that if medical expenditures increase more rapidly than income, policy makers agree that other budgets must decrease. In contrast, the United States has an organized political force supporting the “collective bad” of increased prices and increased expenditures.

A participant asked whether biomedical research could be part of the solution to increased medical care costs. Dr. Marmor explained that biomedical research in nutrition or any other area should be justified by its beneficent effects on population health, not its potential to reduce costs. Dr. Marmor supports developing nutritional and other interventions but is concerned about the potential for overselling the results of this research.

When asked what might be necessary to trigger health care reform, Dr. Marmor noted that the American political structure is designed to make action difficult; an 18th century construction designed to prevent tyranny does not always have desirable effects in a 21st century political system. The major interests at stake need to join together and, in the U.S. political system, this requires tremendous social mobilization by a president and a party. What must be mobilized is not technical understanding but, rather, the distinction between the ordinary market society and society’s treatment of merit goods. Until medical care is regarded more widely as something to be allocated according to the ability to benefit and medical need—as opposed to the ability to pay and willingness to pay (WTP)—an ideological and moral conflict will occur that, given America’s institutional structure, will make real reform difficult.

American Exceptionalism and Cost-Effectiveness Analysis in the United States: A Historic Perspective

Dr. Peter Neumann, Tufts Medical Center

Dr. Neumann invoked “American Exceptionalism,” to explain why the United States appears to be more resistant than other countries to cost-effectiveness analysis (CEA) of the incremental costs and health effects associated with different health interventions. American culture emphasizes liberty and freedom in a way that other cultures do not, so the U.S. political system rarely produces big government solutions. Discussions of comparative effectiveness research in the United States have highlighted the danger of government’s intervening between patients and doctors.

Medicare program officials have tried, at times, to incorporate CEA into their decision-making processes. In the late 1980s, the Medicare program’s proposal to use CEA in making coverage decisions for new medical technology met fierce opposition from the pharmaceutical and device industries, the American Association of Retired Persons, and many medical professional societies. The proposal was eventually withdrawn.

Medicare officials state that they do not use CEA when they make coverage decisions about new technologies, but some signs indicate that this is changing. Medicare covers several technologies that have incremental cost-effectiveness ratios of above \$100,000 per quality-adjusted life year (QALY) and other inefficient technologies, yet resistance to CEA remains strong.

Private health plans do everything possible to manage utilization but tend not to use CEA in an open, explicit way. Some exceptions exist, however, and the industry appears to be changing slowly.

Despite resistance to CEA, the landscape may be changing, in large part due to the unsustainable growth in medical costs. Peter Orszag, Director of the Office of Management and Budget (OMB), has stated that “better information about the costs and benefits of different treatment options...could eventually lower health care spending...” At the highest levels of the federal government, CEA and the notion that it can help inform decision makers is gaining recognition.

Dr. Neumann and colleagues created a database of cost-effectiveness studies (available at www.cearegistry.org). An analysis of the registry shows that the number of publications on cost-utility analysis (CUA)—CEA that measures health benefits in terms of QALYs—is increasing. About half of these studies took place in the United States and some were funded by NIH.

Evidence also shows that the methodological underpinnings of CEA and CUA are improving. More and more studies are characterizing uncertainty and trying to understand the robustness of conclusions under different assumptions. An increasing number of economic analyses are carried out alongside clinical trials and the focus on good practices is increasing.

Medicare makes 10–15 national coverage decisions each year and program officials have begun citing CEA in a number of these decisions. Regression equations show that the value of technologies, measured as cost-effectiveness, is an independent predictor of what Medicare covers. The Medicare Improvement Patient and Provider Act of 2008 allowed Medicare to cover prevention for the first time without explicit congressional authority, as long as evidence for the intervention has a high rating from the U.S. Preventive Services Task Force. The legislation also allows the DHHS Secretary to assess the relation between predicted outcomes and the

expenditures for prevention services. Medicare now has the authority to use CEA for prevention services and used this authority recently when it decided to cover HIV screening.

