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Abstract

In recent years, cost-effectiveness data have strongly influenced clinical practice guidelines for several cardiovascular treatments. Economic considerations are increasingly common as health systems are under mounting pressure to maximise value for money. The quality-adjusted life year (QALY) – an outcome measure that expresses both the duration and quality of life – is the main pillar of cost-effectiveness analyses. It is widely used in assessments of the clinical and economic value of new cardiovascular treatments, but how the QALY is derived is often unclear to clinicians. In this article, we first explain how QALYs are defined and calculated. We then review a selected set of cost-effectiveness analyses of recently-introduced cardiovascular treatments and outline how these studies derived their QALYs. Finally, we discuss the limitations of the QALY and how the presentation of the measure could be improved in cost-effectiveness studies.

Introduction

In many health systems, clinical effectiveness evidence is no longer enough on its own to inform coverage, reimbursement, and treatment decisions for new health technologies. In recent years, cost-effectiveness data have strongly influenced clinical practice guidelines for several cardiovascular treatments, including statins,[1] drug-eluting stents,[2] and, more recently, novel oral anticoagulants.[3] Economic considerations are increasingly common as health systems are under mounting pressure to maximise value for money.[4, 5] The quality-adjusted life year (QALY) – an outcome measure that combines both the duration and quality of life – is the main pillar of cost-effectiveness analysis.[6] When coupled with cost data, QALYs allow decision makers to compare the cost-effectiveness of competing medical options.

Given its high relevance to the practice of cardiovascular medicine, it is important that cardiologists are familiar with the information and assumptions that underlie a QALY. In this article, we first describe what a QALY is and how it is calculated. To illustrate this further, we examine how recent cost-effectiveness analyses of cardiovascular treatments – both drugs and medical devices – derived their QALYs. Finally, we discuss the limitations of the QALY and how the measure can be improved.

What is a QALY?

Economic evaluations can guide the allocation of scarce health-care resources. Researchers usually compare the differences in costs and health benefits of two treatments for the same condition in cost-effectiveness analysis. If these studies use clinical endpoints – for

example, to calculate the cost per heart attack prevented for two blood-thinning drugs – it is not possible to compare the results across health conditions.

To compare the cost-effectiveness of various treatments, it is necessary to place all health outcomes on a single scale. To do this, health economists have developed the QALY, a metric that combines the quantity and quality of life. The QALY is a measure of survival time adjusted by the quality of that life, which can change over time. The QALY is measured on a scale of 0 to 1, where 0 and 1 correspond to the worst and best possible health outcomes, respectively; most health conditions lie somewhere in between, although it is possible for the lower bound to have a negative value. The 0 to 1 spectrum is an interval scale: an improvement in quality of life from 0.1 to 0.2 is considered as equally valuable as a gain from 0.9 to 1.0.[7]

The QALY is widely used to describe the quantity and quality of life of the average patient with a particular condition. For example, a recent study reported that the health-related quality of life of a patient with monthly angina is 0.76, implying that 1 year of life with monthly angina is equivalent, quality-wise, to 0.76 years in perfect health.[8] Cost-effectiveness studies that use utility as the measure of health benefit (e.g., QALYs) are called cost-utility studies, although most researchers use the two terms interchangeably.

Calculating QALYs

Health economists estimate QALYs in several ways. The most common method consists of three steps (**Figure 1**): (1) obtain national preferences about different aspects of health; (2) match these preferences to specific conditions to obtain quality-of-life weights – also called utilities; and (3) estimate the time spent in a condition to calculate QALYs.

[**Figure 1** around here]

In the first step, researchers usually ask a random sample of the general public how willing they would be to give up years of life with various disabilities to return to perfect health.[9] This is typically done in individual countries to account for international differences in people's preferences. In these surveys, health states are presented to the respondents, often using the EuroQol five-dimension (EQ-5D) questionnaire, shown in **Figure 2**. The EQ-5D includes five general aspects of physical, mental, and social well-being, each measured on a three-point scale; this corresponds to 243 possible health states. Once a respondent has answered the time trade-off question (**Figure 2**) for numerous hypothetical health states, it is possible to estimate the quality-of-life preferences for all 243. Researchers collect these answers from large groups of individuals to form nationally-representative preferences about the reduction in quality of life associated with various disabilities (see Drummond et al[10] for a review of alternatives to the time-trade off question, some of which are more commonly used outside of Europe).

