PIGLET'S FOOTPATH IN THE SNOW OR A TRAP FOR UNWARY HEFFALUMPS: THE DERIVATION OF VALUES FOR COST-EFFECTIVENESS THRESHOLDS

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1. BACKGROUND

"In which Pooh and Piglet go hunting and nearly catch a woozle" (Milne,1920,p32)

One of the questions which health economists try to answer is "whether health technologies are worth using?" Some also address the question of "how much are technologies worth?" The conventional view has been that such questions of value can only be addressed by cost-benefit analysis (CBA) rather than cost-effectiveness analysis (CEA).[1] However, in practice health care decision-makers place an implicit value on health benefits each time they use cost-effectiveness data in allocating resources.

The point at which the marginal benefits are considered to be of equal value to the marginal resources used in their realisation has become generally known as the cost-effectiveness threshold.

If we knew the value of the cost-effectiveness threshold, answering questions of value would be much easier. Decision-makers in health care, health economists in academia and in pharmaceutical companies would all like to have a number, and certain numbers are cited regularly. Whether a single true value does (or can) exist is not at all clear. Arbitrary values from one country seem to have been adopted elsewhere in a circular process without empirical foundation. In what follows we revisit the nature and the origins of official and de facto cost-effectiveness thresholds currently used in decision-making regarding the utilization of health technologies in different countries. In Section 2 we discuss the conceptual approaches to threshold value that emerged over time. In Section 3 and 4 we describe the attempts and methods used to create thresholds and the values that have been put out into the public arena. We try to establish the link between these and the theoretical approaches. In Section 5 we discuss the merits of having one or multiple threshold values. Given our familiarity with the UK system we will consider the implications of our findings for NICE and the NHS of the different approaches.

2. CONCEPTS OF A COST-EFFECTIVENESS THRESHOLD

Tracking what?[...] I shall have to wait until I catch up with it…(Milne,1920,p34)

CEA compares costs and outcomes of a treatment to that of a relevant alternative and can exclude interventions that are both more costly and less effective. For a range of treatments

such unequivocal judgment is not available. Alternatives can be rank-ordered in terms of their incremental cost-effectiveness ratio (ICER) and after ruling out extended dominance presented in league tables.

There are many unresolved questions regarding the economic foundations of CEA (e.g., Koopmanshap & Brouwer 2000). Consequently, there are serious problems with comparability, reliability and relevance of the data presented in CEA league tables as highlighted by Drummond et al. (1987, 1993) as well as Gerard and Mooney (1993). Whether technical efficiency can be achieved in health care resource allocation with the help of CEA has also been subject to a debate (see Birch & Gafni 1992, 1993; Johannesson & Weinstein 1993). Under very strict assumptions about the comparator, marginal costs and benefits, divisibility and resource constraints, and correct application of decision rules this may be achieved. Although, as Birch and Gafni argue, these conditions are unlikely to hold in practice, while discussing the conceptual background of the threshold we shall assume they do.

To determine whether a non-dominated and non-dominant intervention represents an appropriate use of resources two different algorithms were distinguished in the literature (e.g., Karlsson & Johannesson 1996). Although the apparent appeal of CEA lies in its avoidance of explicitly putting a price on health benefit, both approaches contain a step when a monetary value has to be put on the unit of health benefit to make decisions about health resource allocations. The two approaches will be referred to as the "fixed budget – variable threshold" (shortly the "fixed budget"), and the "fixed threshold–variable budget" (or just "fixed threshold"), approaches.

Let us assume we have all the information to compile a theoretically correct league table of treatments belonging to the same or different treatment classes. There are two different decision rules to maximise health effects subject to a constraint. In one the constraint is in the form of a fixed budget. One starts to implement programmes starting with the one with the lowest ICER, implementing all the interventions until the health care budget is exhausted. The ICER of the last programme, i.e., the marginal cost of the least effective treatment adopted is the shadow price of the budget constraint.

In the dual of this problem the constraint is given in the form of a 'fixed price.' This algorithm may use the same league table. Instead of defining the budget, a maximum price per unit of effectiveness is set in advance. All interventions with a more favourable ICER will be implemented, which in turn yields the health care budget. The fixed price approach is labelled as the 'willingness-to-pay (per QALY)' (Johannesson & Meltzer 1998) or a little confusingly

the 'explicit shadow price' (Briggs & Gray 1999) approach. It is the fixed price that is often referred to as the threshold or cut-off value (Laska et al. 1999). Outside of the theoretical literature however this distinction is not clear and the threshold often seems to refer to the shadow price of the fixed budget.

We shall not enter a discussion on the normative frameworks that may determine one's standpoint. Hurley (2000) in his summary of the normative theory of health economics concludes, that in contrast with other issues in health economics, the normative framework cannot inform choices of methods and practices in cost-effectiveness analysis coherently. We shall also stay clear of the debate about the equivalence of CEA and CBA, although it is relevant to our discussion, and assume away the difference between LYs and QALYs, ignoring for the moment not just their difference but the issue whether QALY is the right measure of relevant benefits.

