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A primer for clinical researchers in the emergency department: Part X

Understanding Economic Evaluation alongside Emergency Medicine Research

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Abstract

In this series, we address research topics in emergency medicine. While traditionally there was an almost exclusive focus on the efficacy and effectiveness of interventions in emergency research, analysis of the costs and the societal impact of different approaches and pathways have become increasingly important. In this paper, we will address what

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health economics means and discuss the different types and key features of economic evaluation relevant for clinical researchers.

Introduction

Clinical research produces evidence regarding the efficacy or effectiveness of a diagnostic tool or treatment strategy, and this informs clinical decision-making. If resources were unlimited, clinicians would choose the most effective strategy for each patient regardless of cost. However, health care workers, especially in the emergency department (ED), are familiar with increasing service demands and limited resources, and make decisions daily balancing risk and benefit, where providing care for one patient delays care for another.[1] Health economics is the application of economic principles to the distribution of scarce resources used for the delivery of health care to improve patient cutcomes.[2,3]

Health from an economic perspective is measured in terms of mortality and morbidity: either as natural units (life years gained, or disability days saved) or healthy years described as quality adjusted life years (QALY). QALY is the combination of health related quality of life (Qol) and life expectancy (quantity), which creates a generic outcome measure of utility an individual derives from health, and in turn health care.[2]

Economic evaluation provides a systematic approach of comparing relevant alternatives in terms of costs and outcomes to measure which strategies provide the most value for money.[2] Incorporating an economic evaluation alongside clinical research provides additional information that extends beyond the individual patient, to reflect the impact of clinical decisions on resources used in the ED, the health system and society. Further, it is a framework of analysis that incorporates the opportunity cost of health foregone elsewhere in the health system based on the value placed by society on health and access to health care. Therefore, incorporating cost-effectiveness in evidence-based medicine provides a system level measure of comparative efficiency and resource optimization.[2,4]

The clinical outcome effect can be obtained from multiple study sources (randomised control trials, observational trials, administrative data bases or long-term epidemiological

studies). If the survival benefit is not measured, intermediate outcomes such as average blood pressure control or cancer cases detected are used. The economic evaluation can be performed alongside a clinical study, using individual patient data or by using decision-analytic modelling, synthesising information from multiple studies, adjusting for uncertainty in the estimates.[2] Health outcomes as clinical effects are measured as either natural units (the percentage of patients with a concussion from sports related head trauma), or improved mortality (as life years gained) using descriptive data.

Example: *You are preparing a study protocol to evaluate the effectiveness of a neurocognitive intervention initiated in the ED for the treatment of concussion in children. The funding agency would like you to include your plan for a cost-effectiveness analysis of your intervention.*

The Features of an Economic Evaluation

The key features of an economic evaluation are, firstly, the analysis of costs and outcomes of all relevant alternatives. Secondly, the comparison of one or more alternatives to either current practice or often a "do nothing / usual care" alternative if there is no gold standard or evidence based established practice (option A in Figure 1).

The cost-effectiveness plane[5] (Figure 1) plots the difference in cost and effectiveness between the alternatives (option A and B) being compared. The x-axis depicts the relative difference in outcome and the y-axis the cost difference; this creates four quadrants relating clinical effectiveness to cost effectiveness.

If the most effective option is also the cheapest (quadrant II), then this is a "cost saving, adopt" strategy. When the option is both more costly and less effective (quadrant IV), it is a "reject, dominated" strategy.

When there is no clear dominant strategy (quadrant I or III), the difference in the costs compared with the difference in the effects is measured as the incremental cost-effectiveness ratio (ICER).[2]

$$ICER_B = \frac{Cost^B - Cost^A}{Effect^B - Effect^A}$$

The ICER is then compared with the "willingness to pay threshold" (dash line in figure 1), which represents the acceptable cost the health system or decision makers are willing to spend for the additional benefit gained from the intervention. In Australia, this is AUD $50,000/QALY gained.[6] Thus in quadrant I, since the cost per QALY gained with option B is less that the willingness to pay (WTP) threshold of $50,000/QALY ($ICER_B$ lies below the WTP threshold), option B it is considered cost-effective. It is important to note that the $50,000/QALY is an arbitrary value and there is an accepted range of $50,000/QALY to $175,000/QALY. Interventions with ICER less than $50,000/QALY considered as providing high value, interventions with ICER greater than $175,000/QALY as low value, and those in between with intermediate value.[7] There are however exceptions to this rule (for example, orphan drugs for rare genetic disorders), in cases where as a society we decide it worth funding.[8,9]

Economic perspective

The economic perspective taken will determine the impact of decisions on resources, and the relevant costs incurred. As a clinician working in the ED, one could take the perspective of the local ED or hospital. Here, direct costs associated with the delivery of health care (such as hospital admission or medication costs) and the direct health benefits (improved survival or treatment failure at 48 hours) from the treatment are considered. This could be extended to health systems that reimburse health care expenses. Here the agencies have to decide which health care programmes to fund, for example, preventive services (colon cancer screening) are more cost-effective than oncological treatment. If a societal

perspective is taken, then impact on the individual (lost wages and out of pocket expenses) is considered in addition to the health system. It is recommended to take as broad a perspective as possible, to consider the long-term spill over effects on other health services.

