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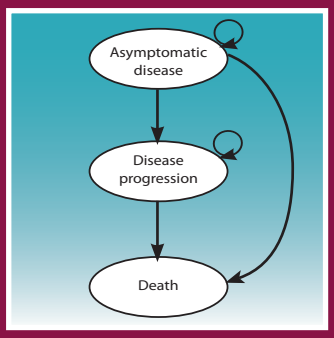

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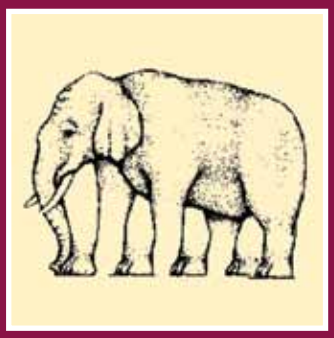

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WHAT IS HEALTH ECONOMICS AND OUTCOMES RESEARCH? A PRIMER FOR MEDICAL WRITERS*

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ABSTRACT

Increasingly, medical writers are being asked to work with health economics and outcomes research (HEOR) information. HEOR uses data from both economic and clinical research to assess the clinical and economic value of new treatments. Many medical writers have the underlying skills required to incorporate HEOR concepts into their work but need more background to do this comfortably. This article provides an introduction to health economics study design, key terms, and commonly used outcomes research approaches. It also describes how health economics writing resembles and differs from traditional medical writing. It briefly explores the present and future role of HEOR in US health policy.

Fundamentally, health economics and outcomes research (HEOR) consists of two areas: analyses that attempt to estimate the economic effect of a specific intervention before it is implemented, and outcomes research or tools used to assess the economic and/or quality-of-life value of an ongoing or anticipated intervention. Health economists evaluate the economic and clinical aspects of health and health care provision, with a focus on the costs (otherwise known as inputs) and the consequences (outcomes) of health care interventions. Outcomes research evaluates the effect of health care interventions on patient-related clinical, humanistic, and economic outcomes. Pharmacoeconomics, a subdiscipline of health economics, is used to estimate the value of pharmacy costs and services.[1,2]

** This article is based, in part, on a presentation delivered at AMWA's 72nd Annual Conference in Sacramento, CA, October 2012.*

Many organizations use health economics data. For example, private insurance plans use health economics information to determine which drugs will be covered, under what circumstances, and at what price level. Health care purchasing agents (for example, in hospital settings) may use health economics data to guide durable equipment purchase choices.[2] National health care systems in many European nations have long used health economics information when determining whether treatments are eligible for coverage. The United States, on the other hand, has only more recently started to acknowledge the role of health economics.[2,3]

Because of the progressive rise of health care expenditures, HEOR analyses are being given closer attention in the United States. For some time, health care costs have been rising at more than the average rate of inflation, and it has been estimated that US health care costs will continue to rise at an annual rate of more than 6% between now and 2020.[4] These rising expenditures are driven, in part, by increased rates of chronic disease, as well as a heightened volume of care (in which new treatments are introduced, expanding the spectrum of care but without replacing existing treatments).[5]

TYPES OF HEALTH ECONOMICS RESEARCH

At the most basic level, health economics analyses assess the cost differences between two alternative treatments. Table 1 lists and briefly describes some of the most common types of health economics analyses. It is important to understand how cost estimates are categorized. The common categories are direct medical costs, direct nonmedical costs, indirect costs, and intangible costs (Table 2). Box 1 defines two common concepts used in cost-effectiveness analyses (CEAs) and cost-utility analyses (CUAs): the incremental cost-effectiveness ratio (ICER), and the quality-adjusted life-year (QALY).

