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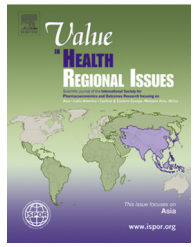

Investigation of Evidence Sources for Health-Related Quality of Life in Cost-Utility Analysis of Pharmaceuticals in Japan

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ABSTRACT

Objective: To provide an overview of how current utility values were obtained in the cost-utility analysis (CUA) for pharmaceuticals in Japan on the basis of methodological guidelines developed in England and Wales, Australia, Canada, France, and Japan by conducting a systematic review of the published literature. **Methods:** We searched and reviewed CUAs conducted for pharmaceuticals in Japan, reporting the results as cost per quality-adjusted life-year (QALY). The databases we used were PubMed, EconLit, Centre for Reviews and Dissemination, and the Japan Medical Abstracts Society. The search terms were "QALY" and "Japan" or "cost utility" and "Japan" in the PubMed database, Centre for Reviews and Dissemination, and EconLit. In the search on the Japan Medical Abstracts Society database, we used the term "QALY." **Results:** In total, 41 CUA articles met the selection criteria and the most common method of obtaining utility values was derived from the published literature (31 CUAs, 168 utility values). Five CUAs were elicited by directly asking the participants regarding their own health state, and four CUAs used "mapping" techniques in which utility values were linked to clinical results. The most commonly used instrument was the EuroQol five-dimensional questionnaire followed by the time-trade-off. A few CUAs mentioned how they selected the literature for the utility values, and some utility values were combined across different sources, using different methods, and obtained from different locations. **Conclusions:** Practical methodological guidelines need to be developed to provide standardized methods of presenting the procedure of using utility values from the literature. Although transferability of utility values across jurisdictions has not been discussed fully, this topic should be covered in methodological guidelines and recommend best practices for evaluations.

Keywords: cost-effectiveness, cost-utility, health-related quality of life, QALY.

Introduction

The concept of cost-effectiveness has been used as a decision-making criterion for the allocation of scarce resources for health care in several countries, such as in the United Kingdom, Australia, and Canada. Cost-utility analysis (CUA) is one of the major methods used for determining cost-effectiveness, and it has been used in these countries for more than a decade. Last year, France composed its own set of cost-effectiveness guidelines for use in the pricing of pharmaceuticals. In April 2012, Japanese government's consulting body called the Central Social Insurance Medical Council (Chu-i-kyo) set common ground for the discussion of the possible introduction of the cost-effectiveness concept for health technologies, including pharmaceuticals. In parallel, a methodological guideline was proposed by an academic group in early 2013 [1]. After 2 years of deliberations, Chu-i-kyo now focuses more attention on drugs as cost-effectiveness evaluation targets, either the newly listed ones or those with a certain period passed since listing. In addition, from April 2014, pharmaceutical companies are being requested to submit economic evaluations for designated products, as a trial.

To conduct CUAs for pharmaceuticals, a substantial amount of data is required. This data not only includes clinical data but also data that are not usually taken from clinical trials, such as long-time transition. One piece of such necessary data is the utility values used when calculating quality-adjusted life-years (QALYs). It was not common to take utility data in clinical trials in Japan; therefore, CUAs often used utility values that were derived from the literature, sometimes derived from studies conducted at different locations, with different instruments. The transferability of utility values, however, has not been fully discussed. Although some analysts have argued that utility scores can be used across studies, because there were no substantial differences across jurisdictions [2], others insisted that differences in ethic and cultural backgrounds might affect perceptions of health [3,4]. Badia et al. [4] suggested that efforts should be made to obtain local health state indices, wherever possible, and further cross-national comparisons of preference values should be conducted.

Conflict of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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Another issue surrounding the utility values is that different utility measurement methods or instruments yield different utility values. This could occur in direct methods, such as the standard gamble (SG), the time trade-off (TTO), and the rating scale (RS), as well as in indirect methods, such as the EuroQol Five-Dimension (EQ-5D) the Health Utilities Index (HUI), and so on. Among the direct methods, for example, it was reported that for the same patient, the scores derived from the SG were generally greater than their scores on the TTO [5–7]. A Japanese study by Noto et al. [8] reported that the elicited utility scores from students and medical staff under hypothetical stroke rehabilitation revealed greater scores on the RS than on the TTO. Similarly, with reference to indirect methods, Neumann et al. [9] reported that scores of patients with dementia on the HUI 2 were greater than their scores on the HUI 3, for all levels of severity. Furthermore, systematic reviews of 28 empirical studies that compared direct and indirect methods of estimating utilities revealed that direct methods (SG and TTO, in this case) resulted in higher scores than indirect methods (the EQ-5D and HUI 3, in this case) [10].

