Health Related Quality of Life for Economic Evaluations in Cancer

What is CREST?

The Centre for Health Economics Research and Evaluation (CHERE) at UTS has been contracted by Cancer Australia to establish a dedicated **Cancer Research Economics Support Team (CREST)** to provide high quality, expert advice and support to Multi-site Collaborative Cancer Clinical Trials Groups.

Factsheets

CREST will produce a series of factsheets as resources for cancer collaborative group researchers wishing to include economic evaluation in their clinical trials.

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SUMMARY

- An economic evaluation alongside a cancer clinical trial needs to include measurement and valuation of the health impacts of the interventions.
- The gold standard in economic evaluations is to use Quality Adjusted Life Years (QALYs) to combine length and quality of life into one measure which provides valuation of the health impacts.
- Instruments called Multi-Attribute Utility Instruments are the preferred option as they have had societal valuations for the health states.
- The common MAUIs used in cancer research are the:
  - EQ-5D
  - SF-6D
  - AQoL-8D
  - HUI3
- Different MAUIs will be suitable for different types of cancer research, depending on how the particular cancer and/or treatment impacts on quality of life. It is useful to also include cancer specific QOL instruments.
- Economic evaluation is used to determine the incremental value of the new treatment compared with the comparator.

For more information about CREST, or for other factsheets in this series, please see our website:

www.chere.uts.edu.au/crest

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Why do clinical trials need economic evaluation-specific quality of life measures?

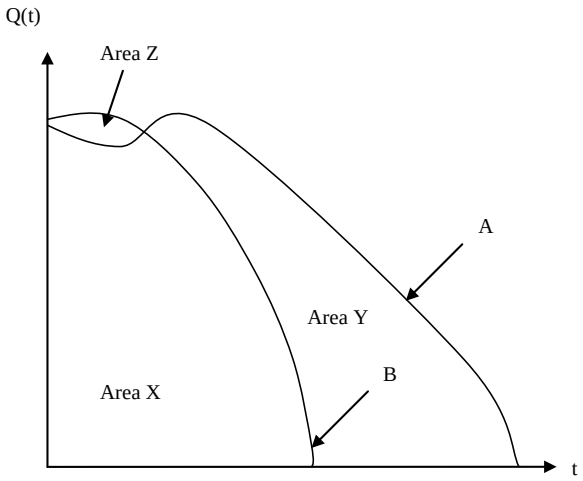
Many trials already collect quality of life data alongside clinical trials (such as the QLQ-C30 or FACT-G). However, quality of life measurement for use in economic evaluation requires a specific sub-category of quality of life measures which aim to value the health impacts of the intervention compared with the current treatment or comparator. This valuation should reflect strength of preference for different quality of life outcomes.

Gold-standard economic evaluation techniques attempt to combine effects of interventions on both mortality and quality of life into one metric. An economic evaluation which does this is termed a cost-utility analysis (CUA). The most common outcome measure in this type of analysis is the quality-adjusted life year (usually shortened to QALY). This is defined as one year of full health for one individual. QALYs are calculated by applying a weighting between 0 (for dead) and 1 (for full health) to the time in each heath state. QALY weights of less than zero are also possible, reflecting the fact that some health states may be considered worse than death. These weights are often called QALY weights or utility weights. A QALY weight of 0.5 applied to a health state implies that 2 years in that health state is equivalent in value to one year of life in full health. Thus, QALYs capture a trade-off between quality of life and survival.

The value of a health profile is the product of life expectancy and quality of life. Therefore, the health gain associated with an intervention is the difference between the product of mortality and quality of life for the intervention minus the same product for an appropriate comparator. This is explained diagrammatically below.

In Figure 1, two health profiles are plotted looking at quality of life Q(t) over time. The two health profiles are resulting from two competing interventions A and B.

Figure 1: Alternative health profiles over time



Thus, for people receiving intervention A, they have a loss of quality of life immediately (perhaps due to treatment) but a gain in survival (life expectancy) (as A reaches the axis after B). If two competing health

programs A and B are considered in terms of the average health-related quality of life experienced by individuals receiving them, the value placed on them by the QALY model is (X+Y) for intervention A, and (X+Z) for intervention B (for economic evaluation, we are interested in the incremental value, which is equal to (Y-Z)).

Multi-attribute Utility Instruments

For an economic evaluation to be conducted alongside a cancer clinical trial, measurement of quality of life is essential, to capture all the relevant impacts of the treatment. The quality of life instrument should capture quality of life across a range of domains (such as mobility, pain or anxiety). It is preferable that the instrument used is also one for which there are existing societal valuations for the health states in the instrument on the 0-1 scale discussed above. These instruments are sometimes called multi-attribute utility instruments, and are a specific sub-set of quality of life instruments, for which valuations have been obtained by an appropriate method such as a Time Trade-Off or Standard Gamble (Torrance, 1986). While many quality of life instruments have a scoring system, most of these are not appropriate to be treated as QALY weights, as they do not have certain necessary properties. In particular, QALY weights have a cardinal interpretation, whereas most scoring systems for quality of life instruments are ordinal. This is a particularly important distinction because of the valuation aspect of QALYs.

