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REVIEW ARTICLE

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The economics and cost-effectiveness of critical care medicine

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Introduction

Critical care is expensive and accounts for a large share of inpatient expenditures. In the United States, for example, intensive care units (ICUs) comprise between 5% and 10% of all hospital beds but consume 20–34% of all acute care resources, a figure that ultimately amounts to over 1% of the American gross domestic product (GDP), or $ 67 billion (in 1994 U.S. dollars) [1–7]. Although the consumption of resources by critical care in the rest of the industrialized world does not approach the fiscal heights reached in the United States, it nevertheless remains disproportionately high relative to other services [8–10]. Overall, health care costs in the United States have risen at nearly twice the rate of inflation of the consumer price index. This higher rate of inflation, together with an increase in the rate of growth in real spending, means that this sector represents a rapidly increasing percentage of the GDP. Health care currently accounts for approximately 14% of the U.S. GDP, roughly double the percentage for 1970, and many predict that this figure will rise to 16% or higher by the end of the century if left unchecked. A gain of 1% of GDP in an economy of over 6 trillion dollars is significant; health care costs in the United States increase by this amount every 3 years [11–13].

The rise in health care costs and the growth in expensive, high-tech services such as are provided in ICUs have caused many to investigate the efficiency of services provided relative to expenditures and outcomes. In all societies, health care must compete with other individual and social endeavors for its share of limited economic resources. Tradeoffs invariably are made, for the decision to fund certain programs necessarily implies that others cannot be undertaken. As health care systems based on retrospective, cost-based reimbursement, fee-for-service physician compensation, and indemnity insurance develop into ones characterized by prospective payment, managed care, capitation, and rigid budgetary constraints, resources become less and less available. As a result, physicians, administrators, and payers must find ever shrewder ways of distributing scare resources in the face of a variety of competing needs [14, 15].

Increasingly, cost-effectiveness analysis has been used in this process to study the clinical and economic ramifications of medical interventions. This type of analysis enables one to make more rational decisions in an atmosphere of heightened cost-consciousness, diminished financial reserves, and competing demands for limited health care resources. This article will discuss the basic approach and tenets of cost-effectiveness analysis and will review stituations where it has been applied to clinical critical care medicine in the United States and Europe.

Cost-effectiveness analysis

Definitions

Cost-effectiveness analysis facilitates the joint assessment of economic and clinical outcomes. Thus it helps to ensure that informed decisions are made and that the best possible outcome is obtained for the resources expended for any clinical intervention [16]. Over the past several years, cost-effectiveness analysis has been used to evaluate the impact of multiple medical interventions for the care of the critically ill, including – but not limited to – coronary artery bypass surgery [17], thrombolytic therapy [18–21], and the use of monoclonal antibodies against endotoxin in the treatment of patients with gram-negative sepsis [22, 23].

Cost-effectiveness analysis needs to be distinguished from different yet similar analytic methods, including cost-minimization, cost-benefit, and cost-utility analyses (see Table 1). In brief, cost-effectiveness analysis measures all costs which accrue for a given set of alternatives, calculates all concurrent benefits, and subsequently determines a cost-effectiveness ratio for each alternative. For health care, costs are usually (but not necessarily) stipulated in monetary terms, and effectiveness (i.e. benefits) is usually quantified in terms of clinical outcome, such as number of survivors, years of survival, probability of survival, or quality-adjusted life years (QALYs) [24]. This contrasts with a simple cost-minimization analysis, which merely assesses costs and thus implicitly assumes the equivalence of all yielded benefits [24]. The terms "cost-benefit" and "cost-effectiveness" are often confused and erroneously interchanged. The techniques of these methods are similar and the two may be performed simultaneously. However, they differ in that cost-benefit analyses require both costs and benefits to be valued in monetary terms, a condition that does not apply to cost-effectiveness analysis. Thus, true cost-benefit analysis is rarely applied to clinical problems because of the inherent difficulty of ascribing a fiscal value to health care outcomes. Cost-utility analysis is a subset of cost-effectiveness analysis. Costs are the same in both analyses; however, a cost-utility analysis attempts to incorporate mortality and morbidity into a single summary effectiveness measure, e.g. QALYs, and to adjust survival according to health-related quality of life [24].