Acronyms

BIA: budget impact analysis
CBA: cost-benefit analysis
CCA: cost-consequences analysis
CEA: cost-effectiveness analysis
CER: comparative effectiveness research
CMA: cost-minimization analysis
CHEERS: Consolidated Health Economic Evaluation Reporting Standards
DRG: diagnosis-related group
HCUP: Healthcare Cost and Utilization Project
HEOR: health economics and outcomes research
HRQoL: health-related quality of life
ICER: incremental cost-effectiveness ratio
ISPOR: International Society for Pharmcoeconomics and Outcomes Research
PCORI: Patient-Centered Outcomes Research Institute
PROs: patient-reported outcomes
QALY: quality-adjusted life-year

The most common format for presenting HEOR results is the retrospective database analysis. These analyses evaluate health care utilization as it occurs in routine clinical care. Typically, these studies obtain information from patient databases (maintained by payers and other organizations). In this way, these studies can track a large number of patients over time. It is a relatively inexpensive way to evaluate the effect of treatment at the population level.[1,2]

There are two other concepts to keep in mind when reading and evaluating health economics literature: discounting and sensitivity analyses. "Discounting" is a method to adjust

Table 1. The Most Common Types of Health Economic Analyses[1,2]

Cost-consequences analysis (CCA)	Estimates the cost and value of interventions, but leaves it to the reader to draw conclusions based on available data. ***Example:*** *A CCA could be used to compare two drugs to prevent transplant organ rejection in a hospital setting. To accomplish this, the study must determine costs associated with key inputs (eg, drugs, rejection treatment, graft survival/dialysis), as well as the probability of consequences associated with both treatment approaches (eg, rejection).*
Cost-minimization analysis (CMA)	Compares input costs, but assumes outcomes are equivalent. ***Example:*** *A CMA could be used to compare the hospital costs associated with inpatient versus outpatient care of pregnant women following the administration of prostaglandin E2 gel to stimulate labor. This analysis assumes that patients have the same outcomes, regardless of treatment, and direct cost comparison is the primary goal.*
Cost-effectiveness analysis (CEA)	Measures costs in dollars and reports outcomes in natural health units (for example, mm Hg reduction for blood pressure studies) or ratios (differences in cost divided by difference in outcomes). ***Example:*** *A CEA could be used to compare three different ulcer treatments, each with varying annual costs and projected healing rates. To make the study results meaningful for clinicians, outcome units unique to the study (eg, gastrointestinal symptom–free days) are often applied.*
Cost-utility analysis (CUA)	Measures outcomes based on years of life gained and quality of life obtained with treatment. ***Example:*** *Two oncology drugs could be evaluated by using a CUA to determine how their cost, associated months/years of life gained, and/or effect on patient quality of life interact. By taking patient outcomes and preferences into account, a CUA provides a more comprehensive, but still cost-based, understanding of the drugs' effects.*
Cost-benefit analysis (CBA)	Enumerates and compares costs and benefits achieved in monetary terms. ***Example:*** *A health authority could use a CBA to project whether a vaccination program is likely to lead to an improved cost-benefit outcome versus not implementing the program.*
Budget impact analysis (BIA)	Estimates effect of an intervention in terms of overall cost to organization or health plan. ***Example:*** *A health plan might use a BIA to assess how much it will cost to treat multiple myeloma patients with Drug A compared with Drug B. The study would measure the net cumulative direct costs of treatment for a given number of patients in a specific population.*

future costs and benefits (in particular, those occurring over periods longer than 1 year) to their present economic value. Discounting is a common practice in multiyear economic analyses. Typically, future costs are discounted between 3% and 5% annually. Discounting should not be confused with upward price adjustment for inflation, which is also commonly performed in retrospective studies lasting more than 1 year.[1,2]

Additionally, sensitivity analyses are often incorporated into HEOR evaluations. A sensitivity analysis assesses the effect of uncertainty on an economic analysis or decision. It is a widely accepted way to verify the strength of the results. In a sensitivity analysis, selected assumptions underlying the analysis are altered to see how this affects overall results. For example, if the initial study protocol assumed a mortality rate of 3% with a particular treatment, investigators might rerun the analysis with mortality rates of 1% and 5%.[1,2] Other variables that might be subject to sensitivity analysis include drug costs, length of hospital stay, or treatment duration.

One final requirement of a successful health economics analysis is the a priori identification of the study's perspective. In HEOR, the term *perspective* refers to exactly which costs, or "whose costs," will be measured based on the purpose of the study. For example, if the perspective is that of the payer (an insurance company or national health care system), the analysis is likely to consider direct medical costs that accrue to the health plan over the short or long term. If the analysis is assessing costs to a hospital, an institutional perspective would be appropriate. In this case, evaluation would typically be limited to the direct costs associated with treatment and/or costs due to preventable readmissions.

