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What is cost-effectiveness?

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- **Cost-effectiveness analysis** compares the costs and health effects of an intervention to assess the extent to which it can be regarded as providing value for money. This informs decision-makers who have to determine where to allocate limited healthcare resources.
- It is necessary to distinguish between **independent interventions** and **mutually exclusive interventions.** For independent interventions, average cost-effectiveness ratios suffice, but for mutually exclusive interventions, it is essential to use incremental cost-effectiveness ratios if the objective – to maximise healthcare effects given the resources available – is to be achieved.
- **Cost-effectiveness ratios** should be related to the size of relevant budgets to determine the most cost-effective strategies.
- **Cost–utility analysis** is the approach required by the National Institute for Health and Clinical Excellence, and other assessment agencies (for example, the Scottish Medicines Consortium and the All Wales Medicines Strategy Group), to determine the relative cost-effectiveness of therapeutic interventions.
- All cost-effectiveness analyses should be subjected to **sensitivity analysis,** which should be included as part of the reporting of the findings.
- Cost-effectiveness is only one of a number of criteria that should be employed in determining whether interventions are made available. Issues of **equity, needs** and **priorities,** for example, should also form part of the decision-making process.
- Care should be exercised in interpreting cost-effectiveness studies to ensure that all **underlying assumptions** have been made explicit and the context and **perspective** of the study are adequately reported.

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What is cost-effectiveness analysis?

The term **cost-effectiveness** has become synonymous with health economic evaluation and has been used (and misused) to depict the extent to which interventions measure up to what can be considered to represent value for money. Strictly speaking, however, **cost-effectiveness** analysis is one of a number of techniques of economic evaluation, where the choice of technique depends on the nature of the benefits specified. **Cost-effectiveness analysis** has been defined by the National Institute for Health and Clinical Excellence (NICE) as an economic study design in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided or cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.[1]

In **cost–utility analysis** the benefits are expressed as quality-adjusted life-years (QALYs) and in **cost–benefit analysis** in monetary terms. As with all economic evaluation techniques, the aim of cost-effectiveness analysis is to maximise the level of benefits – health effects – relative to the level of resources available.

What constitutes a cost?

Costs are seen differently from different points of view. In economics the notion of cost is based on the value that would be gained from using resources elsewhere – referred to as the **opportunity cost.** In other words, resources used in one programme are not available for use in other programmes, and, as a result, the benefits that would have been derived have been sacrificed. It is usual, in practice, to assume that the price paid reflects the opportunity cost, and to adopt a pragmatic approach to costing and use market prices wherever possible.

In cost-effectiveness analysis it is conventional to distinguish between the **direct costs** and **indirect** or **productivity costs** associated with the intervention, as well as what are termed **intangibles,** which, although they may be difficult to quantify, are often consequences of the intervention and should be included in the cost profile.

- **Direct costs:** *Medical:* drugs; staff time; equipment. *Patient:* transport; out-of-pocket expenses.
- **Productivity costs:** production losses; other uses of time.
- **Intangibles:** pain; suffering; adverse effects.

It is essential to specify which costs are included in a cost-effectiveness analysis and which are not, to ensure that the findings are not subject to misinterpretation.

How to use cost-effectiveness analysis

A distinction must be made between those interventions that are completely **independent –** that is, where the costs and effects of one intervention are not affected by the introduction or otherwise of other interventions – and those that are mutually **exclusive –** that is, where implementing one intervention means that another cannot be implemented, or where the implementation of one intervention results in changes to the costs and effects of another.

Independent programmes

Using cost-effectiveness analysis with independent programmes requires that **cost-effectiveness ratios (CERs)** are calculated for each programme and placed in rank order:

$$\text{CER} = \frac{\text{Costs of intervention}}{\text{Health effects produced (eg life-years gained)}}$$

For example, in Table 1 there are three interventions for different patient groups, with the alternative for each of them of 'doing

nothing'. According to cost-effectiveness analysis, programme Z should be given priority over X since it has a lower CER; however, in order to decide which programme to implement, the extent of resources available must be considered (Table 2).

If a further programme becomes available, it should be considered on the basis of its CER figure compared with Table 1. Resources for the new programme should be considered in the same manner as above.

