The Value of Critical Care

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NOTE TO THE READER

Your humble correspondents, in seeking editorial guidance as to the scope of this essay, were advised to interpret our charge as we see fit. Whereas your essayists generally feel no qualms regarding what to write, the term “value” has many meanings and connotations. At the risk of imposing our own “values” (biases) on the reader, it is hoped that the reader will find “value” from the reading of this contribution.

INTRODUCTION

“Value” has many connotations (Box 1, Fig. 1). Applied to critical care, the meaning may be economic (is this a “reasonable” use of resources?), ethical (is this something that the patient wants?), or philosophic (the old cliché, “how do you put a value on a human life?”). The only aspect that can really be quantified is the former, and even then the numbers of studies are few that have brought analytical rigor to the question of the “value of critical care.” With the predicates that lower mortality/better surgical outcomes and lower resource use are desirable, and that measuring and

KEYWORDS

• Critical care • Cost-effectiveness • Cost analysis • Value definitions

KEY POINTS

• The rapid growth in health care expenditure has engendered careful scrutiny of the practice of medicine with regard not only to effectiveness but also to efficiency.
• Physicians must understand the effectiveness of their interventions and the cost at which this effectiveness is obtained.
• As physicians and policy-makers encounter cost-effectiveness analyses in the literature, they must evaluate such studies as they would any clinical study—with caution, skepticism, and attention to the methods used.
• There is a growing interest in the application of emerging methodology to quantify the value of health care interventions by applying the methods of economics.
• Specific critical care inventions have been demonstrated to be cost-effective.
recording outcomes remains challenging, especially for heterogeneous patient populations or when the interactions of multiple coexisting conditions may be confounding, the primary focus of this review is on the cost-effectiveness of critical care.

Surgical mortality appears to be decreasing. Using the Nationwide Inpatient Sample, Semel and colleagues compared deaths within 30 days of admission for patients

| Box 1 |
| Dictionary definition of “value” |

val·ue [val-yoo] noun, verb, val·ued, val·u·ing. Noun, verb.

c.1300, from Old French value “worth, value” (13c.), noun use of feminine past participle of valoir “be worth,” from Latin valere “be strong, be well, be of value” (see valiant). The verb is recorded from late 15c.

noun

1. Relative worth, merit, or importance: the value of a college education; the value of a queen in chess.

2. Monetary or material worth, as in commerce or trade: This piece of land has greatly increased in value.

3. The worth of something in terms of the amount of other things for which it can be exchanged or in terms of some medium of exchange.

4. Equivalent worth or return in money, material, services, etc.: to give value for value received.

5. Estimated or assigned worth; valuation: a painting with a current value of $500,000.

6. Denomination, as of a monetary issue or a postage stamp.

7. (Mathematics). (A) Magnitude; quantity; number represented by a figure, symbol, or the like: the value of an angle; the value of x; the value of a sum. (B) A point in the range of a function; a point in the range corresponding to a given point in the domain of a function: The value of $x^2$ at 2 is 4.

8. Import or meaning; force; significance: the value of a word.

9. Liking or affection; favorable regard.

10. Values (Sociology). the ideals, customs, institutions, etc., of a society toward which the people of the group have an affective regard. These values may be positive, as cleanliness, freedom, or education, or negative, as cruelty, crime, or blasphemy.

11. (Ethics). any object or quality desirable as a means or as an end in itself.

12. (Fine Arts). (A) Degree of lightness or darkness in a color. (B) The relation of light and shade in a painting, drawing, or the like.

13. (Music). the relative length or duration of a tone signified by a note.

14. Values (Mining). the marketable portions of an ore body.

15. (Phonetics). (A) Quality. (B) The phonetic equivalent of a letter, as the sound of “a” in hat, sang, etc.

verb (used with object)

16. To calculate or reckon the monetary value of; give a specified material or financial value to; assess; appraise: to value their assets.

17. To consider with respect to worth, excellence, usefulness, or importance.

18. To regard or esteem highly: He values her friendship.


Surgical mortality appears to be decreasing. Using the Nationwide Inpatient Sample, Semel and colleagues compared deaths within 30 days of admission for patients
undergoing 2520 different surgical procedures in 1996 and 2006. The inpatient 30-day death rate was examined for all procedures, procedures with the most deaths, high-risk cardiovascular and cancer procedures, and patients who suffered a recorded complication. Logistic regression modeling was used to adjust 1996 mortality rates to the age and gender distributions for patients undergoing surgery in 2006. In 1996 there were 12,573,331 admissions with a surgical procedure (95% confidence interval [CI], 12,560,171–12,586,491) and 224,111 inpatient deaths within 30 days of admission (95% CI, 221,912–226,310). In 2006 there were 14,333,993 admissions with a surgical procedure (95% CI, 14,320,983–14,347,002) and 189,690 deaths (95% CI, 187,802–191,578). The inpatient 30-day mortality decreased from 1.78% in 1996 to 1.33% in 2006 (P<.001). Of the 21 procedures with the most deaths in 1996, 15 had significant decreases in adjusted mortality in 2006 (Table 1). Among these 15 procedures, 8 had significant decreases in operative volume. Comparing 1996 and 2006, the inpatient 30-day mortality rate for patients who suffered a complication decreased from 12.10% to 9.84% (P<.001). Although there are myriad factors that contribute to
decreased surgical mortality, the decreases among elderly patients, after high-risk procedures, and after major complications suggest that the decreases in mortality are due in part to advances in surgical critical care. Note in particular the decreases in mortality from complications related to infection/sepsis (see Table 1).

