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Time Trade-Off Derived EQ-5D Weights for Australia

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A B S T R A C T

Background: Cost-utility analyses (CUAs) are increasingly common in Australia. The EuroQol five-dimensional (EQ-5D) questionnaire is one of the most widely used generic preference-based instruments for measuring health-related quality of life for the estimation of quality-adjusted life years within a CUA. There is evidence that valuations of health states vary across countries, but Australian weights have not previously been developed. **Methods:** Conventionally, weights are derived by applying the time trade-off elicitation method to a subset of the EQ-5D health states. Using a larger set of directly valued health states than in previous studies, time trade-off valuations were collected from a representative sample of the Australian general population (n = 417). A range of models were estimated and compared as a basis for generating an Australian algorithm. **Results:** The Australia-specific EQ-5D values generated were similar to those previously produced for a range of other countries, but the number of directly valued states allowed inclusion of more interaction effects, which increased the divergence between Australia's algorithm and other algorithms in the literature. **Conclusion:** This new algorithm will enable the Australian community values to be reflected in future economic evaluations.

Keywords: cost-utility analysis, EQ-5D, outcomes research, quality-adjusted life years.

Introduction

Economic evaluation of health interventions is integral to the decision-making process in many countries, particularly for government reimbursement decisions. The tools used in the construction of such analyses are, therefore, of increasing importance. Cost-utility analysis (CUA) is the preferred approach in many countries, including Australia. An increasing focus on health-related quality of life has seen the development of standardized descriptive quality of life instruments that allow for direct measurement of the quality of life of patients in clinical settings, trials and observational studies, and valuation via a single index derived from a population-based preference elicitation study. These instruments (termed multi-attribute utility instruments) describe health in terms of a set of dimensions and items and include an algorithm that assigns an index number to each health state (defined as a specific profile of attribute items representing alternative levels of the different dimensions) represented by the instrument space on a scale with one representing full health and zero representing death. Attaching a value greater than zero to a health state implies it is better than dead, whereas a negative value represents a state worse than dead. Existing instruments include the EuroQol five-dimensional (EQ-5D) questionnaire [1], the six dimensional health state short form (SF-6D) [2], the health utilities index 3 (HUI3) [3,4], and assessment of quality of life (AQoL) [5].

Australia is an unusual case. Although CUA has become the preferred approach for the evaluation of pharmaceuticals [6], Australian general population specific weights exist for only one of the more common multi-attribute utility instruments (the AQoL). Therefore, Australian CUAs performed using EQ-5D or SF-6D data have relied on weights from other countries, particularly those from the United Kingdom [1,2].

Multi-attribute utility instruments have been compared and their role in the economic evaluation of health technologies has been discussed widely in the literature [5,7]. In this article, the focus is on the EQ-5D, because it represents the most commonly used generic quality of life descriptive system. The primary aim of this study was to develop Australian based weights for the EQ-5D descriptive system, based on data collected from a sample representative of the Australian general population and using methods that are largely comparable to those used previously to develop weights for other countries.

A secondary aim was to explore methodological issues in the derivation of weights for the EQ-5D, particularly in relation to the choice of health states to be directly valued, and the impact of this choice on the weights derived. In this study the choice of health states was informed by undertaking a simulation study. Several different methods were used to define subsets of health states to be directly valued, and simulation data were generated. The results from each of these subsets were analyzed separately and the resulting utility weights were compared for all health states defined by the EQ-5D descriptive system to determine a preferred set of health states to be directly valued. This set was then used for the data collection for the Australian valuation study.

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The second section of the article briefly describes the EQ-5D and its development, including the methods that underlie the existing algorithms, and in particular the selection of health states for direct valuation. This section motivates the simulation approach used in this study and provides a rationale for the approach. Section 3 describes the methods for the simulation study and for the data collection and analysis for development of the Australian algorithm. Section 4 presents the results and Section 5 discusses the choice of algorithm.

Overview of the EQ-5D and valuation studies

The EQ-5D was originally developed by a European team of researchers. The measurement and valuation of health (MVH) study, based at the University of York, produced the United Kingdom algorithm [8]. The EQ-5D has five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Each dimension has three levels corresponding to no problems, some problems, and severe problems. Consequently there are 243 (3^5) possible health states.

Valuation algorithms exist for a variety of countries, including Spain, the United Kingdom, Zimbabwe, The Netherlands, the United States, Japan, Denmark, and New Zealand [1,9–14]. Most of these used the time trade-off (TTO) to value individual states, although a visual analogue scale was used in New Zealand [15]. Further, all used direct valuation of a sample of health states, with regression analysis used to develop a linear additive model to predict the values of all other health states. One advantage of the use of a common method for development of algorithms across countries is that it allows comparison between national attitudes to poor health [9,16]. Recent evidence suggests that characteristics of the population may drive health state valuations, and that differences in valuations between countries are due to differences in national attitudes to ill health, rather than being artifacts of variations in valuation methods [17].

