

## *Position Paper*

# **A Systematic Review of Health State Utility Values for Osteoporosis-Related Conditions**

J. E. Brazier<sup>1</sup>, C. Green<sup>2</sup> and J. A. Kanis<sup>3</sup> on behalf of the Committee of Scientific Advisors, International Osteoporosis Foundation

<sup>1</sup>Sheffield Health Economics Group, School of Health and Related Research, University of Sheffield, Sheffield; <sup>2</sup>Medtap, London; <sup>3</sup>WHO Collaborating Centre for Metabolic Diseases, University of Sheffield Medical School, Sheffield, UK

**Abstract.** An important weakness of economic models in the field of osteoporosis has been the dependence on assumptions or expert judgements rather than empirical estimates for the utility values of key health events associated with osteoporosis such as hip, vertebral, wrist fracture and established osteoporosis. This paper seeks to identify the best available utility estimates for health states associated with osteoporosis and make recommendations about their use. It is based on a systematic search of the main literature databases. Studies meeting inclusion criteria have been reviewed in terms of the appropriateness of the valuation technique, the validity of the descriptive system (if one was used), the number and type of respondents, and overall quality of the study. Twenty three estimates of health state values (HSVs) were found across the four conditions from five studies. These empirical estimates were found to differ significantly from the commonly used assumptions in economic evaluation, but with a wide variation between estimates for the same state (0.32 to 0.80 for vertebral fracture states). This variation can be partly explained by the valuation technique, health state description and the background and perspective of respondent, and leaves scope for considerable discretion that could be abused. There are also problems in using values obtained from the study populations to those in economic models and the difficulty of predicting health state values in those who avoid a fracture. The review recommends a set of health state values as part of a 'reference case' for use in

economic models. Due to the paucity of good quality of estimates in this area, further recommendations are made regarding the design of future studies to collect HSVs relevant to economic models.

**Keywords:** Health state utility values; Osteoporosis

---

## **Introduction**

The ever-increasing demands on health care resources have stimulated much interest in the cost effectiveness of health care interventions. In the UK, the recent establishment of the National Institute for Clinical Excellence (NICE) reflects the Government's commitment to investigating cost-effectiveness alongside clinical effectiveness for drugs and other interventions, in order to make efficient use of scarce health care resources [1]. There have been similar developments in a number of other countries [2,3].

An influential approach to the assessment of cost-effectiveness has been to compare interventions in terms of their incremental cost per 'quality adjusted life years' (QALYs) [4]. The QALY combines increased life expectancy and improvements in health status by assigning to each period of time a weight ranging from 0 to 1, corresponding to the health related quality during that period, where a weight of 1 corresponds to optimal health, and a weight of 0 corresponds to a health state judged to be equivalent to death [5]. The QALYs given to a particular outcome from an intervention is the value given to each state associated with that outcome multiplied by the length of time spent in each state.

---

*Correspondence and offprint requests to:* Prof. J. Brazier, Sheffield Centre for Health & Related Research, University of Sheffield, Regent Court, 30 Regent Street, Sheffield S1 4DA, UK. Tel: 0114 222 0715. Fax: 0114 272 4095.

The QALY approach uses a health state value (HSV) to 'quality adjust' survival, thus a person expected to survive 10 years at a quality of 0.8 has eight QALYs. The benefits of a treatment that increases survival at a quality of 0.8 (from 10 to 20 years) or improves the quality of the 10 years (from 0.8 to 0.9) can be valued in terms of the QALY gain (i.e. gains of eight and one, respectively).

The attraction of this approach for health economic evaluation in osteoporosis is twofold. Firstly, there are multiple clinical outcomes (vertebral fracture, hip fracture, etc.) each with different consequences for morbidity. The approach permits multiple outcomes to be converted into a single currency. Secondly, the single currency permits a comparison across different diseases. Thus, the disability occasioned by osteoporosis can be quantified and compared with other diseases [6]. So too can the cost effectiveness of interventions be compared. Ultimately the field of osteoporosis, if it is to succeed, will have to demonstrate its viability in an increasingly competitive financial environment.

The cost-effectiveness of the treatment and prevention of osteoporosis has been a comparatively poorly researched area with 20 published studies in the last two decades [7,8]. Moreover, an important weakness of these economic evaluations has been a dependence on the use of assumption or judgement rather than on empirical evidence for the utility values of key health events associated with osteoporosis such as hip, vertebral and wrist fracture. Yet, the cost per QALY estimates of these economic models has been found to be highly sensitive to the values of these states in the models [7]. More recently, there have been a number of studies that report HSVs using recognized preference elicitation techniques. The values reported in these studies have differed markedly from the judgements previously used in economic models, and are likely to have far reaching implications for estimates of cost-effectiveness of interventions in this area. However, the empirical estimates for some states cover a wide range of values and the methods used to obtain values have varied between studies. This leaves a considerable amount of uncertainty regarding which set of values to use in an economic evaluation.

