

# Expensive care — a rationale for economic evaluations in intensive care

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Resources in the health care system are limited, and there is a constant challenge to maximise health benefits to patients within the available resources. This is particularly relevant in intensive care, where there is an increasing demand for services coupled with newer and more expensive technologies. In the United States, it has been estimated that intensive care unit costs represent up to a third of all hospital costs.<sup>1</sup> New interventions are often significantly more expensive than the previous standard of care, and concerns have been raised about their financial impact.<sup>2</sup> Economic evaluations enable the clinical and resource implications of health care interventions to be explicitly considered, aiding decisions about which therapies to implement in an environment of heightened cost consciousness and competing demands for limited resources.<sup>3</sup>

This commentary is the first in a planned series outlining the underlying rationale and conduct of economic evaluations in Australian critical care. Subsequent articles will detail how to read and appraise published economic evaluations, methods to collect Australian costs for economic evaluations, the different outcome measures, and guidance on putting it all together to conduct a critical care economic evaluation in the Australian setting.

## What is an economic evaluation?

Economic evaluations compare the costs and benefits of an intervention. A treatment is said to be “cost effective” if it provides greater health gains than could be achieved by using the resources in other ways.<sup>4</sup> The potential combinations of additional resources needed for a new intervention and additional benefits to patients fall into four categories (shown in Figure 1):

- An intervention can cost less and be more effective, in which case it is considered “dominant” and should be adopted;
- It can cost more and be less effective, in which case it is “dominated” and should not be adopted;
- It can cost less but be less effective; or
- It can cost more and be more effective.

In these latter two cases (the bottom left and top right quadrants of Figure 1), a decision is needed about what one is willing to pay to obtain an extra unit of effectiveness (or willing to save to lose a unit of effectiveness). Table 1 lists

## ABSTRACT

The demand for intensive care services is growing, and the cost of these services is increasing, with newer technologies consuming larger portions of the health care budget. We contend that both the costs and benefits of interventions must be considered to truly understand their value in critical care. Economic evaluations provide an explicit framework to compare the costs and benefits of an intervention. If these factors are not considered together, decisions may be made that do not result in the most efficient use of constrained resources. Despite limitations arising from variations in economic evaluation methodology, logistical complexity and problems of generalisability, the Australian trial environment provides an ideal opportunity to obtain robust economic data to help decision-making. Here, we outline the rationale for conducting economic evaluations in the critical care setting and argue that these evaluations need to be routinely incorporated into all large-scale clinical trials.

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the ratio of cost to outcomes (the cost-effectiveness ratio) of various interventions, determined in the Australian setting. These studies include preventive therapies, diagnostic tests and interventions in both ICU and non-ICU settings and measure patient outcomes as life-years gained or generic quality-adjusted life-years (QALYs). A QALY is a composite measure that combines survival and quality of life into a single index and allows comparisons across a range of interventions with disparate clinical outcomes.

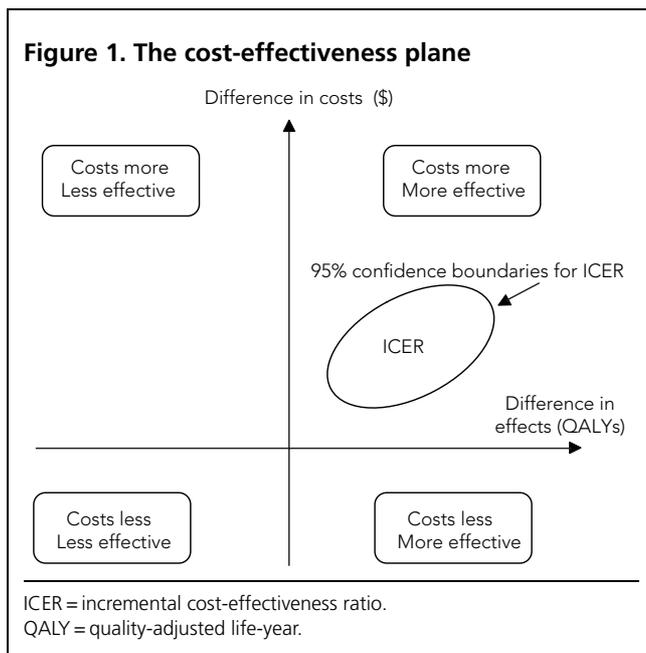
Economic evaluation is increasingly used to aid decision-making, often by reimbursement authorities, but also by individual hospitals and clinical decision-making units. Examples include Australia’s Pharmaceutical Benefits Advisory Committee and Medical Services Advisory Committee, and the United Kingdom’s National Institute for Health and Clinical Excellence. More recently, the United States has passed legislation establishing a “Comparative Effectiveness” institute, with a mandate to consider methods for the economic evaluation of health care technology. As it is likely that the recommendations of these bodies will increasingly affect bedside availability of therapies and interventions, it