Dr. Neumann concluded by making the following predictions: the number of published CEAs in the United States will continue to increase; resistance to CEAs will continue; new comparative effectiveness research (if included in the health care reform legislation) will not include CEAs; and CEAs will play a more important role in clinical guidelines and in coverage and reimbursement decisions.

Discussion

Dr. Martin Brown of the National Cancer Institute (NCI) commented that the Centers for Medicare and Medicaid Research (CMS) is increasingly willing to use CEA to make coverage decisions, partly because of methodological improvements in the field. Similarly, the U.S. Preventive Services Task Force appears to have increased its acceptance of modeling related to CEA. Dr. Neumann said that, overall, the comfort level with CEA has increased somewhat.

One participant noted that although European nations conduct many CEA studies, these countries do not usually use the results to help keep costs down. Dr. Neumann commented that Northern Europe has been more inclined to use CEA studies than other parts of Europe. Studies outside the United States could be informative here and vice versa.

In response to a question, Dr. Neumann explained that economic analyses that are part of clinical trials raise challenges, such as ensuring large enough sample sizes to examine economic endpoints. Some well-done economic analyses have helped inform decisions and a task force of the International Society of Pharmacoeconomics and Outcomes Research discussed methodological challenges and recommendations in *Value and Health*.

Dr. Johanna Dwyer, Senior Nutrition Scientist at ODS, noted that about 30 years ago, William B. Schwartz and Henry J. Aaron published *The Painful Prescription*,² a book on economic analysis. She asked whether the field had changed much since this analysis. Dr. Neumann commented that Schwartz and Aaron discussed the inevitability of technological innovation and this has not changed. However, the crisis has deepened and the increasing comfort level and appreciation of the methods and modeling improvements have moved the field forward, creating the opportunity to conduct more of these studies in the future.

Methodological Overview of Medical Cost-Effectiveness Analysis

Dr. David Meltzer, University of Chicago

Dr. Meltzer noted that since 1960, health care spending has grown 2.5 % more rapidly per year than the rest of the economy.³ Much of this growth is due to growth in quantity; in essence, Americans are spending more on health care because they are undergoing more procedures, receiving more care, or both. CEA may be able to show how best to decrease these costs and identify ways to increase the value obtained with current expenditures.

There is a growing demand for CEA, which has its roots in academic medicine. Other countries, such as the United Kingdom, have used CEA in their national health systems. In the United States, the use of CEA is much more informal. For example, some private payers use CEA to encourage greater use of cost-effective treatments, and pharmaceutical companies regularly publish CEA studies.

Dr. Meltzer identified three types of CEA:

- *Cost Minimization.* This approach identifies the least expensive method for accomplishing a fixed objective, such as finding a tumor. However, this approach assumes that the objective will be met and does not measure the health benefit of the procedure. Instead, the goal should be to maximize benefits with the available resources, which is the fundamental theory underlying all CEA approaches.
- *Cost Benefit.* In this approach, costs and benefits are measured in dollar terms, and all treatments for which the net benefit is greater than 0 are selected. This approach requires placing a dollar value on health outcomes.
- *Cost-Effectiveness.* This approach examines the ratio of changes in cost relative to changes in effectiveness and selects treatments with the lowest cost-effectiveness ratio (the lowest amount of incremental cost relative to the level of incremental effect) to determine the most efficient use of resources.

Dr. Meltzer presented equations demonstrating that the fundamental underlying theory of CEA has a strong basis in “constrained maximization,” which is the standard approach to maximize utility or benefit, subject to the constraint of the total amount of resources available) The goal is to maximize utility, which depends on how much medical care is consumed subject to a budget constraint (income) minus the expenditures for medical care consumption.

The possible outcomes of cost and effectiveness comparisons are:

- Cost increases and effectiveness decreases, indicating that the intervention should not be done.
- Cost increases and effectiveness increases, indicating a need for CEA.
- Cost decreases and effectiveness decreases, indicating a need for CEA.
- Cost decreases and effectiveness increases, indicating that the intervention should always be done.

