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Implementing QALYs

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- Economic evaluations such as cost-effectiveness analysis can provide useful information to inform healthcare decision making, and make choices in healthcare more explicit.
- Quality-adjusted life-years (QALYs) provide an estimate of the extra quantity and quality of life provided by an intervention combined within a single measure.
- Cost utility analysis can be extremely useful, since it provides a common unit (cost per QALY) that allows comparisons to be made between interventions in the same therapy area, and also across therapy areas.
- Estimates of cost per QALY can help to determine whether or not an intervention provides good value for money.
- However, caution should be applied when using cost per QALY estimates, as there are several currently unresolved methodological difficulties.
- Furthermore, QALYs alone cannot form the basis of decision making. Other factors, such as population health needs and local priorities, must be considered as well.

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Implementing QALYS

The advent of the National Institute for Clinical Excellence and the more general shift towards evidence-based medicine have made cost-effectiveness an increasingly important part of healthcare decision making in the UK. Choices based upon cost per quality-adjusted life-year (QALYs) are, inter alia, more explicit, transparent and rationally consistent. QALYs are one of the few tools available that allow comparisons between interventions in a common unit.

What is a QALY?

A 'QALY' is an outcome measure that takes into account both the quantity and the quality of the extra life provided by a healthcare intervention – it is the arithmetic product of the life expectancy and the quality of the remaining years. As outlined in a previous bulletin in this series,[1] additional life expectancy is relatively easy to measure. Assessing the quality of that additional life is more difficult, but it can be assessed by quality of life questionnaires or by preference studies.

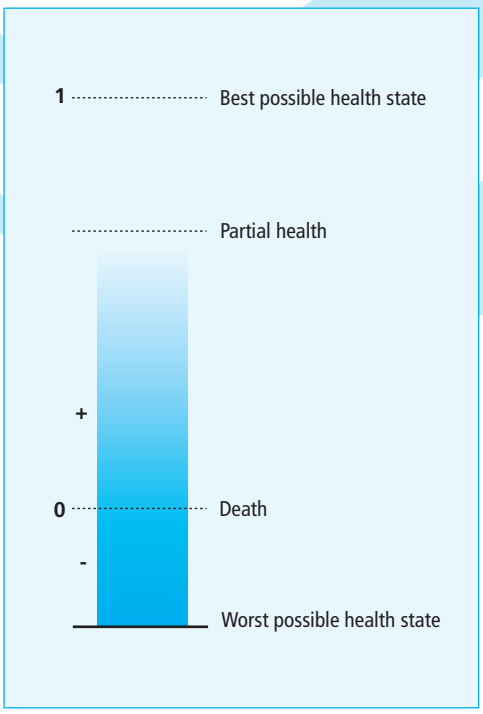

Figure 1. Preference or utility values for health states

The technical term for this preference is 'utility', and utility values can be gathered by asking people about their preferences for various health states. In general, utility values range from 1 (indicating perfect health) to 0 (indicating death). Negative utility values are possible for some health states. For example, some people may consider being in a permanent vegetative state less preferable than death, and so would give that health state a negative utility value. These concepts are illustrated in Figure 1.

Once utility values are available, calculation of QALYs is straightforward. One simply multiplies the utility value of a health state by the length of time spent in that health state. For example, one year of perfect health (utility value of 1) equals one QALY. Similarly, two years spent in a health state with a utility value of 0.75 equals 1.5 QALYs, or 1.5 years of perfect health. Some other examples are shown in Table 1.

Why use QALYs?

One of the most useful aspects of QALYs is that they allow the 'value for money' provided by different interventions to be measured in a common unit – cost per QALY'. This can provide information on the comparative effectiveness of interventions within the same disease area (for example, conventional versus keyhole surgery for uterine fibroids), but more importantly it allows comparisons of the relative effectiveness of interventions from different therapy areas (for example, keyhole surgery for uterine fibroids versus screening for breast cancer). This information can help to inform both treatment decision making within a therapy area and resource allocation decisions across therapy areas.

Value for money – calculating 'cost per QALY'

Utility values, and therefore QALYs, can be calculated for any healthcare intervention

where there is a measure of utility for health states following the intervention. If the costs associated with the intervention can also be calculated, then a cost utility value can be derived. This is expressed in units of cost per QALY and provides an estimate of how much it would cost to provide one year of perfect health (that is, one QALY) following that intervention. In other words, these estimates represent a measure of the value for money that the intervention provides.