Table 2. Cost Categories[2]

Cost Category Type	Examples
Direct medical costs	• Medications
	• Medication monitoring
	• Medication administration
	• Patient counseling and consultation
	• Diagnostic tests
	• Hospitalizations
	• Clinic visits
	• Emergency department visits
	• Home medical visits
	• Ambulance services
	• Nursing services
Direct nonmedical costs	• Travel costs to receive health care (bus, gas, taxi)
	• Nonmedical assistance related to condition (eg, Meals on Wheels, homemaking services)
	• Hotel stays for patient or family for out-of-town care
	• Child care services for children of patients
Indirect costs	• Lost productivity for patient
	• Lost productivity for unpaid caregiver (eg, family member, neighbor, friend)
	• Lost productivity because of premature mortality
Intangible costs	• Pain and suffering
	• Fatigue
	• Anxiety

Box 1. Key Concepts: the ICER and the QALY[2,6]

ICER: Incremental Cost-Effectiveness Ratio	QALY: Quality-Adjusted Life Year
• ICERs can be used in cost-effective analyses and cost-utility analyses. • The ICER is the ratio of the difference in cost, divided by the difference in outcomes. • It answers the question, "How does one treatment compare with another in terms of costs and outcomes?" • If the ICER calculation leads to a negative number, one treatment is "dominant" (ie, more effective and less expensive) compared with the other. If the ICER is positive, other factors must be taken into consideration to determine which treatment is preferable in which circumstances.	• QALYs are typically used in cost-utility analyses. • A QALY combines in a single measure gains or losses to both quantity of life (ie, mortality) and quality of life, for each treatment option. • The QALY equation assumes that 1 year of life lived in perfect health is worth 1 QALY. • The use of this single, common measure enables comparisons of outcomes across multiple studies, and even multiple disease states (for example, for resource allocation decisions). • QALYs are most applicable to research or population-based decision-making; they do not translate very well for day-to-day or individual patient decisions.

It is also important to mention the societal perspective. This approach is considered the most comprehensive method to evaluate a program from a health economics viewpoint, although it is most applicable where health care is nationalized. The societal perspective is not widely applied in US studies. This perspective incorporates all the cost considerations discussed above but also considers the direct and indirect treatment-related costs that patients and society must bear, such as copayments and financial losses due to decreased productivity.[2,3]

THE ROLE OF MODELING IN HEOR ANALYSES

Health economics research is heavily dependent on modeling techniques. Some modeling approaches require a computer and dedicated software, whereas others are more straightforward. The creation of a decision tree is a common first step in model design (Figure 1). A decision tree provides a framework to systematically compare different decision options and subsequent potential patient outcomes.

In this example, Figure 1 compares two treatment options for pressure ulcer (Treatment A and Treatment B). Immediately after treatment application, three disease states are possible (epithelialized, proliferative, or necrotic wound). Over time, three outcomes are possible (closure, granulation, or an ongoing chronic wound). In a more detailed decision tree, probability data for the three final outcomes would also be displayed on the tree branches. This image depicts a straightforward decision tree and represents a situation in which treatment options, duration of therapy, and timeframe under consideration are limited. The condition of the wound and the outcomes of treatment can be easily classified into a manageable number of states.

However, this type of model would not be feasible in situations in which multiple treatment options and multiple patient outcomes are possible (for example, when assessing the effect