It is important to understand the reasons for the variations in HSVs. They may partly result from the choice of respondent (whether they were obtained from a patient population or the general population), the technique used to elicit values (e.g. visual analogue scaling, standard gamble or time trade-off), the variant of the preference elicitation technique, the perspective of the task (e.g. whether it was to value one's own health or someone else's), sample size and overall quality of the study. These issues need to be systematically reviewed in order to assist the research community and ultimately policy makers in the assessment of cost-effectiveness of interventions in this important field.

The purpose of this report is to identify the best available utility estimates for health states associated with osteoporosis. It presents a systematic review of

published and unpublished studies reporting empirical estimates of utility values for key health states used in economic models. These key states include hip, wrist and vertebral fractures and established osteoporosis. This review has been based on a systematic search of the key literature databases and a review of the findings in terms of the appropriateness of the valuation technique, the validity of the descriptive system (if one was used), the number and type of respondents, and the overall quality of the study. The review recommends a set of HSVs to be used as part of a 'reference case' for use in economic models in this area. Due to the paucity and poor quality of estimates in this area, recommendations are made regarding future research to obtain health state utility values for use in economic evaluations of new and existing interventions for osteoporosis.

## Health State Utility Values

There are several strategies for determining health state utility values: (1) to use expert opinion; (2) to use indices obtained from the literature and (3) to directly measure the preferences of an appropriate population [9]. The first two approaches have been widely used in the field of osteoporosis where economic evaluations have used judgements either by the authors or by expert panels, or have extracted values from previous studies using these methods. There is evidence that experts may focus on different aspects of health to patients [10]. Moreover, valuations obtained from the literature, such as those found by this review, may be inappropriate.

The preferred approach is to collect stated preference data for a set of health states using techniques, such as standard gamble and time trade-off, from an appropriate population. This raises a number of important issues regarding how health states should be described, how they are to be valued, who should value them and how the values should be used [11]. These form the basis for this review.

### *How Health States Should be Described*

Estimates can be obtained by asking patients to value their own health state or by asking an appropriate population of respondents (who may or may not be patients) to value hypothetical descriptions of the states. Having patients value their own health has the advantage of avoiding the need to describe health states and may ensure they have a better understanding of the impact of the state on their lives. However, for reasons considered later it is often deemed appropriate to obtain the values of people not currently in the state.

Respondents can be asked to value specially constructed vignettes to describe each health state [12] or to use generic health state descriptions that are not specific to the condition, such as the EQ-5D [13]. The generic measures are administered to a patient population and a set of values already obtained from a general population

sample, sometimes known as ‘preference-based’ measure of health, is applied. The specific approach has the advantage of being more relevant and sensitive to the condition than the generic measures [14]. The disadvantage is that the descriptions are less flexible and cannot be used in clinical trials. The descriptions cover a few states associated with or thought to be typical of the condition, and indeed in some cases there is only one such health state. These may poorly reflect the range of states found in the population and any changes found in a trial may not be well reflected in these vignettes. The advantage of the generic approach is that health state questionnaires can be administered in trials in the same way as other measures of health related quality of life, and hence there is a direct link between the descriptive data being valued and the clinical evidence. Commonly used examples of generic instruments for obtaining health state utility values are the EQ-5D [13] and the Health Utility Index (HUI)-III [15].

### *How to Value Health States*

Another important difference between estimates has been the valuation technique used to elicit HSVs, whether for patients to value their own states or to value hypothetical condition-specific or generic states. The techniques used to value health states are visual analogue scales, standard gamble (SG) and time trade-off (TTO) and these are described in Table 1. It is currently recommended for economic valuation, that health state utility values should be obtained using a choice-based technique such as standard gamble or time trade-off rather than a rating scale [16]. However, there is no consensus as to which of these two should be used.

For deriving QALYs it is important to bear in mind that the aim is to value health states on a scale from zero to one, where zero is for states judged to be equivalent to death and one is full health. (Health states can be and often are regarded as worse than death and hence they

**Table 1.** Health state valuation techniques

#### *Visual analogue scale*

A line, usually with well-defined end-points, on which respondents are able to indicate the desirability of a health state. There are many variants of the technique. An example is the ‘thermometer rating scale’ used by the EuroQol Group [13]

#### *Standard Gamble (SG)*

Asks respondents to make a choice between alternative outcomes, where one of them involves uncertainty. They are asked how much in terms of risk of death, or some other outcome worse than the one being valued, they are prepared to accept in order to avoid the certainty of the health state being valued.