is important that clinicians gain an understanding of economic evaluations.

**The need for economic evaluations in intensive care**

The costs of intensive care are high, and demand is increasing. The National Hospital Cost Data Collection indicates that the average cost of a public hospital admission in Australia in 2007–08 was \$3907.<sup>19</sup> This contrasts with an average of \$62 256 for some of the most common diagnosis-related groups associated with intensive care (A06Z, tracheostomy or ventilation >95 hours; W01, ventilation or craniotomy procedures for multiple significant trauma; and F03Z to F06B, cardiac valve and coronary bypass surgeries).<sup>20</sup>

Economic evaluations provide a framework for consideration of competing alternative interventions, helping maximise the value we get from every health dollar. They enable determination of whether, despite being expensive, a treat-



**Table 1. Examples of Australian cost-effectiveness studies**

Intervention	Cost (A\$)*	
	Per QALY	Per life-year
Antimicrobial-coated central venous catheters <sup>5</sup>	Dominant†	–
Valaciclovir prophylaxis after renal transplantation when donor is cytomegalovirus-positive and recipient is negative <sup>6</sup>	Dominant	Dominant
Exogenous surfactant given with assisted ventilation for extremely low birthweight infants (500–999 g) <sup>7</sup>	Dominant	Dominant
Australian mass media anti-tobacco campaign <sup>8</sup>	–	\$1 509
National skin cancer primary prevention campaign <sup>9</sup>	–	\$2 170
Pre-hospital thrombolytic therapy for STEMI patients <sup>10</sup>	\$3 248	\$4 281
Glucosamine sulfate for osteoarthritis <sup>11</sup>	\$3 746	–
Total hip replacement for osteoarthritis <sup>11</sup>	\$8 741	–
Annual cervical cancer screening using conventional cytology in kidney transplant recipients <sup>12</sup>	–	\$14 481
Zanamivir prescribed in general practice to treat those at high risk of influenza <sup>13</sup>	\$17 069	–
Non-specific NSAIDs for osteoarthritis <sup>11</sup>	\$18 731	–
Ramipril ACE inhibitor (10 mg/day) <sup>14</sup>	–	\$22 781
Flexible sigmoidoscopy every 10 years for colorectal cancer prevention <sup>15</sup>	–	\$25 087
Tamoxifen for breast cancer prevention <sup>16</sup>	\$58 175	–
Recombinant factor VIIa (NovoSeven [Novo Nordisk]) home-treatment intravenous push injection for children with haemophilia <sup>17</sup>	\$76 949	–
Pneumococcal conjugate vaccination, four doses at ages 2, 4, 6 and 12–15 months <sup>18</sup>	–	\$345 752

QALY = quality-adjusted life-year. STEMI = ST elevation myocardial infarction. NSAID = non-steroidal anti-inflammatory drug.

ACE = angiotensin converting enzyme.

\* All values were converted to 2009 Australian dollars

† Dominant = lower cost, greater effectiveness.

ment is cost-effective (good value for money). Economic evaluations should aid decisions on competing alternative interventions within intensive care itself, and also facilitate funding decisions for intensive care services, in comparison with allocating resources elsewhere in the health system.

