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Research article

An International comparative Study on EuroQol-5-Dimension Questionnaire (EQ-5D) tariff scores between the UK and Japan

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Abstract

The purpose of this study is the evaluation of the difference in elicited EuroQol-5-Dimension Questionnaire (EQ-5D) health utility values across the range of different health states derived from the UK, Japanese tariffs. Hence, we conducted a comparative study on UK and Japanese Value Sets of EQ-5D-3L and 5L. Distributions of EQ-5D-3L tariffs were compared between the Japanese and UK versions. For the Japanese tariff, the mean value of Utility was 0.423 (mean)±0.217 (standard deviation: SD), and that for the UK tariff was 0.147±0.312; the median value for the Japanese tariff was 0.466, the minimum value -0.106, and for the UK tariff, the median was 0.122, the minimum value -0.594. Furthermore, distributions of EQ-5D-5L tariffs were compared between the Japanese and UK versions. The mean values of Utility for the Japanese and UK tariffs were 0.449±0.154 and 0.391±0.228, respectively; the median value for the Japanese tariff was 0.450, minimum value -0.0.25, and for the UK tariff, the median was 0.396, the minimum value -0.281. The correlation between the Japanese and UK tariffs for EQ-5D-3L was R2＝0.739, RSME＝0.160. For EQ-5D-5L, the correlation between the Japanese and UK tariffs was R2＝0.907, RSME＝0.069. We clarify Japanese and UK value sets was closer in EQ-5D-5L than in EQ-5D-3L. Moreover, the correlation was observed more prominently in EQ-5D-5L than in EQ-5D-3L as well. Therefore, it is recommended that in the future we should use EQ-5D-5L in Japan when conducting a clinical study to collect health state data using EQ-5D.

Keywords: EQ-5D, Health state values, Utility, Japan, UK

Introduction

An increase in medical expenses has recently been a matter of concern to many countries [1]. One of the factors of this concern is the higher cost of novel medical technologies (new pharmaceutical products and medical devices) compared to that of pre-existing technologies [2]. Against this background, it has been a global issue to efficiently distribute the limited medical expenditures.

In 2016, new decision-making processes for the pricing of health technologies in medical fields based on economic evaluations were started in Japan [3]. In the field of oncology, the trial subjects included Trastuzubab-emtansine (Kadcyla, Roche) a therapeutic agent for HER2-positive metastatic breast cancer, and Nivolumab (Opdivo, Ono Pharmaceutical Co.Ltd) for Non-small cell lung cancer. As it is anticipated in cancer treatments that development of expensive pharmaceutical products such as molecular target drugs and immune checkpoint inhibitors will further progress, we will need to consider cost-utility in the clinical practice of oncology. Hence, it will be important for physicians including oncology specialists to understand health economics assessment in the future.

The Health Technology Assessment (HTA) system which has been provisionally used in Japan was established based on a UK's method [3]. The guidelines for the economic evaluation of drugs/medical devices in Japan

also follow methodology of National Institute for Health and Care Excellence (NICE)[4], an HTA agency in the UK, and recommend using Quality Adjusted Life Years (QALYs), namely, life years adjusted with quality of life (QOL), as an outcome indicator of HTA and conducting cost-utility analysis (CUA) [5]. The quality adjustment of QALYs is performed with Utility and calculated using the Value Set of health state obtained from general population called tariff. The EuroQol-5-Dimension (EQ-5D) is a questionnaire, which is the most generally used for calculating Utility [6, 7]. The EQ-5D includes EQ-5D-3L [9, 10] which evaluates 5 items in 3 levels and EQ-5D-5L [11, 12] in 5 levels.

According to the Japanese guidelines, it is allowed to extrapolate foreign data in the CUA if there is no Utility data available for subject items investigated in Japan [5]. However, the correlation between the Value Set created in foreign countries and that created in Japan is not very clear, and it is unknown whether foreign data are extrapolatable or not.

Hence, we attempted to conduct an international comparative study on the UK, known as the leading country of HTA, and Japanese Value Sets of EQ-5D-3L and 5L.