Mortality in the intensive care unit (ICU) may also be decreasing. Although data from population-based samples are lacking, data are available from sequential reports from major centers,9–14 and inferences can be drawn from results of clinical trials (eg, severe sepsis/septic shock).15–19 Ironically, the decreased mortality from septic shock occasioned by the implementation of evidence-based best practices, perhaps unanticipated or of greater magnitude than believed possible, may be confounding ongoing clinical research in the field.19,20

**METHODS FOR EVALUATING COST-EFFECTIVENESS**

**Quality of Life**

Quality of life (QoL) is an amorphous concept that has usage across many disciplines, including health economics. It is a vague concept; it is multidimensional and

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>30-Day Mortality Rate</th>
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<tbody>
<tr>
<td></td>
<td>1996% (95% CI)</td>
<td>2006% (95% CI)</td>
<td>P Value</td>
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<td><strong>Admission type</strong></td>
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<tr>
<td>Emergency</td>
<td>3.65</td>
<td>2.62</td>
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<tr>
<td>Urgent</td>
<td>1.83</td>
<td>1.48</td>
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<td><strong>Charlson Comorbidity Index</strong></td>
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<tr>
<td>3</td>
<td>4.73</td>
<td>3.27</td>
<td>&lt;.001</td>
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<tr>
<td>≥4</td>
<td>6.94</td>
<td>4.84</td>
<td>&lt;.001</td>
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<tr>
<td><strong>High number of deaths</strong></td>
<td></td>
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<tr>
<td>Coronary artery bypass</td>
<td>2.80 (2.62–3.00)</td>
<td>1.67 (1.51–1.84)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Debridement wound/burn</td>
<td>4.04 (3.61–4.52)</td>
<td>2.23 (2.02–2.46)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Small bowel resection</td>
<td>10.38 (9.37–11.50)</td>
<td>6.83 (6.29–7.42)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>Temporary tracheostomy</td>
<td>22.51 (20.92–24.21)</td>
<td>15.94 (14.80–17.14)</td>
<td>&lt;.001</td>
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<tr>
<td>Ventriculostomy</td>
<td>38.09 (34.25–42.35)</td>
<td>29.21 (26.81–31.72)</td>
<td>&lt;.001</td>
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<tr>
<td><strong>High-risk operations</strong></td>
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<tr>
<td>Cystectomy</td>
<td>3.31 (2.50–4.39)</td>
<td>1.85 (1.38–2.47)</td>
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<tr>
<td>Esophagectomy</td>
<td>9.07 (6.72–12.23)</td>
<td>4.77 (3.42–6.60)</td>
<td>.012</td>
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<td>Lower extremity bypass</td>
<td>3.12 (2.84–3.42)</td>
<td>2.09 (1.82–2.33)</td>
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<td>Mitral valve replacement</td>
<td>9.86 (8.62–11.29)</td>
<td>7.59 (6.83–8.42)</td>
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<tr>
<td>Pancreatic resection</td>
<td>7.10 (5.21–9.68)</td>
<td>4.10 (3.37–4.97)</td>
<td>.016</td>
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<td><strong>Major complications (failure to rescue rate)</strong></td>
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<tr>
<td>Postoperative pneumonia</td>
<td>8.54 (7.93–9.19)</td>
<td>7.34 (6.93–7.77)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>18.69 (17.81–19.61)</td>
<td>14.03 (13.40–14.68)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Shock/cardiac arrest</td>
<td>53.82 (51.72–56.02)</td>
<td>44.15 (42.07–46.26)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Upper gastrointestinal bleeding</td>
<td>9.96 (8.82–11.24)</td>
<td>6.86 (6.03–7.79)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>8.69 (7.97–9.49)</td>
<td>5.43 (4.90–6.00)</td>
<td>&lt;.001</td>
<td></td>
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</tbody>
</table>

theoretically incorporates all aspects of an individual’s life. Research on valued states of existence has reported that health is the most valued state, and there is a rapidly expanding literature on health-related QoL (HRQoL). Patients’ expectations of a morbidity-free life at older age have also increased, and have led to attempts to measure health expectancy. Moreover, purchasing debates in health care now focus on health care cost in relation to “health gain,” or benefit from the treatments and interventions that are contracted for. The increasing emphasis on health care provision as a scarce resource has given impetus to this trend.