[**Figure 2** around here]

The EQ-5D is a generic questionnaire that can be used to describe the quality of life of any patient. It is the most common questionnaire in Europe, where it is considered easy to administer and sufficiently detailed. Thus far, EQ-5D surveys have been conducted in 13 countries on randomly-selected samples of between 300 and 4,048 individuals; a Europe-wide survey was also conducted on 8,709 individuals.[11]

Second, to estimate the quality-of-life weight associated with specific diseases and health conditions, participants in clinical studies are asked to complete the EQ-5D. Their

responses are then matched to the respective nationally-representative preferences. For example, if a heart-attack survivor in a UK-based clinical study provides an EQ-5D response of 2 for mobility, 2 for self-care, 1 for usual activities, 1 for pain/discomfort, and 2 for anxiety/depression, these responses would correspond to a quality weight of 0.675 using the official UK figures.[12] The average value from a clinical study can be used to represent the quality of life of the average patient with a particular condition.

In the third step, researchers multiply the quality-of-life weight for a specific condition by the length of time spent in that health state. For example, if a heart-attack survivor lives, on average, 10 years with a constant quality of life of 0.675, this corresponds to 6.75 undiscounted QALYs (10*0.675). In practice, the quality of life associated with an intervention often varies over time. Most studies also discount QALYs by around 3.0% per year – as conventionally done in economic analyses – under the assumption that people generally prefer immediate health benefits over future gains.

In cost-effectiveness analyses, researchers estimate the difference in QALYs between two interventions over the study time period. In the hypothetical example shown in **Figure 3**, patients with heart failure receiving treatment A accrue, on average, 2.15 QALYs over 4 years, whereas those treated with treatment B accrue 1.25 QALYs. In this scenario, treatment A is associated with an increase of 0.9 QALYs over 4 years compared with treatment B.

[**Figure 3** around here]

Modelling health outcomes

As described above, cost-effectiveness analyses compare the health outcomes of a treatment to those of an alternative, which may be the best, cheapest, or most common

treatment (or no treatment). When modelling health outcomes, researchers choose which health states to include in their analysis. The key assumption is that the treatment alternatives only influence the health states considered in the cost-effectiveness model, and that there are no other significant differences in health outcomes between the two treatment arms. This ensures that cost-effectiveness analyses are parsimonious and incorporate as few health states as possible, instead of the full spectrum of health conditions.

To model the natural history of a condition, cost-effectiveness studies incorporate data on the probability of a patient moving from one health state to another. For example, a model will include the probability of a patient experiencing a given event – for example, dying or having a stroke – as informed by randomised trials and epidemiological studies.

The main result of a cost-effectiveness study is the incremental cost-effectiveness ratio: the difference in costs between the two competing interventions divided by the difference in outcomes – measured in QALYs. The incremental cost-effectiveness ratio is presented as the cost per QALY gained. It is outside the scope of this article to review the methods for estimating the costs associated with alternative interventions, such as clinician visits, procedures and tests, hospitalisations, and medicines; interested readers may wish to consult Drummond et al[10] for a review of costing approaches.

QALYs in cost-effectiveness analyses

To illustrate how QALYs are used in practice, we reviewed four recent cost-effectiveness analyses (**Table 1**). These studies were selected to cover a variety of interventions (i.e., both drugs and medical devices) and countries. The four studies evaluated the cost-effectiveness of: (1) dabigatran versus warfarin for patients with atrial fibrillation;[13] (2) cardiac resynchronisation therapy versus optimal medical therapy for patients with

asymptomatic to mild heart failure;[14] (3) ticagrelor versus generic clopidogrel for patients with acute coronary syndrome;[15] and (4) catheter-based renal sympathetic denervation versus best medical therapy for patients with resistant hypertension.[16] The second and third studies were conducted as part of the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction)[14] and PLATO (Platelet Inhibition and Patient Outcomes) trials,[15] respectively. The other two studies obtained many of the clinical inputs from the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy)[13] and SYMPLICITY[16] trials.

