

# Health-Related Quality of Life after Stroke: Review of the Literature and Implications for Future Research

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**Abstract-** Limits on health care resources mandate that resource-allocation decisions be guided by consideration of cost in relation to the associated expected benefits. It therefore leads to an increased demand for economic evaluation and medical technology assessment. Nowadays, cost-effectiveness analysis (CEA) has emerged as a favored analytic technique for economic evaluation in health care. Currently the leading standard in Western countries is the use of health-adjusted life years (HALYs) in CEA of medical care and health interventions, as well as in estimating burden of disease. Being an umbrella term of a family of measures, HALYs include quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs). In this review we give a concise overview on QALYs and DALYs, and examine variations in QALYs and DALYs estimates currently used in stroke studies. Given the lack of reliable and valid measurement methods in eliciting utility values in QALYs or disability values in DALYs, CEA needs to be addressed in a clear and transparent way to ensure its proper use in practice.

**Key Words:** Cost-effectiveness analysis, Quality-adjusted life years (QALYs), Disability-adjusted life years (DALYs), Stroke

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## INTRODUCTION

Limits on health care resources naturally mandate that resource-allocation decisions be guided by consideration of cost in relation to expected benefits. It therefore leads to an increased demand for economic evaluation and medical technology assessment. There are some major kinds of economic evaluation in health and medicine<sup>(1,2)</sup>. Among them, cost-effectiveness analysis

(CEA) has emerged as a favored analytic technique. As the National Health Insurance (NHI) system in Taiwan is trying to control costs while maintaining or even improving quality of care, it is not surprising to find that CEA would attract more and more attention in our health care decision-making.

In CEA, the resources (costs) used and the health outcomes (effects) associated with each specific intervention (such as drugs, devices, procedures, and pro-

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grams) are estimated and compared to show the tradeoffs involved in choosing among interventions. Health outcomes have long been evaluated by mortality-based indicators such as life expectancy, all-cause and disease-specific mortality. However, these mortality-based rates are insufficient for evaluating disease burden, health outcomes, or the comparative impact of an intervention because the burden of chronic disease, injury, and disability among survivors are unrecorded. Moreover, to assess relative worth in different health interventions across diverse diseases, a standard measurement is required.

Nowadays, the leading standard in Western countries is the use of health-adjusted life years (HALYs) in CEA of medical care and health interventions, as well as in estimating burden of disease. Theoretically, HALYs are summary measures of population health that merge estimates of life expectancy with measures of the quality of life with a disease. Being an umbrella term of a family of measures, HALYs include quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs). Of note is that the particular type of CEA that uses QALYs or DALYs is sometimes referred to as cost-utility analysis (CUA)<sup>(1)</sup>. Following some authors<sup>(2)</sup>, we make no distinction between CEA and its variant, CUA, throughout our discussion. We simply describe these analyses as CEA with QALYs or DALYs when they are used as the measure of effectiveness. Meanwhile, we use the terms 'utility', 'value', and 'preference' interchangeably, although in fact they are different<sup>(1)</sup>.

The purpose of this article is to give a concise review on QALYs and DALYs, and to examine variations in QALYs and DALYs estimates currently used in stroke studies.

## THE CONCEPT OF QALYS

As a common metric for health, QALYs combine information regarding both length and quality of life. Every QALY is equivalent to one year of life in full health. For example, if major stroke is assumed to have a quality of life 0.4, then for a patient suffering a major stroke, each year spent in that state of health is consid-

ered to be 0.4 QALY, and 8 years lived after a major stroke would be counted as 3.2 ( $8 \times 0.4$ ) QALYs. Thus, the number of QALYs gained is the arithmetic product of the additional life expectancy gained owing to the health care intervention and the quality of these years.

In CEA, information regarding additional life expectancy gained after a disease, usually measured from clinical trials or epidemiological data, is relatively easy to obtain. Assessing the quality of that additional life, however, is more difficult. The preferences or utility values for different health states, also called quality-of-life (QoL) weights, have to be assessed with appropriate measurement instruments. Such instruments include, for example, standard gamble (SG), time trade-off (TTO), and direct rating (DR) methods (including category rating and visual analogue scales)<sup>(1,2)</sup>. These are the three most widely used methods to measure directly the preferences of individuals for health outcomes. An alternative that is also widely applied is to use any of the multi-attribute health status classification systems such as Health Utilities Index (HUI), Quality of Well-Being (QWB), or the European Quality of Life Questionnaire (EuroQoL)<sup>(1)</sup>.

In general, utility values range from 0 for death to 1 for perfect health. 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 thus the health state would be given a negative utility value.