HRQoL, a subjective health status, is patient-based but focuses more on the impact of a perceived health state on the ability to live a fulfilling life. It is a double-sided concept, assessing positive as well as negative aspects of well-being and life by incorporating social, psychological, and physical health. It also includes some assessment of the patient’s level of satisfaction with treatment, outcome, and health status, and with future prospects. It is distinct from QoL as a whole, which includes adequacy of housing, income, and perceptions of the immediate environment. It is also ultimately a dynamic (unstable?) concept, for as health status deteriorates, perspectives on life, roles, relationships, and experiences change.

Some investigators are skeptical about patient-based indicators, but others believe that it is important to include patient-based indicators in assessments of outcome because they do not necessarily correlate with objective measures of physical functioning. There is often poor agreement among physicians in relation to supposed objective clinical findings and variations in physicians’ clinical judgments. Subjective indicators such as HRQoL are increasingly popular because of the recognition of the importance of patient satisfaction and how individuals feel, rather than what statistics imply they ought to feel. In this view, clinical indicators of outcome are no longer sufficient; assessment of QoL as a measure of outcome redirects clinicians from limiting the measurement of outcome to postintervention survival, complication rates, and various physical or biochemical indicators toward consideration of the impact of disease and therapy on the patient’s emotional and physical functioning and lifestyle.

The measurement of health outcomes of clinical interventions has become a cornerstone of health services research, and is also linked to the assessment of the appropriateness of health care interventions. QoL assessment as a supplement to the documentation of symptom rates, toxicity, adverse effects, and survival patterns is given more urgency in the light of data that some surgery is inappropriate or ineffective. QoL assessment is also popular among pharmaceutical companies, with most reporting that they have used some type of QoL instrument in their clinical trials of drugs, but the US Food and Drug Administration (FDA) considers the state of the art of QoL measurement too immature to merit mandatory inclusion in clinical trials.

Cost-utility studies (see later discussion) need a common measurement of health outcome. With these cost-utility analyses, the cost of an intervention is related to the number of quality-adjusted life years (QALYs). A QALY is a year of full life quality; poor health may reduce the quality of a year (eg, from 1 to 0.5). In QALYs, improvements in the length and QoL are amalgamated into one single index. Each life-year is quality-adjusted with a utility value, where 1 = full health. The utility value aims to reflect the HRQoL. Thus, QALYs are not really measures of QoL per se, but rather are measures of units of benefit from a medical intervention, combining life expectancy with an index of, for example, disability and distress. That they are based on invalidated value judgments has led to criticism.

Values of QALYs can be derived by several different methods. The disadvantages of all these methods are their cost, the requirements for skilled interviewers, and complexity (leading to reliance on nonrandom or unrepresentative samples). One of
the main debates surrounding the use of these techniques is who should provide the utility values: the general public, health care providers, or patients and their families? Bowling\textsuperscript{21} provides a comprehensive discussion of QoL research, oriented toward the social sciences.

**Defining “Value”**

“Value” is a key parameter in determining whether the cost of something is “appropriate.” Any level of spending may be acceptable, depending on the value provided by that expenditure. However, revelations about the prevalence of medical errors and their high cost,\textsuperscript{22} as well as the challenges inherent in translating evidence into practice,\textsuperscript{23} underscore that health care delivery can be excessive and wasteful. The practice of medicine is being scrutinized regarding the efficient allocation of resources, in the belief that optimal resource allocation may improve both clinical and economic outcomes.\textsuperscript{24} Medical cost has been increasing for years at a rate exceeding the general rate of inflation, heightening the sense that translation of (often expensive) new diagnostics and therapeutics into practice must be done efficiently.

Conceptually, efficiency represents the attempt to obtain the most value and output for every dollar spent. Hence, there is a growing interest in the application of emerging methodology to quantify the value of health care interventions by applying the methods of economics.

**Types of Cost**

What is meant by “cost?” An important distinction exists between charges and costs. Charges reflect the desired reimbursement rates for a hospital or provider. Included in this value are the true expenditures for care and some measure of reasonable profit.\textsuperscript{25} Charges are basically an accounting tool that may bear little relation to expected reimbursement from third-party payors (or cost, for that matter), except that they are set higher invariably to maximize reimbursement. Because of the variable nature of charges, cost is the preferred numerator for cost-effectiveness analyses (CEAs, see later discussion), as they are meant to represent actual resource consumption.