[**Table 1** around here]

The studies included the quality-of-life weights of the key health states that patients may experience during the course of their disease (**Table 1**), such as atrial fibrillation, heart attack and failure, hypertension, and stroke. The weights were sometimes listed as decrements to health – also called disutilities – which represent the reduction in quality of life when a health event occurs (e.g., heart attack) or treatment is initiated (e.g., renal sympathetic denervation). All studies discounted the QALYs by either 3.0% or 3.5% per year.

Here we decompose – using the steps detailed in **Figure 1** – the data presented in these articles to outline how the researchers arrived at QALYs.

Nationally-representative preferences (step 1):

The four studies were conducted in various countries – Germany, Sweden, and the UK. Only two of the studies, however, explicitly stated which national quality-of-life

preferences were used.[13, 15] None of the studies noted which technique was used to elicit the national weights (e.g. time trade-off).

Quality-of-life weights (step 2):

The relevant details about the quality-of-life weights were not always reported. Some of the studies did not state which patients were asked to complete quality-of-life questionnaires and which questionnaires were used (e.g. EQ-5D) (**Table 2**).

Two studies obtained the quality-of-life weights from clinical-trial participants. In the first,[16] EQ-5D responses from 18,624 PLATO trial participants were collected at trial onset, 6 months, and 12 months. The authors of the second study[14] obtained responses to the Minnesota Living With Heart Failure questionnaire – a disease-specific questionnaire – from REVERSE participants; these responses were converted to the equivalent EQ-5D responses using a published formula. When necessary, the authors of both studies complemented these responses with published quality-of-life weights.

In the other two studies[18, 16] – which were not conducted alongside clinical trials – the researchers did not collect any responses to quality-of-life questionnaires and instead relied entirely on published quality-of-life weights.

QALYs (step 3):

To extrapolate long-term outcomes and the duration spent in various health states, the studies relied primarily on the clinical pathways observed in trials, including PLATO (12 months),[15] REVERSE (24 months),[14] RE-LY (24 months),[13] SYMPLICITY HTN-1 (24

months),[16] and SYMPLICITY HTN-2 (6 months).[16] The modelling assumptions were tested in sensitivity analyses.

[**Table 2** around here]

Overall, there was considerable heterogeneity in the description of the quality-of-life data in the models. While some of the studies reported most of the pertinent details about the data, others included minimal description of how QALYs were derived (**Table 2**). Notably, none of the studies listed the technique that was used in the first step to estimate the quality-of-life weights (e.g. time trade-off), and only two of the studies noted which national weights were used.

The limitations of QALYs

Although QALYs appeal to health economists, several criticisms are raised against the use of QALYs to inform treatment decisions.

First, many health-care practitioners question the face validity of QALYs. All methods used to derive quality-of-life weights make assumptions that are often violated.[7, 17, 18] For example, the question presented in **Figure 2** is only reliable if the respondent provides the same answer regardless of number of years of life in ill health. In other words, it assumes that if a respondent is willing to give up two of ten years to return to perfect health, they would be willing to give up four of twenty years. If a person provides two different answers – which is often the case – it is not possible to elicit the true preference.[19] There is empirical evidence that most people do not trade duration of life for quality of life in a linear fashion.[20] For example, many individuals do not agree that six months in good health is equivalent to

one year with quality of life reduced by 50%. More generally, individuals must be very well-informed about their preferences to answer time trade-off questions accurately. It is a challenging conceptual exercise to determine one's exchange rate between disability and full health. In short, the idealized notion of utility put forth by economists is difficult to measure in real life.

Second, the aim to maximise the number of QALYs gained from health spending raises equity concerns.[21-23] All QALYs are of equal value, regardless of who gains or loses them, hence the expression that "a QALY is a QALY is a QALY." However, this is not always aligned with societal preferences about the distribution of resources. For example, societies may prefer to first help the most vulnerable and unhealthy members, before improving the health of those who are already relatively healthy.[7, 24] QALYs may also discriminate against some groups, such as the elderly, for whom interventions may not be as cost-effective. As treating younger patients is expected to confer a greater number of QALYs, all else equal, QALY maximisation has been labelled by some as "ageist."[25] The debate about QALYs is fraught with philosophical and ethical dilemmas.