Health related costs

Cost analysis specified from the perspective taken, involves including all costs associated with the intervention and outcome. If there is only one treatment being evaluated, then comparing it with doing nothing provides meaningful information. There are two types of direct costs, health care related (drugs, tests, hospital and health care provider fees), and non-health care related costs (family member time, cost of transportation). Indirect costs relating from loss of wages or pain and suffering are much harder to measure and are often not included in the economic analysis.[2]

Opportunity cost is the fundamental economic principle that describes the health cost associated with the next best alternative that was not chosen. This represents the health benefit that is lost elsewhere in the health system as a result of scarce resources. For example, the National Health System (NHS) in the United Kingdom operates with a health care budget funded by the taxpayer. Since all the health care costs are borne by the health system, the cost of a stroke prevention programme should also include the opportunity cost of not funding the next best alternative programme.[2]

The most common resources for cost information in Australia are the Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS).[6] They provide information for the government-subsidized cost of care to the public health system. Additionally, there are various repositories for ED visits and hospital admission related cost (Emergency Department Data Collection or National Hospital Cost Data Collection).[10] Relevant costs for physician services and drug costs can be obtained form national, regional or local hospital level resources, however it is much harder to assess the cost of physician time. Most cost-

effectiveness studies do not consider the cost of physician time since it is assumed to be a common factor in both arms of the study.

When designing this clinical study, it is important to consider and capture the economic burden of concussion on the patients and their family. These costs would not be available in the MBS or PBS datasets. Some of the questions included are:

- *How many days of paid work have you missed to look after your child being unwell because of the concussion?*
- *How many days of unpaid usual duties have you missed to look after your child being unwell because of the concussion?*
- *How many days overall have you needed an additional carer (other family members or baby-sitters) to look after your child for being unwell because of the concussion/injury?*
- *Approximately how much have you spent out of your own pocket as a result your child's concussion/injury?*
    - *Medication*
    - *Gap payments*
    - *Transport and accommodation*

Time horizon, discounting and inflation

The time horizon of the outcome measures should be specified *a priori*, recognizing that the health benefits are achieved some time after the costs are incurred. The time-period considered will vary for different diseases and if it is an acute or chronic process. It is critically important to systematically include all relevant costs incurred at different time periods adjusted for time preference and inflation. Time preference is an economic concept that states that individuals value the present more than the future. This results in comparing both present and future costs and benefits adjusted to the same base time-period of analysis.[2]

Inflation reflects the decreasing purchasing power of the dollar in the present compared with the past. Therefore, costs and outcomes measured in the past are adjusted to the same base year or the year of the analysis to account for inflation.[2] The inflation rate for health care is either the Consumer Price Index (CPI) or the Australian Institute of Health and Welfare (AIHW) Health Price Index.

If the concussion study is run for 5 years 2019-2024, all the costs (drugs, doctor visits, out of pocket expenses) for each year will be adjusted for inflation to 2025 when the data is being analysed.

Discounting follows the principle of time preference where future money is less valuable than the present. Discounting future costs back to a present value allows for the comparison of costs that occur at different times from the intervention to a common denominator – the present. The discount rate of 3% or 5% per year reflects the interest rates of long-term government bonds that money can be invested in the current time-period for use in the future. For consistency, since future costs are discounted to a present value, the outcome in terms of future health is discounted as well. [2]

For example, a paediatric concussion rehabilitation programme, that costs the health system $10,000/ year for 5 years: the future 4 years are discounted at 3% back to the present and added to the present cost of $10,000 in the first year, with a total present value of $47,171. The health gain from early diagnosis and treatment can last for much longer than 5 years, perhaps the lifetime of the patient. Using the same principle that present health is more valuable than future health, the future years of additional survival measured as QALYS are discounted as well and added to the QALY gained in the first year of the programme. This way, the total costs and QALYs are compared at the same time point after adjusting for the time horizon of the study.

Health economic outcomes

The ideal instrument to quantify the outcome for an economic evaluation is a generic measure of health, where the summary score is a common metric to compare health gain across different programmes or diseases. The Quality adjusted life-years (QALYs) is one such measure, and is obtained from either "marginal cost per QALY league tables" or generic preference-based instruments like the EuroQoL EQ-5D, the Health Utilities Index Mark 3 (HUI-3), or the Child Health Utility 9D (CHU-9D).[2,11] People's preference of a health state is reflected in a utility (weights) scale from 0 to 1; where 0 is death and 1 is perfect health, and one QALY is one year of perfect health. The QALY is a measure of utility from this descriptive system of health with a set of preference weights.

For the concussion study you decide to use the CHU9D questionnaire which covers areas pertaining to sleep, physical activity, school work, pain and emotion health. Patient reported outcomes in terms of health related quality of life measures, captures treatment effects reflecting health related patient satisfaction and wellbeing.