A multi-attribute utility instrument has three key features: (1) a set of questions that cover a comprehensive range of quality of life dimensions and levels, such that the instrument can describe a large range of possible health states, (2) a scoring algorithm that provides a QALY weight for each health state described by the instrument (3) the requirement that the scoring algorithm is based on a preference elicitation task that reflects strength of preferences for quality of life compared with survival. The most widely used preference elicitation tasks are the Standard Gamble and the Time Trade-off (more on these below).

The advantage of a multi-attribute utility instrument is that it allows the direct measurement of quality of life of the participants in the trial with a relatively simple easy-to-complete quality of life instrument, but because a MAUI has been used, valuations of the health states are readily available via the scoring algorithm.

What are the existing instruments in this area?

There are four widely used quality of life instruments in the area:

- **EQ-5D** (Dolan, 1997, Dolan, et al., 1996),
- **SF-6D** (Brazier, et al., 2002),
- **AQoL-8D** (Richardson and Khan, 2009),
- **HUI3** (Feeny, et al., 1995, Torrance, et al., 1995).

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For a complete bibliography relating to each of these instruments (plus licensing information and the instruments themselves), the respective websites are excellent resources:

- www.euroqol.org/
- www.sheffield.ac.uk/scharr/sections/heds/mvh/sf-6d
- www.aqol.com.au/
- www.healthutilities.com/

Each instrument has a number of dimensions (between 5 and 8), each dimension having between 3 and 6 levels. The ability of each of the instruments to detect changing quality of life depends on the comprehensiveness of the dimensions across the relevant domains of quality of life, and the fineness of the distinctions possible between levels in each dimension. These two ideas are closely related to the number of possible health states within the instrument, which is described in the table below.

The use of cost-utility analysis (which needs these kinds of instruments) has grown significantly over the last 20 years, to the point that government decisions about subsidy of new interventions generally mandate the use of such instruments.

Brauer *et al.* (2006) identify that the use of the EQ-5D and HUI in published cost-utility analyses have increased significantly in the period 1998-2001 relative to the period 1976-1997, and it would be reasonable to expect that this trend would have continued, and be replicated in the more recent instruments (SF-6D and AQoL). A simple summary of some key points regarding the four major quality of life instruments is provided in Table 1 below.

What are the major techniques used to value health states?

To gain values for individual health states, studies follow two general stages. Firstly, a selection of the states within an instrument are directly valued using a preference elicitation technique such as a Time Trade-Off or a Standard Gamble. For more information on these, see Torrance (1986).

These publically available valuations are derived from general population samples (rather than clinicians or patients for example). This is because economic evaluation of health technologies is most commonly considered to be informing social decision-making.

Table 1: Summary of 4 major MAUIs

	EQ-5D	SF-6D	HUI3	AQoL-8D
Number of health states	243	18,000	972,000	2.37×10^{23}
Usual functional form	Additive*	Additive*	Multiplicative	Multiplicative / exponential
Direct valuation technique	Time Trade-Off & Rating Scale	Standard Gamble	Standard Gamble & Rating Scale	Time Trade Off
Completion time (Richardson, et al., 2011)	1 minute	2.5 minutes	3 minutes	5.5 minutes

* Both instruments do not assume a wholly additive structure; however, both approaches are better classified as additive than multiplicative

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While there are some criticisms of general population valuations, for example, whether respondents have an adequate understanding of how a specific disease affects quality of life, the MAUIs are designed to describe health states in generic terms that would apply across diseases. It has also been argued that patients with the disease may not reflect society's preferences, particularly f they adapt to their condition.

Can the survey be completed by someone other than the patient?

There are situations in which patients are unable to complete surveys, and hence cannot have their health state valued using these quality of life instruments. For example, it is usually assumed that valuations for very young children, people with dementia, or people with intellectual impairment cannot be reasonably taken from responses from the person themselves. In these instances, proxy completion may be appropriate, although not all MAUIs have been validated for proxy use.

How sensitive are these instruments in cancer?

Each instrument consists of a number of dimensions which aim to include all major areas in which health (or lack thereof) can manifest. If a particular cancer impacts on quality of life in ways not captured by one of these dimensions, then the instrument is likely to be fairly insensitive. Hawthorne (2001) provides a good summary of the types of areas each instrument is particularly good (or poor) at describing quality of life.

Australian valuations of health states

As yet, published valuations of health states in these instruments are limited to non-Australian settings (other than for the AQoL). The most commonly used valuation sets in an Australian setting are from the UK for the EQ-5D and the SF-6D (Brazier, et al., 2002, Dolan, 1997), or from Canada for the HUI3 (Feeny, et al., 2002). Australian values for AQoL are downloadable from the AQoL website as a STATA do-file. Australian values derived through a Time Trade-Off for the EQ-5D states are in press (Viney, et al., 2011), and Australian weights for the SF-6D and the EQ-5D are currently being produced using a different technique called a Discrete Choice Experiment. For more information, contact CREST.

If I have not included these questionnaires in my trial, can I still do a cost-utility analysis?

Existing QALY weights for a wide range of health states are available in the published literature. A good summary of this, with a helpful search function, can be found here: https://research.tufts-nemc.org/cear4/default.aspx. However, using these weights relies on assumptions about the similarity of the patient population and health states, which may not be appropriate. Ideally, QALYs should be collected alongside clinical, cost and other quality of life data in a trial.

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