CEA allows researchers to describe the cost-effectiveness of medical interventions in terms of their additional cost per additional unit of benefit (e.g., life-years). For example, screening neonates for phenylketonuria saves money and lives, so this intervention would always be advantageous no matter what value is placed on benefits. Conversely, a screening ultrasound every 5 years for abdominal aortic aneurism costs \$907,000 per life-year saved and is not cost effective.

Studies suggest that people would give up about \$50,000- \$200,000 to gain a year of life, providing a baseline for determine which interventions are cost-effective.

CEAs should be based on multiple perspectives, including private; public; and societal. Analysts should make explicit the impact of these different perspectives on CEA results.

QALYs are a composite measure reflecting changes in length and quality of life. CUA is the use of QALYs in CEA and is clearly the dominant methodology in the field. The primary approaches to measuring health-related quality of life (HRQOL) include linear analog scale, standard gamble, and time trade-off.

Discussion

A participant noted that the dominance of QALYs in the field can be attributed to peer reviewers insisting that QALYs be used in published studies. For some interventions, accounting for changes in HRQOL is important but for others, life-years saved is acceptable. Dr. Meltzer agreed, noting that many of the clearest examples of cost-effectiveness depend on life-years saved, not QALYs. Other approaches to valuing health effects, such as WTP, can be important in certain settings.

A participant asked whether any models are available to compare QALYs for different members of society. Dr. Meltzer noted that no simple methods can, for example, allow researchers to measure whether happiness for one person is worth more or less than happiness for another.

A participant asked about the equations Dr. Meltzer presented. The lambda in one equation is based on the assumption that a balance exists between the value of spending on medical care and the value of spending on everything else. Cost-effective interventions typically improve health at an increased cost, and paying more for health care results in having less money to spend elsewhere. Dr. Meltzer noted that the U.S. population tends to be very uncomfortable with tradeoffs between health care and other activities. CEA is never used for making “black and white” decisions; it is part of the input to help make decisions. Cost-effectiveness ratios are important for deciding whether to carry out an action but they do not help scale the benefits.

Institute of Medicine Recommendations for Valuing Health in Regulatory Cost-effectiveness Analysis

Dr. Wilhelmine Miller, Robert Wood Johnson Foundation Commission to Build a Healthier America, George Washington University School of Public Health and Health Services

Dr. Miller reviewed the work of the Institute of Medicine (IOM) Committee to Evaluate Measures of Health Benefits for Environmental, Health, and Safety Regulation, which published recommendations in 2006 for applying CEA in the economic assessment of federal regulations.

The OMB has required some form of economic analysis and centralized review of some federal regulations since the early 1970s. Historically, cost-benefit analysis (CBA) has been the predominant approach used to assess the economic impacts of major U.S. health and safety regulations. In 2003, OMB issued *Circular A-4: Regulatory Analysis*, requiring that agencies also conduct CEA whenever “a valid effectiveness measure can be developed.” The next year, OMB and several federal agencies asked the IOM to convene a consensus committee to consider

technical and ethical issues related to the selection of integrated effectiveness measures, such as QALYs.

The IOM committee included several members of the U.S. Panel on Cost-Effectiveness in Health and Medicine, convened by the U.S. Public Health Service in 1993 to assess the state of the science and to define best practices for conducting CEAs in health care. The recommendations for conducting and reporting on CEA in the panel's report, *Cost-Effectiveness in Health and Medicine*, have been adopted by many journals and practitioners as the standard approach.⁴

The IOM committee deemed QALYs to be the most appropriate metric for regulatory analysis because of their simplicity, wide use, and extensive evaluation. The committee also followed the U.S. panel's endorsement of direct preference elicitations for health states of interest in the regulatory framework. However, the committee acknowledged that direct elicitations of preferences for health states probably would not be practical in regulatory studies. The committee therefore recommended basing QALY estimates on generic indexes. Because preference-based EuroQol 5D (now known as EQ-5D, www.euroqol.org/) index values had been estimated for the general U.S. population recently, the EQ-5D index was deemed the "leading candidate" for adoption in the U.S. regulatory context. The dimensions of EQ-5D include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.