General approach

The determination of cost-effectiveness involves making comparisons among different choices; therefore, at least two alternatives need to be studied explicitly. The economic measures and clinical outcomes for each analysis will depend the problem under investigation and on the specific set of clinical circumstances. However, all cost-effectiveness analyses should follow the same general principles and steps [15, 25, 26]:

1. The explicit identification of all clinical strategies and choices under analysis. Calculation of a cost-effectiveness ratio for just one strategy does not constitute a cost-effectiveness analysis. The cost-effectiveness of two or more different approaches to the same problem, such as of two alternative antibiotics or two different inpatient settings for treating the same condition (e.g. ICU care vs routine hospital care) need to be compared.

2. The explicit stipulation of the study's perspective. At the outset, the specific perspective assumed by the study needs to be defined. An intervention may be cost-effective for society in general yet may be deemed cost-ineffective for a smaller sector, such as a local political area, a third party insurer, or an acute-care institution. This is because both the costs and the benefits accrued depend upon one's perspective. Most published studies assess cost-effectiveness for society in general and determine cost-effectiveness in terms of the cost per year of life saved (or gained) or cost per QALY. However, costs and benefits accrued are not necessarily standard and may vary considerably among different sectors of society [27].

Table 1 Comparison of cost-effectiveness analysis, cost-benefit analysis, and cost-utility analysis (adapted from Drummond et al. [26])

	Cost-effectiveness analysis	Cost-benefit analysis	Cost-utility analysis
Costs	Monetary units (e.g. currency)	Monetary units	Monetary units
Benefits	Outcome (e.g. years of life saved) Change in health status (e.g. reduction in blood pressure)	Monetary units	Outcome measures which incorporate morbidity and quality of life (e.g. quality-adjusted-life-years)
Summary measures	Cost-effective ratio (e.g. dollars per year of life saved)	Net gain or loss (in Monetary units)	Cost-utility ratio (e.g. cost per quality-adjusted life year)

3. Determination of all costs. All costs accrued from a particular perspective need to be delineated carefully, and the distinction between costs and charges should be addressed, if not reconciled. Usually only direct costs (those costs that can be directly measured) are assessed. However, many favor a more complete assessment of total costs, which include (1) direct costs, (2) costs accrued as a result of adverse events, and (3) savings that are achieved as a result of better health status [14, 28]. Some argue that medical care costs resulting from increased life expectancy should also be included; however, this point remains controversial [14].

4. Specification and determination of benefits. Cost determination may be complicated, as it is often difficult to capture every specific component. However, estimation of accrued benefits is usually the most onerous task, as the quantitative valuation of benefit and effectiveness often retains an inherently subjective element. Benefits are usually reported as changes in life expectancy, probability of survival, or alteration in survival as a result of a particular intervention.

5. Specification of the time frame. Costs and benefits are usually time dependent and are rarely spent or accrued immediately. Thus, all analyses need to specify the period of time for which an analysis applies. If the time frame exceeds 1 year, the costs and benefits may need to be discounted and converted to present values. Discounting takes into account the notion that costs that are immediately defrayed are more "valuable" than ones of an identical numerical value that are defrayed in the future. Similarly, benefits accrued immediately are often preferable to those accrued only at a future date [26, 29]. Usually, future costs (C_t) are converted to a present value (PV) according to the number of years involved (T) and a preselected discount rate (r):

$$PV = \sum_{t=1}^{T} C_t/(1+r)^t \ .$$

Although in theory many different values can be proposed for a rate of discount, the rate often selected is that of the yield on long-term government bonds, in which the maturity on the bond corresponds to the number of years [29].

