

INTERNATIONAL SURVEY ON WILLINGNESS-TO-PAY (WTP) FOR ONE ADDITIONAL QALY GAINED: WHAT IS THE THRESHOLD OF COST EFFECTIVENESS?

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SUMMARY

Although the threshold of cost effectiveness of medical interventions is thought to be £20 000–£30 000 in the UK, and \$50 000–\$100 000 in the US, it is well known that these values are unjustified, due to lack of explicit scientific evidence. We measured willingness-to-pay (WTP) for one additional quality-adjusted life-year gained to determine the threshold of the incremental cost-effectiveness ratio. Our study used the Internet to compare WTP for the additional year of survival in a perfect status of health in Japan, the Republic of Korea (ROK), Taiwan, Australia, the UK, and the US. The research utilized a double-bound dichotomous choice, and analysis by the nonparametric Turnbull method. WTP values were JPY 5 million (Japan), KWN 68 million (ROK), NTS 2.1 million (Taiwan), £23 000 (UK), AUS 64 000 (Australia), and US\$ 62 000 (US). The discount rates of outcome were estimated at 6.8% (Japan), 3.7% (ROK), 1.6% (Taiwan), 2.8% (UK), 1.9% (Australia), and 3.2% (US). Based on the current study, we suggest new classification of cost-effectiveness plane and methodology for decision making. Copyright © 2009 John Wiley & Sons, Ltd.

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1. INTRODUCTION

Cost-effectiveness analysis (CEA) is used to distribute healthcare resources more efficiently in many countries. In CEA, the additional consumption of medical resources is divided by the benefits (e.g. quality-adjusted life-years; QALYs) gained from healthcare interventions, in order to calculate an incremental cost-effectiveness ratio (ICER). Generally, an intervention is considered cost effective if the ICER (e.g. cost per QALY) is below a predetermined threshold.

For example, £20 000–£30 000 per QALY has been accepted as the threshold in the UK to decide whether or not the National Institute for Health and Clinical Excellence (NICE) should recommend use of a new healthcare technology (NICE, 2004). In the US, the threshold of US\$ 50 000–\$100 000 per QALY often is mentioned in medical literature, despite the fact that these values are not based on clear scientific evidence. George *et al.* (2001) found that the Australian Pharmaceutical Benefits Advisory Committee was unlikely to recommend a drug for listing if the ICER (cost per life-year) exceeded AU\$ 76 000.

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The origin of the threshold level (US\$ 50 000–\$100 000) in the US dates back to at least 1982, when discussed in a paper by Kaplan *et al.* (Kaplan and Bush, 1982; Ubel *et al.*, 2003) Although Kaplan and colleagues classified the value of ICER into three categories ‘cost effective’ (when $ICER < US\$ 20\,000$), ‘controversial’ (when ICER is US\$ 20 000–\$100 000), and ‘questionable’ (when $ICER > US\$ 100\,000$), reasonable grounds for the classification were not described in the paper.

In Canada, Laupacis *et al.* (1992) suggested a similar categorization: ‘strong evidence’ for adoption and appropriate utilization (when $ICER < CA\$ 20\,000$ per QALY), ‘moderate evidence’ (when ICER is CA\$ 20 000–100 000 per QALY), and ‘weak evidence’ (when ICER is $> CA\$ 100\,000$ per QALY). Despite the differences of exchange rate and time period, the cut-off value in the 1980s and 1990s was the same as Kaplan *et al.* had cited.

The uncertainty of threshold levels creates some controversies. Although the threshold of US\$ 50 000 or US\$ 100 000 per QALY is widely used, Ubel *et al.* (2003) pointed out that inflation was not considered in that threshold. If the high range of the threshold was determined to be US\$ 100 000 in 1982, it is not reasonable that the same value continues to be adopted until the present time. In a literature review published in 2000, Hirth and colleagues suggested that the threshold should be US \$265 000. (Hirth *et al.*, 2000) If this higher threshold is utilized in analysis, however, almost all the new healthcare technologies are judged to be cost effective. We think that the cut-off value of US \$265 000 is too high to be acceptable.

In the UK, Claxton *et al.* recently pointed out that NICE’s threshold may be too high. (Claxton *et al.*, 2008) In Japan, the Republic of Korea (ROK), and Taiwan, there is no consensus on the threshold of cost effectiveness.

The objective of the current study was to measure and compare the thresholds in some developed countries in East Asia and the West, using the contingent valuation method (CVM). There are two methods to determine the threshold: the first is by consensus of professionals considering a healthcare budget, meaning that the goal is to optimize the resource allocation within a restrictive expenditure for healthcare. The second is by people’s willingness-to-pay (WTP) for healthcare. As people may not think about the overall healthcare budget when completing these exercises, it may cause an increase in healthcare expenditures if people are willing-to-pay more.

We think that both of these methods are reasonable approaches. Regardless of the amount of money that people are willing-to-pay, healthcare expenditure is not infinite. On the other hand, it is important to reflect people’s preference to healthcare policy or allocation of budget. In our research, we explored WTP.