Considering only the cost of expensive new interventions, or not considering costs at all, will inevitably lead to misguided decisions. If only the expense of a new intervention is considered, yet the intervention results in clinical outcomes that dramatically reduce downstream costs and provides a health outcome at a reasonable cost, then there is a risk of failing to adopt a cost-effective intervention. An example is the use of activated protein C in patients with severe sepsis. With a treatment cost > \$12 000 per patient, this might be considered expensive. However, considering the cost to an ICU budget alone, without considering the value of the clinical benefits, might undervalue the intervention overall. It is clear that cost effectiveness requires clinical effectiveness; the higher the quality and strength of the evidence for clinical effectiveness, the less the uncertainty about cost effectiveness. It is important to recognise that treatments with high acquisition costs may still be cost effective when one considers costs and benefits that accrue outside the ICU. Not considering benefits may lead to the failure to adopt some important innovations.

Alternatively, if only outcomes are considered (in the absence of cost), there is potential for interventions to be adopted that do not provide good value for money, wasting valuable resources that could be used elsewhere in the health care system for greater benefit. For example, the SAFE (Saline versus Albumin Fluid Evaluation) study conducted by the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG) was the largest study to date in an intensive care setting. This landmark 7000-patient study found no discernible difference in death rates between intensive care patients resuscitated with human albumin and those resuscitated with saline.<sup>21</sup> No economic evaluation was conducted alongside the trial. Currently in Australia, the cost of 500 mL of 4% albumin is \$46.67 (National Blood Authority, personal communication), while the cost of 500 mL normal saline is less than \$2.20 (Baxter Australia, product catalogue). Within the Australian health care system, only the cost of saline is included within the ICU budget, while the cost of albumin is borne by federal, state and territory governments. Thus, for a hospital in Australia (as opposed to Europe or the United States), use of albumin rather than saline results in additional available money within the hospital budget, but, at a national level, increases the cost of care.

These examples highlight the role of the perspective taken in any evaluation. When one considers only a limited budget perspective (such as an ICU drug budget), one may

make a different decision than when a broader perspective is taken. If maximising health gain within society's budget constraints is the objective, then all costs and health outcomes need to be included, irrespective of who bears those costs.

### Existing economic evaluations in intensive care

To date, economic evaluation has had limited application in critical care. The few existing cost-effectiveness analyses (CEAs) in clinical comparative trials in critical care between 1993 and 2003 were summarised by Talmor and colleagues.<sup>2</sup> Their systematic review comprised 19 CEAs with varying quality scores, resulting in only 48 cost-effectiveness ratios, most using a lifetime horizon, and most assessing either activated protein C or mechanical ventilation. The cost-effectiveness ratios ranged from cost saving to US\$958 423 per QALY and from US\$1150 to \$575 054 per life-year gained.<sup>2</sup> These wide ranges reflect different interventions and different patient groups. For example, the cost effectiveness of activated protein C ranged from \$12 570 to \$33 100 per life-year gained and \$20 047 to \$48 800 per QALY; however, when stratified by risk, patients with an APACHE II score < 25 had a cost of up to \$575 054 per life-year gained and \$958 423 per QALY, compared with \$19 723 per life-year gained and \$32 872 per QALY in those with an APACHE II score  $\geq$  25.<sup>2</sup>

More recently, CEAs have been published on a variety of intensive care interventions including antimicrobial-coated central venous catheters,<sup>5</sup> integrated sepsis treatment protocols,<sup>22,23</sup> anti-fungal therapy,<sup>24,25</sup> recombinant human erythropoietin for reducing red blood cell transfusions,<sup>26</sup> meropenem versus imipenem plus cilastatin in the treatment of severe infections in intensive care,<sup>27</sup> extracorporeal membrane oxygenation,<sup>28</sup> and daily versus alternate-day haemodialysis in the management of acute kidney injury.<sup>29</sup> To date, only one of the published economic evaluations of intensive care therapies has been performed in Australia — an analysis of antimicrobial-coated central venous catheters.<sup>5</sup>

### Limitations of economic evaluations

Despite the strong rationale for using economic evaluations to facilitate decision-making about health care resource utilisation, and the evidence that their use is increasing, there remain limitations. In the health care system, decisions need to be made about the type and quantity of care available and who that care is available to. Recommendations based on economic evaluations are often designed to maximise the societal health gain for a given expenditure. This may conflict with the clinician's goal of maximising the health gain for their individual patient. For example, a hospital formulary

may use the results of an economic evaluation to restrict access to a particular drug, or restrictions may be placed on capital expenditure for new equipment.