6. Determination of the cost-effectiveness ratio. Once all costs and benefits are specified, the cost-effectiveness ratio is determined. This ratio essentially provides a summary measure of the resources that are needed to achieve a certain level of health. Some common examples of cost-effectiveness ratios include the cost per year of life saved (or gained), the cost per survivor, and the cost per QALY. The cost-effectiveness ratio may also be determined on the basis of other outcomes, such as the cost per correct diagnosis, in the case of a screening test [24]. Determination of cost-effective ratios allows for a quantitative comparison of alternatives. A higher ratio implies that more resources must be procured to obtain the same outcome; a lower ratio, that similar outcomes may be achieved with fewer resources.

7. Sensitivity analysis. Most cost-effectiveness analyses rely to varying degrees upon certain underlying assumptions. As such, costs may vary under different conditions or settings and benefits may not accrue equally. Studies are strengthened by sensitivity analysis, which varies the values of these underlying assumptions throughout a clinically significant and economically relevent range. This enables one to determine how responsive a model is to change and thereby to extrapolate the findings to other situations.

8. Other factors. It should be pointed out that cost-effectiveness analysis is an economic efficiency test for the alternative being considered and, as such, should be used only as an adjunct by decision makers to provide important information. Cost-effectiveness is just one of many factors to be considered in the decision-making process and should be balanced against ethical and equity considerations as well as other clinical and societal projects. For example, a strategy that is deemed cost-effective may affect certain groups in the population more adversely than others, and thus it may not be feasible, or even ethical, to undertake it.

The imperative for cost-effectiveness analysis

Since the birth of the ICU as a distinct clinical entity, critical car medicine has grown steadily in terms of the number of ICU beds, the percentage of hospitals supporting ICU services, and the number of clinicians with advanced training and qualifications in critical care medicine [30–33]. Although clinical practice suggests that ICU care has a beneficial effecton many conditions, empirical evidence is often lacking, as most of the data is derived from isolated retrospective studies and anecdotal reports [34, 35]. Furthermore, ICU admission is not standard, is often independent of severity, and often depends upon such factors as bed availability and individual bias. Strauss and colleagues [36], for example, studied the impact of bed availability upon ICU triage and demonstrated that severity of illness was higher when ICU beds were scarce and that length of stay in the ICU increased when patient numbers were low and available beds were abundant. Similarly, significant international variations are noted in ICU care in terms of case mix, triage, and discharge. American hospitals tend to have more ICU beds and to devote a greater percentage of their budgets to critical care services than other industrialized nations [37]. They also have a greater propensity for admitting patients requiring only close physiological monitoring. Yet in spite of these differences, outcomes in the United States tend to be similar to those in other nations in terms of ultimate ICU and hospital survival [38, 39].

Nevertheless, despite this variability and the lack of standardization, a certain core percentage of patients appear to benefit from ICU admission. However, it is difficult – perhaps even impossible – to identify precise situations in which ICU care definitively improves clinical outcome. Some patients who receive ICU care may often be treated just as efficaciously in a less aggressive and less expensive setting, particularly those who require only close physiological and electrocardiographic monitoring [40]. Conversely, many terminally ill patients who will most likely die with or without critical care intervention are also frequently treated in ICUs. The clinical variability among ICUs and the dearth of data conclusively documenting the benefits of ICU care have great ramifications in terms of cost-effectiveness, for significant resources are devoted to the care of patients, the accrued benefit to whom has yet to be demonstrated. An expensive clinical intervention or program may yet be cost-effective if it improves outcome relative to all other choices and to all expended resources. Conversely, a less expensive alternative may be cost-ineffective if the change in outcome is minimal relative to the resources expended. The difficult decisions involve the comparison between a strategy that yields great benefits at high cost to one that provides much lower benefits at a very low cost. The cost-effectiveness ratio may be favorable to the lower-benefit strategy, despite the fact that no benefit will be realized if the cost-effective strategy is adopted. In general, the cost-effectiveness of an intervention will be relatively low if it consumes vast resources but yields little clinical benefit. However, this discussion illustrates that cost-effectiveness analysis is not free from controversy, for it ultimately puts an implicit value on benefits in a similar, although not as direct, manner as the much-criticized cost-benefit analysis.