#### *Time Trade-off (TTO)*

Technique developed as an alternative to SG, designed to overcome the problems of explaining probabilities to respondents. The choice is between two alternatives, both with certain prospects, i.e. years in full health ( $x$ ) and years ( $t$ ) in the health state being valued. The respondent is asked to consider trading a reduction in their length of life for a health improvement. The HSV is the fraction of healthy years equivalent to a year in a given health state, i.e.  $x/t$ .

can have a negative value.) All valuation exercises must therefore have the same reference (or ‘anchor’) states of full health and death. Full health needs to be defined in an agreed manner as one of the possible outcomes of the choices presented in SG and TTO and the other must be instant death. Where this is not done, for example full health is replaced by best imaginable for age (and there are instances of this in this field) then the valuations should be ‘chained’ onto the full health–death scale using a value for this best imaginable state on the full health – death scale for use in economic evaluation (for a further description see [9]).

### *Whose Values*

An important issue is the question of whose values should be used to value the health states. They may be patients, professionals or other experts, members of the general population or some other population deemed appropriate. These constituencies have been found to yield different valuations. Though the picture is mixed, there is evidence that patients value poor health states more highly than members of the general population trying to imagine the same states [17–19]. This has been explained in terms of adaptation to disabilities, a change in reference point [19] or perhaps a more insidious lowering of expectations [11].

Whatever the source of the difference between patients and the general population, this can have important implications when valuing changes. For dramatic changes, such as those that may arise from a hip fracture where the patient moves from near full health to substantially less, then the change in HSV is greater when made by the general population than by patients. However, where the change is rather less dramatic, such as where a patient moves between severely disabled states, then general population values are poor at distinguishing between them and may result in lower valuations of the change [19].

There are arguments both ways regarding which values to use in economic evaluation. Having patients value their own health ensures they have a better understanding of the impact of the state on their lives. However, the appropriateness of current patient values has been questioned for future health services since this ignores the views of future patients. More generally, it has been argued that for the purposes of informing resource allocation we require the values of society at large and hence those studies using a representative sample of the general population would be more appropriate [20].

### *How the Values Should be Used*

An economic evaluation estimates the health loss for each individual from a health event as the difference between the HSVs before and after the event. When evaluating a new treatment for a symptomatic condition,

this can be assessed by undertaking health assessments before and after treatment. However, economic models of interventions in osteoporosis are typically driven by health events, such as hip fractures, where there are limited pre-event data. In economic models it is often assumed that the pre-event HSV is either 1.0, or that of some control group, or some age-matched and sex-matched average. These methods at least control for the fact that the prevalence of fractures is related to age and sex, but they do not provide true assessments of the likely health state of those who avoid a fracture. People who have a hip fracture probably have a poorer health status than average before the fracture. This has

important implications for the use of health state valuation data, and the nature of the control is considered in this review.

## Systematic Search

This review has been based on a systematic search of the key literature databases, including Medline, EMBASE, SCI, and NEED for the years 1980–1999. The search identified papers reporting economic evaluation of the prevention and treatment of osteoporosis and those reporting quality of life, health state values, QALYs,

**Table 2.** Empirical estimates of utility values for osteoporosis-related health states

Condition	Study	Health state description	Health state value	How valued	Who valued
Normative	NOF Kind et al, 1998 [25]	EQ-5D completed by general population	1.0	Judgement	Panel of experts General population ( <i>n</i> =3381)
		45–49	0.840	TTO	
		50–54	0.850		
		55–59	0.802		
		60–64	0.829		
		65–69	0.806		
		70–74	0.747		
		75–79	0.731		
'Established osteoporosis'	Gabriel et al. 1999 [12]	Own health: Patients with non-traumatic vertebral fracture in last five years (excluding multiple fractures)	0.84 (±0.29)	TTO anchored by best imaginable for age and death	Patients ( <i>n</i> =75, mean age 76).
		Health state constructed from clinician views and focus groups (including reference to future risk)	0.43 (±0.40)	TTO anchored by current health and death, transformed by valuation of own health against perfect health and death	Clinical attendee with no fracture in last 2 years ( <i>n</i> =199, mean age 68)
Hip fracture	NOF Review	First year: assumes time spent in acute care, rehabilitation and so forth	First year: 0.3817	Judgement	Expert panel
		Assumed distribution across defined disability states	Subsequent years: 0.855		
	Gabriel et al. 1999 [12]	37 Patients mean age 76 with hip fracture in the last 5 years completing: HUI-II	0.68 (0.18)	SG (estimated from a transformation of VAS).	Parents of school children from Hamilton, Canada ( <i>n</i> =203)
		QWB	0.61 (0.08)	VAS	Representative sample of the general population of San Diego
		Own health state	0.72 (0.16)	VAS	Patients
		Own health state	0.70 (0.41)	TTO anchored by best imaginable for their age and death	Patients
		Disabling hip fracture state	0.65 (0.45)	TTO anchored by best imaginable health for age and death	Patients ( <i>n</i> =33, mean age 76) who regarded their own state as worse than hypothetical state
			0.28 (0.37)	TTO anchored by own health and death with former transformed by own health state valuation (itself anchored against best imaginable for age and death)	Recent clinic attendees who have never had a fracture ( <i>n</i> =198, mean age 68)
	Salkeld et al. (2000) [22]	Life after a 'good' hip fracture.	0.31 (IQR=0.0–0.65)	TTO anchored by a typical health state of someone of similar age to the respondent and death	Older people at risk of fracture ( <i>n</i> =194, mean age 81)
	Brazier et al. (2000) [24]	39 Patient completed EQ-5D before and after fracture (mean age 76)	6 mths: 0.49 (0.32) 12 mths: 0.48 (0.38)	TTO	General population ( <i>n</i> =3381)
Confined to a nursing home due to a hip fracture	NOF Review	Nursing home	0.4	Judgement	Expert panel
		Salkeld et al. (2000) [22]	Life after a 'bad' hip fracture that included being in a nursing home	0.05 (no range given)	TTO anchored by a typical health state someone of similar age to the respondent and death