Study Subjects and Method

Overview of EQ-5D questionnaire

EuroQol-5-dimension (EQ-5D) questionnaire is a scale for generic QOL measurement developed by the EuroQol groups. It is characterized by simplicity and appropriateness for multi-national comparisons and used primarily for quality adjustment when calculating QALY. Using 5 elements of health state, including mobility, self-care, usual activity, pain/discomfort, and anxiety/depression, the EuroQol group created a questionnaire form called EQ-5D [13]. With EQ-5D-3L, evaluations are made on these 5 elements in 3 levels: (1) no problems, (2) some problems, (3) major problems, and expressed in scores of 1-3 [9]. For instance, the Health State 11223 means “no problems with mobility (1), no problems with self-care (1), some problems with performing usual activity (2), moderate pain/discomfort (2), and major anxiety/-depression (3)”. Thus, using EQ-5D-3L, 243 patterns of health state from 11111 to 33333 and 245 patterns of conditions including unconsciousness and death can be defined. In 2011, the EuroQol group developed EQ-5D-3L [11], which evaluates the same elements used in EQ-5D-3L in 5 levels. Using this questionnaire form, 3125 patterns of health state from 11111 to 55555 can be defined.

Method

In literature review, data were extracted from literatures [9, 10, 12, 14] in order to create tariffs for EQ-5D-3L and 5L calculated for general populations in the UK and Japan. Based to these literatures, we investigated the method to evaluate Utility, the number of samples, the method to assess subjects, and the number of outcome measures of hypothetical health state in preparation of Japanese and English tariffs. Subsequently, using coefficients estimated from the previous study, we completed 245 patterns and 3125 patters of tariffs for EQ-5D-3L(Table.S1) and EQ-5D-5L(Table.S2), respectively. With these tariffs for EQ-5D-3L and 5L, we investigated the difference in Japanese and UK Utility, and then evaluated correlation of tariffs for EQ-5D-3L and 5L. For correlation, Root Mean Squared Error (RMSE) and correlation coefficients were calculated. JMP13（SAS Institute Inc., Cary, NC, USA）was used for all statistical analyses.

Results

Tariff development procedure for EQ-5D (Table1)

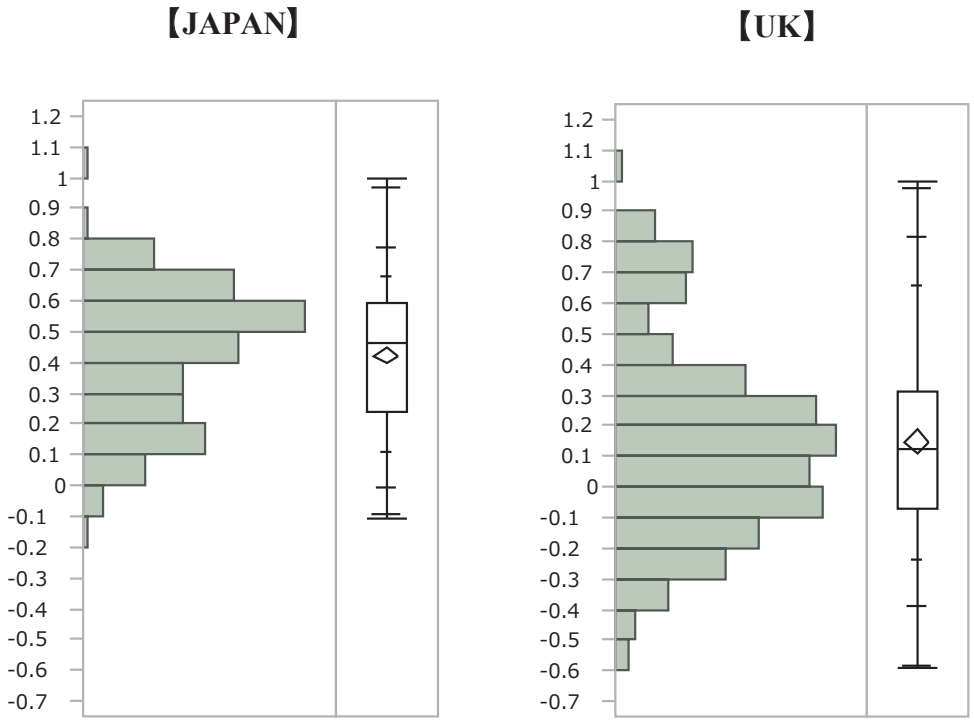
The tariffs for EQ-5D had been developed using different methods for 3L and 5L. For the Japanese version of EQ-5D-5L, the tariff had been prepared according to the Valuation Protocol [15] created by the EuroQol group as for the UK version. It had been designed to evaluate 3125 patterns of health state using both the Time-trade-off (TTO) method and the discrete choice experiment method; 86 patterns of health state obtained with the experimental design method were evaluated using interviews, and coefficients were calculated. In order to prepare the Japanese and UK versions, 1026 and 996 subjects were selected from general population of Japan and the UK, respectively. On the other hand, there were some differences in the tariff preparation procedure for EQ-5D-3L. The numbers of subjects used to prepare the Tariffs were 543 and 2997 for Japanese and the UK versions, respectively. For the hypothetical health state, there were 12 patterns for the Japanese version and 42 patterns for the UK version evaluated to calculate the coefficients. The common point, on the other hand, between the Japanese and UK versions was that the tariffs had been prepared with the TTO method using interviews.

