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Economic Analysis of Secondary Trial Data

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Abstract Clinical trials may furnish data to conduct economic analyses. An economic analysis requires us to identify all opportunity costs associated with the intervention over the time horizon chosen for the analysis and enumerate the improvements in benefits from the intervention of interest. We review the basic steps used when performing economic studies based on secondary analysis of data from clinical trials using examples from myocardial infarction studies. Different types of economic analyses and the potential contributions of Markov modeling are described. Issues of measuring quality of life, patient utilities, cost of care, and potential sources of cost data are reviewed. The interpretation of incremental cost-effectiveness ratios is discussed and economic benchmarks for defining good and poor value interventions are provided. (Prog Cardiovasc Dis 2012;54:351-356)

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Clinical trials have the potential for furnishing data to conduct economic analyses based on secondary analysis of trial data. The strength of an economic study based on such post hoc analysis will depend on the trial variables available and how well the trial population and outcomes measured can be combined with cost and epidemiological data available for the disease [1]. The general approach to studies that compare the economic differences between 2 treatment approaches is often termed a "cost-benefit analysis." However, a true cost-benefit analysis is rarely performed for medical interventions because it requires translating of the study benefit, such as preventing a myocardial infarction (MI) death, into a monetary value (eg, 1 death, $500,000) to calculate a net monetary benefit for a treatment. Thus, most economic analyses reported for medical interventions compare costs per health benefit achieved. These types of economic comparisons are called "cost-effectiveness analysis" (CEA) or "cost utility analysis" (CUA) studies [2]. A cost-effectiveness study compares the cost of achieving the main clinical outcome for the study, such as cost per MI death avoided. A cost utility study compares the cost per additional quality-adjusted year of life (QALY) expected for patients given the different study treatments. A CEA may rely mainly on the short-term clinical differences observed at the end of a trial, whereas a CUA would estimate the difference over patients remaining life expectancy based on archival epidemiological data for the condition. Clearly, the lifetime estimate is more likely to capture the full benefit of the intervention, whereas the short-term cost-effectiveness approach is less vulnerable to bias from assumptions related to prediction of future outcomes based on historical data.

The general approach to either a CEA or a CUA is similar with regard to resource use and cost data but differ in regard to the kind of clinical or patient-related outcomes measured. Fundamentally, an economic analysis requires us to identify all opportunity costs associated with the intervention over the time horizon chosen for the analysis and enumerate the improvements in benefits from the intervention of interest. The first step is to define the

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Abbreviations and Acronyms

ADL = activities of daily living

CEA = cost-effectiveness analysis

CR = cardiac rehabilitation

CUA = cost-utility analysis

HRQoL = health-related quality of life

ICER = incremental cost effectiveness ratio

LOS = length of stay (hospital)

MI = myocardial infarction

QALY = quality-adjusted life years

costing perspective of the analysis. The perspective can be that of society, which includes medical care and lost employment time and wages. Often the perspective is defined in a more limited way to costs incurred within the medical care system or even more narrowly as the perspective of the payer. The strengths and weaknesses of each perspective and specifications for which types of costs to include in each perspective are defined in recommendations developed for the United States by an expert group [3]. Step 2 is to identify the clinical benefits, which includes identifying how best to link clinical trial data on secondary health indicators, such as reduction in blood pressure or improvement in ejection fraction, to primary health indicators such as level of morbidity, improved life expectancy, quality of life measures, and/or patients' preferences for specific health outcomes (utility weights). Once all costs and benefits have been identified, we can calculate the cost required to get an additional unit of benefit. This is called an incremental cost-effectiveness ratio (ICER), which is the accepted economic measure of the value of a new intervention. For a study of an intervention to improve the outcomes for a MI, a CEA would calculate cost per death averted, whereas a CUA would report cost per QALY gained by using the improved treatment. Throughout this article, we use MI as the example, but any cardiovascular outcome could be considered for an economic analysis.

Myocardial infarction is responsible for nearly 1 million acute hospital admissions per year in the United States. The condition costs $15,000 to $20,000 per admission to treat [4]. Thus, a new approach to treating MI could potentially have large economic implications for hospitals, insurers, and patients. The new approach could reduce the length of stay (LOS) in the coronary care unit as well as decrease hospital LOS. If it decreases the damage to the heart, it may also reduce posthospital care and greatly improve patients' health-related quality of life (HRQoL). However, the changes in the prehospital process because of the new approach may require extra resources and, thus, incur an added cost. In an era of increasing pressures to contain health care costs, it is important that the cost implications of new treatments be understood before new approaches are broadly implemented. This may help speed along the adoption of a cost-effective new treatment and slow or halt the diffusion of interventions that do not deliver good value for our health care dollars.

Table 1
Variables required for a cost-utility analysis

Variables	Essential	Nice to Have	Can be Derived From Other Sources
Outcome measure	x		
Hospital length of stay	x		
Source of admission (from home, from nursing home)		x	
Discharge destination (home, home health, rehabilitation, nursing home)	x		
HRQoL		x	
ADL	x		
Comorbidities	x		
Utility weights			x
Cardiac rehabilitation use		x	
Cost of hospital admission			x
Postdischarge visits			x
Drug costs postdischarge			x

To perform a detailed "piggy-back" economic study on a clinical trial ideally requires some data on resource use both prehospital and posthospital admission. Table 1 gives suggestions of what would be needed. Data on HRQoL and activities of daily living (ADL) would facilitate understanding of the effect of the new approach on each stage in the continuum of care.

Estimating cost for the MI episode

The major difference in cost for an MI episode treated with a new approach may be assumed to be apparent after 30 days. For other cardiovascular outcomes, this time frame may differ. Within the first month of an MI, most patients will accrue all the acute care hospital cost and a substantial amount of the cardiac rehabilitation costs that may be expected to be affected by difference in the percent of loss of myocardium. After that time, much of the variation in cost may be influenced by the patient's preference for (or economic access to) cardiac rehabilitation and/or the success with which patients follow medical directions to prevent worsening of their condition. If a time horizon of more than 30 days is used, then the measured resource use will also, increasingly, be affected by patients' adherence (or nonadherence) to the recommended lifestyle changes as well as the effects of their comorbid conditions.

Assuming the data will come from multisite trials, neither charges nor estimated costs may be assumed to be similar across the sites; only data on resource use would