Cost per QALY estimates can be either average or incremental. An average cost per QALY estimate simply takes the costs of an intervention and divides it by the QALYs provided by that intervention. However, the most useful type of cost per QALY estimate available is the incremental cost per QALY estimate. As the name suggests, incremental estimates focus on the extra costs and benefits compared with another intervention. Incremental cost per QALY estimates assess the additional cost per health gain that is expected when choosing one intervention over another, and so most closely reflect the impact of choices made in the real world.

Calculating cost per QALY: a working example

A useful example of how to calculate QALYs can be based upon medical interventions to treat recurrent metastatic breast cancer. This example estimates the extra cost and health gain associated with treatment with docetaxel compared with two other agents paclitaxel and vinorelbine. Estimates of utility, costs and incremental cost per QALY have been calculated using an updated version of a cost utility model proposed by Hutton *et al.*[2]

The estimates of costs, QALYs and incremental cost per QALY for docetaxel versus paclitaxel are shown in Table 2.

According to Table 2, docetaxel costs £172 more than paclitaxel but results in an extra 0.0862 QALYs, which is equivalent to an extra 31 days of perfect health (if one QALY equals one year of perfect health). The incremental cost per QALY for docetaxel versus paclitaxel is £1,995. In other words, the extra cost to gain one additional QALY (that is, one year of perfect health) by using docetaxel instead of paclitaxel is £1,995(Data on file, Aventis Pharma).

Table 1. Calculation of QALYs

Length of time in health state	Utility value for health state	Number of QALYs (equivalent to number of years of perfect health)
0.8 years	0.67	0.54
2.4 years	0.53	1.3
5.2 years	0.84	4.4

Table 2. Calculating incremental cost per QALY for docetaxel versus paclitaxel

	Docetaxel	Paclitaxel	Difference (or increment)
Mean costs of treatment per patient (£)[x]	7,817	7,645	172[a]
Mean utility (QALYs)[y] per patient	0.7347	0.6485	0.0862[b]
Average cost per QALY (=x/y)	£10,640	£11,789	–
Incremental cost per QALY of docetaxel versus paclitaxel (=a/b)	–	–	£1,995

Results from a Markov decision analysis model. Data on file, Aventis Pharma

The estimates of costs, QALYs and incremental cost per QALY for docetaxel versus vinorelbine are shown in Table 3.

According to Table 3, docetaxel costs £3,549 more than vinorelbine but results in an extra 0.2525 QALYs, which is equivalent to an extra 92 days of perfect health. The incremental cost per QALY of docetaxel compared with vinorelbine is £14,055. In other words, the extra cost to gain one additional QALY by using docetaxel instead of vinorelbine is £14,055 (Data on file, Aventis Pharma).

The values for average cost per QALY in Table 3 highlight why average values can sometimes be misleading. The average values suggest that vinorelbine may provide greater value for money than docetaxel (as its average cost per QALY estimate is lower), whereas the incremental values (which most closely reflect the choices faced in healthcare decision making) show that docetaxel can be considered good value for money compared with vinorelbine due to the extra QALYs it provides.

Other cost–utility estimates in advanced breast cancer

A recent publication[3] suggested that palliative chemotherapy in advanced breast cancer may have economic advantages, in terms of cost per quality-adjusted progression-free survival, over taxoids such as docetaxel and paclitaxel. However, these estimates lack robustness as the cost model was constructed retrospectively and patient numbers were small, with the result that differences in the utility estimates are not statistically significant.

Implementing QALYs

Two methods to assess whether a cost per QALY estimate represents good value for money are the league table approach and the threshold approach. By using these approaches, the estimates of cost per QALY calculated for docetaxel in the above examples can be assessed to determine whether docetaxel provides good value for money.

Cost per QALY league tables rank interventions by their average cost per QALY estimate, and an example table is shown in Table 4.

In theory, such league tables can help to inform decisions as to how a limited amount of money should be spent to achieve the greatest health gain for the population. However, many problems with this approach have been identified. QALY league tables have been accused of simplifying complex clinical situations. The studies underpinning the estimates may have been conducted in different settings and at different times, limiting their direct comparability.