The determination of cost-effectiveness for critical illness is often difficult, for one must document a beneficial change in clinical outcome relative to the costs expended. In critical illness, assessment of improved outcome can be difficult because it is often hard to establish a direct link between clinical improvement and ICU care and even harder to assess clinical utility beyond the measurement of increased life expectancy. Furthermore, the true determination of the cost of and allocation of resources to critical care services and ICU patients are complex matters that are often fraught with methodological inconsistencies [41].

Cost-effectiveness of critical care: a literature review

Formal organization of a critical care service

As critical care medicine has become increasingly established as a unique clinical specialty among the primary certifying boards of internal medicine, surgery, pediatrics, and anesthesia, more data has surfaced regarding the clinical and economic impact of ICU care and organized critical care services (see Table 2). Pollack and colleagues [42], for example, prospectively studied the impact of an intensivist-lead critical care service patient outcome and on admission and discharge decisions in a university hospital pediatric ICU. Admissions solely for monitoring and for patients with a low severity of illness significantly declined. After adjusting for severity of illness, ICU mortality also fell, although patients generally received more therapeutic interventions [42].

Table 2 Summary of economic and cost-effectiveness studies in critical care medicine

Topic	Country	Citation
Elderly SICU Patients	Sweden	Vang et al. 1985 [45]
Multidisciplinary ICU	The Netherland	Bams and Miranda 1985 [46]
Septic shock	United States	Reynolds et al. 1988 [43]
Pediatric critical care	United States	Pollack et al. [42]
Intermediate care versus coronary care	United States	Fineberg et al. [47]
Low birth weight neonates	United States	Walker et al. [44]
ICU cost-effectiveness and clinical performance	United States, Canada, Europe	Rapoport et al. [50]
Ventilator management teams	United States	Cohen et al. [53]
Elderly ICU patients	United States	Cohen et al. [55]
Thrombolysis in acute MI	United States	Kalish et al. [59]
Thrombolysis in acute MI	United States	Mark et al. [22]
Thrombolysis in acute MI for the elderly	United States	Krumholz et al. [19]
ICU cost-performance model	United Kingdom	Smithies et al. [48]
ICU cancer patients	United States	Shapira et al. [56]
Monoclonal antibodies in gram-negative sepsis	United States	Schulman et al. [23]
Monoclonal antibodies in gram-negative sepsis	United States	Chalfin et al. [22]
Monoclonal antibodies in gram-negative sepsis	United Kingdom	Chang et al. [67]

A similar investigation evaluated severity of illness, length of stay, procedures, and patients charges for all patients with septic shock admitted to the adult ICU at an inner-city teaching hospital for the years immediately prior to and immediately following the formal organization of a critical care service [43]. Severity of illness was similar during both periods, although mortality fell after the change. However, ICU care became more "costly", as patient charges and length of stay increased. Per capita charges, for example, increased from $ 29, 111 to $ 34,609 [43]. Clearly, improved outcome was accompanied by higher cost; however, cost-effectiveness, in terms of charges per survivor, was improved as this ratio fell from $ 126,570 to $ 96,136 [43]. Similarly, the marginal cost-effectiveness for the critical care service, defined as the change in per capita charges divided by the change in survival, was $ 42,292 [($ 34,609 − $ 29,111)/(0.36 − 0.23)]. Thus, critical care service for septic shock generated higher charges, although these additional expenditures led to better outcomes [43].