QALYs were developed in the late 1960s, primarily for use in CEA. A CEA of chronic renal disease is among the earliest<sup>(3)</sup>. After much deliberation, the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine, as well as other consensus groups, concludes that a QALY measure is required for generalizable cost-effectiveness calculations<sup>(2)</sup>. However, different elicitation methods (and perspectives of the evaluators) tend to yield different preferences or utility values from the same respondents for the same health states, and there is little consensus on which is to be preferred. Readers are referred to the literature<sup>(1,2,4,5)</sup> for a more detailed discussion on QALY.

## THE CONCEPT OF DALYS

DALYs were first introduced in the World Development Report (World Bank 1993) as a method for estimating the global burden of disease, and as an outcome measure for use in CEA<sup>(6,7)</sup>. DALYs are the sum of the present value of years of lifetime lost through premature mortality and the present value of years of lifetime adjusted for the average severity of disability (mental or physical) caused by a disease or injury. That is to say, DALYs are the sum of years of life lost (YLLs) and years of life lived with disability (YLDs). It is noted that DALYs are a measure of something 'lost' rather than 'gained'.

With the DALY approach, each state of health is assigned a disability weighting factor on a scale from 0 (perfect health) to 1 (death) by an expert panel. Future burdens are discounted (usually at a rate of 3% per year), and years of life in childhood and old age are counted less. Specifically, the general equation for YLLs is as follows:

YLL =

$$\frac{KCe^{ra}}{r+\beta^2} [e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] - e^{-(r+\beta)a}[-(r+\beta)a-1]] + \frac{1-K}{r} (1-e^{-rL})$$

where  $a$  is the age at death,  $L$  the remaining standard life expectancy at death,  $r$  the discount rate,  $\beta$  the parameter for the age-weighting factor,  $K$  the age-weighting factor, and  $C$  a constant (0.1658).

The formula for YLD is basically the same except for that it is multiplied with a numeric disability weight ( $D$ ), and that  $a$  is the age of onset of disability and  $L$  is the duration of disability:

YLD =

$$D \left\{ \frac{KCe^{ra}}{r+\beta^2} [e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] - e^{-(r+\beta)a}[-(r+\beta)a-1]] + \frac{1-K}{r} (1-e^{-rL}) \right\}$$

Just like the increasing awareness that valuations for QALYs may differ when the QALYs accrue to different patients or are evaluated at different times, there are concerns about the ethics and validity of DALYs.

Particularly, the DALY framework not only is health-weighted, but also contains a weighting of life years that accentuates the dependency of the very young and the very old. This unique property of DALY has naturally caused some controversy. On the other hand, however, the assumption that all QALYs are of equal value no matter who gains them or when they occur during the life span is just equally controversial<sup>(2,8)</sup>.

## QUALITY OF LIFE AFTER STROKE

Although utility values are the key component of QALYs, given the nature of QALYs, it is not surprising to find that different studies report different utility values after stroke. In their comprehensive review of all QoL estimates for stroke appearing in the peer-reviewed literature between 1985 and 2000, Tengs et al<sup>(9)</sup> found that QoL estimates range from -0.02 (indicating that major stroke is worse than death) to 0.71 for major stroke, from 0.12 to 0.81 for moderate stroke, from 0.45 to 0.92 for minor stroke, and from 0.29 to 0.903 for general stroke. Possible reasons for this variation include the aforementioned different utility assessment methods, different types of respondents (patients, general population, or clinicians), and the defined bounds of the scale (1 corresponds to perfect health or merely the absence of stroke).

Post et al<sup>(10)</sup> did a similar review published soon after the aforementioned one, and found that patients at risk for stroke assigned utilities of 0.26 and 0.55 to major (Rankin Scale 4 to 5) and minor (Rankin Scale 2 to 3) stroke, respectively. Stroke survivors assigned relatively higher utilities, 0.32 for major stroke and 0.71 for minor stroke.

Meta-analyses of QoL studies are rare in general. A meta-analysis of QoL estimated for stroke<sup>(11)</sup> reported utility values of 0.87 for minor stroke, 0.68 for moderate stroke, and 0.52 for major stroke if the TTO method is used and respondents are community members when the scale bounds range from death to perfect health. Furthermore, the same study found that the utility values are sensitive to severity of stroke and the bounds of the scale, but not to the elicitation methods or who the respondents are.