Mutually exclusive interventions

In reality, the likelihood is that choices will have to be made between different treatment regimens for the same condition, different dosages or treatment versus prophylaxis – that is, mutually exclusive interventions. The key question is: what are the additional benefits to be gained from the new therapeutic intervention, for example, and at how much greater cost? In order to answer such a question, **incremental cost-effectiveness ratios (ICERs)** are used:

$$\text{ICER} = \frac{\text{Difference in costs between programmes P1 and P2}}{\text{Difference in health effects between programmes P1 and P2}}$$

The alternative interventions are ranked according to their effectiveness – on the basis of securing maximum effect rather than considering cost – and ICERs are calculated as shown in Table 3.

The least effective intervention (P1) has the same average CER as its ICER, because it is compared with the alternative of 'doing nothing'.

$$\text{ICER for P2} = \frac{\text{Cost of P2} - \text{Cost of P1}}{\text{Effect of P2} - \text{Effect of P1}} = \frac{100{,}000 - 125{,}000}{1{,}500 - 1{,}300} = \frac{-25{,}000}{200} = -125$$

The negative ICER for P2 means that by adopting P2 rather than P1 there is an improvement in life-years gained ***and*** a reduction in costs. The ICER for P3 works out to be 120, which means that it costs £120 to generate each additional life-year gained compared with P2.

Alternatives that are more expensive and

Table 1. Cost-effectiveness of three independent programmes

Programme	Cost (£) [C]	Health effect (life-years gained) [E]	Cost-effectiveness ratio [C/E] (£/life-years gained)
Z	150,000	1,850	81.08
X	100,000	1,200	83.33
Y	120,000	1,350	88.89

Table 2. The extent of resources

Budget available (£)	Programme(s) to be implemented
<150,000	As much of programme Z as budget allows
150,000	All of programme Z
150,000–250,000	All of programme Z and as much of X as budget allows
250,000	All of programmes Z and X
250,000–370,000	All of programmes Z and X and as much of Y as budget allows
370,000	All 3 programmes

Table 3. Incremental cost-effectiveness ratios

Programme	Costs (£) [C]	Effects (life-years gained) [E]	Incremental cost [ΔC]	Incremental effect [ΔE]	ICER [ΔC/ΔE]
P1	125,000	1,300	125,000	1,300	96.15
P2	100,000	1,500	–25,000	200	–125
P3	160,000	2,000	60,000	500	120
P4	140,000	2,200	–20,000	200	–100
P5	170,000	2,600	30,000	400	75

less effective are excluded. In Table 3 both P1 and P3 are followed by programmes that have increased effectiveness and reduced cost. In other words, P2 and P4 are associated with a negative ICER. P1 and P3 are therefore excluded.

Having excluded P1 and P3, ICERs are recalculated for P2, P4 and P5 and are as shown in Table 4. P2 is **'dominated'** by P4 as the latter is more effective and costs less to produce an additional unit of effect (£57.14 compared with £66.67). The dominated alternative is then excluded and the ICERs are recalculated again (Table 5).

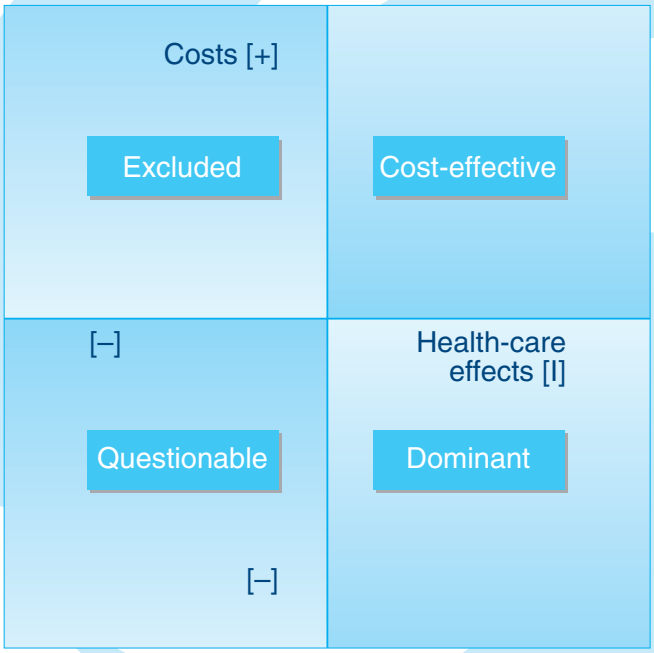

Figure 1. Cost-effectiveness plane

The process can be illustrated as shown in Figure 1. In our example, programmes P4 and P5 would be in the **cost-effective** quadrant. In deciding between them, the size of the available budget must be brought to bear. If the available budget is £140,000, all patients should receive intervention P4, while, if the available budget is £170,000, all patients should receive the more effective P5. However, if the budget is, say, £150,000, then, since the cost difference between P4 and P5 is £30,000 and the budget surplus is £10,000, it is possible to switch one-third of patients to P5 and still remain within budget.