A comparison on tariff distribution for EQ-5D

Distributions of EQ-5D-3L tariffs were compared between the Japanese and UK versions (Figure 1). For the Japanese tariff, the mean value of Utility was 0.423 (mean)±0.217 (standard deviation: SD), and that for the UK tariff was 0.147(mean)±0.312(SD); the median value for the Japanese tariff was 0.466, 75 percentile 0.594, 25 percentile 0.236, the minimum value -0.106, and for the UK tariff, the median was 0.122, 75 percentile 0.31, 25 percentile -0.072, and the minimum value -0.594. Furthermore, distributions of EQ-5D-5L tariffs were compared between the Japanese and UK versions (Figure 2). The mean values of Utility for the Japanese and UK tariffs were 0.449 (mean)±0.154 (SD) and 0.391 (mean)±0.228 (SD), respectively; the median value for the Japanese tariff was 0.450, 75 percentile 0.557, 25 percentile 0.341, minimum value -0.0.25, and for the UK tariff, the median was 0.396, 75 percentile 0.554, 25 percentile 0.229, and the minimum value -0.281.

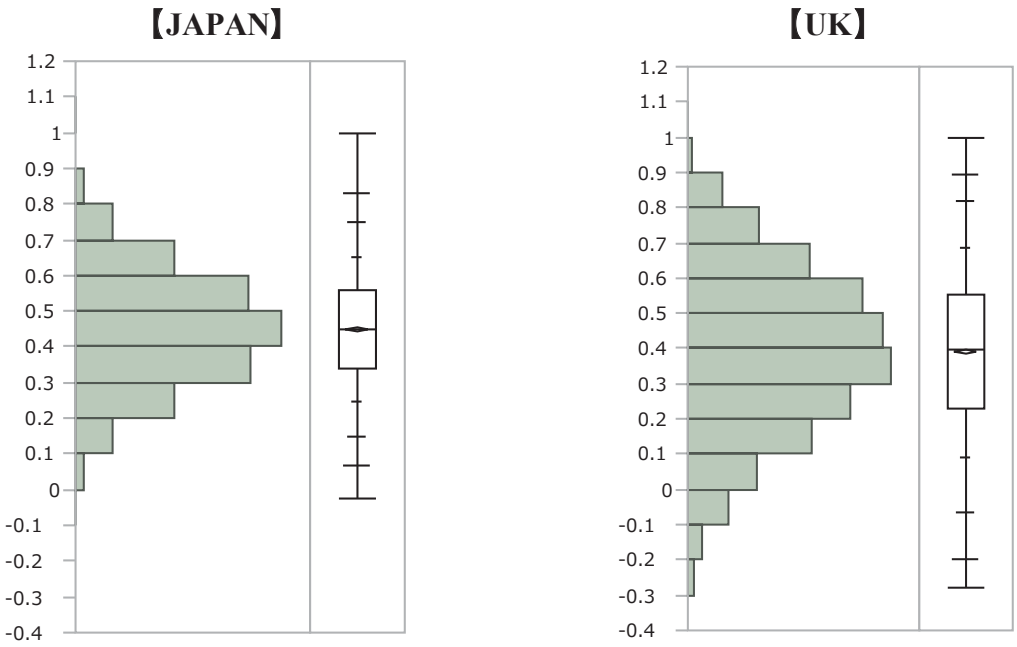
Table 1. Comparison of the methodology of EQ-5D tariff between Japan and UK.