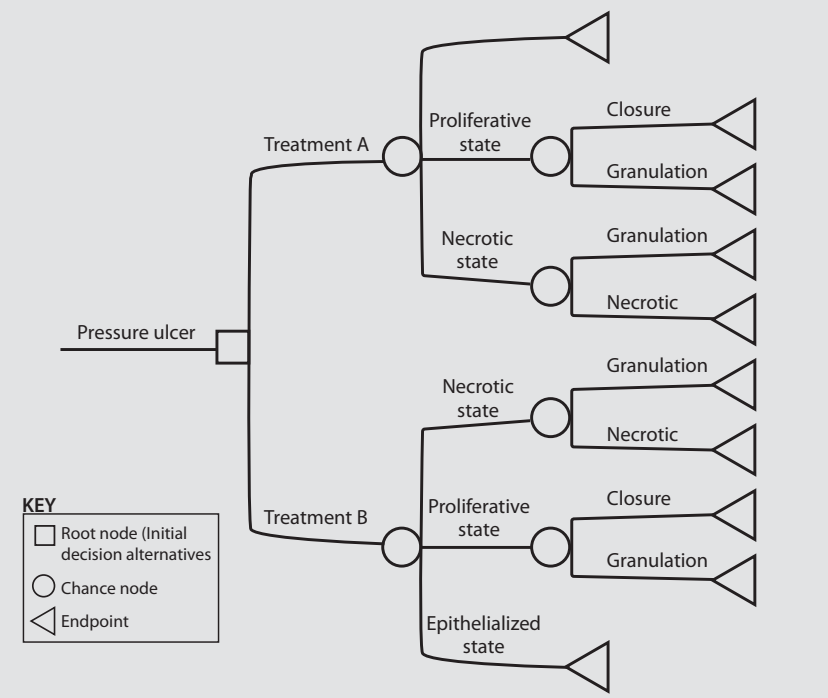

Figure 1. *A decision tree comparing two treatments for pressure ulcers.*

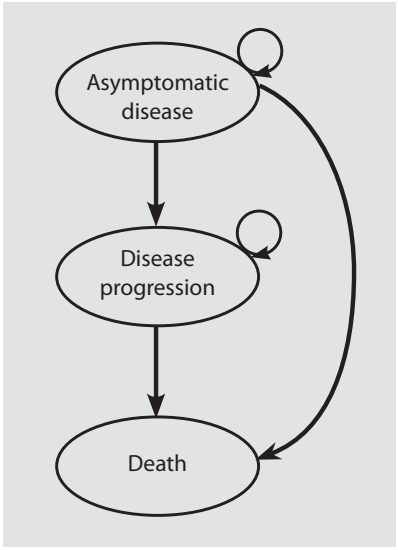

Figure 2. *Representation of a Markov model of disease progression.*

of different treatments over time in patients with type 2 diabetes). In such cases, a more sophisticated approach, such as a Markov model of disease progression, is more appropriate. Markov models are useful in situations in which patient risk is ongoing over time, multiple outcomes are possible, event timing must be considered or cannot be predicted, and disease-related events (eg, a myocardial infarction) may occur more than once.[7]

Markov models are programmed using a theoretical patient cohort; these data are often obtained from clinical trials. Within the model, it is assumed that a patient is always in one of a finite number of discrete health states. Patient "events" take place when a transition occurs from one state to another, and the model typically concludes for all patients in death or some other predetermined endpoint.[7] Figure 2 shows a basic representation of a Markov model, in which patients can move from asymptomatic disease to disease progression to death—or can transition back and forth between asymptomatic and progressive disease.

DATA SOURCES FOR HEALTH ECONOMICS ANALYSES

The accuracy of any health economics analysis is dependent on the quality and applicability of study data. The primary inputs used in HEOR analyses are clinical outcomes, their associated costs, and patient preference information.

Often, clinical outcomes and cost data are obtained from clinical trials of the treatment in question. Economic evaluations may be conducted simultaneously with clinical trials. However, when this is not feasible, investigators must rely on the published literature, existing databases, and even expert opinion (in cases in which limited evidence is available) to identify appropriate inputs. One of the greatest challenges in identifying appropriate cost data is determining whether the information available is generalizable to the patient population being evaluated.[2,8]

Data sources can include clinical trials conducted by other investigators, medical records, or reimbursement claims.[9] Costs can also be estimated by using standard reimbursement information, such as that available from the Centers for Medicaid and Medicare Services for diagnosis-related groups (DRGs), or via databases that track hospital charges and costs.[2] One such database is the Agency for Health Quality and Research's Healthcare Cost and Utilization Project (HCUP). HCUPnet, at **http://hcupnet.ahrq.gov**, is a free, online query system that provides diagnosis- or procedure-specific data for US hospital inpatient and emergency departments, as well as associated hospital charges and costs.[10]