Third, for decision makers to act on information from cost-effectiveness studies, it is often necessary to define a threshold monetary value that a society is willing to pay for a given health improvement, such as an additional QALY gained from an intervention. In practice, it is difficult to establish a valid threshold, and there is no consensus on which method is most appropriate. The implicit thresholds used in the UK (£20,000-30,000 per QALY gained),[26, 27] the USA ($50,000 per QALY gained),[28] and other countries are the subjects of much debate.

Fourth, the ability to return to work or to care for family members might be equally important to an improvement in health for some people.[29] QALYs, which focus on absolute levels of health, do not capture such benefits.

Fifth, generic quality-of-life questionnaires do not cover all dimensions of health benefit. For example, as previously described, the EQ-5D (**Figure 2**) focuses on five general aspects of health. Disease-specific questionnaires have also been developed to emphasise the aspects of quality of life that are most relevant to patients suffering from particular conditions. Notable examples in cardiology include the Seattle Angina[30] and Kansas City Cardiomyopathy[31] questionnaires. The responses to disease-specific questionnaires are then converted to the equivalent response on the EQ-5D or another questionnaire for which nationally-representative preferences are available.

Finally, there is disagreement over which members of the general population should be asked to complete the questionnaire described in **Figure 2** to generate national quality-of-life preferences.[32] Most studies rely on responses from a random sample of the general public, as described in this article, to generate societal preferences. Some researchers ask patients instead. Patients may overstate the quality of life with their conditions, however, if they adapt to life with an illness or disability; conversely, it is possible that the general public understates the quality of life with various conditions. Others suggest that researchers should ask clinicians given their medical expertise and daily interaction with patients.

The need for standardised reporting

As shown in the reviewed cost-effectiveness studies, the way that QALYs are reported and used in cost-effectiveness studies is often non-transparent and difficult to scrutinise. The lack of transparency and standardisation in reporting fuels the scepticism around QALYs. It is essential for authors to include key information to allow readers to accurately interpret the results (**Table 2**).

Nearly two decades ago, the Panel on Cost-Effectiveness in Health and Medicine, an expert panel convened by the US Public Health Service, published recommendations for reporting cost-effectiveness analyses.[33, 34] The Panel recommended that studies include a "complete description of estimates of quality-of-life weights."[33] This includes all relevant information on how the weights are derived, such as the population that completes the qualify-of-life questionnaire and the questionnaire that is used. A second panel has been convened to update the earlier recommendations.

Researchers should strive to adhere to these guidelines, especially as cost-effectiveness evidence continues to grow in prominence. **Figure 1** outlines the key components for reporting standardised information on how QALYs are derived. If there are space constraints in a journal, these details can be published in online appendixes.

Conclusions

Cost-effectiveness studies influence the coverage, reimbursement, and use of many cardiovascular health technologies. QALYs are a widely-used metric in these studies that capture both the morbidity and mortality gains of an intervention. The metric allows payers to choose between treatments based on how much they prolong the lives and improve the health of patients.

Despite the limitations of QALYs, cost-effectiveness studies that incorporate QALYs provide a useful indication of whether new medical interventions provide good value for money. Alongside other information, such studies can help inform decisions about whether to adopt new treatments. There is a need to educate cardiologists and the wider medical community about how QALYs are used in cost-effectiveness analyses to bridge the divide between the clinical and health-economic communities. As illustrated by the studies reviewed

in this article, the sources of QALYs are not always clearly outlined in such analyses. To enable fruitful dialogue about the strengths and limitations of QALYs, it is important that studies report all relevant information in a standardised way.