Applications of cost-effectiveness analysis

The assessment of cost-effectiveness is an essential component in determining whether a therapy is approved for reimbursement and for formulary inclusion. Health technology assessment agencies such as NICE place considerable weight on the relative cost-effectiveness of therapies in making their judgements. NICE requires the use of cost–utility analysis, in which the outcome measure is expressed as a QALY, and which enables comparisons to be made across therapeutic areas – using the QALY as the 'common currency'. In cost–utility analysis the ICER therefore becomes the cost per QALY gained and can be compared with those of other interventions, or with a notional

Table 4. Exclusion of more costly and less effective alternatives

Programme	Costs (£) [C]	Effects (life-years gained) [E]	Incremental cost [ΔC]	Incremental effect [ΔE]	ICER [ΔC/ΔE]
P2	100,000	1,500	100,000	1,500	66.67
P4	140,000	2,200	40,000	700	57.14
P5	170,000	2,600	30,000	400	75.00

Table 5. Exclusion of dominated alternative

Programme	Costs (£) [C]	Effects (life-years gained) [E]	Incremental cost [ΔC]	Incremental effect [ΔE]	ICER [ΔC/ΔE]
P4	140,000	2,200	140,000	2,200	63.64
P5	170,000	2,600	30,000	400	75.00

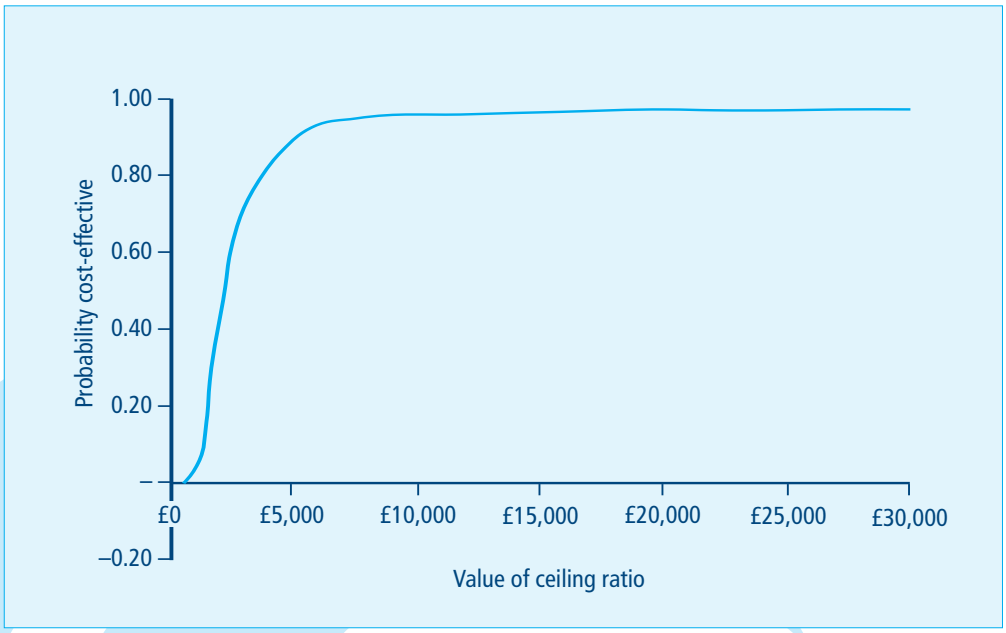

Figure 2. Cost-effectiveness acceptability curve

threshold value of what is considered to represent cost-effectiveness (see *What is cost–utility analysis?*[2] for further discussion).

Cost-effectiveness analysis (or cost–utility analysis) is far from being a precise science, and there is often considerable uncertainty associated with the findings and wide variation around the estimate generated. For example, one of the early technology appraisals undertaken by NICE was on interferon beta and glatiramer acetate for the treatment of multiple sclerosis. Estimates of the cost-effectiveness varied enormously due to differing assumptions relating to the duration of treatment, the number, severity and impact on quality of life (QoL) of relapses that occurred, and the extent to which progression was compromised by the interventions.

It is therefore imperative that the assessment of cost-effectiveness should be subjected to a sensitivity analysis to enable decision-makers to be fully aware of the range of possible eventualities.