(Continued over)

**Table 2.** Continued

Condition	Study	Health state description	Health state value	How valued	Who valued	
Vertebral fracture	NOF Review	Assumes 33% experience no change, 57% QoL reduced by 0.5 for 1 month, 10% experience complete loss and then 0.5 loss for 7 weeks	0.97	Judgement	Expert panel	
	Gabriel et al. (1999) [12]	94 Patients with vertebral fracture in the last 5 years completed: HUI-II	0.80 (0.16)	SG (estimated from a transformation of VAS).	Parents of school children from Hamilton, Canada ( <i>n</i> =203)	
		QWB	0.66 (0.09)	VAS	Representative sample of the general population of San Diego	
		Own health state	0.76 (0.17)	VAS	Patients ( <i>n</i> =94)	
		Own health state	0.81 (0.32)	TTO anchored by 'best imaginable for age' and death	Patients ( <i>n</i> =94)	
		Multiple vertebral fracture state		0.68 (0.4)	TTO anchored by best imaginable health and death	Patients ( <i>n</i> =24) who regarded their health as worse than the hypothetical state
			0.31 (0.38)	TTO anchored by own health state and death with the former transformed by own health state valuation (itself anchored against best imaginable for age and death)	Clinic attendees with no fracture in last two years ( <i>n</i> =199)	
	Wrist fracture	Oleksik et al. (2000) [23]	Patients with radiographically confirmed fracture in the last 5 years completed the EQ-5D		TTO	General population ( <i>n</i> =3381)
			No.	<i>n</i>		
			0	293	0.82 (0.21)	
1			130	0.75 (0.23)		
2			69	0.74 (0.25)		
3			36	0.81 (0.18)		
≥4			60	0.66 (0.30)		
Lumbar			42	0.78 (0.20)		
Thoracic			145	0.68 (0.34)		
Wrist fracture	NOF Review	Assumes 0.7 for 7 weeks Assumes long-term dependency for 2% of cases with QoL reduction to 0.7	Year 1 0.96 Subsequent years 0.98	Judgement	Expert panel	
	Dolan et al. (1999) [21]	EQ-5D completed by 50 wrist fracture cases (mean age 72 years) in outpatient clinic at first and final visit (average 48 day interval). QALY loss over a year assuming a linear progression between initial and last assessment 0.018 (0.014)	0.982	TTO	General population ( <i>n</i> =3381)	

preference-based measures and so forth in osteoporosis related conditions. This was a very broad search strategy that identified papers well beyond the interests of this paper in health state utility values and was designed to ensure that no papers were missed. Studies were also identified by hand searching, citation searching, reference list checking and those known to researchers involved in the study.

This broad search strategy found a total of 1014 papers. The abstracts were initially sifted in order to identify those with any potential to be relevant to this review and the number of papers was thereby reduced to 173. These papers were ordered and reviewed to identify those papers presenting HSVs. It was found that most of the papers were concerned with measuring quality of life in general and did not present health state utility values. Just four published papers [12,21–23] were found to report HSVs for one or more of the osteoporosis related conditions (Table 2). A number of papers reported more than one state and elicited valuations from different groups of respondents and/or used more than one valuation technique. As a result, there were 23 HSVs

in all, with two health state valuations for established osteoporosis, seven for hip fracture in general, one for hip fracture resulting in home confinement, 12 for vertebral fracture and one for wrist fracture. These were supplemented by one unpublished study containing a hip fracture valuation [24]. These are now reviewed.

## Review

Table 2 presents the study, the health state descriptions, the mean and standard deviation of the values, the valuation technique employed and the source of the valuations for each of the osteoporosis-related conditions. For comparison, normative HSV data have been presented by age group for the UK. These values were obtained from the EQ-5D being administered to over 3,000 representative members of the UK general population [25]. The values used by the National Osteoporosis Foundation (NOF) [26] have also been presented for comparative purposes, since these are the

values commonly being used in current economic evaluations.