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References

1. Lazar, L.D., et al., *Cost-Effectiveness of Statin Therapy for Primary Prevention in a Low-Cost Statin Era.* Circulation, 2011. **124**(2): p. 146-U93.
2. Schafer, P.E., et al., *Cost-effectiveness of drug-eluting stents versus bare metal stents in clinical practice.* Circ Cardiovasc Qual Outcomes, 2011. **4**(4): p. 408-15.
3. Coyle, D., et al., *Cost-Effectiveness of New Oral Anticoagulants Compared with Warfarin in Preventing Stroke and Other Cardiovascular Events in Patients with Atrial Fibrillation.* Value in Health, 2013. **16**(4): p. 498-506.
4. Boriani, G., *How do cardiologists face health economics and health technology assessments?* European Heart Journal, 2012. **33**(22): p. 2757-2758.
5. Miller, G., J.T. Cohen, and C. Roehrig, *Cost-Effectiveness of Cardiovascular Disease Spending.* Journal of the American College of Cardiology, 2012. **60**(20): p. 2123-2124.
6. Whitehead, S.J. and S. Ali, *Health outcomes in economic evaluation: the QALY and utilities.* British Medical Bulletin, 2010. **96**(1): p. 5-21.
7. Weinstein, M.C., G. Torrance, and A. McGuire, *QALYs: The Basics.* Value in Health, 2009. **12**: p. S5-S9.
8. Kohn, C.G., et al., *Cost-Effectiveness of Ranolazine Added to Standard-of-Care Treatment in Patients With Chronic Stable Angina Pectoris.* American Journal of Cardiology, 2014. **113**(8): p. 1306-1311.
9. Dolan, P., et al., *The time trade-off method: Results from a general population study.* Health Economics, 1996. **5**(2): p. 141-154.
10. Drummond, M., *Methods for the economic evaluation of health care programmes*. 3rd edition. ed. 2005, Oxford: Oxford University Press. xv, 379 s.
11. EuroQol Group. *EQ-5D*. 2014 [cited 2014 November 2]; Available from: http://www.euroqol.org/home.html.
12. The Economics Network. *EQ-5D Index Calculator*. 2014 [cited 2014 June 24]; Available from: www.economicsnetwork.ac.uk/health/EQ_5D_index_calculator.xls.
13. Davidson, T., et al., *Cost-effectiveness of dabigatran compared with warfarin for patients with atrial fibrillation in Sweden.* European Heart Journal, 2013. **34**(3): p. 177-183.
14. Linde, C., et al., *Cost-effectiveness of cardiac resynchronization therapy in patients with asymptomatic to mild heart failure: insights from the European cohort of the REVERSE (Resynchronization Reverses remodeling in Systolic Left Ventricular Dysfunction).* European Heart Journal, 2011. **32**(13): p. 1631-1639.
15. Nikolic, E., et al., *Cost-effectiveness of treating acute coronary syndrome patients with ticagrelor for 12 months: results from the PLATO study.* European Heart Journal, 2013. **34**(3): p. 220-228.
16. Dorenkamp, M., et al., *Potential lifetime cost-effectiveness of catheter-based renal sympathetic denervation in patients with resistant hypertension.* European Heart Journal, 2013. **34**(6): p. 451-61.
17. Neumann, P.J., D.E. Zinner, and J.C. Wright, *Are methods for estimating QALYs in cost-effectiveness analyses improving?* Medical Decision Making, 1997. **17**(4): p. 402-408.
18. Arnesen, T. and M. Trommald, *Are QALYs based on time trade-off comparable? - A systematic review of TTO methodologies.* Health Economics, 2005. **14**(1): p. 39-53.
19. Dolan, P. and P. Stalmeier, *The validity of time trade-off values in calculating QALYs: constant proportional time trade-off versus the proportional heuristic.* Journal of Health Economics, 2003. **22**(3): p. 445-458.

20. Nord, E., N. Daniels, and M. Kamlet, *QALYs: Some Challenges.* Value in Health, 2009. **12**: p. S10-S15.

21. Wagstaff, A., *Qalys and the Equity-Efficiency Trade-Off.* Journal of Health Economics, 1991. **10**(1): p. 21-41.

22. Rawles, J., *Castigating Qalys.* Journal of Medical Ethics, 1989. **15**(3): p. 143-147.

23. Mooney, G., *Qalys - Are They Enough - a Health Economist's Perspective.* Journal of Medical Ethics, 1989. **15**(3): p. 148-152.

24. Caro, J.J., *How relevant is cost-effectiveness anyway?* European Heart Journal, 2013. **34**(4): p. 245-246.

25. Tsuchiya, A., *QALYs and ageism: Philosophical theories and age weighting.* Health Economics, 2000. **9**(1): p. 57-68.

26. McCabe, C., K. Claxton, and A.J. Culyer, *The NICE cost-effectiveness threshold - What it is and what that means.* Pharmacoeconomics, 2008. **26**(9): p. 733-744.

27. Appleby, J., N. Devlin, and D. Parkin, *NICE's cost effectiveness threshold - How high should it be?* British Medical Journal, 2007. **335**(7616): p. 358-359.