In what follows we will only discuss how the currently circulating threshold values came about and how they relate to these approaches. Throughout the text, when we wish to distinguish between a societal WTP and the shadow price we will spell it out, otherwise will use the term threshold.

3. CURRENTLY CIRCULATING THRESHOLD VALUES

Do you think it's a woozle(VOSL?)…sometimes it is and sometimes it isn't. (Milne,1920,p34)

Despite these controversies threshold values are commonly 'used.' Firstly, individual study results are placed into a comparative context. Neumann et al. (2000) analysing reporting practices in cost-utility analyses between 1976-1997 found that 57% of the 228 articles compared their results with those of related cost-utility analyses, and 34 % of articles mention an explicit dollar threshold value. In their analysis of 40 studies in oncology Earle et al. (2000) found that 30% cited an explicit threshold value to compare their results against.

At the health policy level there are also values quoted as the threshold. Although NICE denies the existence and the use of an explicit threshold, in the updated document on appraisal methods it does specify that above a £30,000/QALY "the case for supporting the technology […] has to be increasingly strong" (NICE 2003). In other countries values are regularly quoted by practitioners of economic evaluation: AUS$20,000/QALY in Australia, €20,000/QALY in the Netherlands, €30,000 in Spain. Ontario, Canada almost included $20,000 in its economic evaluation guidelines, but decided to take it out (O'Brien at iHEA, York, 2001).

The threshold is also used in a macroeconomic work. First Murphy and Topel (1999) then Cutler and Zeckhauser (2001) tried to answer the question of whether the technological advances between 1950 and 1990 in health care have been worth their costs. They looked at the new and displaced treatments for four conditions, aggregating all their costs and benefits. Crucial to their calculation is the applied value for a life year in the absence of disease of $100,000, which leads them to the conclusion that the medical spending has produced positive net benefit for the US population.

Numerous papers and conferences have discussed the value of the threshold. (e.g., Towse et al. 2002); the ISPOR Annual Meeting in US in 2004 had a plenary session about cost-effectiveness thresholds and in the 2004 OHE annual lecture Alan Williams just recommended that the UK threshold should be £18,000 instead of £30,000.

Where have these values come from? How can they be calculated?

4. METHODS TO CREATE A THRESHOLD

…walking round and round in a circle, thinking of something else…(Milne, 1920,p33)

To guide ourselves in the ontological search we classified the approaches to determine a threshold based on their de facto or claimed method. We will see that some of these methods are clearly lacking any theoretical or empirical foundations and they cross-reference each other, i.e., they do not provide supportable values for decision-making. The classification includes whether it is from the health care or non-health care field; from individual or social choices; hypothetical or relates to actual actions by individuals or society.

1. Values from health economics, based on:
    a. CEA studies
    b. Individual choices
    c. Past explicit decision making
    d. Expert opinion
2. Non-health economics (VSL literature), based on:
    a. Revealed preferences
    b. Contingent valuation studies (stated preferences)
    c. Past explicit decision making

A. Values from health economics: analysis of published CEAs

One way to estimate the threshold is to look at past decisions with regards to health technologies. By relating the acceptance or rejection of technologies to their ICERs, it might be possible to infer the implicit social valuation of health benefits, whether the studies were specifically commissioned to inform decisions or not. Prior to the widespread use of economic evaluation looking at the whole spectrum of health technologies and finding the one with the marginal ICER had little meaning. Infrequently explicit health technology utilisation decisions were made and threshold figures were inferred from them. One often cited example is a 1973 US Congress ruling about financing the dialysis of patients with renal failure. Although the calculated $50,000 figure was the annual cost for such a patient, not an ICER, this number still seems to anchor the US ICER comparisons. Garber and Phelps (1997) among others remark that this is "arbitrary and owes more to being a round number than to a well-formulated justification for a specific dollar value." Recent moves have been to an equally arbitrary $64,000 (see ISPOR, May 2004, Arlington, VA).

The Can$ 20,000–100,000 range as the acceptable and potentially good value for health technologies published by Laupacis et al. (1992) is labelled by Weinstein (1995) as a "rule of thumb," although the authors claim that it is based on some evaluation of past decisions:

> '…These arbitrary limits were chosen after a review of available economic evaluations and previously suggested guidelines. Technologies that cost less than Can$ 20,000/QALY are almost universally accepted as being appropriate ways of using society's and the health care system's resources.' (Laupacis et al. 1992:476.)

As Weinstein pointed out, this is exactly the same range as the one published in 1981 by Kaplan and Bush in US dollars. A similar recommendation framework was set up in the Wessex region in the UK for local health care contracting purposes, with the cost-effectiveness categories ranging from £3,000 to £20,000 per life year (Stevens et al. 1995). The similarity (and circularity) of the argument for the range is illustrated by the following citation:

> 'These [categories] are not immutable, but are broadly related to expectations of the range of estimates likely to arise and those that have been encountered elsewhere.' (Stevens 1995)

We do not know what evidence the authors had when defining their range in the early 90s. What we can examine is whether these, or any other values, could be inferred by looking at the available evidence on CEAs in the recent past.