The 23 empirically derived HSVs for the four conditions (i.e. hip, vertebral and wrist fracture and established osteoporosis) differ considerably from the NOF values obtained by a panel of experts. For example, the NOF value for vertebral fractures of 0.97 compares with values obtained empirically that range from 0.31 to 0.80. There is also a considerable range of values for each condition, probably due to differences in the derivation of the estimates. Differences include what is being valued, the valuation technique, who did the valuing and the anchor states used in the valuation task. These results are discussed in more detail for each condition.

### *Established Osteoporosis*

Gabriel et al. [12] compare health state TTO valuations by patients who have experienced a non-traumatic fracture in the last five years (that is not multiple) and the valuation of a hypothetical case by a sample of non-fracture cases. The health state values were 0.84 and 0.43, respectively. This large difference can be partly accounted for by the fact that the one is a health state valuation by patients and the other is for a hypothetical state by a group who have not experienced a fracture. However, there were also differences in the state being valued since the hypothetical state did not describe any particular type of fracture but included a discussion of future risk, whereas own health was valued using an anchor of best imaginable for age.

For economic models, a conceptually better approach to valuing established osteoporosis is to base it on the worst fracture experienced by the patient.

### *Hip Fracture*

Five out of the seven values in Table 2 report preference-based HSVs and range between 0.28 and 0.72. The lowest values of 0.28 and 0.31 were for condition-specific states, but the health state descriptions were very different: 'disabling' [12] and 'good' [22], respectively. Both were elicited using TTO, with the former anchored against best imaginable and the latter a good health state typical for their age. Adjusting for these anchors would increase the values to some extent. It is noteworthy that the valuation of the disabling state by those who were experiencing a worse state was significantly higher at 0.65.

The remaining two cross-sectional HSVs were very similar. The HUI-II valuation for those who had a hip fracture in the last five years was 0.68 compared to the TTO own HSV of 0.70. Although the patient-derived value might have been expected to be higher, this may have been partly offset by the fact that TTO values are often lower than SG valuations [11].

Brazier et al. [24] collected HSVs using the TTO-weighted EQ-5D before and after hip fracture in a population recruited into a clinical trial. This prospective data set offers a more valid estimate of the loss in health status associated with a hip fracture. The mean HSVs at 6 and 12 months after hip fracture were 0.49 and 0.48 respectively. These figures are lower than those reported by Gabriel et al. [12] for the HUI-II and this could be due to the use of TTO rather than SG and/or the fact that the population is significantly older. Brazier et al. [24] also found that prior to the fracture, patients had a significantly lower HSV compared to the average for their age of 0.60 compared to 0.731 [25]. The estimated proportionate loss using these figures is comparable to that indicated by comparing the HUI estimate of 0.68 to the age/sex norm found in Canada of 0.82 [27].

Whichever estimate is used, these results all imply a significant impact for hip fracture on HSVs. These results support the usual finding that patients give higher valuations than non-patients and that an explicit description of a state seems to elicit a lower value. However, there is no empirical evidence for distinguishing between the first and subsequent years. The results of Gabriel et al. [12] were for those who had experienced a fracture in the last 5 years and the study by Brazier et al. [24] is currently limited to a 12 month follow-up.

### *Nursing Home*

There is only one published estimate for hip fracture cases in a nursing home. Salkeld et al. [22] asked a group of elderly respondents to value a 'bad' hip fracture state that included being in a nursing home. The estimated HSV of 0.05 compared to the NOF assumption of 0.4. The upper anchor used in the TTO question was anchored by a state regarded as good for respondents of their age, which given they were an elderly population is not the same as full health. Another concern with using this HSV is the prevalence of this particular health state description in a nursing home population. Without this information it cannot readily be incorporated into an economic evaluation.

### *Vertebral Fracture*

Nine of the 10 preference-based HSV estimates for vertebral fracture lie between 0.66 and 0.81 and are considerably below the NOF assumption of 0.97. The EQ-5D data from the study by Oleksik et al. found evidence of a relationship between number of fractures and HSV. Thoracic fractures had lower values than fractures located at the lumbar spine. TTO own health values were not higher than the HUI value, again possibly due to the different valuation technique (0.81 vs. 0.80), but higher than the estimates by Oleksik et al. [23] based on a general population TTO valuation of the EQ-5D. The other value of 0.31 was obtained from non-fracture respondents for a hypothetical state of 'multiple'

fractures. It would seem that once again, an explicit description of the condition has resulted in a lower value than the generic descriptions.