Although some researchers (Gyrd-Hansen, 2003; King *et al.*, 2005) previously have tried to measure WTP per QALY, the results were quite variable (Glick *et al.*, 2006) and appear unreliable. By using the same methodology to measure WTP per QALY, however, we estimated and compared cost-effectiveness thresholds between countries in East Asia, the Pacific Rim, Europe, and North America.

2. METHODS

2.1. Questionnaire design

To determine the incremental ICER threshold, we developed a questionnaire in Japanese, which measured WTP for one additional year of survival with perfect health status, which is equal to one additional QALY. The questionnaire was pretested on 10 Japanese people, who were then interviewed as a way to review the questionnaire. From their feedback, we were able to reevaluate the questionnaire description and survey feasibility. Following these interviews we performed a small online pilot study ($N = 121$) to confirm feasibility of a web-based survey, and then completed the original questionnaire.

The survey instrument was a detailed questionnaire regarding two main and two additional categories of WTP. The two main WTPs (1) WTP_{sei} : WTP for the respondent’s additional QALY, and

(2) WTP_{sel} : WTP for the respondent's additional QALY 5 years later were used to establish decision-making rules and calculate a discount rate of outcome. The two additional WTPs (3) WTP_{fam} : WTP for an additional QALY for a family member, and (4) WTP_{soc} : the cost that the respondent thought society should pay for someone's additional QALY were used to evaluate monetary value of other people's QALY for comparison with respondents' own QALY. However, it is noteworthy that WTP_{soc} is not considered to be an exactly accurate WTP, as citizens do not pay out of their own pockets. As such, this value merely represents social consensus.

The presurvey results demonstrated that the more complicated questionnaire, for example, which involved descriptions of health states, was difficult to understand and answer. We therefore decided to use simple questionnaire to obtain reliable answers. In this questionnaire we considered the WTP for one additional life year in perfect health as WTP for a QALY. While the questionnaire did not assume or mention a specific disease state, our description of the disease was described as a life limiting illness such as metastatic cancer rather than chronic disease (see the section 'Discussion').

Following translation into English and other languages, the questionnaire was then translated back into Japanese to confirm that the meaning had been retained. The Japanese and British versions of the survey are provided in Figure 1 and Appendix A. Questionnaires were adjusted to specifically adapt to the healthcare system in each country.

In the present study, a double-bound dichotomous choice was utilized in the questionnaire. Six bid values (Table I) were randomly shown to the respondents, and the respondents were asked whether or not they would pay for the new healthcare technology that can result in one additional QALY. The second-stage bid values were modified, depending on the first answer of each respondent.

Imagine that you are stricken with a serious illness that immediately threatens your life. Now, please assume that Medication A has been developed to treat your illness and if you take it your life will be extended for one full year and you will be completely healthy (without being confined to bed) for one full year.

Please assume, however, that Medication A will not be covered by health insurance [NHS (National Health Service) or private medical insurance (*in the British version*)] and you will have to pay the full amount to receive the product, which will cost JPY xxxx* [£ xxxx*].

In this case, would you purchase the product?

(*xxxx is bidding value)

Figure 1. A questionnaire on WTP for their own additional QALY (WTP_{sel})

Table I. Bid values in double-bound dichotomous choice

No	First bid value	Second bid value (JPY)	
	(Q1)	Q1 = No	Q1 = Yes
1	500 000	250 000	1 000 000
2	1 000 000	500 000	2 500 000
3	2 500 000	1 000 000	5 000 000
4	5 000 000	2 500 000	7 500 000
5	7 500 000	5 000 000	10 000 000
6	10 000 000	7 500 000	15 000 000

These bid values were converted to each currency.

Following completion of the double-bound dichotomous choice, we initiated the continuous bidding game. The continuous bidding game measures individual WTP values, but results are influenced by starting-point bias and outliers more than dichotomous choice (Drummond *et al.*, 2005). Both tests were repeated for each of the four WTP categories.

The maximum WTP that a respondent could enter was 50 million JPY (or US\$ 500 000). The bid values were determined by the small pilot study in Japan, and the same bid values are shown in the survey of all countries converted to each currency. For the calculations, the exchange rate applied was KWN 1 = JPY 0.1, NT\$ 1 = JPY 3.3, £1 = JPY 250, AU\$ 1 = JPY 100 and US\$ 1 = JPY 100.

2.2. Data collection

Internet survey data was collected from approximately 5 500 respondents who were randomly sampled from panels in six countries: Taiwan (500 respondents), Japan, the Republic of Korea (ROK), Australia (AU), the United Kingdom (UK), and the United States (US). The population size of the field panels maintained by various companies in different countries are 150 000 people in Taiwan, 120 000 in ROK (Hankook Research), 760 000 in Japan (INTAGE Interactive Inc.) 150 000 in Australia, 500 000 in the UK, and 3.5 million people in the US (Harris Interactive Inc.). The research in Japan, ROK, UK, and Australia, and the UK was conducted in October 2007, whereas the research in Taiwan and the US was performed in March 2008. Respondents ranging from 20 years of age to 59 years of age were recruited for this survey and stratified by age and gender in each country.