With the more widespread use of CEAs and CUAs in health care, different research groups have tried to identify and describe their trends and tendencies. Significant effort has recently been put into the compilation of methodologically consistent league tables. The first most comprehensive one published is the medical section of a list of 500 life-saving interventions compiled by Tengs et al. (1995). All entries in this table are in cost/life year saved. The second one was compiled at the Harvard School of Public Health. Cost-utility analyses published between 1976 and 1997 were collected, and results of analyses were retrospectively standardised by using some of the US Panel's reference case criteria. As its name suggests, all entries are in cost/QALY.

Briggs and Gray (BG) compiled a league table of UK-based cost-effectiveness studies, in which ICERs with both cost/QALY and cost/LY have been included. The last year the UK league table included was 1996. As the number of CEAs/CUAs has been growing since the middle of the 1990s we conducted a search to complete the list of the UK CEAs with studies published between 1997 and the beginning of 2002. Although the comparability of studies is a contentious issue, 180 ICERs were extracted from 84 new studies and were grouped by disease and intervention. (Full details of the search and results are given in Appendix A.)

ICERs were all converted to 1996 GB£ based on the HCHS inflation index, and compared to those in the BG league table (Table 1). The distribution of ICERs seems to be fairly similar as described by the mean and the median: both are right skewed. A t-test for the equality of means has a p value of 0.904 and a non-parametric test for independent samples (Mann-Whitney U statistic) has an asymptotic 2-tailed significance of 0.316. This suggests that there has not been a significant shift of the distribution of published ICERs over time. Some real increase in the values can be seen.

The median values for disease areas with at least ten observations show a higher than overall median for neoplasms but it is still under £20,000. The only outlier is the category of nervous system diseases – almost entirely made up of drugs for multiple sclerosis. No such divergence can be seen when the grouping variable is the intervention type. The same is not true in the Harvard database (data not shown): the 'other medical procedures' and medical devices come out much higher than the average.

Table 1. Mean, Median, and Percentiles of ICERs

	New	Old (BG)
Mean	£31,574	£30,376
Median	£6,500	£4,961
Min	£44	£9
10th	£773	£854
20th	£2,311	£1,428
30th	£3,355	£1,907
40th	£4,536	£2,822
50th	£6,500	£4,961
60th	£8,661	£11,381
70th	£14,484	£21,061
80th	£31,004	£33,139
90th	£50,746	£62,059
Max	£1,052,780	£909,001

Table 2. ICERs by Disease Category in the UK, 1997–2002

DISEASE CAT	N	Median	Mean	Std. Deviation
Circulatory system	66	£4,608	£15,676	32349
Congenital anom	2	£70,533	£70,533	46280
Digestive sys	1	£52,530	£52,530	.
Endocr/nutri/metab	2	£970	£970	371
Genitourinary	1	£1,542	£1,542	.
Infectious/parasit	40	£5,162	£14,664	25187
Mental	12	£596	£5,105	7448
Musculoskeletal	3	£2,587	£6,224	6875
Neoplasms	33	£8,645	£11,248	9699
Nerv. Sys/sense organs	18	£46,824	£188,781	333823
Respiratory sys	2	£7,935	£7,935	66
Total	180	£6,500	£31,574	118118

Three quarters of the interventions with published ICERs have ICERs below £30,000 as seen from the tables above.

There are several limitations of our search. The UK filter potentially left out some articles. The selection and classification of articles was carried out by one person only (AB) subject to subjective bias (ideally more people would do this and resolve any disagreements). However, there are further reasons why we cannot say much about a threshold value looking at the results.

Table 3. ICERs by Intervention Type in the UK, 1997–2002

INTERVENTION	N	Median	Mean	Std. Deviation
Pharmaceutical	134	£6,631	£36,080	135048
Surgical	17	£7,550	£33,802	54883
Screening	11	£3,789	£14,970	18548
Other Medical procedure	3	£7,521	£5,625	4295
Care delivery	3	£746	£17,787	30090
Immunisation	4	£8,041	£8,620	1263
Other public health	8	£463	£569	315
Total	180	£6,500	£31,574	118118

- To judge whether there are some gaps and some under-studied disease areas we should show how the available CEAs relate to the range of health technologies that are actually in use in the NHS, and the proportion of NHS activity and resource use in each of the disease class. This information is not readily available in the UK, although we did try to use pharmaceutical or hospital expenditure by ICD-9 categories. In the absence of such data we can only note the difference between the UK and US proportions.
- Cost-effectiveness results do change over time and some of these studies are quite old. There can be at least three reasons for a change in the ICER:
    i. Better data become available. This has been the case with Beta interferon (see Forbes 1999; Parkes 2000; Tappenden 2001).
    ii. Clinical practice changes over time, which was the case with EPO (see Leese 1992; Remak 2003).
    iii. The perspective of the analysis changes. For example, antenatal HIV screening had one of the highest ICERs with children's benefit not included (Gibb 1999), and one of the lowest with it included, which actually led to the introduction of screening (Ades 1999).
- Studies might not have the right comparators or stand up to other quality checks.
- Most of these CEAs have never formed the basis of a formal decision.