Sensitivity analysis

Sensitivity analysis is used to report the robustness of the cost-effective analysis resulting from the economic evaluation.[12] It is equivalent to the test of significance using p-values and 95% confidence intervals of effectiveness research in medicine. In model-based economic evaluations, the process incorporates the uncertainty of the point estimates of cost and QALY inputs (95% confidence interval limits or maximum/minimum values) in the model, and quantifying the changes in the results and recommendations.[8] Since the information on the relevant health care costs and benefit are often obtained from multiple studies and different study types (RCTs, observational studies, etc.), it is important to rigorously measure the effect of uncertainty and the interaction of multiple factors on the results.[2] By changing single input parameters "one-way" or multiple parameters simultaneously "multi-way", uncertainty in the estimates used are considered in the

economic conclusion. Additionally, modelling the best case scenario (also known as value of perfect information) helps identify the key factors that if improved upon with research will have the most impact on the outcome.[2]

In this study of concussion, if the neurocognitive intervention in the ED results in shorter duration of illness this will translate to higher QALY outcomes in the patients. Additionally, the minimum and maximum costs of the intervention are noted. First, a base case analysis is made using the average costs and QALY gains in the average aged patient with concussion. If the average QALY gain is 0.3 with a 95% CI of 0.2 – 0.4, then we would repeat the analysis using different values for QALY gains varying from 0.2 to 0.4 and report the impact on the cost-effectiveness results using the base case. Similarly, this process would be repeated by using the extreme measures of cost, and patient age and other variables that have a significant impact on outcome. As a result, the sensitivity analysis involves repeated sampling varying different parameters in the model, and reporting the robustness of the economic conclusion.

Types of economic evaluation

There are several types of economic evaluation, and the type of analysis that can be performed alongside the clinical trial will depend on whether the health benefit is reported as money gained or health gained. Cost is always measured in monetary units, and as set out above, costs incurred in the past are adjusted for inflation and future costs are discounted to the present.[1-3,5,11]

- Cost analysis: The cost of illness or burden of disease, although commonly published, does not meet the criteria of a full economic evaluation. This is because it does not consider multiple outcomes to compare the effectiveness of an intervention. *However, it is an important first step in the cost-effectiveness analysis of paediatric*

concussion. It requires a systematic approach, using the predetermined perspective (hospital/health system/society) to account for all relevant costs.

- Cost minimization analysis: When interventions have equivalent outcomes, the least costly option is the most efficient use of resources. This is often done using data from a single trial, in order to incorporate the uncertainty of point estimates (95% confidence intervals) in the sensitivity analysis to test the equivalent results. A recent example of a cost-minimisation study reported that nasogastric hydration was associated with a similar hospital length of stay, but least costly than intravenous hydration in children with bronchiolitis.[13]
- Cost-benefit analysis: the relevant costs and outcomes are compared in monetary units. This may be difficult to do, since not all outcomes can be measured in terms of money.
- Cost-utility analysis: The monetary cost is compared with outcomes in terms of a utility measure like the quality adjusted life year (QALY). Multiple disease states can be compared by this generic outcome measure, and provides a framework for decision-making about resource allocation at the national or health system level.
- Cost-effectiveness analysis: The most common economic evaluation, where the cost of interventions is compared with a common naturally occurring outcome (life years gained, or reduction in mortality rate). There has been no study on the cost-effectiveness of strategies for the management of paediatric concussion. There are several studies on the cost-effectiveness of clinical decision rules for the diagnosis of traumatic brain injury in children.[6,14,15]

For this example, we decide to use a cost-effectiveness analysis, comparing the neurocognitive intervention with a "usual care" alternative. With the societal perspective, we capture the costs of a 5-year concussion programme and family economic burden. Using the CHU9D, we measure the impact on health in terms of QALY gains. This fulfils the

requirements of an economic analysis, which compares more than one outcome, and considers all relevant costs and healthcare outcomes.

Summary

Ideally, an economic evaluation should be performed alongside/with clinical trials. Incorporating the key elements of costs and relevant outcomes in the study design will help measure the health economic impact of interventions. Evidence based medical decisions affect the care of the individual patient, however collectively, these clinical decisions impact efficiency and resource utilization. The expected economic value of a treatment or programme provides information regarding the efficient use of resources at the health system or societal level.

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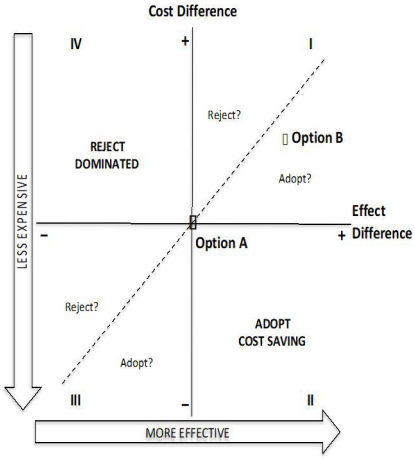

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