The threshold approach can be used alongside league tables to assess whether or not an intervention provides good value for money. The measurement is made by whether or not the cost per QALY estimate falls above or below a threshold value. An arbitrary figure of $20,000–50,000 per QALY has commonly been applied as the threshold.[4] By applying this value to Table 4, the last three interventions would not be considered good value for money. However, being arbitrary, this threshold

Table 3. Calculating incremental cost per QALY for docetaxel versus vinorelbine

	Docetaxel	Vinorelbine	Difference (or increment)
Mean costs of treatment per patient (£)[x]	7,817	4,268	3,549[a]
Mean utility (QALYs)[y] per patient	0.7347	0.4822	0.2525[b]
Average cost per QALY (=x/y)	£10,640	£8,851	–
Incremental cost per QALY of docetaxel versus vinorelbine (=a/b)	–	–	£14,055

Results from a Markov decision analysis model. Data on file, Aventis Pharma

Table 4. Cost per QALY league table[1]

Intervention	Extra cost per QALY gained (1990 £)
GP advice to stop smoking	270
Hip replacement	1,180
Cholesterol testing and treatment (all adults aged 40–69)	1,480
Kidney transplantation (cadaver)	4,710
Home haemodialysis	17,260
Hospital haemodialysis	21,970
Erythropoietin treatment for anaemia in dialysis patients (assuming 10% reduction in mortality)	54,380
Neurosurgery for malignant intracranial tumours	197,780

Figure 2. Recommendations in UK healthcare decision making based on cost per QALY and quality of evidence[6]

Evidence quality	Cost per QALY gained (£)			
	<£3K	£3–20K	>£20K	Negative
I. At least one randomised controlled trial	Strongly recommended	Strongly recommended	Limited support	Not supported
II. Well designed controlled trial	Strongly recommended	Supported	Limited support	Not supported
III. Expert consensus or opinion	Supported	Limited support	Limited support	Not supported
IV. Conflicting or inadequate evidence	Not proven	Not proven	Not proven	Not supported

value is likely to vary in different societies and cultures, depending on how they themselves value healthcare.

Applying the threshold value of £20,000 to the average cost per QALY for docetaxel, £10,640 (Tables 2 and 3), suggests that docetaxel provides good value for money in this setting.

A slightly more sophisticated application of the threshold approach has been described by Stevens *et al*,[5] in a paper on healthcare decision making in the UK. This approach includes a judgement on the robustness of the clinical evidence upon which the cost per QALY estimate is based. In other words, estimates based on data from a randomised controlled trial are considered to be better than those based on expert opinion. A matrix can be drawn which categorises cost per QALY values according to the strength of evidence underlying them. An example of such a matrix is shown in Figure 2.

The incremental cost per QALY for docetaxel compared with paclitaxel is £1,995, and the evidence underlying this estimate falls into category I. According to the matrix in Figure 2, docetaxel would be classified as strongly recommended. Again, this suggests that docetaxel provides good value for money compared with paclitaxel in this setting.

Similarly, as the incremental cost per QALY of docetaxel compared with vinorelbine is £14,055, and as this estimate was based on data from a randomised controlled trial (category I evidence), according to Figure 2, docetaxel would again be classified as strongly recommended. Once more, this suggests that docetaxel provides good value for money compared with vinorelbine in this setting.

Caution with QALYs

Possibly the greatest area of controversy for QALYs is the choice of quality values. In the above examples, it was most appropriate to use proxy utility values, but it could be argued that these may not really reflect the preferences of patients for these health states and so may distort the resulting cost per QALY estimates. Similarly, strengths of preferences for health states are likely to be dependent on factors such as age and lifestyle, and so may be different for different people in similar health states.

Another limitation is that cost per QALY estimates may be derived from different types of studies, in different locations, and using different methods to estimate utility.

QALYs may also lack sensitivity when comparing two similar treatments in the same therapy area or treatments for mild as opposed to severe forms of a disease. In other words, differences that may be important clinically or to the patient may not be shown by cost per QALY estimates.

With these thoughts in mind, it is important to remember that, although flawed, QALYs are one of the few tools that allow comparisons in a common unit between interventions in the same therapy area and across therapy areas. Key advantages and disadvantages of QALYs are shown in Table 5.

QALYs can, and probably should, be used to help inform decision making. However, they should never be used in isolation, as they do not capture all domains and aspects of healthcare. Other important considerations include epidemiology, the health needs of the population, social and ethical factors, and local health priorities.