Relative to other generic health-related quality of life tools, the number of health states in the EQ-5D is small. The SF-6D contains 18,000 health states and the AQoL allows for more than one billion. The study by Tsuchiya et al. [13] discusses issues relating to the number of unique health states. First, there is a trade-off between the richer descriptive system permissible under those instruments with more health states and the ease of use associated with tools such as the EQ-5D. In trial-based evaluation of health technologies, it is preferable to not overburden patients with self-completed questionnaires. The brevity of the EQ-5D is an advantage in this regard. The simplicity of the descriptive system, however, may make it insensitive to changes in health status, and, therefore, to the relative impact of different interventions on health-related quality of life. Further, in valuation tasks, there may be considerable variability among respondents in their interpretation of a particular descriptor (particularly the distinction between moderate and severe levels). A five-level descriptive system has been introduced and represents an improvement in terms of descriptive ability [18,19], but no scoring algorithm has yet been developed and the three-level descriptive system remains widely used [20].

A second issue arises from the number of states that require direct valuation. For any given descriptive system, the higher the proportion of states that are directly valued, the less restrictions are placed on the functional form of the algorithm (for example, allowing estimation of interactions between dimensions).With instruments such as the AQoL, HUI3, and SF-6D that incorporate several thousand separate health states, any valuation study is necessarily limited in the proportion of health states that can be directly valued. In the case of the AQoL and HUI3, the developers of the instrument assume a priori multiplicative functional form, which then limits the number of distinct states that need to be valued. In the case of the SF-6D, the functional form is assumed to be additive, but even a relatively large valuation study can only include a small proportion of the total number of health states, which in effect limits the investigation to a linear additive functional form without interactions.

Tsuchiya et al. [13] notes that a large number of directly valued states per respondent make the evaluation exercise more onerous because the TTO often requires respondents to answer multiple questions to value one health state. In the original valuation study by Dolan [8], 43 states were included in the valuation sample, but Tsuchiya et al. [13] have argued that a subset of 17 states is appropriate. Although there is a potential trade-off between valuation of a larger proportion of states and the burden of data collection, electronic methods of data collection can reduce the marginal cost of data collection, thus allowing a larger number of respondents for the same data collection resources. For example, use of an online panel or computer-assisted telephone interview (CATI) techniques can reduce recruitment and interview costs. Electronic methods for data collection allow more respondents to be questioned, thus either reducing the number of states each respondent has to face, and/or increasing the proportion of states that can be directly valued (rather than estimated through the subsequent algorithm).

A third issue – related to but distinct from the number of health states that need to be directly valued – is the selection of the particular health states that are to be valued. When using the EQ-5D, for example, it is unreasonable to ask a single respondent to value more than a small subset of the total 243 health states within a TTO framework. Two major approaches have been taken to constructing this subset: the 43-state approach used in the UK valuation survey (of which a subset of 13 of the 43 health states was valued by each respondent), and the 17-state approach (of which all 17 were valued by each respondent) used in the Japanese valuation survey [1,13]. The approach to selection of health states used by Dolan et al. [8] was based on classifying health states as very mild, mild, moderate, and severe (based on the levels of each dimension) and then selecting a subset ($n = 43$) that included full health, the worst health state in the EQ-5D, and health states from each of these severity groups. Although the basis of selection was not described in the article, the approach ensures that each dimension is represented at the no problems, some problems, and severe problems levels. The study also excluded "implausible" health states defined as combinations of level 1 on usual activities (no problems with performing one's usual activities) with level 3 on mobility (confined to bed) or level 3 on self-care (unable to wash or dress oneself) [8].

Tsuchiya et al. [13] used a subset of 17 of the original Dolan et al. [8] set of 43, described as "the minimum set of health states required to estimate the value set," although it is not clear from the article on which criteria this statement is made. In neither case is it clear that experimental design principles underlie the choice of health states to be valued. It is noteworthy that the states selected under both the Dolan approach and the Tsuchiya approach have a relatively higher proportion of dimensions at level 1 (i.e., no problems) and a high co-occurrence of level 1 in multiple dimensions. The implication of this is that the point precision will differ between directly valued states, and the uncertainty around the extrapolated values will be greater in those health states with relatively more level 2 and 3 attributes. A recent study has directly valued 101 of the states, but this has not yet been replicated elsewhere [21].

Given the relatively small number of health states in the EQ-5D, it is feasible to value all states directly. This has the advantages of reducing the need to extrapolate between directly valued states, and allowing for estimation of a wider range of interaction effects. Given that some health states are implausible, it may not be appropriate to value all states, because the cognitive task of requiring respondents to imagine an implausible health state may be unrea-