Costs can be derived from charges on the basis of the published hospital-specific cost:charge ratios from The Centers for Medicare and Medicaid Services (CMS). Costs may be direct, indirect, or intangible; or either fixed or variable. Direct costs are those of labor and goods used in the delivery of the intervention. Indirect costs, on the other hand, are those attributable to lost productivity resulting from illness (from the patient perspective), or those that are amortized (from the institutional perspective, eg, depreciation, debt service). Intangible costs incorporate the pain and suffering resulting from the disease or intervention. Fixed costs are those that remain the same regardless of the amount of production output. In a hospital setting, these include costs associated with running the physical plant and equipment, or the minimum level of staffing and inventory to remain open and functional for patient care. Variable costs are those that change in the short term with the changes in production output, such as costs of having to increase the number of nursing staff because of a temporary surge in ICU volume. There is controversy regarding whether CEA should address fixed, variable, or total (the sum of fixed and variable) cost. Although most studies analyze total cost, variable costs are influenced by externalities.\textsuperscript{26} Fixed costs cannot be reduced short of closing the facility; they accrue no matter what transpires. However, fixed costs are also subject to external influences, albeit to a lesser degree and over longer periods of time.

Analyzing fixed versus variable costs can result in vastly different estimates of the cost of an illness. For example, Dasta and colleagues\textsuperscript{27} estimated the total cost for
a patient with respiratory failure on the first day of ICU care in the United States to be $8000, diminishing for subsequent days to $3600 to $3900 (2002 US dollars). By contrast, Kahn and colleagues calculated the direct variable costs of the last ICU day in a cohort of similar patients who survived beyond ICU day 3 to be $400, with the first day on the ward costing only $280. By this reckoning, a hypothetical intervention that reduces the ICU length of stay (LOS) by 1 day saves the hospital only $120, which lacks face validity unless, for example, transfer out of the ICU is delayed by a lack of floor beds.

Types of Cost Analysis

There are 5 major types of cost analysis: (1) cost minimization; (2) cost-benefit; (3) cost-consequence; (4) cost-effectiveness; and (5) cost-utility; the last 2 being encountered most frequently in the medical literature. Cost minimization compares the infrequent situations in which 2 interventions produce identical effects. Cost-benefit analysis examines both cost and benefit in terms of monetary units, whereas cost-consequence analysis evaluates costs and consequences separately, allowing users to choose the costs and the consequences relevant to a specific circumstance.

In medicine generally, most economic research takes the form of either CEAs or cost-utility analyses. CEA examines the ratio of the cost of a particular intervention to a chosen unit of effectiveness. The need for a CEA or cost-utility analyses (these terms are sometimes used interchangeably) usually arises when the value proposition of a new intervention is unclear. (A value proposition is a business or marketing statement that summarizes why a consumer should buy a product or use a service. This statement should convince a potential consumer that one particular product or service will add more value or solve a problem better than other similar products. In practical terms, companies use the value proposition to target customers who will benefit most from using the company’s products, and this helps maintain an economic “moat” [ie, imperviousness to competition]).

When a new therapy (A) is both less expensive and more effective than its comparator (B), it is said to “dominate” the comparator; in such a case (albeit rare in medicine) the decision to adopt therapy A is clear. Conversely, A is dominated by B if A is less effective and more costly than B. Ambiguity arises when either A is more effective and more costly than B or A is less effective and less costly than B. It is important to understand that being cost-effective does not necessarily mean cost-saving. Some effective therapies are expensive. Under these circumstances, it is important to articulate the resource expenditure per unit of effectiveness by a formal means for balancing the trade-offs between the 2 interventions, yielding a rational decision that maximizes outcome. Consensus-based recommendations for the conduct of CEAs have been published.

Perspective

“Perspective” is the point of view taken when conducting a CEA. Perspective is crucial because it determines which costs and outcomes are likely to matter more than others. For example, in an ICU study, the cost of averting one case of ventilator-associated pneumonia (VAP) is borne almost completely by the hospital, and this is therefore an outcome that is important from the hospital’s perspective. However, the development of VAP may affect morbidity but not necessarily the direct cost that the patient must pay. Other perspectives may represent those of payors, pharmacies, the ICU (as a cost center), or society as a whole. The costs and benefits of an intervention may not be borne equally; therefore, if the assessment is not made from a sufficiently broad perspective, the assessment of an intervention may be
skewed and lead to potential bias. Moreover, cost shifting may be attractive to those whose costs would be diminished, but not to those who would bear the additional cost. This dilemma led to the principle in CEA that one should adopt whenever possible a societal perspective from which all costs may be incorporated, regardless of who bears the burden.

When considering CEAs, it can be ascertained quickly whether the investigators have used a societal perspective. In general, such articles describe results in terms of a reference case (baseline scenario) that is being explored, which serves as the frame of reference for other comparisons. The reference case incorporates QALYs in the denominator of the cost-effectiveness ratio. By definition, this represents the societal perspective, and is therefore most important for public health and overall resource allocation. The calculation of the reference case requires a long-term evaluation of both cost (lifetime health care cost) and effectiveness outcomes. Because some interventions may restore a person to perfect health, whereas others (while extending life) leave the person debilitated, not only are expected years of survival included in the denominator but also the quality of those years of life. The usual denominator in cost-utility studies is the QALY, and cost/QALY serves as the reference case. In addition, reference cases are useful because they provide a baseline scenario against which to compare alternative resource allocation decisions; it is valid to compare the costs per QALY in reference cases across unrelated conditions and interventions. In general, a cost/QALY of less than $100,000 is considered the threshold for determining that a therapy is cost-effective (the lower, the better).