The direct cost-effectiveness of critical care medicine

The latter two studies indirectly imply a favorable cost-effectiveness ratio for critical care services. However, a few investigators have directly attempted to determine ICU cost-effectiveness. Walker and colleagues [44] determined a cost-effectiveness ratio for low-birth-weight (500 − 999 g) neonates and concluded that intensive care may not be cost-effective for infants weighing less than 900 g at birth. Vang et al. [45] retrospectively looked at the cost-effectiveness of ICU admission for elderly surgical patients at a community hospital in Sweden between 1978 and 1980; they determined the cost per year of life gained (in 1984 US dollars) to be $ 190.00 (SEK 1,700). In another investigation, which was not truly a cost-effectiveness study because only one option was studied, Bams and Miranda [46] determined the cost-effectiveness ratio of surgical critical care at the University Hospital in Groningen, in terms of the cost per survivor, to be $ 7,095.

Fineberg et al. [47] investigated the cost-effectiveness of an intermediate care unit versus a coronary care unit for the treatment of patients with a low probability of a myocardial infarction from the societal perspective. Intermediate care units were deemed highly cost-effective for patients with a life expectancy of 5 or more years, and conventional coronary care units were calculated to cost $ 2.04 million per life saved and $ 139,000 per year of life saved (in 1980 dollars). When the risk of infarction was increased (to 20% in sensitivity analysis) these figures fell to $ 485,000 per life saved and $ 33,000 per year of life saved, respectively [47].

Cost-effectiveness, cost performance, and severity of illness

In all hospitals in the industrialized world, ICUs tend to care for the sickest patients. Nevertheless, ICU patients are very heterogeneous and display a wide variability in terms of severity of illness and patient acuity. Most economic studies in critical care implicitly neglect this fact, however, as they tend to lump all ICU patients, together into one large group. This limits one's ability to assess cost-effectiveness according to patient acuity or case mix, for patients with a low severity of illness are combined with those who have a worse prognosis and a lower probability of survival. Intuitively, cost-effectiveness should vary according to case-mix and acuity. For example, higher severity of illness has been linked to higher resource consumption; thus, higher mortality may imply low cost-effectiveness, as a great amount of resources are allocated to the care for those with a minimal chance of meaningful recovery. Thus, ICU cost-effectiveness may be evaluated more precisely by dividing patients into various strata according to severity of illness.

Smithies et al. [48, 49] developed a cost-performance profile to assess jointly the economic and clinical performance of their ICU according to APACHE II scores. In this study, patients were grouped into deciles of increasing risk, and the costs per survivor (CPS) and per non-survivor (CPNS) and the effective cost per survivor (ECPS) were determined for each decile. ECPS provides the meaningful cost-effectiveness measure per survivor, as it was determined by adding all the costs incurred by all patients within each strata and then dividing the sum by the total number of survivors. A standardized mortality ratio (SMR) was also developed by dividing the expected mortality, as determined from the mean APACHE II risk of death, into the actual mortality [48].

Patients were analyzed over a 3-year period (1 June 1990 − 31 May 1993). For all years, most of the patients were clustered in the first two deciles. The CPS and the CPNS remained within a relatively narrow range throughout the study. However, the ECPS showed an exponential rise as the risk of death increased. As the number of survivors within each decile decreased, more and more resources were expended for the care of fatalities, and thus collective costs rose while the survivor pool decreased. In the 1st fiscal year, for example, the CPS and CPNS remained relatively stable, never exceeding £20,000. However, the ECPS rose from £ 1,315 in the lowest decile (0 − 10% risk of death) to £ 91,625 in the eighth decile. An ECPS of £ 8,910 was obtained in the ninth decile; however, only five patients were in this stratum and four of them died. No ECPS was obtained for the highest decile because the observed mortality was 100%. Although this model showed quantitatively how the ECPS dramatically increased as the expected probability of mortality rose, the major purpose was to compare cost-performance and cost-effectiveness after ICU reorganization. In the 2nd year of analysis, the ICU staff assumed direct responsibility for patient care and instituted several other changes, including the uses of a "gut protection" protocol and of continuous venovenous hemodiafiltration. As in the previous year, ECPS rose exponentially with increasing risk, although it was markedly lower for all strata and never exceeded £ 22,000. In the 3rd year, the ECPS again rose due to the addition of nitric oxide and extra-corporeal membrane oxygenation protocols for the treatment of ARDS; however, the ECPS for all strata still remained far below the levels from the 1st year [48].