There could be plenty of routine interventions with high ICERs on average (for all patients) that have not been evaluated. Almost certainly each intervention could be provided to subgroups that have a higher ICER than the average, potentially very high.

There is an inevitable bias in the published literature because of the selection of topics for evaluation. NHS studies are more likely to be undertaken where there is uncertainty over the effectiveness of interventions or fear of excessive costs. This is evidenced by the fact that ICERs in the NICE appraisals are higher than average for UK published studies (data not shown). Studies published by manufacturers and sponsors of technologies tend to have more favourable results. However, in the absence of data on the comprehensiveness and/or representativeness of the published CEAs, let alone their accuracy, all we can say is that more than 70% of the published ICERs are below £30,000.

B. Values from Health Economics: Social Choices

Some of the CEAs did provide the basis for an explicit decision about the implementation of health technologies. In Australia, Canada, New Zealand and the UK, national institutes have been carrying out health technology assessments to aid formal decisions about their adoption. These lend themselves to analyses in search of a threshold. Decisions of the national institutions in the UK and Australia (NICE and the PBAC) were analyzed and surprisingly narrow ranges have been obtained as the borderline for acceptance and rejection. (Towse 2002, and George et al. 2002).

It is tempting to interpret the inferred ranges as a shadow price of a fixed budget, especially in the Australian case where all new drugs are evaluated. This would definitely not be appropriate in the UK given the arbitrary selection and the small number of health technologies appraised from the plethora of services funded.

Even though not published by New Zealanders themselves, the figures obtained from Pharmac via personal communication (see Pritchard 2002) might be fitted into the fixed budget – variable threshold model. In New Zealand the budget is considered fixed and new drugs can be added or the use of funded ones extended if there are savings expected elsewhere. Pritchard provides *average* CE ratios for three subsequent years: covering a wide range of 'marginal' services, with ICERs of two to four times the average CE ratio. The fact that both the average ICER and the marginal ICER change over time could demonstrate that New Zealanders might think in terms of a fixed budget approach.

There is a different implicit threshold value for New South Wales in Australia that has been obtained from a less cited research project. Cromwell et al. (1998) took the current health budget, certain capacity constraints, such as time of skilled staff and bed availability, and the currently provided services, and determined the service mix that maximised QALYs for the population. The marginal service happened to be renal dialysis for nephrotic syndrome and

other chronic renal failure. There were around 16 more services very close to the margin, and estimates were very sensitive to the effectiveness data.[1] The cost-utility ratio of the marginal service was around Aus$ 30,000/QALY.[2]

The results of the unique New South Wales experiment, that is indeed the shadow price of their budget constraint, have never been applied, given the lack of good quality effectiveness data. The authors themselves expressed a sceptical view about the future of such an approach for reasons of political feasibility.

Most recently Devlin and Parkin (2004) examined the technologies appraised by NICE and tried to infer a threshold value from the decisions to adopt or reject the technology given its cost-effectiveness, budget impact and other factors. From their best model specification they inferred a marginal threshold value at which the probability of acceptance is 50% of £35,380 with an interquartile range of £29,000–42,000.

C. Values from Health Economics: Individual Choices

Although the idea has been around for some time, the first published research we are aware of that estimates individuals' WTP for a QALY is a Danish survey of 3200 people (Gyrd-Hansen 2003). After establishing a preference ordering for two random health states based on the EQ-5D health state descriptions people were asked if they were willing to pay a certain amount per month for medical treatment that would put them in the preferred state. The mean WTP for a QALY was estimated to be about £7,000.

Gyrd-Hansen argues that the WTP for QALY is so low because first, the question related to a small improvement in health, and second because it involved a valuation of health state ex post (respondents had to imagine themselves in it), stripping it of the option value. Questions about the value of life and death could have easily resulted in a much higher value. This idea is supported by the experience from labour market studies.

D. Values from Health Economics: Expert Opinion

Expert opinion seems to be a trivial choice of source. Surveying health economists in the UK Newhouse (1998) compared the answers about the threshold value from his questionnaire to that of US health economists. He found similar mean responses – around US$ 60,000 – and high non-response rates, a sign of reluctance to answer. A rapid survey of 28 health

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[1] Most effectiveness data were adopted from the Oregon experiment, and only in a few cases were locally conducted CEAs at hand.
[2] Personal communication with author.

economists at the above mentioned OHE conference in 2002 resulted in an average of £29,000. Although a handy alternative, expert opinion is rather problematic for it is not known what is in mind when quoting a value. The US values from Newhouse seem to be in line with the Laupacis et al.'s values, whereas the UK value comes very close to the NICE figure of £30,000, suggesting that experts rely on methods listed above therefore their opinions do not have added value. Throughout the UK discussion the concept a fixed threshold independent of the budget was mixing with the concept of an NHS-budget dependent calculated threshold invoking the fixed budget approach (see Culyer 2002).