After allowing for the expected HSV in the age groups prone to vertebral fracture, the apparent difference to the NOF assumption is considerably reduced for some of the estimates. The HUI-II estimate for those who had a fracture in the last 5 years of 0.8, for example, compares to the normative value based on Canadian data of 0.82 for a comparable age group. The study by Oleksik et al. [23] produced values of 0.66–0.81 compared to general population norms of 0.81.

One concern with these studies is that they recruited patients who had had a fracture up to 5 years ago. There are no HSV estimates against time of fracture and hence no separate estimates for year one and subsequent years. Furthermore, these studies used cross-sectional controls. The control cases in the study by Oleksik et al. [23] were patients who met the same inclusion criteria of age and *T*-score (<−2.5), but the authors found the controls were significantly younger (by 2.5 years), had a higher lumbar spinal bone mineral density (BMD), and a lower prevalence of non-vertebral fractures. The consequences of these differences for EQ-5D score before fracture (or as would have pertained if the fracture had not occurred) is not known.

### Wrist Fracture

Some earlier economic evaluations have assumed that a wrist fracture has no impact on health status. The NOF model had values of 0.96 for year 1 and 0.98 for subsequent years for long-term dependency in a small proportion of cases. The single empirical study of wrist fractures has found a significant impact over short periods of time [21]. The researchers administered the EQ-5D at admission and at final visit to the accident and emergency department and were able to estimate a mean loss in HSV over this period from the wrist fracture by assuming a linear progression between the first and last visit of 0.982.

A concern with this estimate is whether the EQ-5D is sensitive to some of the problems associated with wrist

fracture, particularly the longer-term complications found in a small proportion of patients as indicated by the NOF estimate.

### A Reference Case Set of Values

There was a wide range of preference-based HSVs for each condition primarily due to differences in the descriptive systems and the sample of respondents used in the valuation. One recommended solution in such a situation is to have a reference case of values for all analysts to use. This does not imply that analysts should only use the reference case in future economic evaluation, but they should be used in at least one analysis of each economic evaluation of an intervention for osteoporosis.

The influential Washington Panel on Cost-Effectiveness recommends the use of a generic instrument with social valuations of health states obtained using a preference-based instrument [20]. This allows comparison between health care programs, such as cardiac or cancer versus osteoporosis, as well as within program. The problem to date with the condition-specific approach has been that this has been limited to one or two vignettes, and these do not necessarily reflect the full range of states associated with each condition. Furthermore, they can not be easily linked to patients in trials. Generic instruments can be administered to patients in trials or other clinical studies and hence provide a more accurate quantitative basis to the descriptive results. Whilst accepting there may be problems with generic health state classifications for some condition, such as insensitivity to the consequences of wrist fracture, another approach would be to produce a preference-weighted condition specific measure.

This review found two generic preference-based measures being used, the EQ-5D and the HUI-II. There are few data on their relative performance in osteoporosis, and no methodological basis for preferring one to the other [11,16]. Currently the EQ-5D has the advantage of being available on more osteoporosis related conditions than the HUI-II and hence is preferred for the reference case set of values presented on Table 3.

**Table 3.** Reference case health state values to be applied to population norms<sup>a</sup>

Health state	Value	Source
Established osteoporotic	Use values associated with the type of fracture (see below)	
Hip fracture	0.797 95% CI 0.651-1.012	Brazier et al. (2000) [24]
Nursing home	0.4	NOF
Vertebral fracture	0.909 95% CI 0.84-0.97	Oleksik et al. (2000) [23]
Wrist fracture in first year	0.981 95% CI 0.978-0.986	Dolan et al. (1999) [21]
Proximal humerus	0.981 95% CI 0.978-0.986	Dolan et al. (1999) [21]

<sup>a</sup>These values are the multipliers for the proportionate effect of a fracture on HSVs in the first year. For subsequent years, see suggestions in text.

This decision limits the choice of HSVs for the reference case to: (1) hip fractures – Brazier et al. [24], which has the additional advantage of providing an estimate of the health loss; (2) vertebral fractures – Oleksik et al. [23] using the value for a single fracture, though an analyst could also use values for multiple fractures; (3) wrist fractures – Dolan et al. [21]. The figures for hip and vertebral fractures apply to all years following fracture. Due to lack of evidence it is not possible to distinguish between first and subsequent year, as done by the NOF.

### *Using the HSVs in Economic Models*

The HSVs found in this review do not cover all possible age groups. Some studies are limited to one age group (e.g. [24]) and others are based on small numbers and it has not been possible to estimate reliable age-specific values. To extrapolate the findings from these studies to specific age groups, one approach would be to assume a constant absolute reduction regardless of age. Another is to assume a constant proportional effect on HSVs. There is no evidence to support one assumption or the other. The latter approach has been used for the reference case data set since it assumes that the better your health status the more you have to lose and this was thought to be the most realistic assumption.