The committee's additional recommendations included the following:

- *Valuing and calibrating health states.* Life-year and QALY estimates should reflect actual population health as closely as possible, comparing the estimated HRQOL and life expectancy of the affected population to predicted, post-intervention estimates.
- *Constructing and reporting cost-effectiveness ratios.* Multiple cost-effectiveness ratios should be reported. Incremental cost-effectiveness ratios are usually the most useful summary measure for comparing different regulatory interventions. In addition to reporting effects in the aggregate, researchers should report QALY estimates separately for each health impact. Cases of disease avoided and cause-specific mortality should also be reported. Information on related uncertainties and on non-quantified effects should accompany all reported CEA results.
- *Use of QALYs in cost-benefit analysis.* Regulatory analyses should not assign monetary values to QALY estimates to value health states because this approach lacks theoretical and empirical support.
- *Information for regulatory decisions.* The regulatory decision-making process should explicitly address and reflect distributional, ethical, and other non-quantified implications of a proposed intervention. Analysts should consider whether the pre- or post-regulatory costs or risks disproportionately affect certain population groups. Analysts and regulators should select subgroups for comparative analysis of impacts that could experience disproportionate benefits, burdens, or both.

- *Public involvement.* Policy makers and agency administrators should involve a broad range of individuals and groups at all stages of policy development for regulating risks. Greater consistency and transparency in presenting analytic results will facilitate public understanding and participation.
- *Data collection and research.* Improving the data used to assess the health risks addressed by regulatory interventions should be a research priority. DHHS and other federal agencies should collect HRQOL information through routinely administered population health surveys and other major risk-assessment and monitoring data collection efforts. DHHS should coordinate the development of an integrated research agenda to improve the quality, applicability, and breadth of integrated measures for use in regulatory CEA.

The U.S. Environmental Protection Agency relies primarily on CBA and has provided “illustrative” CEAs in response to OMB requirements. FDA and the National Highway Traffic Safety Administration have historically reported CEA and CBA results. The Environmental Protection Agency does not use monetized QALYs in its CBAs, but they are commonly used in FDA and National Highway Traffic Safety Administration analyses.

Implementation of the IOM committee’s recommendations has been inhibited by time and resource constraints and by competing priorities. OMB has not issued guidance on implementing the recommendations. The most controversial or problematic recommendations for some agencies is the recommendation not to use monetized QALYs in CBA, even though WTP estimates—the theoretically appropriate source of values for CBA—often are not available.

Dr. Miller suggested the following activities to encourage implementation of the IOM committee’s recommendations:

- Assess the informational needs of decision makers.
- Develop criteria for matching particular measures to the circumstances in which those measures are most useful instead of routinely reporting numerous results.
- Promote cross-agency collaboration.
- Separate funding for improved data and methods from specific rulemakings.

Discussion

A participant noted the juxtaposition between the IOM recommendations on CEA in the regulatory environment with the U.S. tendency to separate costs from policy considerations for health care. Dr. Miller commented on the irony that the IOM was precluded from examining CEA use in the very fields for which it was developed (i.e., population health and clinical health care services); the committee was charged with examining federal regulatory programs only.

A participant asked how estimate ranges in the monetary values assigned to QALYs affected the committee’s recommendations. Dr. Miller explained that the committee’s charge was to develop an alternative to CBA, and the literature has values of statistical life and of statistical life year estimates. Whether agency CBAs should use monetized QALYs is based on the strong preference for collecting new WTP estimates for morbidity outcomes rather than relying on a

fixed dollar/QALY conversion factor. One participant noted the wide range of WTP estimates for a QALY. According to WTP studies, preventing morbidity is valued differently from preventing mortality.

Dr. Miller said that, in isolation, a cost-effectiveness ratio only helps identify the absurd outliers and is not a definitive decision point.

Health-Related Quality of Life and Health Status

Dr. Robert M. Kaplan, University of California, Los Angeles Schools of Public Health and Medicine

A variety of methodologies can be used to measure health. Dr. Kaplan discussed their role in population health data systems and how they might be implemented in public health.