Since the publication of the results of NINDS rtPA Stroke Trial in December 1995, a number of comprehensive CEA of rtPA therapy for acute ischemic stroke have been conducted<sup>(12-14)</sup>. The utility values used in these studies vary greatly<sup>(15)</sup>. In a recent CEA of rtPA<sup>(16)</sup>, a survey using the EuroQoL with a random sample of 100 first-ever stroke patients alive 1 year after discharge found the mean utility values were 0.22 for disabled (Barthel Index <95) and 0.77 for autonomous (Barthel Index ≥95) patients. Among the more recent studies reporting utility values after stroke, O'Brien and Gage<sup>(17)</sup> use 0.75, 0.39 and 0.12, respectively, as QoL estimates for mild residua, moderate to severe residua, and residua from recurrent stroke. Their utility estimates were based on a study<sup>(18)</sup> published almost 10 years ago. In the Duke Stroke Policy Model (DSPM)<sup>(19)</sup>, utility values, which were based on a large survey of patients at risk for major stroke, were 0.9 for TIA, and 0.8, 0.65, 0.5, 0.35 and 0.2 for Rankin Score 1 to 5, respectively. In a study on the cost-effectiveness of clopidogrel versus aspirin in secondary prevention after vascular events<sup>(20)</sup>, the utility value for peripheral arterial disease was 0.8, for mild stroke, 0.76, for moderate stroke, 0.39, and for severe stroke, 0.11. In a study of CEA of screening for obstructive sleep apnea (OSA) in stroke patients<sup>(21)</sup>, utility of stroke without OSA was 0.6 and stroke with untreated and treated OSA were 0.4 and 0.6, respectively, in their reference cases.

None of the above mentioned CEA of rtPA therapy applied the DALY approach. However, DALYs have been used in CEA across various conditions<sup>(22,23)</sup>, including one that compared aspirin therapy with thrombolytic therapy in stroke care<sup>(24)</sup>. Different disability weights for stroke have been used in different studies. In the 1990 Global Burden of Disease (GBD) study, disability weights for first-ever stroke with long-term disability is 0.224 for treated patients and 0.262 for untreated patients<sup>(25)</sup>, so is in the GBD 2000 study. The main reason not to estimate the disability weights according to level of severity in the GBD 1990 study is the lack of disability data from the vast majority of the world regions. A Dutch study, however, provides some information: disability weights for first-ever stroke with mild, moderate

and severe level of long-term disability are 0.36, 0.63 and 0.92, respectively<sup>(26)</sup>.

## DISCUSSION

Although noted to be of great importance in health care decision-making, less are known about the underlying "true" QoL weights of QALYs that reflect the desirability of living in some health state or set of outcomes. There are continuing debates over which method (to obtain the required preference weights) and whose preferences to use in QALY calculations<sup>(1,2)</sup>. According to a review focusing on utility values elicited with the TTO method and from the patient's perspective regarding own current health<sup>(24)</sup>, CEA based on currently published TTO QoL weights should not be trusted as a tool for setting priorities among diagnostic groups. Worse still, studies have found that individual preferences may be inconsistent with the strict assumptions of expected utility theory that underline the QALY concept<sup>(1,2,27)</sup>. For all the criticism of QALYs, no acceptable alternative has yet arisen<sup>(1,27)</sup>.

Recently, scholars at the Harvard School of Public Health and Tufts-New England Medical Center developed a comprehensive registry of CEA (<http://www.tufts-nemc.org/cearegistry/>) and updated the utility values catalog to 2001<sup>(28)</sup>. Given the lack of consensus in estimating QoL after stroke, any of the published QoL weights may be used in a CEA of stroke management. This naturally raises concerns about the meaningfulness in calculating the cost per QALY when considering public reimbursement of interventions or decision-making in health care resource allocation.

To our knowledge, very little is known about QoL after stroke patients in Taiwan. Data reported in other countries may not be fully applicable to Taiwan because of cultural differences. Furthermore, stroke patients with moderate to severe cognitive impairments and those who exhibit communication difficulties may not be able to respond to various methods for measuring preferences. Meanwhile, although using measures of functional independence status (such as the Barthel Index) to estimate the patient's QoL has been considered<sup>(29)</sup>, a notable

degree of heterogeneity in QoL was reported among patients with similar levels of functional status after stroke<sup>(30)</sup>.

In conclusion, regardless of the competing views on economic foundations of CEA<sup>(31)</sup>, a comprehensive and valid economic evaluation of any stroke management requires valid QoL measurements. The need for improved outcome measures for stroke, including QoL measures, is becoming increasingly important in view of the recent development of thrombolytic and neuroprotective therapies. Nevertheless, studies of CEA in general, and the CEA of stroke treatment in particular, are still limited in Taiwan. As CEA becomes more essential to health care policy, we need to understand the strengths and limitations of such analyses. Given the lack of reliable and valid measurement methods in eliciting utility values in QALYs or disability values in DALYs, CEA needs to be addressed in a clear and transparent way to ensure its proper use in practice.

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