Sensitivity analysis

The need for sensitivity analysis arises because of a number of factors. These include:

- Methodological issues arising from different approaches and methods employed in the evaluation
- Potential variation in the estimates of costs and effects used in the evaluation
- Extrapolation from observed events over time or from intermediate to final health outcomes
- Transferability of results and the validity of results from different populations/patient groups.

ICERs therefore require some indication of the confidence that can be placed in them. What would happen, for example, if the 'true cost' of one of the treatment strategies was somewhat higher or lower than the estimate used in the investigation, or if there were significant changes in the life-years gained or other parameters used? Sensitivity analysis tests all the assumptions used in the model and enables the impact of changes on the baseline estimates to be investigated.

The use of probabilistic sensitivity analysis is now recognised as the appropriate format for undertaking and reporting sensitivity analysis, via a cost-effectiveness plane and acceptability curve, as shown in Figures 1 and 2.

These are generated by costs and effects data being simulated repeatedly (usually 1,000 times) to generate a vector of CERs, which are plotted on the cost-effectiveness plane, and from which the cost-effectiveness acceptability curve is derived. This indicates the likelihood that the CER lies below a

Box 1. Checklist for assessing cost-effectiveness studies[5]

Study design

(1) The research question is stated
(2) The economic importance of the research question is stated
(3) The viewpoint(s) of the analysis are clearly stated and justified
(4) The rationale for choosing the alternative programmes or interventions compared is stated
(5) The alternatives being compared are clearly described
(6) The form of economic evaluation used is stated
(7) The choice of form of economic evaluation is justified in relation to the questions addressed

Data collection

(8) The source(s) of effectiveness estimates used are stated
(9) Details of the design and results of effectiveness study are given (if based on a single study)
(10) Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)
(11) The primary outcome measure(s) for the economic evaluation are clearly stated
(12) Methods to value health states and other benefits are stated
(13 Details of the subjects from whom valuations were obtained are given
(14) Productivity changes (if included) are reported separately
(15) The relevance of productivity changes to the study question is discussed
(16) Quantities of resources are reported separately from their unit costs
(17) Methods for the estimation of quantities and unit costs are described
(18) Currency and price data are recorded
(19) Details of currency of price adjustments for inflation or currency conversion are given
(20) Details of any model used are given
(21) The choice of model used and the key parameters on which it is based are justified

Analysis and interpretation of results

(22) Time horizon of costs and benefits is stated
(23) The discount rate(s) is stated
(24) The choice of rate(s) is justified
(25) An explanation is given if costs or benefits are not discounted
(26) Details of statistical tests and confidence intervals are given for stochastic data
(27) The approach to sensitivity analysis is given
(28) The choice of variables for sensitivity analysis is justified
(29) The ranges over which the variables are varied are stated
(30) Relevant alternatives are compared
(31) Incremental analysis is reported
(32) Major outcomes are presented in a disaggregated as well as aggregated form
(33) The answer to the study question is given
(34) Conclusions follow from the data reported
(35) Conclusions are accompanied by the appropriate caveats

certain threshold (ceiling), which represents a benchmark against which to assess whether the intervention can be regarded as representing value for money. There are obviously a number of issues that surround the use of such explicit approaches to informing what therapies are made available, many of which are contentious and controversial – see, for example, the discussion surrounding the NICE preliminary determination relating to therapies.[3,4]

Implications of cost-effectiveness analysis

While cost-effectiveness analysis is a useful technique for assisting in the decision-making process, there are important issues to consider.

- Cost-effectiveness analysis can indicate which one of a number of alternative interventions represents the best value for money, but it is not as useful when comparisons need to be made across different areas of healthcare, since the outcome measures used may be very different. As long as the outcome measure is life-years saved or gained, comparisons can be made, but even in such situations cost-effectiveness analysis remains insensitive to the QoL dimension. In order to know which areas of healthcare are likely to provide the greatest benefit in improving health status, a cost–utility analysis needs to be undertaken using a 'common currency' for measuring the outcomes across healthcare areas. If information is needed as to which interventions will result in overall resource savings, a cost–benefit analysis has to be done, although both cost–utility analysis and cost–benefit analysis have their own drawbacks.

- The quality of cost-effectiveness analyses is highly dependent on the quality of effectiveness data used, and all cost-effectiveness analyses should include a detailed sensitivity analysis to test the extent to which changes in the parameters used in the analysis may affect the results obtained. A useful checklist for assessing cost-effectiveness studies is to be found in Box 1.[5]

- Cost-effectiveness is only one of a number of criteria that should be employed in determining whether interventions are made available. Issues of equity, needs, priorities and so on should also form part of the decision-making process.

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Further reading

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