Concerns in population health include morbidity (illness, or how people feel and how health problems affect them) and mortality (death, or how long people live). To compare widely different interventions, the measure of health must encompass differences not only in length of life but also in quality of life, symptoms, and ability to function.

Population health can be measured by evaluating mortality and life expectancy rates, as well as by using morbidity-based measures that include HRQOL indexes. HRQOL measures include cost-utility analyses based on decision theory that require eliciting utility weights, or preferences, for health states. These measures are scored on a scale of 0 (dead) to 1 (perfect health).

The purpose of quality-adjusted survival analysis is to summarize life expectancy with adjustments for quality of life. A QALY is a health outcome measure that assigns to each time period a weight ranging from 0 to 1 that corresponds to the quality of life during that period. The QALY combines morbidity and mortality into a single index, represents life expectancy with adjustments for QOL, and represents a year of life free of all disabilities and symptoms. QALYs can be used to measure the impact of a treatment and can be evaluated over time, with and without treatment. Similarly, cost with and without treatment can be evaluated.

Prospective studies are needed that measure HRQOL over time and characterize these life states, ultimately estimating the impact of treatment. The field has developed an increasing interest in alternative ways of estimating QALYs using existing datasets. Cross-sectional methodologies allow researchers to estimate HRQOL at a point in time and combine this measurement with life tables and other methods.

A small set of potential HRQOL indexes is available today. Each of these tools has an associated questionnaire ranging from 5 to nearly 60 questions. The developers of these indexes have collaborated in recent years to try to develop an aggregate index.

Utility-based measures are available to estimate the impact of nutrition at the population level and nutritional interventions at the individual level, and generic methods allow comparisons of investments in nutrition with investments in other aspects of health care. Very few applications

currently exist, and the field looks forward to the development of these methods for comparative effectiveness studies.

Discussion

Dr. Kaplan explained that the questions asked to generate utility weights are straightforward and quality-of-life ratings tend to be surprisingly consistent. Ratings tend to vary minimally across socioeconomic states, and much less variability exists between people who have experienced a condition than among those who have not. Although quality-of-life ratings vary, those of individuals in wheelchairs and people who have never been in a wheelchair are remarkably similar.

A participant asked about the use of disability-adjusted life years (DALYs). Dr. Kaplan explained that certain areas of the world have embraced this measure, which uses a similar methodology to the QALY and adjusts life expectancy for years without disability

Dr. Marmor suggested that using the term “quality of life” hides heterogeneity in how individuals construe the quality of their lives and presents problems for communicating about health to political leaders. Two people in the same physical state can have dramatically different perspectives about their personal happiness, functional capability, and depression status. Dr. Kaplan added that although multiple indicators are important, a judgment must ultimately be made about whether a treatment is effective, and explicitly quantifying that in a single measure is helpful.

Estimating Costs

Dr. Martin Brown, National Cancer Institute, National Institutes of Health

Dr. Brown reported that NCI, AHRQ, and the Veterans Administration (VA) sponsored a workshop on cost estimation (<http://healthservices.cancer.gov/publications/workshops/hcc>) that resulted in a supplement published in *Medical Care*.⁵

Aggregate estimates of current incidence, survival, and costs burden and future trends are useful for policy and program planning. These estimates can be used to evaluate specific services or components of care or to evaluate the care trajectory. For nutritional interventions, aggregate costs could be used in broad policy analyses. Longitudinal costs represent longitudinal per-person estimates that are useful for CEA and at the disease category level for tracking costs for individuals over long periods. These estimates reflect current patterns of care, not idealized care.

Challenges in measuring longitudinal patterns of cost include

- The clinically appropriate definition of “episode of care” can vary by disease or condition, severity of disease, or nature of the disease control intervention.
- The flow of cost might not be constant within episodes of care.
- The assignment of mutually exclusive and exhaustive costs (making sure that all costs are assigned to some disease or condition) to disease entities is not obvious.
- Medical technology, practice patterns, and cost are dynamic, but health cost data are cross-sectional or longitudinal over a relatively short observation period.