**Modeling**

Whereas data regarding long-term outcomes for chronic conditions may be available for researchers to apply in CEA, those for acute and short-lived episodes may not exist, such as those that arise in the ICU. To circumvent this challenge, investigators may adopt the technique of decision modeling, in which assumptions about long-term outcomes, based on previous work in published populations, are entered into a mathematical formula to generate the outcome estimates of interest. This method is a preferred approach to building a reference case, as practical considerations, such as the urgency of the need for cost-effectiveness information and the enormous resources required, preclude real-time collection of actual long-term outcomes.

**Incremental Cost-Effectiveness Ratio**

Comparative effectiveness research (CER) represents a useful application of CEAs and cost-utility analyses. The purpose of CER is to compare explicitly the effectiveness of 2 interventions used for the same condition. The single value representing comparative cost-effectiveness is the incremental cost-effectiveness ratio (ICER). For example, Shorr and colleagues examined the cost-effectiveness of linezolid as compared with vancomycin for the treatment of methicillin-resistant *Staphylococcus aureus* VAP. The ICER was calculated as the ratio of the differences in costs to the differences in effectiveness measures of the compared therapies. By definition, the lower the ICER, the better the cost-effectiveness profile. In the base-case analyses, the estimates were approximately $67,000, $22,000, and $30,000 for incremental costs per survivor, per life-year saved, and per QALY, respectively.

**Sensitivity Analysis**

Because model inputs are based on assumptions, they invariably include some degree of uncertainty. Sensitivity analyses are designed to estimate how this
uncertainty in the assumptions may affect the precision of the outcome estimates. These sensitivity analyses usually include univariate (one input is varied at a time), 2-way (2 inputs with the strongest effect on the outcome variability are varied simultaneously), and multivariable analyses (all inputs are varied at the same time across their plausible ranges). The extent of uncertainty used in sensitivity analyses is most appropriate if derived from actual clinical data, and should represent the 95% CIs around various point estimates. In the literature the reader may encounter Markov analysis or Monte Carlo simulation, with which the reader should be familiar; these are described briefly in Box 2.

A CEA that does not report a sensitivity analysis should be viewed with skepticism. For example, a recent cost-effectiveness simulation of a silver-coated endotracheal tube as a preventive measure for VAP found the tube to be cost-saving in the base case. Univariate analyses indicated that VAP costs and the risk reduction resulting from use of the novel endotracheal tube accounted for most of the model uncertainty. A 2-way sensitivity analysis revealed outcome estimates ranging from savings of $34,000 to an expenditure of $205 to prevent one case of VAP.

Another useful type of sensitivity analysis is a worst-case scenario analysis, wherein all inputs are biased against one of the comparators (usually the novel intervention). In a study of the cost-effectiveness of micafungin as compared with fluconazole for empiric treatment of candidemia in the ICU, the calculated base-case cost/QALY was $35,000 (well below the traditional non–cost-effective threshold of >$100,000 per QALY). In the worst-case scenario, the cost-utility ratio gave a cost of $72,000 to save one additional QALY. A threshold analysis suggested that when the prevalence of azole resistance reached 1.5%, micafungin was no longer cost-effective relative to fluconazole.

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**Box 2**

**Descriptions of Markov analysis and Monte Carlo simulation**

**Definition of Markov Analysis**

A method used to forecast the value of a variable whose future value is independent of its past history. The technique is named after Russian mathematician Andrei Andreyevich Markov, who pioneered the study of stochastic processes, which are processes that involve the operation of chance. The Markov Analysis introduces a method for forecasting random variables. Markov analysis has several applications in the business world. Two common applications are in estimating the proportion of a company’s accounts receivable that will become bad debts, and forecasting future brand loyalty of current customers.

Read more:

http://www.investopedia.com/terms/m/markov-analysis.asp#ixzz1wjU5xcYi

http://en.wikipedia.org/wiki/Markov_chain

**Definition of Monte Carlo Simulation**

A problem-solving technique used to approximate the probability of certain outcomes by running multiple trial runs, called simulations, using random variables.

Monte Carlo simulation is named after the city in Monaco, where the primary attractions are casinos. Gambling games, such as roulette, dice, and slot machines, exhibit random behavior.

Read more:

http://www.investopedia.com/terms/m/montecarlosimulation.asp#ixzz1wjZ7w0sV

http://en.wikipedia.org/wiki/Monte_carlo_simulation
Inflation Adjustments and Discounting

Adjustment of costs for inflation, and to discount both future costs and effectiveness estimates, can be used as markers of study quality.\textsuperscript{28} Inflation adjustment is necessary for several reasons. Medical cost inflation increases rapidly, therefore cost needs to be adjusted to the current time; a dollar spent today presumably has more value than a dollar spent in the future. Inflation adjustment to the same year confers uniformity and the ability to compare “apples with apples.” Any analysis that quantifies future cost (eg, lifetime health care cost) and outcomes (eg, QALYs) needs adjustment for inflation in both the numerator and the denominator of any CER. The recommended annual base discount rate (the general inflation rate in the United States) is 3%, whereas medical cost inflation increases by at least twice that rate.

