How oncology studies obtain QALY weights: a literature review

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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

- Multi-attribute utility instruments (MAUIs) are the gold standard for determining QALY weights but have not been commonly used in cancer studies.
- There is no clear preference for which MAUI should be used; the EQ-5D is most commonly used. However, there are concerns that this tool may not be sufficiently sensitive. Other instruments, such as the HUI-3 or disease specific MAUIs, may be more appropriate in the field of oncology.
- It is likely that the valuations obtained from different MAUIs are not comparable. This raises concerns given the number of papers that rely on QALY weights from secondary references that may have employed multiple methods that are not comparable.
- If MAUIs are not available, a health state valuation experiment is preferable to a non-preference-based approach to determine QALY weights.
- The general public or patients should be used to value health states rather than medical professionals.
- If QALY weights are obtained from the literature, information on how they have been derived should be provided. In general, the preferred sources for QALY weights are economic research articles or databases, rather than cost-effectiveness analyses.

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How oncology studies obtain QALY weights: a literature review.

Introduction

Economic evaluation is important to inform appropriate resource allocation in health care and can be characterised by two features; it involves the comparison of two or more different options, and it compares these options in terms of costs and consequences (Drummond et al., 2005). Economic evaluation determines the cost per outcome of an intervention by comparing the result with the cost per health outcome of an alternative different intervention; the results are usually reported as an incremental cost-effectiveness ratio (ICER). As the cost of health care rises, so does the importance of understanding the cost-effectiveness of alternative treatments. In turn, we need to ensure that the parameters used in cost-effectiveness analyses are both accurate and robust.

One form of economic evaluation, cost-utility analysis (CUA) involves capturing different aspects of quality of life and survival into a single measure, Quality Adjusted Life Years (QALYs). Intrinsic to the idea of QALYs is measuring health-related quality of life (HRQOL) across the years of life remaining. HRQOL was defined by Patrick and Erickson (1993) as "*The value assigned to duration of life as modified by the impairments, functional status, perceptions and social opportunities that are influenced by disease, injury, treatment or policy*". QALYs are used to represent utility values associated with health states and incorporate two separate aspects of health status into one value; the description of the health state and the attribution of a value to it. Best practice dictates that the descriptive component should capture all relevant aspects of quality of life and that its valuation should be preference based, representing its value to society. Multi attribute utility instruments (MAUIs) are considered the gold standard method of obtaining QALY weights. For detailed information about QALYs and related topics, see the CREST Factsheet *Health related quality of life for economic evaluations in cancer* http://www.chere.uts.edu.au/crest/pdfs/factsheet_hrqol.pdf

It is important to understand how the QALY weights reported in the literature are determined and the level of uncertainty associated with them. This is particularly the case in medical fields such as oncology where the incremental cost per QALY gained for interventions is typically high. In this Factsheet we report the results of a project which investigated the sources of QALY weights reported in published economic evaluations of oncology interventions.[1]

[1] This work was undertaken by Tristan Gonzalez as part of a treatise in the Masters of Health Economics Programme at the University of York. It focused on a review of economic

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Methods

A literature review was conducted of all economic evaluation papers reporting QALY weights in the field of oncology published in the years 1995, 2000, 2005 and 2010. Data regarding the derivation of QALY weights were extracted from all relevant studies and compiled in a spreadsheet for analysis. The information extracted from the papers addressed the following questions:

- Were QALY weights derived alongside clinical data?
- Did the patient complete a MAUI?
- If the patient did not complete a MAUI, what was the source of valuation?
- How were utility values derived?
- Were QALY weights derived from a secondary/tertiary reference?

Each year was analysed separately and statistical analysis was undertaken to determine whether the proportion of sources that appeared to show trends over time was statistically significant. The papers were also reviewed to determine the nature and extent of sensitivity analyses conducted with respect to QALY weights. The aim was to determine whether it was standard for the QALY weights to be tested in sensitivity analyses and if so, what type of sensitivity analysis was used. The site and stage of cancer was also recorded, to investigate whether these variables had any effect on how the QALY weights were determined and if any patterns were able to be observed. The cost per QALY was also included in the data extraction as well as whether cost per life year gained was measured.

Results

The initial search produced a total of 167 papers. 11 of these were found to be unrelated to either cancer or QALY weights and so were removed. Papers were then removed if they were unrelated to oncology, did not use QALY weights or if they were review papers. Two papers could not be obtained; one was written in German and a copy of the second paper could not be located. A total of 112 papers were included in this review.

Table 1 shows the dramatic increase over time in the number of papers that used QALYs and QALY weights or are cost-utility analyses. Consequentially, 65% of all of the papers included in this study were published in 2010.

Table 1: Number of relevant studies in each year

Year	Number of Relevant Studies
1995	4
2000	12
2005	23
2010	73
Total	**112**

Table 2 summarises the methods used to obtain the QALY weights where these were obtained as part of the current research project being reported in the literature. Only 16/112 studies collected information on QALY

evaluations in oncology to identify trends over time in how utility weights are derived.

weights as part of the original study and of these, only 8 used a MAUI to obtain QALY weights.

Table 2: Summary of the methods used to obtain QALY weights in original research projects

Number of Studies	Methods Used to obtain QALY weights
4	EQ-5D MAUI
2	SF-6D (converted from SF-36 Questionnaire)
1	EORTC QLQ-C30
1	Subjective Health Estimation Survey
8	Non-MAUI method used

Abbreviations: EORTC QLQ-C30 denotes European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30, EQ-5D EuroQol 5 dimension, SF-36 short form 36, SF-6D short form 6 dimension, MAUI multi-attribute utility instrument, QALY quality adjusted life year.