To review the current practices related to these two issues, we examine what was addressed in the national methodological guidelines for economic evaluation across different countries because these guidelines represent the best practices in economic evaluation. Thus, we examined the guidelines provided by the following organizations: the National Institute for Health and Care Excellence (NICE) in the United Kingdom (England and Wales) [11], the Pharmaceutical Benefits Advisory Committee in Australia [12], the Canadian Agency for Drugs and Technologies in Health in Canada [13], the Haute Autorité de Santé (HAS) in France [14], and the proposed guideline provided by an academic group in Japan [1] that was funded by the Japanese Ministry of Health and Welfare.

Methods to Derive Utility Values as Prescribed in the National Guidelines of Five Countries

Although most of the guidelines prioritized the utility values derived from the studies conducted in their own county, the guidelines from all five countries allowed for the elicitation of utility values from the literature subject to the fulfillment of certain conditions. For instance, in France, the utility values and the life-years were recommended to be extracted from French empirical data. If French data were not available, the use of foreign data was allowed if the methodological quality of the study was good (although "good" was not defined) and its external validity was justified. The NICE guideline requires the utility values to be measured directly from the patients using the EQ-5D. If such information is not available in data from relevant clinical trials, it recommends the use of EQ-5D data from the literature, provided it is identified using a systematic and transparent method and there is clear explanation of the justification for choosing a particular data set. The Australian guideline recognized that utility estimates might sometimes be derived from the literature. It specifies, however, that the details of the methods used to identify the studies and to elicit the utility estimate should be presented clearly, so that validity should be assessed. According to the Canadian guideline, if utility values (preference scores) were not measured in a prospective study, they could be sourced from the literature if they are appropriate for the population of interest. In the proposed Japanese guideline, it is recommended that utility values be, in principle, elicited from the public. If Japanese studies, however, are not of optimal quality, the use of study results from other country settings is allowed.

Situations in which more than one plausible set of utility data for a health state was available from the literature, the guidelines from the five countries differed on their recommendations. The NICE and HAS guidelines recommended that scores from a single source should be used and sensitivity analyses should be conducted to show the effect of the alternative utility values. The Australian guidelines provide a warning that combining utility weights across different sources, for different health states, makes it difficult to interpret the results, particularly across those using different methods. We also noted that this issue was not addressed by the Canadian and Japanese guidelines.

Measuring Utility Values as Prescribed in the National Guidelines of Five Countries

Recognizing the variation in the utility values depending on the instrument, the NICE guideline applied strict criteria by specifying that only the EQ-5D measurement scale should be used for utility measurements. We also found that the recommendations in the guidelines may be influenced by the availability of the instruments in the country. For instance, the French authority recommended the use of "validated preference-based scores available in France"; currently, only the EQ-5D and HUI 3 meet this criterion. The proposed Japanese guideline recommended the use of index-type instruments with a newly developed Japanese scoring algorithm, which is currently met by the EQ-5D. The Canadian guidelines are relatively flexible and encouraged using indirect methods, such as HUI, the EQ-5D, the Short Form 6 Dimension (derived from the MOS 36-Item Short-Form Health Survey), and the 15D because they are easy to obtain, compare, and interpret. The guidelines, however, recommended that analysts select in advance the most appropriate instrument for the condition, one that best suits the study question and that prevents bias. The Australian guidelines are realistic in this regard and do not specify any particular instrument because such instruments were not always used in all the trials. The guidelines generally preferred, however, the indirect methods of multiattribute utility instruments. Although the five guidelines varied in terms of the instruments used to measure the utility values, all guidelines recommended at least the EQ-5D.

Considering these issues surrounding utility values, the objective of this study was to provide an overview of how current utility values were obtained in CUAs for pharmaceuticals in Japan on the basis of recommendations in these five methodological guidelines. If the values were elicited from the literature, we examined the original sources (original study or not/study location/instrument used), the criteria and methods used to choose those selected original sources, and if more than one plausible set of utility data was available, methods of dealing with or selecting the data. We accomplished these objectives by conducting a systematic review of the published literature on CUAs for pharmaceuticals in Japan.

Methods

Literature Review

We searched the published literature on the CUAs conducted in Japan that reported the results as cost per QALY. The following databases were used for this search: PubMed, Centre for Reviews and Dissemination (CRD) in the University of York, EconLit, and the Japan Medical Abstracts Society (Ichushi). We included all articles that fit the search criteria, irrespective of the language of publication. The search terms used for the PubMed, EconLit, and CRD databases were "QALY" and "Japan," or "cost utility" and "Japan." For the Ichushi database, we used "QALY" as the search term. We conducted the search on February 20, 2013, and the search period was not specified. We also searched reference lists of the included studies.