IS ICU CARE COST-EFFECTIVE?

Several rigorous examples do demonstrate that critical care is cost-effective. Among 937 critically ill patients treated in the critical care setting at a major European university teaching hospital, the influence was examined of using different HRQoL instruments on the calculation of the number of QALYs gained and the cost per QALY.\textsuperscript{32} Two HRQoL tools were used at 6 and 12 months after the start of treatment, and QALYs were calculated using 4 different sets of assumptions (Box 3). Each of the 8 conditions ($2 \times 4$ factorial) generated unique information regarding QALYs gained and cost/QALY, with the former ranging from 49 to 150 QALYs gained, and cost/QALY ranging from $\text{€38,405}$ to $\text{€118,668}$. Thus, critical care was considered to be cost-effective in 7 of the 8 scenarios.\textsuperscript{32}

Box 3
Effect of health-related quality of life assessment and QoL calculation using several methodologies and assumptions

\begin{itemize}
  \item **Assumption 1**
  Without treatment, patients would die (HRQoL = 0, QALYs gained = 0).
  After treatment, HRQoL is increased to the 6-month time point, then changes linearly with QALY thereafter. Thus, for those who die before the first follow-up, the QALY gain is zero. The maximum number of QALYs to be gained is 1.

  \item **Assumption 2**
  Without treatment, patients would die (HRQoL = 0, QALYs gained = 0). After treatment, HRQoL increases linearly with QALY thereafter. The maximum number of QALYs to be gained is 0.75.

  \item **Assumption 3**
  Without treatment, patients would stay at their same baseline HRQoL for the entire follow-up period. Nontreated patients are not assumed to die. With treatment, the HRQoL changes immediately to the level measured at 6 months, after which it increases linearly to the 12-month follow-up period. The maximum number of QALYs gained depends on the baseline HRQoL score.

  \item **Assumption 4**
  The assumptions are those set forth in Assumption 3, except that with treatment the change in HRQoL increases linearly from baseline through all follow-up periods. The maximum number of QALYs gained depends on the baseline HRQoL score.
\end{itemize}

Edbrooke and colleagues\textsuperscript{33} studied 7659 patients (11 hospitals, 7 European countries) referred to the ICU who were stratified by whether or not they were accepted for ICU admission. Stratified by age, Karnofsky score (one of the earliest of the QoL assessment tools, developed in 1948; it is limited by its exclusive emphasis on physical functioning), reason for admission, and severity of illness. The two groups were compared in terms of cost and mortality using multilevel regression. Admission to the ICU reduced the risk of mortality overall (relative risk [RR] 0.70, 95% CI 0.52–0.94), and was related inversely to the predicted risk of death (for 40% predicted mortality, RR 0.55, 95% CI 0.37–0.83). Cost per life-year (CPLY) was $7065 overall, and $4088 for 40% risk of death. Results were robust when subjected to sensitivity analysis. Thus not only did ICU care reduce mortality, but CPLY decreased with increasing severity of illness, underscoring the cost-effectiveness of critical care.

QoL and lifetime cost-utility for critically ill patients with acute respiratory failure were assessed in a nationwide prospective study of 958 consecutive patients treated with mechanical ventilation in 25 Finnish ICUs.\textsuperscript{34} One-year mortality was 35% (95% CI 32%–36%). Of the 619 survivors, 288 completed a QoL questionnaire. For the survivors, QoL at 1 year was lower than that reported by an age-matched and gender-matched general population. Among the 288 survivors, the mean predicted lifetime QALYs were 15.4 and 11.3 after adjustment for the missing data (reflecting all 958 patients). The mean estimated cost was €20,739 per hospital survivor, and the mean predicted lifetime cost-utility for all patients was €1391/QALY. Among age subgroups (10-year intervals), mean QALY decreased and mean cost/QALY increased for older patients, but despite lower HRQoL compared with healthy matched patients, the cost per hospital survivor and lifetime cost-utility remained reasonably low regardless of age, disease severity, or type or duration of mechanical ventilation.