28. Neumann, P.J., J.T. Cohen, and M.C. Weinstein, *Updating Cost-Effectiveness - The Curious Resilience of the $50,000-per-QALY Threshold.* New England Journal of Medicine, 2014. **371**(9): p. 796-797.

29. Coast, J., *Is economic evaluation in touch with society's health values?* British Medical Journal, 2004. **329**(7476): p. 1233-1236.

30. Spertus, J.A., et al., *Development and Evaluation of the Seattle Angina Questionnaire - a New Functional Status Measure for Coronary-Artery Disease.* Journal of the American College of Cardiology, 1995. **25**(2): p. 333-341.

31. Green, C.P., et al., *Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: A new health status measure for heart failure.* Journal of the American College of Cardiology, 2000. **35**(5): p. 1245-1255.

32. Neumann, P.J. and D. Greenberg, *Is The United States Ready For QALYs?* Health Affairs, 2009. **28**(5): p. 1366-1371.

33. Siegel, J.E., et al., *Recommendations for reporting cost-effectiveness analyses.* Jama-Journal of the American Medical Association, 1996. **276**(16): p. 1339-1341.

34. Gold, M.R., et al., *Cost-effectiveness in health and medicine.* 1996, New York: Oxford University Press. xxiii, 425 p.

Figure 1. The sequential steps for estimating quality-adjusted life years (QALYs).
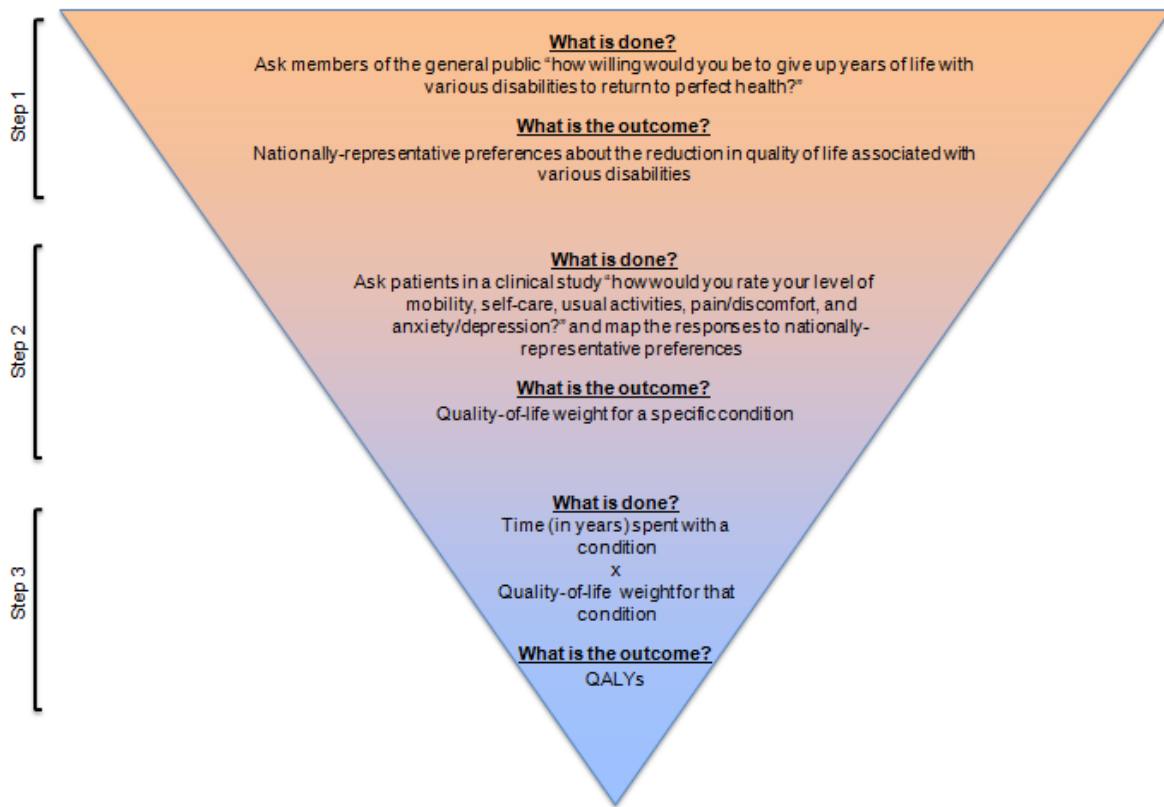

Step 1

What is done?
Ask members of the general public "how willing would you be to give up years of life with various disabilities to return to perfect health?"