E. Values from Non-Health Economics: Individual Choices

An alternative threshold calculation can be based on individual choices. The impact of environmental and transport schemes on mortality is usually assessed through changes in the risk of death. For a given change in risk the expected number of lives saved (or lost) is estimated from data on population exposure to the hazard. The value one is willing to pay for reducing this risk can be used to calculate a value of a statistical life (VSL). To see an example, if there is a project that reduces the risk by 5 in 10,000, and the average person is willing to pay £Z to avoid that risk, then the willingness to pay for a project that saves one life (that is 2000 times a 0.0005 risk of death) is 2000*£Z. This life is referred to as a "statistical life", because it is the aggregate sum of small risk reductions, and the individuals whose deaths are avoided (or caused) are not identified.

People reveal their preferences between health (mortality or morbidity) risks and monetary rewards in real life situations. Since the markets for health care goods are fraught with failures, other markets have been the targets of such research. The *revealed preferences approach* looks at labour markets where decisions involve trading off occupational risk for higher wages, and markets for safety products (purchase of smoke detectors, seat belts) to provide risk-income/wealth estimates. The *contingent valuation approach* faces people with hypothetical situations involving such trade-offs between risk and money.

Both revealed preferences and contingent valuation methods are fraught with problems with regard to people's perception of risk. The major criticisms are described in detail elsewhere (see Viscusi 1993 and Hammitt & Graham 1999). Baseline risk values influence obtained values. Risk perception may well change over time. Methodology also makes a difference. Revealed preference studies produced higher estimates than CV studies, although there is evidence for the opposite relationship (De Blaeij 2003, Aldy & Viscusi 2003). The WTP for risk reduction is significantly higher when the commodity in question is a private rather than a

public good (De Blaeij 2003). Within CV studies the payment vehicle and elicitation format within the survey design also make a difference in results. The magnitude of the VSL estimates was shown to depend on age and income (e.g., Aldy & Viscusi 2003). However, the effect of these covariates seems to depend on the method: US and Canadian survey data reported by Alberini et al. (2004) showed very weak evidence of VSL declining with older age and hardly any relationship with health status.

Despite these criticisms, the list of studies estimating a VSL has grown enough to be a worthy subject of reviews and meta-analyses summarising the findings. Table 4 lists the reviews and meta-analysis since 1989 that present ranges of VSL or pooled estimates from labour market, road safety, safety product market and contingent valuation studies. The ranges presented seem to narrow over time, and there is some correspondence between the figures.

How to turn VSL into value of a life year? The extensive literature on the value of a statistical life did not aim for a value per life year. However, assuming a given life expectancy, a discount rate, and relative weights for the remaining life years, potentially reflecting quality adjustments, any given VSL can be turned into different values of LY, depending on the assumption about the weights.[3] This approach has been applied in health economics for some time now (for a few examples see French et al. 1990, Weinstein 1995, Hirth 2000, Loomes 2002). Some even considered quality adjustment in the calculation.[4] This cannot be reconciled with the authors' caution against automatic transfer of the values between sectors and outside the age range that described the population of the primary research.

Loomes (2002) showed that applying certain parameters and the currently used UK transport safety value from the CV study, the value of a LY might come out around £30,000. However, the UK revealed preference studies all produced extremely high VSL values (see in Aldy & Viscusi 2003), translating into a very different result using the same parameters.

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[3] Jones-Lee (1987) found an inverted U-shaped relationship between age and value of a life year. It is an interesting question whether the end of the U reflects people's expectation of the quality of their life when they get older. The Beaver Dam Health Outcomes Study, interviewing 1,356 people found declining average utilities by age, but when examining a relatively healthy subgroup, the quality scores were independent of the age bracket (Fryback et al. 1993). That suggests that a quality adjustment might be validly imposed on the top of a differential value.

[4] The Health and Safety Executive commenced work on the valuation of injuries and accidents in the consumer and transportation fields using the Relative Utility Loss Approach (RULA) (Soby et al. 1993). Serious road traffic injury was subdivided into eight classes. Utility loss scores were assigned to each of these groups. Because of different duration of effects from each class of injuries, Lost Years of Functioning were calculated, which is the same as quality adjusted life years lost due to an accident. The study went on to value a year of life to arrive at monetary estimates of an injury that may be used in a cost-benefit analysis. Only illustrative calculations were made using the then official VSL of £664,000 and assuming an age-independent value per life-year and different discount rates. The RULA approach has been abandoned.

Not only do the starting points of these estimates range very widely, but the results are also very sensitive to the discount rates, the assumptions about life expectancy and the value of a life year as a function of time. However, this calculation method can be clearly linked to the fixed threshold approach and might suggest that there is no single valid value. If anything, this line of research suggests a multitude of threshold values.