A study by Rapoport et al. [50] also used severity scoring to assess the cost-effectiveness of intensive care; it different from the previous investigation, however, in that it analyzed the performance of not just one but many ICUs. Briefly, a total of 3,397 patients admitted to 25 ICUs in Europe and North America during a 4-month period in 1991 were evaluated using a lenght-of-stay index (weighted hospital days) for cost measurement and the difference between observed and predicted survival as measured by the mortality probability (MPM) model [51, 52]. Most of the ICUs fell within 1 SD of the mean for both clinical and economic performance: 21 out of 25 fell within 1 SD for clinical performance and 17 of 25, within 1 SD for economic performance. Few cost or clinical outliers were therefore noted, and no tradeoff was noted between outcome (i.e. clinical performance) and resource consumption (i.e. economic performance) [50].

Economic impact of a ventilatory management team

Other investigators have analyzed the economic impact of specific components of critical care services. Cohen et al. [53], for example, looked the impact of a multidisciplinary ventilatory management team upon costs and outcomes. Briefly, costs and outcomes were assessed for all ventilated patients in a 450-bed, community teaching hospital during the year prior to and following the establishment of the team. Outcomes during the two periods were similar; however, ICU length of stay, duration of mechanical ventilation, and the number of arterial blood gases and indwelling arterial catheters all decreased with the ventilator team, leading to a saving of $ 1,303 per episode of mechanical ventilation. Even though specific ratios were not derived, the lower costs and higher outcomes imply relative cost-effectiveness [53].

Cost-effectiveness of mechanical ventilation in the elderly

The use of very expensive therapies in the elderly is clearly an area of great clinical and ethical controversy. Debate continues on the issue of the impact of age on ICU outcome, but it is generally agreed that age alone should not be used as criterion for ICU access. It has been estimated by many that a small percentage of ICU patients (less than 10%), who, for the most part, require prolonged mechanical ventilation, consume as much as 50% of all ICU resources and experience significantly worse outcomes [54].

Cohen et al. [55] investigated the charges per year of survival in 45 patients aged 80 years and older who required 3 or more days of mechanical ventilation in a combined medical-surgical ICU. They introduced a post hoc, rule-of-thumb index [age in years (A)+duration of mechanical ventilation in days (D): A+D]. Using this approach, they noted that approximately 75% of all hospital charges for these patients were accrued after the 3rd day of mechanical ventilation, and that nearly 40% of total hospital charges for the entire group were generated by 22 patients after A+D exceeded 100. The cost-effectiveness ratio, defined as dollars per year of life saved, ranged from $ 86,000 to $ 123,899 (in 1992 dollars), and rose to $ 300,790 when the A+D index was 100 [55].

Cost-effectiveness of critically ill cancer patients

The cost-effectiveness of specific diagnoses, such as ICU patients with cancer, has also been studied. Schapira et al. [56] investigated the cost-effectiveness of critical care for ICU patients with both solid- and soft-tissue malignancies during a 2-year period at the H. Lee Moffitt Cancer Center in Tampa Florida. The cost per year of life gained was $ 82,845 for patients with solid tumors and $ 189,339 for those with soft-tissue malignancies. Furthermore, the costs for a projected year of life at home for patients with solid tumors and hematologic malignancies were $ 95,142 and $ 449,554, respectively. As the authors note, these values greatly exceed similar cost-effectiveness ratios, including those of $ 4,500 for chemotherapy for small-cell lung cancer and $ 10,000 for bone marrow transplantation for acute myeloid leukemia [56–58]. Relative to these and other critical care interventions, the admission of certain critically ill cancer patients to the ICU may be deemed cost-ineffective, for limited expected survival is achieved at very high cost [56].

