ARTICLE

Economic evaluation of medicines

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SUMMARY

In Australia the government must balance access to new drugs against the cost to the Pharmaceutical Benefits Scheme. Economic evaluations can be used to ensure health resources are allocated efficiently, maximising patient outcomes for every dollar spent.

There are several methods available to assess the efficiency of funding decisions in health care. Examples are cost-effectiveness, cost-utility, cost-minimisation and cost–benefit.

The Incremental Cost Effectiveness Ratio is a statistic used to summarise the cost-effectiveness of a new medicine relative to a comparator. It allows the decision maker to compare one treatment to another, thereby quantifying the opportunity cost of decisions.

Introduction

Funding medicines in a sustainable manner is an enduring challenge for health policy in many countries. In Australia, where the Federal Government operates as a healthcare monopsony or single payer, a balance must be achieved between access to new and innovative drugs and containing the cost of the Pharmaceutical Benefits Scheme. Recently the government decided to fund an innovative class of new drugs to treat hepatitis C, costing more than $1 billion over the forward budget estimates, but providing substantial benefits for patients by effectively curing the disease. This decision was made in part by balancing the benefits of the therapies against their cost through health economic evaluations.

Health economics lies at the interface between economics and medicine, applying economic concepts, such as opportunity cost, to healthcare funding decisions. In a world with scarce resources where choices must be made between competing alternatives, opportunity cost is the value of the best alternative forgone. For instance, if the government chooses to fund hepatitis C drugs instead of new cancer therapies, then the opportunity cost can be defined as the unrealised potential benefit from funding the cancer therapies. Although multiple factors are taken into account when deciding to fund new medicines, invoking this principle of opportunity cost helps us to understand how health resources can be allocated efficiently, and thereby maximise patient outcomes for every dollar spent.

Health economic evaluation methods

There are several methods available to inform funding decisions in health care. These include cost-effectiveness, cost-utility, cost-minimisation and cost–benefit analysis (Table). They allow decision makers to assess the benefits of funding decisions relative to the cost. In Australia these methods are used by the Pharmaceutical Benefits Advisory Committee (PBAC) to meet the legislative requirements in making funding recommendations for drugs to government.

The different types of economic evaluation vary according to the types of costs and outcomes being compared. When evaluating drugs, a key

Table **Summary of types of economic evaluation**

Method	Context	Cost measurement	Benefit measurement	Outcome
Cost-minimisation	When the drug is considered non-inferior to the comparator for health outcomes	monetary	none	cost comparison
Cost-effectiveness	When the drug is considered superior to the comparator for health outcomes	monetary	natural units (e.g. hospitalisations avoided or life-years gained)	incremental cost-effectiveness ratio
Cost-utility	When the drug is considered superior to the comparator for health outcomes	monetary	quality-adjusted life-years	incremental cost-effectiveness ratio
Cost–benefit	When costs and health outcomes are considered in monetary units.	monetary	monetary	cost–benefit ratio

consideration for an economic evaluation is the choice of the comparator or alternative drug. The PBAC currently defines a comparator as the 'therapy that prescribers would most replace in practice' with the proposed medicine.[1] The choice of comparator is critical because when completing an economic evaluation we are essentially interested in the incremental costs and outcomes of the proposed new treatment *over* the comparator. For instance, if placebo is chosen as a comparator instead of an active treatment then the bar is set lower for determining the therapeutic advantage and, by extension, the economic argument for the new treatment. The choice of comparator thus influences the question being posed, such as whether the medicine is considered superior or non-inferior, and the type of economic evaluation to be used.

In general, a cost-minimisation analysis is used when two drugs are considered non-inferior in terms of health outcomes, such as drugs in the same therapeutic class and biosimilar drugs. Net costs are compared to establish the cheapest alternative. Recent examples of drugs listed via a cost-minimisation analysis include a vaccine for the prevention of diphtheria, tetanus and pertussis and an infliximab biosimilar.[2]

In contrast, a cost-effectiveness or cost-utility analysis is presented in tandem with a superiority argument. Net costs are compared to net health outcomes such as life-years or clinical parameters. A cost-utility analysis (considered a subset of cost-effectiveness analysis) compares net costs against net health outcomes as measured by the quality-adjusted life-year (QALY). As a cost-utility analysis provides a consistent unit of measure (incremental cost per QALY gained), comparisons can be made between funding options, and therefore this analysis is preferred by the PBAC. Tamoxifen,[3] for the primary prevention of breast cancer, is a recent example of a drug listed via a cost-utility analysis. Conversely an example of a drug de-listed due to unacceptable cost-effectiveness (calculated via cost-utility analysis) was cinacalcet for the treatment of patients with end-stage renal disease receiving dialysis who have uncontrolled secondary hyperparathyroidism.[4]

A cost–benefit analysis considers costs and health outcomes in monetary units. Health outcomes can be converted to monetary units by calculating society's willingness to pay to avoid poor health, or by calculating the cost of illness through lost wages or the cost of treatment. Although the PBAC does not generally accept cost–benefit analyses (without an accompanying cost-utility analysis), previous submissions have used this type of analysis to assist with determining an appropriate price.[5]

Perspective

When conducting a health economic evaluation, the perspective that is adopted is a fundamental consideration. This determines the scope of the costs and benefits included. Different perspectives can be categorised as single payer (such as government, health insurance or individuals) or a broader societal perspective. Guidelines for submissions to the PBAC mandate applicants to adopt a healthcare system perspective.[1] This considers costs and benefits relevant to the Australian health system which typically includes the patient, and the public or private healthcare provider.