	EQ-5D-3L		EQ-5D-5L	
	Japan	UK	Japan	UK
Valuation method of Utility	Conventional Time-trade off	Conventional Time-trade off	Leadtime Time-trade off	Leadtime Time-trade off and discrete choice experiments
Number of respondents in the valuation data set	543	2997	1026	996
The methodology of data collection from respondents	Interview	Interview	Interview	Interview
Number of hypothetical health states	17	42	86	86



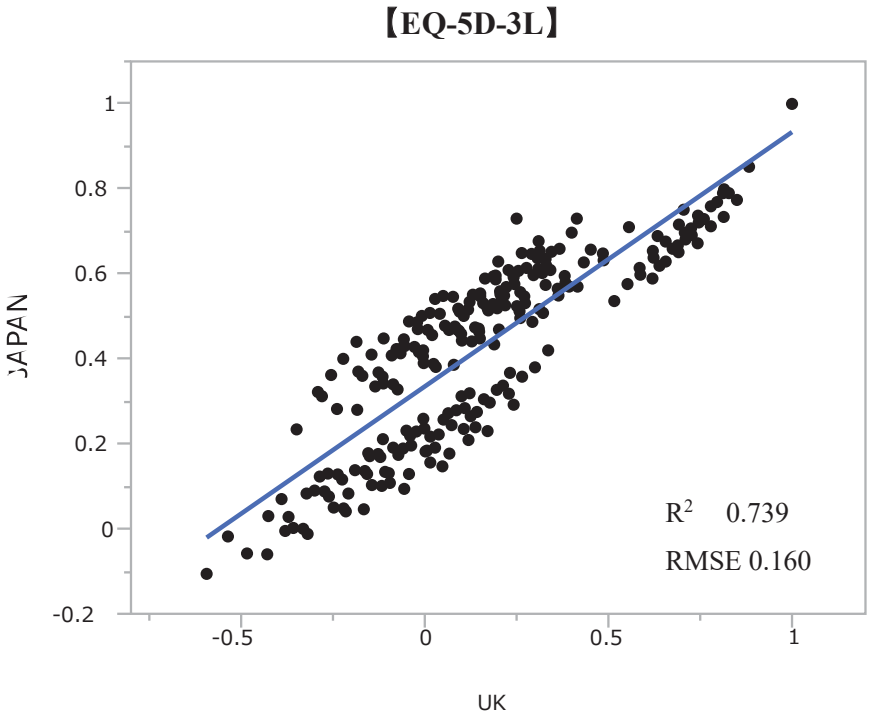
	JAPAN	UK
maximum	1	1
75%ile	0.594	0.31
median	0.466	0.122
25%ile	0.236	-0.072
minimum	-0.106	-0.594

Figure 1. Distribution of EQ-5D-3L



	JAPAN	UK
maximum	1	1
75%ile	0.557	0.554
median	0.450	0.396
25%ile	0.341	0.229
minimum	-0.025	-0.281