F. Values from Non-Health Economics: Social Choices

One might argue that only those VSL estimates should be used for creating a value of a LY that has been used in past government policy decisions about implementing life-saving policies, i.e., that reveal governments' trade-offs in practice. However, the table presented by Aldy and Viscusi (2003, Table 2) shows that values used by US regulatory agencies between 1985 and 2000 ranged from 1.0 million US$ to $6.3 million (in constant 2000 US$) for a diverse set including regulations about ozone-layer protection to portable bed rails.

Table 1. Reviews and Meta-Analyses on VSL

Reference	Number and type of studies included	VSL in million (1998 US$)	Method/Remark
Fisher et al. 1989	21 studies, mixed methodology: labour market, contingent valuation	**2.5 – 12.5**	
Viscusi 1993	24 labour market studies	**4 – 9**	
Neumann & Unsworth 1993	26 studies, incl. 21 labour market studies	**6**	Mean of a Weibull distribution fitted on the data
Miller 1990	27 studies, each incl. more VSL estimates (discarded 30%)	**3 (2.1–3.9)**	mean of subjectively adjusted preferred estimates
Miller 2000	68 best estimates from labour market, contingent valuation and consumer behaviour studies	**4**	(fixed effect from a function of GDP/capita and a dummy variable for study type)
Desvousges et al. 1995	29 "most reliable" VSL estimates	**4**	Meta-analysis, estimates regressed on mean risk from study
Mrozek & Taylor 2002	203 VSL estimates from labour market studies	**1.5 – 2.5**	Meta-analysis
Trawen et al. 2002	11 countries surveyed about official cost of road fatality for CBA	**1.5**	Mean total costs, converted by PPP (fixed prices)
de Blaeij 2002	30 road safety studies with 95 VSL estimates	**–**	No range or single value given. 70% below 5 million
Aldy & Viscusi 2003	46 international wage-risk studies	**5.8 (2.3–14.6)**	Robust regression with Huber weights, including 18 covariates in estimate. The widest estimate

Sources: De Blaeij 2002, Mrozek and Taylor, 2002, Trawén 2002, Aldy and Viscusi, 2003. For conversion rates: http://stats.bls.gov/news.release/cpi.nr0.htm
Note: Meta-analyses on developing countries have been omitted from this table. See Bowland & Beghin (2001)and Liu et al. (1997). De Blaeij et al. (2002) refused to set a plausible range for VSL.

Similarly, in the UK, based on individual WTP and contingent valuation methods – the UK Department of Transport adopted value of £902,500 from the estimated range of £500,000–1,600,000 by Carthy et al. (1998), (in 1998 GBP) for a VSL (Carthy et al. 2000). However, the UK Health and Safety Executive adopted a higher VSL for cancer-related fatalities, due to the fact that people truly dread the disease that outweighs the affects of latency on the WTP (see Andrews & McCrea 1999, quoted by Aldy & Viscusi 2003, p.56). These values seem therefore to depend on the context and the population affected by the regulation.

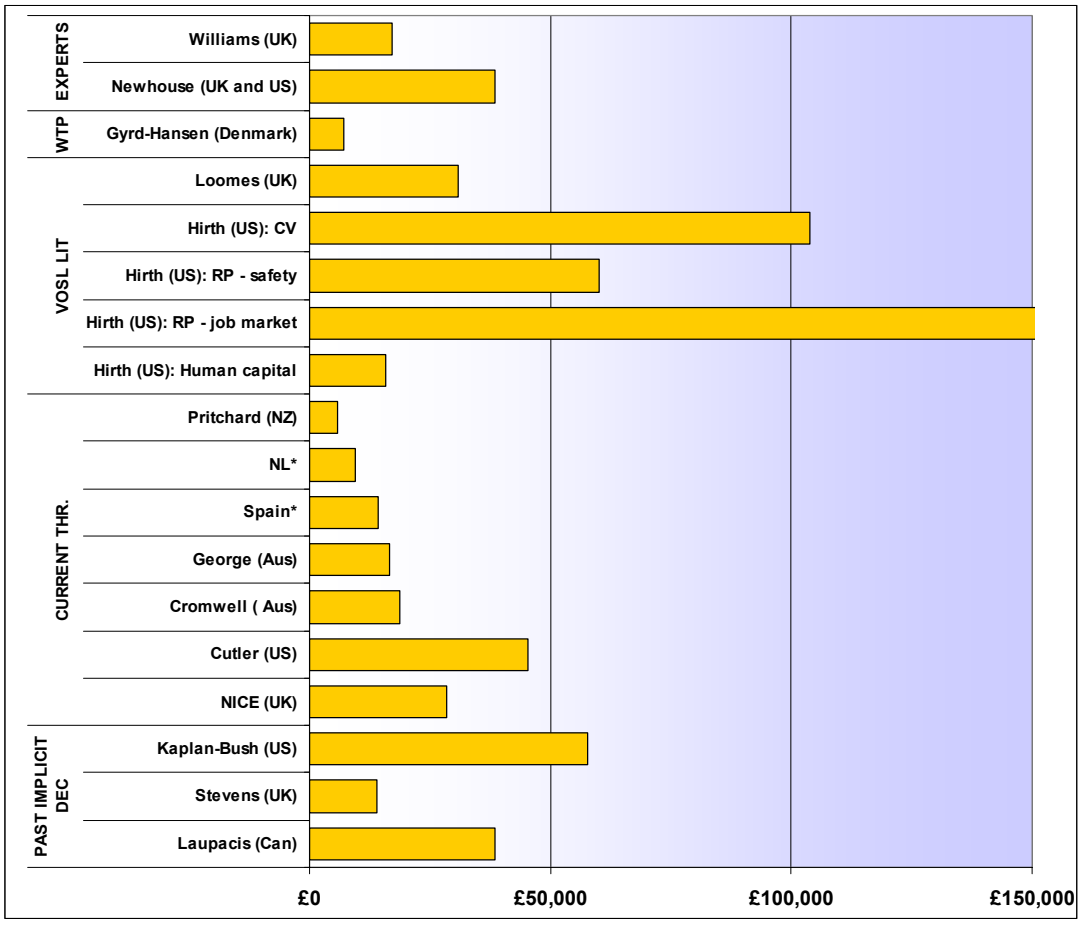
Values compared for similar interventions across countries are also on a broad range. Trawen (2000) published 11 country specific values for the lives lost in road traffic accidents ranging from around US$ 0.9 million in Austria to more than 3.5 million US$ in the US.