The cost-effectiveness of protocolized sepsis care has been examined in 2 studies of comparable design, reaching similar conclusions. In a single-center study from Boston, Talmor and colleagues\textsuperscript{35} compared 79 patients who presented to the emergency department in septic shock with 59 control patients. The analysis was performed from the perspective of the health care system using a lifetime horizon, and incremental cost/QALY gained (ICER) was the primary end point. Mortality was 20.3% in the protocol-treated group versus 29.4% in the control group (P not significant). The integrated sepsis protocol increased cost by $8800/patient, due largely to increased ICU LOS. However, the expenditure was found to be cost-effective, with an incremental cost of $11,274 per life-year saved and $16,309 per QALY gained. By contrast, Suarez and colleagues\textsuperscript{17} evaluated the cost-effectiveness of the protocol derived from the Surviving Sepsis Campaign guidelines\textsuperscript{36} in a cohort of 1465 patients from 59 medical-surgical ICUs located throughout Spain. Comparison was made with 854 patients treated for severe sepsis/septic shock before protocol implementation. The health care system perspective was used. The primary outcome was ICER. There was lower mortality (39.7% vs 44.0%, P<.05) for the protocol-treated patients. Mean costs were €1736 higher (95% CI 114–3356) for protocol-treated patients, largely from increased LOS. Mean life-years gained was 0.54 years higher for the protocol-treated group (95% CI 0.02–1.05 years). The adjusted ICER of the protocol was €4435. Sensitivity analysis showed protocol-based care to be cost-effective in 96.5% of bootstrap replications.

Other Examples Relevant to the ICU

Translating evidence into practice often relies on the adoption of a “bundle” of interventions rather than a single treatment; a prime example is the Surviving Sepsis
### Box 4
**Selected cost-effectiveness analyses of relevance to surgical critical care practice**

**Antibiotic Prophylaxis of Surgery for Closed Fractures**

Slobogean et al, 2010

Comparison of single- and multiple-dose prophylaxis

- Time horizons of 90 days and 1 year
- Base-case analysis, sensitivity analysis, probabilistic. Monte Carlo sensitivity analysis
- Single-dose prophylaxis slightly more cost-effective, $2576 versus $2596 for an average gain of 272 QALD

**Critical Care Interventions**

Etchells et al, 2012

Systematic literature review identified 5 comparative economic analyses that reported 7 comparisons of adequate methodological quality, 4 of which were cost-effective:

- Pharmacist-led medication reconciliation; chlorhexidine for “vascular catheter site care”;
- Implementation of “Keystone ICU Initiative” to prevent CLABSI;
- Counting to detect retained surgical foreign bodies.

The 3 interventions that were “economically unattractive” were bar-coded surgical sponges compared with standard counting, use of erythropoietin for critically ill patients to avoid transfusion, and related adverse events

**Screening for MRSA**

Olchanski et al, 2011

Decision analysis with multivariable sensitivity analysis. PCR-based versus culture-based screening in several ICU populations: “High risk,” ICU, previous MRSA colonization/infection. Screening resulted in cost savings of $12,158–$76,644/month compared with no screening. Same-day PCR-based screening of high-risk patients resulted in fewer infections and the lowest total cost.

Sensitivity analysis showed that the results are sensitive to hospital size, test turnaround time, transmission rate, prevalence rate, and rate of conversion of colonization to infection

**TBI Care**

Whitmore et al, 2012

Decision analytical model of 3 strategies for treating a patient with severe TBI: (1) Aggressive care (including invasive ICP monitoring and decompressive craniectomy); (2) Routine care, in which Brain Trauma Foundation guidelines are not followed; and (3) Comfort care, consisting of only 1 day of critical care, followed by floor care. Glasgow Outcome Scale Scores were converted to QALYs based on estimates of longevity and QoL from the literature. Societal perspective. Monte Carlo sensitivity analysis used for patients aged 20, 40, 60, and 80 years.

Aggressive care yielded an additional 1.7 QALYs; although the cost-effectiveness of aggressive care diminished with advancing age, it was significant at all ages. Aggressive care was significantly less costly up to age 80, whereas comfort care was associated with poorer outcomes and higher costs up to age 80

**Trauma Triage**

Mohan et al, 2012

Comparison of ICERs for current practice with interventions targeting attitudes toward transferring patients to trauma centers (decisional threshold) and ability to identify patients who should be transferred (perceptual sensitivity). Societal perspective. Markov analysis (decision model). Monte Carlo sensitivity analysis. The ICER of an intervention to change perceptual sensitivity was $62,799/QALY, compared with current practice, whereas the ICER of an intervention to change the decisional threshold was $104,795/QALY. Findings were most sensitive to the relative cost of hospitalizing patients with
Campaign treatment guidelines. Hence, it can be asked whether some of the bundled interventions are cost-effective. Two such care bundles include early goal-directed therapy (EGDT) for sepsis (which is itself incorporated into the Surviving Sepsis Campaign guidelines), and a 24-hour intensivist presence model for ICU staffing. Huang and colleagues examined the cost-effectiveness of EGDT from both the hospital and societal perspectives. Use of EGDT had a nearly 100% probability of being cost-effective at a value of less than $20,000 per QALY. On the other hand, the cost-effectiveness of different models of ICU attending coverage remains poorly defined. For example, a 24-hour intensivist coverage model for the ICU is believed to be cost-saving from the perspective of the hospital, because the intensivist’s continuous presence can improve outcomes, enhance patient throughput and the efficient use of resources, and focus efforts on prevention, but cost-effectiveness from the societal perspective has not been demonstrated definitively. The savings associated with implementation of the 24-hour intensivist model derive largely from an anticipated reduction in ICU and hospital LOS, which cannot be assured (see the sepsis protocol data above). This conundrum illustrates the need to be explicit about perspective and sensitivity analyses when conducting CEAs.