Table 3 presents the multipliers for the proportionate effect of a fracture on HSVs in the first year. For hip fractures, for example, the mean HSV at 12 months is divided by the baseline value (i.e.  $0.477/0.597=0.799$ ).

### *Health State Valuations for Subsequent Years*

Economic models have often assumed that the impact on health state utility values from a fracture is less after the first year, presumably to allow for a process of recovery (e.g. [26–28]). It is also likely that the speed and extent of recovery will vary with age. The studies reviewed in this paper did not provide separate values for different years following any of the fractures.

In order to extrapolate these results beyond the first year, it is necessary to assume values for subsequent years. It can either be assumed that fractures have the same relative degree of impact in subsequent years or a set of guesstimates can be made to allow for a possible recovery. A reference set of guesstimates based on previous economic models would be to assume that hip fractures have half the impact in subsequent years (i.e. 0.90) and for consistency the same assumption has been made about vertebral fractures (i.e. 0.955). However, wrist fracture may have no impact beyond the first year and hence we do not suggest any decrement for subsequent years. An important area for future research would be to obtain empirical estimates for subsequent years.

### *Uncertainties Around the Mean Health State Values*

The final selection of HSVs for the reference case are shown in Table 3, including the mean ‘multiplier’ for the proportionate effect that the fracture has on HSV. This multiplier should be applied to the age/sex HSV of patients without a fracture being used in the model. Ninety five percent confidence intervals have also been estimated from the empirical studies using Feiller’s theorem [29].

## **Research Agenda**

The search found remarkably few studies of the impact of osteoporosis-related conditions on HSVs. This finding was confirmed by a recently published listing of 1000 HSVs that contained only six values for these conditions, five for hip and one for vertebral, and all of these were based on expert opinion and not empirical evidence [30].

The studies reviewed in the report have begun to use accepted methods for use in economic evaluation, but they are limited in terms of age range, sample size, and the time period since the event and poor controls. To improve the reference case value data set would require the administration of a preference-based generic health status measure to a large prospective population cohort and long-term follow-up. Such preference-based measures could include the EQ-5D, HUI-III or the recently developed SF-6D that utilizes SF-36 data [16,31]. The choice should depend on evidence of their validity across these conditions. It would be possible and important to estimate the actual loss in HSV over time following each of the fractures (including multiple fractures) by age and generate measures of variance. These data could be collected as part of large clinical trials and observationally. International studies would also allow for cross-national comparisons.

A longer-term agenda should look more critically at the instruments used for estimating HSVs, and in particular the generic preference-based measures for each of the fractures. If generic measures were found to be irrelevant or insensitive to important aspects of one or more of the conditions, then another approach would be to develop condition-specific vignettes, though these are difficult to apply to quantitative data from trials and other studies. Another approach would be to develop condition-specific preference-based measures for use on patients in clinical studies (that could utilize existing measures of health-related quality of life). Another approach would be to estimate preference weights for condition-specific measures (such as the Mini-Osteoporosis Quality of Life Questionnaire [32]).

## **Conclusion**

An extensive search of the literature revealed only five studies on the impact of osteoporosis-related conditions on HSV and these generated 23 values. These values

differed significantly from the assumptions used in previous economic models, such as the NOF model. These have been critically reviewed in order to understand the reasons for the wide range of values and to select values to recommend for use in economic evaluation. Many of the differences reflected the source of value (e.g. patient's own values or social values) or the descriptive system used in the valuation (e.g. condition-specific vignettes or generic preference-based measure). One solution to these differences was to recommend a reference case of values for use in all economic evaluation (Table 2), though it is recognized that analysts may wish to use other values as well, such as those obtained directly from patients.

Osteoporosis must compete alongside other areas of medicine for health care resources and cost-effectiveness has become an increasingly used criterion. The application of this criterion requires HSVs and osteoporosis does not compare well with other fields of medicine in terms of amount and quality of evidence on HSVs. This report recommends the widespread use of the generic preference-based measures (such as the EQ-5D and HUI-III) in clinical trials and observational studies in order to significantly improve the evidence and some more critical methodological work on these measures.

*Acknowledgement.* We are grateful to the International Osteoporosis Foundation and the National Coordinating Centre for Health Technology Assessment (NCCHTA) for their support. The views and opinions in this report do not necessarily reflect those of the NCCHTA.