Health economics cost-utility analyses also use data points know as utilities. A utility is a measure that assesses patients' or other stakeholders' preferences for an outcome. Typically, it is expressed as a value between 0 (representing death) and 1 (representing perfect health). As an example of the utility concept, patients facing dual lower-extremity amputation might rank their utility at 0.2. On the other hand, patients with moderate seasonal allergies might assign a utility of 0.9 to their condition. Utilities may also be calculated from another perspective in cases in which input from another source (such as the treating physician) is relevant. In essence, utility measures provide a way to quantify qualitative input to provide summary scores that

consider both the positive and negative aspects of treatment on health and quality-of-life outcomes.[11]

Utilities often overlap with patient-reported outcomes (PROs), although the terms are not synonyms. PRO is an umbrella term for input provided directly by patients regarding their treatment preferences. Typically, PRO instruments rely heavily on qualitative input for development, but are subsequently translated into a validated numeric scoring system.[12] Information sources for PROs can include assessment tools that capture information on patients' global impressions, functional status, well-being, symptoms, treatment satisfaction, health-related quality of life (HRQoL), and treatment adherence. PROs are increasingly common in economic and clinical research, with multiple instruments (both disease-specific and designed to assess general health) being developed and validated.[1,13] Because patient preferences can substantially influence whether a treatment is properly used or adhered to, payers and regulators are recognizing the value of PROs in drug development. Likewise, drug developers are recognizing the potential for PRO information to improve their products' competitive profiles and likelihood of formulary acceptance.[14] In acknowledgment of the increased relevance of PRO data in clinical research, the US Food and Drug Administration published guidelines in 2009 for the use of PROs in medical product development.[15]

THE ROLE OF THE MEDICAL WRITER IN HEOR

The HEOR field has visibly expanded in the United States in recent years. Numerous journals devoted to the health economics literature have emerged, targeted to managed care plan executives, pharmacy benefit and formulary managers, government officials, and other key decision-makers. Examples of journals in the field include *Health Economics, Journal of Health Economics, Journal of Managed Care Pharmacy*, and *Value in Health*. It is also becoming common for pharmaceutical and device companies, as well as health insurance companies, to have internal HEOR departments. Typically, however, a substantial proportion of the writing and other professional HEOR work of these organizations is outsourced.[16] Academia generates a huge number of HEOR analyses, most often through programs affiliated with pharmacy and/or public health.

Figure 3 illustrates the growth in HEOR-related medical writing over the past 20 years. This image is based on a PubMed search conducted to track the number of published studies with the term "cost-effectiveness" in the title (search term *1992:2012[pdat] AND cost-effectiveness[title]*). Growth has been quite steady, with only 139 publications in 1992 and 1,045 for 2012.

Health economics writers almost always bring value beyond writing skills to an HEOR project. Beyond medical writing capabilities, there are some additional skills an HEOR writer should possess. These observations are based on my 7 years of work in this field. First and most important is a willingness to work directly with numbers. Health economics writers are often presented with raw data or data that must be reviewed closely, double-checked, and formatted before any writing begins. Second, it is not unusual for an HEOR writer to have to fully understand the primary study data. This is because, compared with analyses of clinical trials, health economics analyses are likely to have fewer authors who comprehend the mathematical aspects of the work. Third, a concise writing style is also important, because an additional, documented challenge to preparing HEOR analyses for publication is the need to report cost-related items (that would not be required in a purely clinical study) in the methods section of a document.[17]

HOW HEALTH ECONOMICS INFORMATION IS USED IN THE UNITED STATES

The 2009 American Recovery and Reinvestment Act provided funding to set priorities for comparative effectiveness research (CER) in the United States. The Patient Protection and Affordable Care Act (PPACA), passed in 2010, created the Patient-Centered Outcomes Research Institute (PCORI). PCORI's mission is to commission evidence-based research that enables patients and providers to make informed decisions about the range of available preventive and treatment options for any condition.[18,19] However,