A major criticism of economic evaluations to date is the lack of standardised methodology and the quality of the data on which they are based. There are inconsistencies in costing methods, the components of care that are costed, the perspective used, and the sources of utility weights used to determine QALYs, as a few examples. In addition, a lack of high-quality evidence of effectiveness and limited data for quality-of-life outcomes limits the confidence we can have in their results. In their systematic review, Talmor and colleagues<sup>2</sup> identified significant variability in the methods used in critical-care economic evaluations. For example, only two of the 19 included studies were conducted from a societal perspective, sensitivity analyses were conducted in only 14, and time horizons ranged from 6 months to a lifetime.<sup>2</sup>

This lack of standardisation makes it difficult to compare evaluations and limits their usefulness for informing decision-makers. Recognising this, the American Thoracic Society has published guidelines for conducting CEAs in critical care, to help standardise the methods.<sup>30</sup> The guidelines recommend conducting a base case economic analysis from a societal perspective, estimating long-term costs and quality of life after ICU care, and conducting multiway sensitivity analyses.<sup>30</sup> They also recommend conducting a “data rich case”, generating a cost-effectiveness ratio using data on actual patient outcomes and costs (rather than modelled outcomes).<sup>30</sup> Within Australia, there are no specific guidelines for conducting economic evaluations in critical care, but numerous other guidelines exist, including those from the Medical Services Advisory Committee<sup>31</sup> and the Pharmaceutical Benefits Advisory Committee.<sup>32</sup>

Despite the move towards standardising methods, collecting data for economic evaluations remains complex. The primary inputs are evidence of effectiveness and cost data. For comparing effectiveness of interventions, any economic analysis is only as good as the underlying clinical trial, with the attendant potential for bias and variation in the evidence of effectiveness. The collection of cost data is especially pertinent in critical care, which consumes a very large number of resources.

Another limitation on the usefulness of economic evaluations is their lack of generalisability. Treatment practices vary dramatically between regions and countries, as do the costs (and even availability) of resource inputs. The combination of these factors, their impact on an economic analysis, and the limited ability of those appraising economic evaluations to understand the effect on their conclusions hinder the direct application of results from one setting, country or region to another. This is a rationale for undertaking analyses locally within the region of interest.

## Why undertake economic evaluations alongside clinical trials — the Australian opportunity

The limitations of conducting economic evaluations considered above might be largely overcome if we take advantage of the strength of the critical care clinical trial program in Australia. Conducting economic evaluations alongside large, multicentre, pragmatic clinical trials is an ideal opportunity to efficiently collect detailed information on the costs of care; to provide evidence of clinical effectiveness, including effect on quality of life; and to provide a broad base from which to generalise to other ICUs and hospitals in Australia. In Australian intensive care, large, pragmatic, randomised controlled trials are performed that mimic true clinical practice, such as the SAFE,<sup>7</sup> NICE<sup>33</sup> and RENAL<sup>34</sup> studies. There is a unique opportunity to conduct high-quality, generalisable, economic evaluations relevant to Australian conditions alongside these clinical trials.

## Conclusions

Unquestionably, we must consider the costs as well as the benefits of interventions. Prioritising of health care should incorporate all available information, including cost effectiveness, equity, need and access. This has become increasingly important at a time that both ICUs and the whole health care system lack the money to cover their increasing budgets in a worsening economic environment. Routine incorporation of cost effectiveness studies into randomised controlled trials in intensive care is essential; only with these data can clinicians fully assess the value of new interventions in intensive care. With further research and more CEAs, efficient and robust methods can be refined and standardised. In Australia and New Zealand, we are in the ideal position to help make this happen.

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