Apart from being in actual fact used in regulations at one time, these values do not provide a new method – or a very different value for that matter – for threshold estimation, given that all these are based on the previous research on wage-risk or human capital approach and there is some evidence about the arbitrariness in the choice of value.

5. SO WHERE ARE WE NOW?

As Figure 1 shows the values generated by the different methods (all values are converted to 2000 GBP using average annual exchange rates from www.oanda.com and the UK health care index to update the converted values).

Figure 1. Values of a Life Year from Different Countries by Methods (2000 GB£)



Despite the lack of supporting evidence and the inconsistency with other similarly drawn values (see Figure) the estimates from Laupacis et al. seem to have reached a wide audience and become commonly accepted. In February 2004 the Social Science Citation Index listed 536 articles citing Laupacis et al., most of them being CEAs of particular interventions in the US and other countries. A sub-sample check of articles cited the 20,000-100,000 range

without specifying the year of 1992, and the ICERs of the particular treatment was often directly compared against this range without inflation, or even currency conversion.[5] Authors from outside North America in general took greater care in pointing out that the range may not be applicable in their countries. Without any apparent link to either the fixed budget or the fixed threshold approaches these ranges seem to have been taken on board as some kind of social consensus thresholds. Ironically, even Gyrd-Hansen related to her WTP for QALY figure to Laupacis et al.'s value!

Irony aside, there are some conclusions to be drawn from the above. First, none of the current values have strong foundations. Second, if decision-makers are to continue to use a threshold approach, there is a need to define the meaning and the value of the threshold more clearly. For example, at a time of expanding health budgets estimation of the social value of a QALY might be useful in determining the extent of such expansion (the assumption being that budgetary constraints have produced a shadow price of the national budget constraint which is lower than the societal WTP for health benefits). In reality those charged with releasing the resources to fund the implementation of NICE guidance can only do this at the rate of the local budget shadow price. This is likely to vary between locations (Birch and Gafni, 2001) because of geographical, demographic and historical budgeting factors. Although the societal WTP appears to be easier to estimate, one single value is unlikely to emerge to cover all situations and the challenges to elicit any value remain.

But perhaps any formally estimated value will be a step forward as most of the numbers in use are arbitrary. They came to life, probably with very innocent intentions. However, producers of economic evaluations, including health economists, started to cite these tentative values, reinforcing their validity to an untutored audience. Pooh and Piglet followed their own footprints around the spinney in the snow several times, thinking they were tracking an increasing number of woozles, before Pooh realised that he was "foolish and deluded". However it may well be easier to find a woozle than to estimate the shadow price of a health service budget constraint. On the other hand, it may be easier to elicit social willingness to pay for a QALY than to catch a heffalump, but that's another story……

[5] Health economists are getting better though. At ISPOR US, 2004 a plenary session was titled as "the $64,000/QALY question" that is probably the Can$100,000 exchanged to US dollars.

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Appendix 1

Search

The aim was to identify original applied cost-effectiveness studies with UK resource use and cost data. The search strategy applied by Briggs and Gray (1999) was adopted. The following electronic databases were searched:

MEDLINE(R) SilverPlatter (1996 through January 2002)
Econlit <1969 to January 2002>
OHE – HEED, only year 1999 was available
NHS – EED, all years
SCI – ISI Web of Science Expanded <1945– >
The search strategy was the following:

#1 (YEAR* OF LIFE) AND COST
#2 LIFE YEAR* AND COST
#3 HEALTHY YEAR AND COST
#4 COST UTILITY
#5 UK and (#1 OR #2 OR #3 OR #4)
LIMIT TO
PUBLICATION YEARS 1997–2002
ENGLISH LANGUAGE
PUBLICATION TYPE: NOT EDITORIAL OR LETTER

The search identified 228 articles. Rejection criteria were the following, based partly on Briggs and Gray (1999):

- wrong type of study (analysis of outcomes or costs only)
- no applied results reported (review discussion)
- other cost-effectiveness results, not cost/LY or cost/QALY
- discusses results reported elsewhere
- non-UK resource and cost data

The last couple of years has brought a rise in the number reports from multinational, multicentre studies. Reporting practices differ, but effectiveness data and resource use are not usually reported for each participating country. In some cases national costs are applied for the resources used and therefore country specific ICERs can be reported. Articles with UK specific results were included (e.g. Brown et al. 2002).