Conclusions

- QALYs are a useful tool to aid healthcare decision making.
- Cost per QALY estimates should be incremental to present the additional costs and health gains of choosing one intervention over another. This reflects the choices that have to be made in the real life setting.
- League table and threshold approaches can be used to see if a cost per QALY estimate represents good value for money.
- While QALYs are useful, flaws still remain with the methods used to derive them, and controversy exists in the way they should be used.
- QALYs should not be used in isolation. Many other factors should be considered in treatment decision making.

Table 5. Advantages and disadvantages of QALYs

Advantages	Disadvantages
Provide a framework for valuing the health gains associated with interventions	Values assigned to the quality of life component of the QALY may not reflect the values of patients receiving the intervention
Can be used to help guide priority setting	Controversial – whose quality values should be used?
Combine estimates of both the extra length of life gained from an intervention and the quality of the extra life gained	May lack sensitivity within a disease area
Allow comparisons of the effectiveness of one intervention for a problem with the effectiveness of another intervention for the same problem	Can over-simplify complex healthcare issues and suggest 'quick and easy' resource allocation decisions
Allow comparisons across disease areas to help show which programmes provide the greatest allocative efficiency	

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Further reading
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Taxotere® (docetaxel) Prescribing Information

Presentation: Vials of concentrate for infusion containing 20mg docetaxel or 80mg docetaxel with accompanying vials of solvent. **Indications:** Locally advanced or metastatic breast cancer in combination with doxorubicin for patients who have not received prior cytotoxic therapy for this condition. Locally advanced or metastatic breast cancer after failure of cytotoxic therapy, which should have included an anthracycline or alkylating agent. Locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of prior chemotherapy. **Dosage and Administration:** Taxotere is administered as a one-hour iv infusion every three weeks. The recommended dosage in breast cancer is 100 mg/m^2, or 75 mg/m^2 in combination with doxorubicin (50 mg/m^2). The recommended dosage in NSCLC is 75 mg/m^2. Premedication with an oral corticosteroid is recommended for 3 days, starting one day prior to docetaxel administration. *Elderly:* No special instructions. *Children:* Safety and efficacy not established. *Hepatic impairment:* Reduce dosage; discontinue in severe cases. **Contraindications:** Hypersensitivity to the active substance or excipients, baseline neutrophil count of <1,500 cells/mm^3, pregnancy or breast-feeding, severe liver impairment. **Precautions and Warnings:** Reduce dosage with febrile neutropenia, neutrophils <500 cells/mm^3 for more than one week, severe or cumulative cutaneous reactions, severe peripheral neuropathy, or moderately raised LFTs, ALT and/or AST >1.5 times the ULN concurrent with serum alkaline phosphatase >2.5 times the ULN. Severe hypersensitivity reactions require immediate discontinuation. Severe cutaneous skin reactions, such as eruptions followed by desquamation, may require interruption or treatment discontinuation. Severe fluid retention such as pleural effusion, pericardial effusion or ascites should be monitored closely. With serum bilirubin levels >ULN and/or ALT and AST >3.5 times the ULN concurrent with alkaline phosphatase levels >6 times the ULN, no dose-reduction can be recommended and docetaxel should not be used unless strictly indicated. **Interactions:** Caution with compounds that induce, inhibit or are metabolised by cytochrome P450-3A, which may alter docetaxel metabolism. **Pregnancy and Lactation:** Contraindicated. **Adverse Reactions:** Neutropenia, thrombocytopenia, anaemia, hypersensitivity reactions, fluid retention, cutaneous reactions, peripheral neuropathy, infectious episodes, increased liver enzyme levels, alopecia, asthenia, mucositis, injection site reactions, gastrointestinal events, cardiovascular events (including hypotension and dysrhythmia), arthralgia, and myalgia. Pharmaceutical Precautions: Store vials between +2°C and +25°C; protect from bright light. Reconstitute concentrate with accompanying solvent and dilute with infusion solution (0.9% sodium chloride or 5% dextrose for intravenous injection) before use. Apply usual cytotoxic precautions. **Package Quantities and Basic NHS Price:** Blister cartons containing one vial of TAXOTERE® concentrate and one vial of solvent: TAXOTERE® 20mg £175.00; TAXOTERE® 80mg £575.00.
Legal Category: POM.
Marketing Authorisation Numbers: TAXOTERE® 20mg EU/1/95/002/001; TAXOTERE® 80mg EU/1/95/002/002. Further information available on request from Aventis Pharma Ltd., 50 Kings Hill Avenue, Kings Hill, West Malling, Kent ME19 4AH.
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