Figure 2. Distribution of EQ-5D-5L



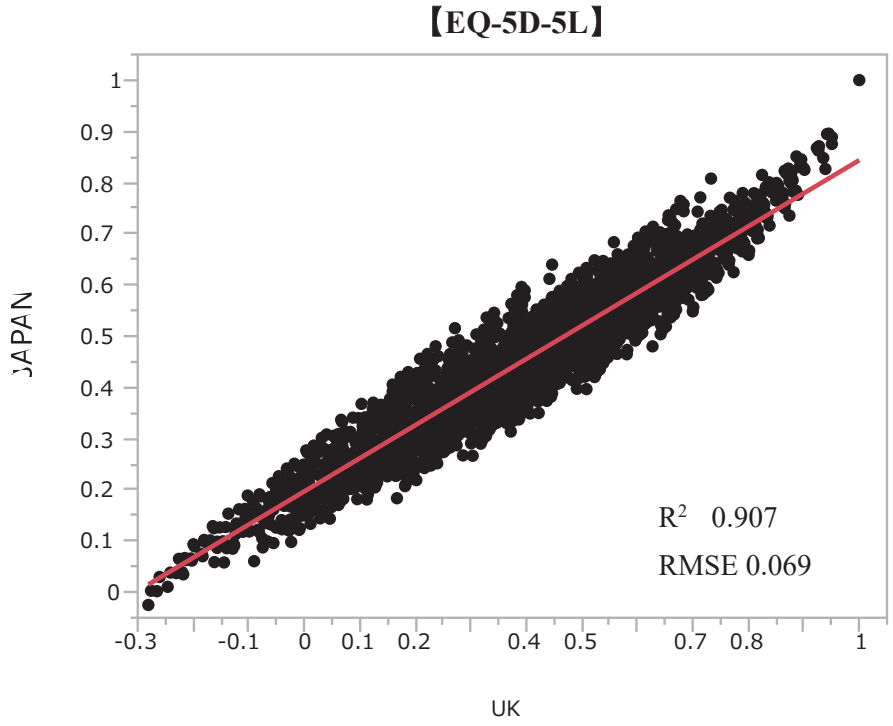


Figure 3. Correlation of tariffs between UK and Japan

Correlation analysis on EQ-5D tariffs (Figure 3)

The correlation between the Japanese and UK tariffs for EQ-5D-3L was R2=0.739, RSME=0.160. For EQ-5D-5L, the correlation between the Japanese and UK tariffs was R2=**0**.907, RSME=0.069.

Discussion

EQ-5D is a questionnaire form which is the most commonly used to evaluate the health state values [6,7]. EQ-5D include EQ-5D-3L which evaluates 5 health states in 3 levels and EQ-5D-3L which evaluates the same health states in 5 levels. The NICE in the UK recommends using EQ-5D-3L when calculating QALY for CUA outcomes to perform HTA [16]. However, the results of analyses conducted in this study suggested that distribution of the Japanese and UK value sets was closer in EQ-5D-5L than in EQ-5D-3L (Figure 1,2). Moreover, the correlation was observed more prominently in EQ-5D-5L than in EQ-5D-3L as well (Figure 3). These findings suggest that, it will be more promising using EQ-5D-5L in Japan when conducting a study using EQ-5D so that international comparisons will be possible in the future. When comparing with a study conducted in the UK using EQ-5D-3L, we can do so by performing mapping of EQ-5D-3L and EQ-5D-5L based on the previous study conducted by Shiroiwa et al. [17].

Then we consider factors for differences in health state values in EQ-5D. As we have discussed so far, even for the same health states, there are some differences in Utility between the Japanese and UK tariffs. As shown inTable.1, differences were observed for EQ-5D-3L in the number of subjects evaluated in tariff preparation as well as in the numbers of hypothetical health states used in coefficient calculation. This factor may have induced differences in Utility. Norman et al. also reported that for EQ-5D-3L, differences observed in the Japanese and UK tariffs might be associated with the differences in the preparation process [18]. In addition, as reported by Jo et al., differences in cultural backgrounds may have induced the differences in Utility [19]. In this study, it was also revealed that the differences in Utility were resolved with EQ-5D-5L. There are two possible reasons for this. First of all, the number of health state patterns increased from 245 to 3125 by evaluating the health states in 5 levels; this enabled us to identify even smaller changes in health states. Secondly, Valuation Protocol [15] had been developed by the EuroQol group; this enabled us to prepare tariffs with the standardized method compared to EQ-5D-3L.

Meanwhile, the differences in tariffs commonly observed in EQ-5D-3L and 5L are associated with bias developed during the translation process of the questionnaire. For SF 36 (the 36-item short form health survey), which is another type of a questionnaire form, Fukuhara et al. reported that bias developed during the translation process [20]. Hence, we cannot deny that bias might have developed due to different nuance of languages in the translation process of EQ-5D as well.

There are limitations however in this study. As we mentioned earlier, the differences in Japanese and UK tariffs of EQ-5D-3L seemed to be associated with differences in the method of preparation process or with cultural backgrounds. However, we cannot judge which of these factors is more involved in these differences. Likewise,

we cannot demonstrate in this study that which one of the factors, either standardization of methodology or increased evaluation scores, contributed more greatly than the other to reduction of Utility differences in EQ-5D-5L. In addition, there is another limitation in this study that we did not mention about the bias issues developed during the translation process of the questionnaire forms.

Thus, there are several limitations in this study. However, from the comparisons between Japanese and UK tariffs of EQ-5D, it was revealed that distribution and correlation of health state values had been improved with EQ-5D-5L compared to 3L.

Conclusions

Based on our study, it is recommended that in the future we should use EQ-5D-5L in Japan when conducting a clinical study to collect health state data using EQ-5D.

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Conflict of Interest Statement

None of all authors has a conflict of interest to declare.

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