Abstracts were read through and where it was evident that the article did not meet inclusion criteria then it was rejected. Out of the identified studies 105 were retrieved (for 1 article only the OHE-HEED record was available). Reading the retrieved items resulted in further rejections and identification of some more CEAs based upon the reference lists of the articles. When two or more studies reported the same research, only the most recent publication was included. This produced a final list containing 84 articles that are listed in Appendix 1. The UK filter potentially left out some articles.

ICERs were extracted on the following basis:

- choose the scenario that was considered to be the most probable by the authors (in a lot of cases it meant choosing the life-span of the model, whether life-time modelling or just limited number of years).
- when results were reported for subgroups ICERs were extracted for each group, independent of whether SA was reported for these as well or only for the overall results.

choose the ICER with 6% discount rate for costs and benefits, so that results are comparable to Briggs and Gray, although the new UK requirement is differential discounting, and authors usually examined the effect of differential discounting at least in SA.

THE SEARCH. The aim was to identify original applied cost-effectiveness studies with UK resource use and cost data. The search strategy applied by Briggs and Gray (1999) was adopted (described in Appendix 1). The search identified 228 articles. International articles with UK specific results were included (e.g. Brown et al. 2002).

Abstracts were read through and in case of evidently not meeting inclusion criteria they were excluded. Out of the identified studies 105 were retrieved (for 1 article only the OHE-HEED record was available). Reading the retrieved items resulted in further

rejections and identification of some more CEAs based upon the reference lists of the articles. When two or more studies reported the same research, only the most recent publication was included. This produced a final list containing 84 articles that are listed in Appendix 2.

For the studies that have been included in the league tables, intervention types were defined in accordance with the Harvard Database's classification (Neumann et al. 2000). The disease areas were classified by the ICD-9 classes.

RESULTS. More than half of the recent UK analyses focus on pharmaceuticals, representing a higher proportion then in the earlier UK studies or in the Harvard Database. This could be related to the activity of NICE, which has focused initially on pharmaceuticals. The number of articles on screening has increased, whereas diagnostic technologies have been hardly looked at in the last couple years. Surgical procedures seem to be neglected relative to the US table.

Table 8 CEAs According to Intervention Type

Intervention	UK 1997–	Briggs and Gray	Harvard
Pharmaceutical	57%	37%	31%
Surgical	9%	10%	18%
Screening	13%	2%	12%
Diagnostic	0%	17%	11%
Other medical procedure	5%	10%	8%
Care delivery	4%	8%	8%
Device	0%	3%	4%
Immunisation	4%	3%	4%
Health education/counselling	0%	3%	3%
Other public health	9%	3%	1%
Various	0%	3%	0%
Total number of articles	84	60	228

Sources: Neumann et al. (2000); Briggs and Gray (1999).

In terms of disease areas, circulatory diseases and neoplasms are in the forefront of CEAs in the UK. Some changes in the recent years can be recognised: there have been fewer studies on circulatory diseases and mental illness, while articles on neoplasms and infectious (mostly HIV and Hepatitis C) and nervous system (including MS) diseases grew most relative to the BG league table. Digestive system, genitourinary and

musculoskeletal diseases remained relatively under-studied compared to the Harvard database.

Table 9 CEAs According to Disease Categories

Disease category	1997–	BG	Harvard
Blood and blood-forming organs	0.0%	0%	2%
Circulatory System	25.3%	33%	26%
Conditions of the perinatal period	0.0%	2%	2%
Congenital anomalies	1.3%	0%	6%
Digestive system	1.3%	0%	4%
Endocrine, nutritional, metabolic and immunity	5.1%	5%	6%
Genitourinary system	3.8%	7%	17%
Infectious and parasitic	16.5%	10%	2%
Injury and poisoning	0.0%	2%	5%
Mental	5.1%	13%	5%
Musculoskeletal system and connective tissue	2.5%	5%	18%
Neoplasms	24.1%	13%	5%
Nervous system and sense organs	12.7%	7%	2%
Respiratory system	2.5%	2%	1%

Sources: Neumann et al. (2000); Briggs and Gray (1999).

Most articles present several ICERs, corresponding to different scenarios, subgroups, one-way or multi-way sensitivity analyses. The rules for extracting the ICERs can be

Appendix 2

List of Articles from New Search:

Ades, Cost effectiveness analysis of antenatal HIV screening in United Kingdom. BMJ 1999. 319: p. 1230-1234.

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