Health outcomes

In Australia, the PBAC predominantly makes funding recommendations based on cost-minimisation or cost-utility analyses. In order to present a cost-utility analysis, health outcomes must be transformed into QALYs. This allows a ratio of net cost to net QALYs to be calculated, which can be compared against other funding options.

A QALY is a measure of disease burden. It includes the length of life and the quality of life (measured as utility) in one summary metric. A QALY of 1 indicates one year in full health and is derived from the length of time (in this case 1 year), multiplied by the utility (for full health, utility = 1). A QALY of 0.5 can mean 0.5 years in full health or one year at 50% of full health (utility = 0.5). The score can be calculated for any condition or disease, so QALYs are useful for comparing one disease with another.

Utility values are based on community-derived preferences for different health states and they can be calculated by several methods. Today it is common for clinical trials to include questionnaires such as the EQ-5D or SF-36 which allow quality-of-life utilities to be calculated. Other methods include Time Trade-Off or Standard Gamble which allow participants to trade years of life for reduced quality of life.

Costs

Common costing approaches in health economic evaluations include patient-specific and non-patient specific. A patient-specific approach involves the task of measuring resource use (services, tests, drugs etc.) based on individual patient data. In contrast, a non-patient-specific approach uses generic cost assumptions for a group of patients such as using national cost weights to estimate the cost of a hospital stay.[6]

Patient-specific costing is generally built stepwise by defining relevant resources, quantifying the resources consumed and, finally, estimating the value of each

resource. Relevant resources will depend on the perspective adopted and often include resources consumed over several years extending to a patient's lifetime. For economic evaluations of new drugs, relevant costs include the drug itself as well as resources associated with its delivery and the 'downstream' consequences of the disease. These costs can include direct costs such as clinical consultations, co-dependent tests, investigative procedures, hospital visits and other drugs, as well as indirect costs such as lost productivity.

Quantifying resource use can be achieved by collecting individual data (prospectively or retrospectively) or by estimating resource use based on sources such as clinical guidelines or expert advice. While prospective individual data collection is more accurate, it must be weighed against the time burden and cost of data collection.

Estimating the value of resources is achieved by assigning a monetary cost to a given resource, which depends on the perspective being adopted. In submissions to the PBAC, where a healthcare system perspective is adopted, it is common to assume the cost of a resource reflects the amount paid by government. This includes pharmaceutical costs, medical and pharmacy service costs, and costs associated with hospital stays, all of which can be sourced from government websites.

Incremental cost effectiveness ratio

The incremental cost effectiveness ratio (ICER) is a statistic used to summarise the cost-effectiveness of a new drug (A) relative to the comparator (B). The ICER is calculated by the net cost divided by the net effect (commonly the net QALYs gained) and is reported in monetary units as cost per health outcome (such as cost per QALY gained).

$$\text{ICER} = \frac{\text{Cost A} - \text{Cost B}}{\text{Effect A} - \text{Effect B}}$$

When considering whether to fund a new medicine, the ICER can be used to guide decision making. It allows the decision maker to compare one treatment with another, thereby quantifying the opportunity cost of decisions.

In Australia, the PBAC does not have a specific threshold for funding new medicines, although a new drug with a cost less than $50 000 per QALY gained is more likely to be recommended for funding. The PBAC will consider the ICER in tandem with other factors such as clinical need and equity issues.[7] More importantly, the PBAC will consider the uncertainty of the ICER to varying underlying assumptions (such as the clinical benefit or the cost of therapy) and the time frame over which it is calculated (such as over the trial period or extrapolated to a patient's lifetime). The ICER is therefore a supportive tool to guide decision making and should be considered within the appropriate clinical and social context.

Conclusion

With the cost of health care continuing to rise, economic evaluations are a tool to help rationalise decision making and ensure that we maximise the health benefits from our expenditure on medicines. In Australia, the PBAC predominantly uses cost-minimisation and cost-utility analyses to quantify the comparative costs and benefits of funding decisions. For new medicines with superior efficacy, cost-utility analysis is used to estimate an incremental cost-effectiveness ratio, which quantifies the opportunity cost of decisions using a consistent unit of measure. ◀

Colman Taylor is an employee of Optum which provides health economics consulting services to industry and government.

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