What is the outcome?
Nationally-representative preferences about the reduction in quality of life associated with various disabilities

Step 2

What is done?
Ask patients in a clinical study "how would you rate your level of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression?" and map the responses to nationally-representative preferences

What is the outcome?
Quality-of-life weight for a specific condition

Step 3

What is done?
Time (in years) spent with a condition
x
Quality-of-life weight for that condition

What is the outcome?
QALYs

Figure 2. Example of how to derive quality of life information on health states.

	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression
Health State X	2	1	2	2	1

Note: 1 = Best; 3 = Worst

Imagine that you will live 10 years in *Health State X* (quality of life is described above).

How many years of life would you be willing to sacrifice to return to perfect health?

Figure 3. Example of average quality-adjusted life years (QALYs) gained from hypothetical treatment (A versus B).
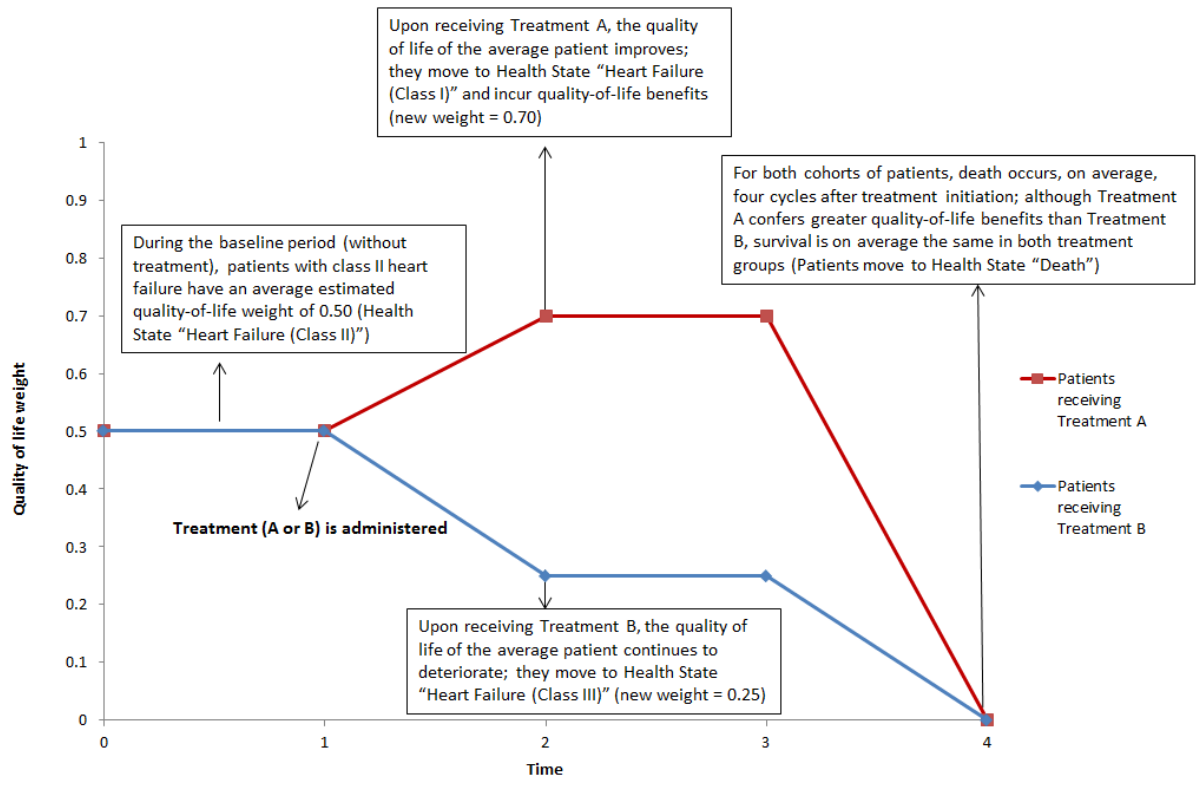
Note: The QALYs accrued with treatment A versus treatment B for the average patient is shown as the highlighted area between the two lines. The figure above only depicts one possible health scenario. As the figure is drawn, treatment A leads to a gradual increase from 0.5 to 0.7 in the average patient's quality-of-life weight during the 2nd year, whereas an alternative representation might be an immediate improvement from 0.5 to 0.7 when treatment begins. Similarly, the figure shows a gradual decline in the quality-of-life weights during the last year for both treatments, whereas a more abrupt decrease might occur. In other cases, one intervention may be associated with longer survival, but no difference in the quality of life. It is also worth noting that time was measured in years in the scenario above, but other studies may use other units (e.g., days or weeks).