In the “phase of care” approach, costs are segmented into phases that correspond to periods of differing average intensities of care, which avoids biases and allows use of the maximal amount of data. Within the observation window, some patients experience an initial phase of care (a high-cost component of care), some patients experience a late stage of care (also a high-cost component), and some patients are in the intermediate stage of care. Data on all of these patients can be used to estimate costs for these different phases of care. These phase-specific estimates can be combined with the population-based incidence data on individuals in those stages to construct a pseudo-longitudinal estimation of cost and combine these phase-specific estimates with prevalence-specific estimates to construct an estimate of prevalence cost. Without this type of approach, researchers risk developing misleading comparisons of cost.

This method can be applied to other aspects of cost, such as patient time costs. Engaging in health care activities uses time that could be used doing other activities, but time costs are not taken into account in the vast majority of health economics studies. Although some studies have shown that time-related costs are substantial, these studies included only small convenience samples, focused on specific aspects of care, and did not compare the intervention studied to “regular” or “routine” care.

Sensitivity Analysis and Uncertainty

Dr. Milton Weinstein, Harvard University

The types of uncertainty associated with economic evaluation include: 1) outcomes (e.g., what will be the outcomes for the actual population of interest?); 2) parameters (e.g., what are the probabilities, utilities, and costs that govern the actual outcomes?); 3) methodology (e.g., what costs and consequences should be included and how should they be valued?); and 4) model structures (e.g., what are the structural and causal relationships among the variables of interest?). Parameter uncertainty can include probabilities of disease prevalence and incidence, rates of disease progression, and treatment efficacy; health state utilities; and costs. Sources of uncertainty in parameter estimates include sampling variation and internal and external study validity.

Probabilistic sensitivity analysis for CEA involves representing the uncertainty about the parameters in a given analysis as probability distributions. Adding this type of analysis to the model used to develop cost-effectiveness ratios produces a distribution of cost-effectiveness results. CEA results consist of an incremental effectiveness change (a QALY gain or loss) and an incremental cost or cost saving. Although doing so is statistically complex, a joint distribution of the incremental effectiveness and incremental costs of an intervention can be compared with those of another intervention.

The most common method for calculating distributions of inputs that lead to distributions of CEA outputs is Monte Carlo decision modeling, which requires the use of subjective distributions. Another approach commonly used with clinical trial data is non-parametric bootstrapping with replacement. Methods to generate distributions around outputs include joint probability distribution of incremental cost and incremental effectiveness, distribution of net monetary benefit, and cost-effectiveness acceptability curves. The joint distribution of

incremental cost and incremental effectiveness can be used to determine the probability that the result is cost effective relative to some WTP threshold.

Common “throw-away” types of statements that often appear in the discussion sections of papers, such as “more research is needed” or “we have insufficient evidence from which to draw definite conclusions,” have little value. How do the authors know whether more research is needed? How consequential is this additional research? Mounting a large, expensive study might not be necessary to resolve a question for which little is at stake. Furthermore, CMS might not have time to wait for such a study to be conducted before making a decision on coverage. The most helpful type of uncertainty analysis for decision makers is the value-of-information analysis that shows, for example, the importance of finding out a parameter’s true value or reducing a parameter’s uncertainty.

¹ Marmor T, Oberlander J, White J. The Obama administration’s options for health care cost control: hope versus reality. *Ann Intern Med.* 2009;150(7):485-489.

² Aaron HJ, Schwartz WB. *The Painful Prescription: Rationing Hospital Care.* Washington, DC: The Brookings Institution; 1984.

³ Hartman M, Martin A, Nuccio O, Catlin A; and National Health Expenditure Accounts Team. Health spending growth at a historic low in 2008. *Health Aff.* 2010;29(1):147-155.

⁴ Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine.* New York: Oxford; 1996.

⁵ Lipscomb J, Yabroff KR, Brown ML, Lawrence W, Barnett PG. Health care costing: data, methods, current applications. *Med Care.* 2009;47(7)(Supp 1):S1-S6.