## References

- Department of Health and the Association of the British Pharmaceutical Industry Guidelines for the economic evaluation of pharmaceuticals [Press release]. London: Department of Health, 1994.
- Commonwealth Department of Health, Housing and Community Service Guidelines for the pharmaceutical industry on the submission to the pharmaceutical benefits advisory committee. Canberra: Australian Government Publishing Service, 1992.
- Ministry of Health (Ontario) Ontario guidelines for the economic evaluation of pharmaceutical products. Toronto: Ministry of Health, 1994.
- Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes, 2nd edn. Oxford: Oxford Medical Publications, 1997.
- Weinstein MC, Statson WB. Foundations of cost-effectiveness analysis for health and medical practices. *N Eng J Medicine* 1977;296:716.
- Murray CJL. Rethinking DALY's. In: Murray CJL, Lopez AD, eds. The global burden of disease. Geneva, WHO 1996:1-89.
- Sculpher M, Torgerson D, Goeree R, O'Brien B. A critical structured review of economic evaluations of interventions for the prevention and treatment of osteoporosis. Discussion Paper 169. York: The University of York Centre for Health Economics, 1999.
- Torgerson DJ, Reid DM. The economics of osteoporosis and its prevention. A review. *PharmacoEconomics* 1997;11(2):126-38.
- Torrance GW. Measurement of health state utilities for economic appraisal: a review. *J Health Econ* 1986;5:1-30.
- Jachuk SJ, Brierley H, Jachuk S, Wilcox PM. The effect of hypertensive drugs on the quality of life. *J R Col Gen Pract* 1982;32(235):103-5.
- Dolan P. The measurement of health related quality of life for use in resource allocation in health care. In Culyer AJ, Newhouse JP, eds. Handbook of health economics, vol. 1, Elsevier Science: Amsterdam 2000.
- Gabriel SE, Kneeland TS, Melton LJ, 3rd, Moncur MM, Ettinger B, Tosteson AN. Health-related quality of life in economic evaluations for osteoporosis: whose values should we use? *Med Decis Making* 1999;19:141-8.
- Brooks RG. 'Euroqol: the current state of play', *Health Policy* 1996;37:53-72.
- Fitzpatrick R, Zeibland S, Jenkinson C, Mowat, A. A comparison of the sensitivity to change of several health status measures in rheumatoid arthritis. *J Rheumatol* 1993;20:429-36.
- Torrance GW, Furlong W, Feeny D, Boyle M. Multi-attribute preference functions. *Health Utilities Index*. *PharmacoEconomics* 1995;7:503-20.
- Brazier J, Deverill M, Green C. A review of the use health status measures in economic evaluation. *J Health Services Res Policy* 1999;4(3):174-84.
- Sackett DL, Torrance GW. The utility of different health states as perceived by the general public. *J Chron Dis* 1978;31:697-704.
- Boyd N, Sutherland H, Heasand K, Trichler D, Cummings B. Whose values for decision analysis? *Med Decis Making*, 1990;10:58.
- Lenert LA, Treadwell JR, Schwartz CE. Associations between health status measures and utilities: implications for policy. *Med Care* 1999;37:479-89.
- Gold MR, Siegel JE, Russell LB, Weinstein MC Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996.
- Dolan P, Torgeson D, Kumar Kalarlapudi TK. Health related quality of life of Colles' fracture patients. *Osteoporos Int* 1999;9:196-9.
- Salkeld G, Cameron ID, Cumming RG et al. Quality of life related to fear of falling and hip fracture in older women: a time trade-off study. *BMJ* 2000;320:241-6.
- Oleksik A, Lips P, Dawson A et al. Health related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fracture. *J Bone Miner Res* 2000;15:1384-92.
- Brazier JE, Kohler B, Walters S. A Prospective study of the health related quality of life impact of hip fracture. Sheffield: SchHARR, University of Sheffield, 2000.
- Kind P, Dolan P, Gudex C, Williams A. Variations in population health status: results from a UK national questionnaire survey. *BMJ* 1998;316:736-41.
- National Osteoporosis Foundation. Osteoporosis: review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis. *Osteoporos Int* 1998;8:1-88.
- Roberge R, Berthelot J-M, Cranswick K. Adjusting life expectancy to account for disability in the population: a comparison of three techniques. *Social Indicators Res* 1999; 48:217-43.
- Zethraeus N, Lindgren P, Johnell O et al. A computer model to analyse the cost-effectiveness of HRT - a revised version. Working paper Series in Economics and Finance, No. 368. Stockholm School of Economics, Sweden.
- Briggs AH, Gray AM. Handling uncertainty when performing economic evaluation of health care interventions. *Health Technol Assess* 1999;3:2.
- Tengs TO, Wallace A. One thousand health-related quality-of-life estimates. *Med Care* 2000;38:583-637.
- Brazier JE, Harper R, Thomas K, Jones N, Underwood T. Deriving a preference based single index measure from the SF-36 *J Clin Epidemiol* 1998;51:1115-29.
- Ioannidis G, Adachi JD, Guyatt GH. Development and validation of the mini-Osteoporosis Quality of Life Questionnaire in osteoporotic women with back pain due to vertebral fractures. *Osteoporos Int* 1999;3:207-13.

Received for publication 6 May 2002  
Accepted in revised form 7 May 2002