Table 1. Summary of QALY data from selected cost-effectiveness studies in the *European Heart Journal*.

Study description	Quality-of-life weight*	Data source	Time horizon	National preferences
Cardiac resynchronisation therapy in patients with asymptomatic to mild heart failure vs. standard medical therapy[14]	Class I (mild) heart failure: 0.93 Class II (mild) heart failure: 0.78 Class III (moderate) heart failure: 0.61	(1) Another study which used the EQ-5D (2) Clinical trial (REVERSE-EU) which used the Minnesota Living With Heart Failure questionnaire; the responses were converted to the EQ-5D	10 years	Not stated
Dabigatran in patients with atrial fibrillation vs. warfarin[13]	Atrial fibrillation: 0.81(65-69 year-old patients) 0.78 (70-74 year-old patients) 0.76 (75-79 year-old patients) 0.71 (80-84 year old patients) 0.05 (decrement to quality of life for each additional year with atrial fibrillation) Ischemic stroke (decrement to quality of life at the time of event): 0.15 Hemorrhagic stroke (decrement to quality of life at the time of event): 0.30 Myocardial infarction (decrement to quality of life at the time of event): 0.19	(1) Other studies which used the EQ-5D	20 years	Sweden
Catheter-based renal sympathetic denervation	Hypertension: 0.98 (0.97-0.99)	(1) Other studies; questionnaire not stated	70 years	Not stated

in patients with resistant hypertension vs. best medical therapy[16]	Myocardial infarction and angina: 0.88 – first year 0.90 – subsequent years	(2) The disutility of percutaneous coronary interventions (obtained from another study) was used as a proxy for the disutility of renal sympathetic denervation		
	Stroke: 0.88 – no sequelae 0.71 – moderate sequelae 0.31 – severe sequelae			
	Heart failure: 0.69			
	End-stage renal disease: 0.70			
	Disutility of renal sympathetic denervation procedure: 0.06 (decrement to quality of life during each year of treatment)			
Ticagrelor in patients with acute coronary syndrome vs. generic clopidogrel[15]	Non-fatal myocardial infarction: 0.87 (<69 year-old patients) 0.84 (70-79 year-old patients) 0.78 (>80 year-old patients) 0.06 (decrement to quality of life at the time of event)	(1) Clinical trial (PLATO) which used the EQ-5D (2) Another study; questionnaire not stated	Lifetime	United Kingdom
	Non-fatal stroke: 0.14 (decrement to quality of life at the time of event)			

EQ-5D, EuroQuol five-dimension questionnaire; PLATO, Platelet Inhibition and Patient Outcomes; QALY, quality-adjusted life year; REVERSE, Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction

* All studies modelled the risk of death at each point in time, with a corresponding quality-of-life weight of 0.

Table 2. Information included in each study about the quality-of-life weights.

	Step 1			Step 2		Step 3
	Questionnaire	**Country**	**Technique (e.g. time trade-off)**	**Questionnaire**	**Respondents (e.g. clinical-trial patients)**	**Duration (i.e. observed or modelled)**
Cardiac resynchronisation therapy in patients with asymptomatic to mild heart failure vs. standard medical therapy[14]				✓	✓	✓
Dabigatran in patients with atrial fibrillation vs. warfarin[13]	✓	✓		✓		✓
Catheter-based renal sympathetic denervation in patients with resistant hypertension vs. best medical therapy[16]						✓
Ticagrelor in patients with acute coronary syndrome vs. generic clopidogrel[15]	✓	✓		✓	✓	✓