Cost-effectiveness of thrombolytic therapy

Laffel et al. [19] developed a model to study the incremental costs and benefits of patients who received coronary thrombolysis. The cost per year of life saved was reduced as the clinical efficacy of thrombolytic therapy improved, and thrombolytic therapy was shown to be more cost-effective for larger infarcts and when it was administered early in a patient's clinical course. For example, the cost per year of survival was $ 35,000 (in 1989 dollars) for large infarcts and $ 800,000 for small ones [19]. In another study, which specifically evaluated the cost-effectiveness of streptokinase for elderly patients, streptokinase was deemed clinically efficacious for patients 75 years or older when the risk of acute myocardial infarction exceeded 9%. The calculated cost per year of life gained for streptokinase never rose above $ 55,000 over a wide range of assumptions concerning underlying incidence, outcome, and cost [18].

In two more recent studies [21, 59] the cost-effectiveness of tPA was compared to that of streptokinase. TPA patients generated higher costs, yet had better outcomes when compared to streptokinase-treated patients in both studies, leading to a marginal cost-effectiveness of $ 32,678 per year of life saved [21] and $ 30,300 per additional QALY [59]. Sensitivity analysis demonstrated that the cost-effectiveness for tPA improved as patient age increased and for patients with anterior wall infarctions [21, 59].

Cost-effectiveness of investigational agents for sepsis

Sepsis afflicts between 150,000 and 400,000 patients per year, many of whom require intensive care [60]. In spite of the aggressive care that is often provided, mortality remains high and may reach 90% for patients who develop hemodynamic shock [61]. Biotechnological agents, such as monoclonal antibodies to endotoxin and interleukin-1 receptor antagonists (IL1-ra), have been studied in phase-III clinical trials as adjunctive agents in the treatment of the sepsis syndrome. The clinical efficacy of many of these agents remains an area of active investigation; however, their potential economic impact has attracted significant attention, as most of them are expected to cost several thousands of dollars and thus questions concerning their cost-effectiveness have been raised.

The cost-effectiveness of monoclonal antibodies against gram-negative endotoxin was evaluated in two separate studies (see Table 3). Schulman and colleagues [23] developed a decision-theory model to assess the cost-effectiveness of one of the monoclonal antibodies that was evaluated in a large phase-III trial: HA-1A. The cost per year of life saved for HA-1A was $ 24,100 in the strategy where HA-1A was given to all patients with presumed gram-negative sepsis, and $ 14,900 when HA-1A was given only to those patients who tested positive with a hypothetical bedside screening test. When subjected to sensitivity analysis, these ratios ranged from $ 5,200 for patients with an expected gain in life expectancy of 20 years to $ 110,000 for an expected gain of only 1 year [23].

Chalfin et al. [22] also used decision analysis to investigate this problem from the perspective of the acute care institution [22]. Total expected costs were always higher for the cohort of patients who received the drug; however, the higher costs were always $ 870 less than the acquisition price of the monoclonal antibodies because increased expected survival led to reductions in other costly expenditures. In terms of cost-effectiveness, monoclonal antibody therapy had a lower cost per survivor and remained the more cost-effective option even when subjected to rigorous sensitivity analysis, including an increase in the acquisition cost to over $ 5,000 [22].

The cost-effectiveness of an IL1-ra has also been evaluated with data obtained from a phase-II randomized trial involving 99 septic adults [62]. Mortality was higher for the controls and declined with increasing doses of the drug (17 mg/h over 72 h to 133 mg/h); however, average hospital and ICU lengths of stay were higher in the treatment groups. From a cost-effectiveness standpoint, the higher survival more than offset the longer ICU stay, and thus the cost-effectiveness ratios, defined as average hospital and length of ICU stay per survivor, were lower in the treatment groups than in the control group [62].