96/112 papers used a secondary source to obtain QALY weights (usually from previous research). 26/96 of the secondary source papers used a MAUI to obtain QALY weights.

The EQ-5D was the most commonly used (8/26), followed by the SF-36 questionnaire (and SF-6D algorithm) (6/26). Other MAUIs used included HUI, QLQ-C30, QWB, PORPUS and the Billewicz Scale. The categories of studies from which QALY weights were sourced (secondary sources) are presented in Table 3.

Overall, 30% of QALY weights were derived from cost-effectiveness analyses reported in other papers (in turn, these cost-effectiveness analyses may have derived utility weights alongside clinical data or obtained them from other literature). The largest proportion of QALY weights (47%) was derived from economic research.

Table 3: Description of types of source study

Category of Source Study	Description
CEA	All types of cost-effectiveness analyses (ie. Cost-utility, cost-benefit and cost-effectiveness analysis)
Clinical Research	Studies reporting results from clinical trials, with no economic analyses attached
Economic Research	Studies designed with the sole purpose of determining QALY weights (no economic analyses or clinical trials attached)
Policy	Studies that are conducted to influence health policy (such as health technology assessments).
Review	Studies that review a number of source studies in order to obtain QALY weights (and specify this as their aim).
Abstract	Abstracts and conference proceedings, where a full paper is not available
Database	Database designed to compile QALY weights for use in studies (e.g. HODaR)
Not stated	Source of QALY weight is either not stated or multiple sources have been used (without being a formal review article).

Abbreviations: CEA denotes cost-effectiveness analysis, HODaR Health Outcomes Data Repository, QALY quality adjusted life year.

Abstracts or conference proceedings were the source of 6% of QALY weights. Due to the incomplete nature of publications of this type, details of how the QALY weights reported in these proceedings were derived are difficult to determine. Of the 2010 papers, 10% referenced QALY weights which were sourced ultimately from an abstract or conference proceeding. Table 4 shows the prevalence of the category of source study used during the different time periods. It is difficult to analyse any changes over time, due to the small number of papers in 1995 and 2000. There does however, appear to be a trend towards using economic research articles, specifically designed to derive QALY weights, with the largest proportion being seen in 2010.

In earlier years, QALY weights were more likely to be derived from pre-existing cost-effectiveness analyses whereas in later years they were more likely to be derived from economic research studies (such as a time trade-off (TTO) experiment). Over time there was a decrease in the incidence of QALY weights being derived from cost-effectiveness analyses. CEAs more often included QALY weights derived using health state valuation experiments and referencing, rather than using a MAUI approach. However, it should be noted that the small number of studies in the earlier years means caution must be applied in interpreting this finding. The data show a trend towards economic research articles being used to derive QALY weights.

Table 4: Number of each category of source studies used to determine QALY weights in each year

	1995	2000	2005	2010
CEA	4	6	11	9
Clinical Research		1	2	6
Economic Research		4	5	38
Policy			1	1
Review		1	1	2
Abstract				8
Database				3
Not stated		1	2	6

Abbreviation: CEA denotes cost-effectiveness analysis, QALY quality adjusted life year.

A number of studies used a combination of methods to derive QALY weights, particularly a combination of health state valuation experiments with non-preference-based methods. 27% (30/112) used the Standard Gamble (SG) technique (although some of these were alongside other techniques) and 28% (31/112) used the TTO method. A total of 48% (54/112) of papers used a health state valuation experiment compared with 6% (7/112) that were derived from non-preference based approaches. Approximately 80% of papers conducted sensitivity analyses on QALY weights (89 out of 112 relevant papers). A further 8% (9 papers) did not clearly state whether sensitivity analyses on QALY weights were conducted. The remaining 12% did not conduct sensitivity analyses on QALY weights, and of these only two derived QALY weights using a MAUI (which would reduce uncertainty in this situation).

Discussion

This review of the literature has shown that only a small proportion of papers derived QALY weights within the scope of the main study. From a total of 112 papers, 16 used this approach, with only 8 of these using MAUIs to obtain QALY weights. As using a MAUI alongside a clinical study is considered the gold standard in terms of determining QALY weights, the small number of studies using this approach is a cause for concern. The EQ-5D is the most commonly used tool, a finding consistent with the results of Brauer et al. (2006). This is followed by the SF-6D, a tool that is popular due to the widespread use of the SF-36 (and SF-12) questionnaires, from which the SF-6D can be derived. The HUI tool is less commonly used again, although it is considered by some to be more suitable in the context of oncology.

Recently there has been an emergence of cancer specific MAUIs, designed to incorporate subtle changes in quality of life that other MAUIs may not be sensitive enough to detect. For example, Rowen et al. (2011) used the EORTC QLQ-C30 questionnaire to describe quality of life and derive values for the corresponding health states. However, this is an emerging field, so few of the papers included in this review used a cancer specific approach.

There are conflicting views in the literature about whether different preference-based measures are comparable. Although Brazier (2004) has suggested that the valuations obtained by the SF-6D and the EQ-5D are comparable, more recent work by Whitehurst et al. (2011) has shown that the group mean results from SF-6D and EQ-5D are not directly comparable, meaning that cross-study comparability of economic evaluations using different methods of deriving QALY weights may not be appropriate.

The combination of MAUIs being used rarely, and a large variability in alternative methods of deriving QALY weights means the comparability of studies where QALYs are used as an outcome measure in the field of oncology is questionable. A problem has also been identified in terms of the techniques used for referencing QALY weights. Many authors appear to be using QALY weights derived from secondary sources without investigating how they have been derived, the original source or the quality of the source study. Given the importance of QALY weights to the end result of cost-utility analyses, it is crucial that such information be provided to allow an assessment of its likely impact on the resulting ICER values.

For more information

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