Surprisingly, some of the bundled interventions for prevention of hospital-acquired infection, which are advocated by many, have not been evaluated either for effectiveness or cost-effectiveness. One such example is the Institute for Healthcare Improvement’s “ventilator bundle.” In a recent systematic review of studies evaluating bundled interventions for prevention of VAP, the investigators found only weak evidence in support. More importantly, no rigorous evaluations of the cost-effectiveness of ventilator bundles for avoiding VAP were identified (one has been published subsequently [Box 4]), but the cost-effectiveness demonstrated was examined only from the perspective of the third-party payor. As additional bundled strategies are promoted as quality improvement initiatives and measures for reimbursement, rigorous assessment of cost-effectiveness will be essential. Given that health care

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<th>Ventilator Bundle</th>
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<td>Mollar et al, 2012</td>
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CER of use of a “ventilator bundle” versus standard care in 2 models for prevention of VAP, for patients ventilated for more than 48 h: One for the prevention of VAP per se; another for the prevention of death. Perspective of third-party payor, thus societal costs and direct medical costs were not considered. The cost per episode of VAP prevented was €4451, and €31,792 per death prevented. The ICER analysis showed that the ventilator bundle was more cost-effective for VAP prevention in 99.9% of cases, and 42.6% of cases was dominant (ie, had both better outcomes and lower cost). The ventilator was more cost-effective for prevention of death in 85.9% of cases, with both lower cost and better outcome (dominance) in 31.6% of cases.

Abbreviations: CER, cost-effectiveness ratio; CI, confidence interval; CLABSI, central line–associated bloodstream infection; CPG, clinical practice guideline; ICER, incremental cost-effectiveness ratio; ICP, intracranial pressure; ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction; QALD, quality-adjusted life-days; QALY, quality-adjusted life-years; QoL, quality of life; RR, relative risk; TBI, traumatic brain injury.
resources are limited, reflexive adoption of some tactics may result in the diversion of resources that prove ultimately to be more cost-effective.

Several other ICU-related therapies have been subjected to cost-effectiveness analysis (see Box 4) and have been found to be cost-effective. However, it should be noted that one therapy of recent interest, off-label administration of recombinant human Factor VIIa (rFVIIa) as rescue therapy for patients with hemorrhage who require massive transfusion, was found to be not cost-effective. Among 353 patients with substantive bleeding at Royal Perth Hospital, Australia, 81 received rFVIIa. The total CPLY gained was $1,148,000, and the ICER was $736,000, greater than the usual acceptable cost-effective limit of $100,000 per life-year. The ICER increased with increasing severity of illness and transfusion requirement. Note that this analysis did not address specifically the use of rFVIIa for trauma.

A Cautionary Tale

The recent example of the introduction and subsequent withdrawal, 10 years later, of drotrecogin alfa (activated) (DAA) therapy for severe sepsis, should serve as a cautionary tale. Angus and colleagues incorporated both real-time data from a clinical trial and modeling in a CEA of the therapy, specifically the incremental health care cost associated with 1 death averted at 28 days as a result of treatment with DAA. To determine cost, the investigators needed not only to establish the costs of DAA but also to account for the cost of the continued care and further health care resource consumption attendant thereto for survivors. Angus and colleagues estimated that DAA cost society $160,000 per life saved. In determining the reference case, which required estimating the life expectancy of sepsis survivors and HRQoL, the cost of DAA was $48,000/QALY. The ICER improved to $27,000/QALY when the estimated risk of short-term death increased, and worsened to the point of cost-ineffectiveness (> $100,000/QALY) if the survivors were expected to live fewer than 5 years.

Of course, a therapy cannot be found to be cost-effective if ultimately the therapy is not effective. Although a single Class I trial and ample Class II and III data implied that DAA was effective, other randomized trials were not supportive. The ensuing heated controversy led to the recent failed trial of DAA for patients in septic shock, leading to its withdrawal from the market.

SUMMARY

The rapid growth in health care expenditure has engendered careful scrutiny of the practice of medicine with regard not only to effectiveness but also to efficiency. This shift necessitates that physicians understand the effectiveness of their interventions and the cost at which this effectiveness is obtained. Cost-effectiveness and cost-utility analyses have become crucial evaluative tools in medicine. Explicit articulation of comparative cost-effectiveness facilitates the allocation of limited resources. As physicians and policy-makers encounter CEA in the literature, they must evaluate such studies as they would any clinical study: with caution, skepticism, and attention to the methods used.

REFERENCES