Conclusions and comments

Clearly, critical care is expensive care, and ICU clinicians will come under increased pressure to contain costs and curtail growth. Pressures for cost containment may emanate from processes within institutions grapping with limited budgets, or from external forces and widescale changes in health care financing, organization, and delivery. Regardless of the origin, the effects are bound to trickle down to the intensive care unit and may influence the scope, quantity, and quality of care provided. The expansion of managed care in the United States, for exam-

Table 3 Comparison of cost-effectiveness and economic studies of monoclonal antibodies against gram-negative sepsis

Study	Agent	Method	Perspective	Summary measure
Schulman et al. [23]	HA-1A	Decision analysis	Society	Cost per year of life gained
Chalfin et al. [22]	HA-1A and E5	Decision analysis	Acute care institution	Cost per survivor
Chang et al. [67]	HA-1A	Cost-performance model	Acute care institution	Effective cost per survivor

ple, and the increased pressure as a result of limited global budgets and capitated reimbursement may further increase the financial pressures faced by acute care hospitals, and these effects may trickle down to critical care services and the scope of care delivered.

Under ideal circumstances, economic pressures and financial constraints can have a positive impact on health care delivery, as processes and structures can be streamlined and waste and redundancy eliminated without reductions in quality. In the ICU, this may manifest itself as improved patient triage, better identification of patients who stand to benefit the most from ICU care, reductions in unnecessary procedures and interventions, and shorter ICU and hospital lengths of stay. However, cost-cutting measures as a result of severe monetary shortfalls can also lead to reduced quality of care and worse patient outcomes. Quality of care in the ICU may be particularly sensitive to financial cuts, because critical care is highly dependent upon both labor and capital. Unlike other inpatient services, such as certain elective surgical procedures which can be shifted to an ambulatory environment, critical care is relatively inelastic, as many critically ill patients need to be cared for in the specialized environment of the ICU [63]. Thus, curtailments in ICU services resulting from budgetary cutbacks may change the overall "mission" of the ICU and lead to diminished quality with poorer outcomes.

As cost-containment efforts become more widespread, clinicians and administrators will face increasingly difficult choices. Many of the changes occurring in health systems in the industrialized world have sharply curtailed the ability to provide a full range of services, including those of great expense and limited benefit, to every patient upon demand. In the past, health care may have been dominated in some societies by a "technological imperative", and clinicians were often immune to the economic consequences of their clinical practice [64]. Now, however, the forces have changed, and cost considerations have become more and more embedded in the clinical process. Appropriate analytical tools that are judiciously and ethically applied, such as cost-effectiveness analysis, should be utilized to facilitate more rational and reasoned decisions, especially in the all-too-common cases where a program yielding better outcomes and a higher quality of care is more expensive than an alternative one. In these situations, cost-effectiveness analysis, the accurate assessment of all costs and benefits, and the determination of a meaningful cost-effectiveness ratio may allow for reasonable and reproducible comparisons among competing alternatives. Alongside the clinical and financial imperatives that may arise, cost-effectiveness analysis has even been proposed as a criterion for the funding of new procedures and technologies [65].

By virtue of its vast expenditures and often indeterminate and varied outcomes, critical care needs to be assessed in terms of both its overall cost-effectiveness and the cost-effectiveness of its specific components. It has also been suggested that the cost-effectiveness and clinical efficacy of critical care services, especially if used in concert with severity of illness scores to stratify patients according to acuity, may even be enhanced by the identification of those patients who stand to benefit the most from ICU care and from expensive therapies along with those at "high risk of high cost" [6, 66, 67]. Limited resources and increased financial scrutiny will limit expenditures for critical care and other costly services that have unclear, minimal, or improbable benefits. In essence, cost-effectiveness analysis can help one set rational-priorities and achieve sensible and clinically reasonable goals. This will facilitate comparisons among critical care services at the institutional, local, and national levels and therefore yield the highest benefit at the most reasonable cost.

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