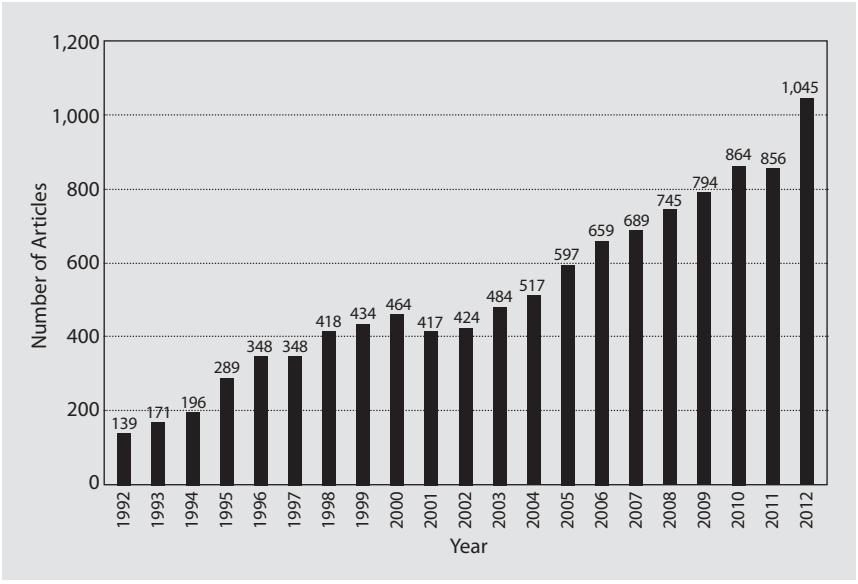

Figure 3. *Growth in health-economics–related publications: 1992 to 2012.*

a stipulation in the Affordable Care Act specifies that PCORI could not develop or employ any instrument with a dollar per QALY approach to set a threshold on which interventions are considered to be cost-effective.[20] This only applies to the federally funded PCORI program; private insurers are free to adopt their own standards or approaches.

Peter Neumann, ScD, a professor of medicine of Tufts University, wrote in a 2012 article that the current health care conversation in the United States "allows little space for cost concerns. It ignores resource constraints and has an unreal, wishful quality to it, as though skydivers could defy gravity by cleverly talking their way around it." He noted that no key stakeholders have yet been willing to acknowledge that getting a handle on cost growth will require uncomfortable trade-offs.[21]

Why is there so much resistance to the use of health economics data in the United States? Perceptions have long existed that US health care resources are not really constrained, although this outlook is changing. There is also substantial political resistance to the use of HEOR in decision-making. Additionally, a lack of trust between payers (insurers) and manufacturers (pharmaceutical/device companies) is a concern. It has also been noted that an overemphasis on health economics requirements might harm innovation or affect the development of new medical technology (where a higher price typically goes hand-in-hand with advancement). Last, there are genuine concerns that health economic information is not currently being developed in a timely and transparent way, and that many key decision-makers lack the expertise to prepare, review, communicate, or fully understand findings from health economics research. These discussions are ongoing, with multiple stakeholders trying to determine the best way to make HEOR communications more straightforward.[2,22]

A step toward optimizing the reporting of HEOR publications was recently taken by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) with the publication of their Consolidated Health Economic Evaluation Reporting Standards (CHEERS). This document consolidates input from multiple prior publications (timeframe 1996 to 2011) into a single standard and provides detailed recommendations and a checklist for the appropriate reporting of HEOR data for publication.[17, 23]

CONCLUSION

Each health care decision made by an individual or institution has clinical and resource implications. Health economics research helps health care purchasers and consumers understand not only the clinical efficacy and safety of treatments, but their overall value in terms of cost and patient preferences. In this way, health economics is broadening our concept of evidence-based medicine and guiding us toward improved decision-making. HEOR analyses are an increasingly common component of clinical research and an emerging area of specialization in medical writing. It is likely that most medical writers will be exposed to HEOR concepts as part of their professional work; therefore, it is important for them to be familiar with HEOR concepts and terminology.

➲ *For readers interested in learning more about HEOR concepts and practices, references 1, 2, 3, 9, 12, and 17 are highly recommended as additional reading.*

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