2.3. Statistical analysis

2.3.1. Nonparametric method. Data from the double-bound dichotomous choice were analyzed by nonparametric Turnbull methods (Turnbull, 1976) to calculate WTP per QALY. The possible answers to the double-bound dichotomous choice questions were classified into four patterns: 'YES' to both the first and second question (YY); 'YES' to the first question, and 'NO' to the second, higher value (YN); 'NO' to the first value, and 'YES' to the second, lower value (NY); and 'NO' to both the first and second value (NN).

In the formula for possible responses, let the higher bid value of i for the individual ($i = 1, 2, \dots, N$) be T_{Ui} , and the lower bid value be T_{Li} . In addition, we can denote each of m bid values as being T_j , $1 \leq j \leq m$, such that, $0 = T_0 < T_1 < T_2 < \dots < T_m < T_{m+1} = \infty$. The probability of the answer pattern can be written as follows:

$$\begin{aligned} P[YY] &= F(T_{M+1}) - F(T_{Ui}) \\ P[YN] \text{ and } P[NY] &= F(T_{Ui}) - F(T_{Li}) \\ P[NN] &= F(T_{Li}) - F(T_0) \end{aligned}$$

where function F is the acceptance curve, which is the probability that the respondent will reject the presented bid values. We can get the nonparametric maximum likelihood estimators of acceptance probability by maximizing the log-likelihood, which can be represented by the following equation:

$$\begin{aligned} \ln L(\mathbf{s}) &= \sum_{i=1}^N \ln \left(\sum_{j=1}^{m+1} \alpha_{ij} [F(T_j) - F(T_{j-1})] \right) = \sum_{i=1}^N \ln \left(\sum_{j=1}^{m+1} \alpha_{ij} s_j \right) \\ s_j &= F(T_j) - F(T_{j-1}) \end{aligned}$$

With respect $\mathbf{s} = (s_1, \dots, s_{m-1})$, subject to $\sum s_j = 1$ and α_{ij} means whether WTP of i , the individual, is included between T_{j-1} and T_j . Therefore, the equation is

$$\alpha_{ij} = \begin{cases} 1 & \text{if } T_{Li} \leq B_{j-1}, B_j \leq B_{Ui} \\ 0 & \text{otherwise} \end{cases}$$

Turnbull suggested an Expectation and Maximization algorithm-like, self-consistency algorithm for the maximization of $L(\mathbf{s})$. For this calculation, let the conditional probability of i 's WTP ranging from T_{j-1} to T_j be I_{ij} . The expectation of I_{ij} is given by the equation

$$E(I_{ij} | \mathbf{s}^{(l)}) = \frac{\alpha_{ij} s_j}{\sum_k \alpha_{ik} s_k} \equiv \mu_{ij}(\mathbf{s}^{(l)})$$

A renewed self-consistency estimate of $\mathbf{s}^{(l+1)}$ can be obtained as a solution to the following equation:

$$s_j^{(l+1)} = \frac{\sum_{i=1}^N \mu_{ij}(\mathbf{s}^{(l)})}{\sum_{i=1}^N \sum_{j=1}^{m+1} \mu_{ij}(\mathbf{s}^{(l)})} = \frac{1}{N} \sum_{i=1}^N \mu_{ij}(\mathbf{s}^{(l)})$$

WTP values are given as the area under the estimated acceptance curve. The values are calculated by dividing the area into j trapezoids, according to the following equation:

$$\text{WTP} : \hat{\mu} = 0.5 \sum_{j=1}^m (\hat{S}_j + \hat{S}_{j-1})(T_j - T_{j-1})$$

The estimator of variance and covariance of s_j^2, σ_{ij}^2 is calculated by the component of the inverse matrix of Hessian, as follows:

$\hat{\sigma}_{ij}^2$ is (i, j) component of $(-\partial L(\mathbf{s}) / \partial s_i \partial s_j)^{-1}$ substituted for the estimator of s_j .

The standard deviation of $\hat{\mu}$, σ_{WTP} is calculated by $\hat{\sigma}_{ij}^2$ and the confidence interval of $\hat{\mu}$ can be constructed as $\hat{\mu} \pm 1.96 \hat{\sigma}_{\text{WTP}}$ using normal approximation.

The implicit discount rate of outcome, r , was also calculated. The values of WTP_{sel} and $\text{WTP}_{5\text{sel}}$ were compared as follows:

$$r = \left(\frac{\text{WTP}_{\text{sel}}}{\text{WTP}_{5\text{sel}}} \right)^{1/5} - 1$$

2.3.2. Parametric method. Also, we used parametric methods to compare the nonparametric methods, estimate the median of WTP, and predict the acceptance probability out of the range of bid values. When the Weibull curve was applied to the acceptance curve, the log-likelihood can be written as follows:

$$\begin{aligned} \ln L(\mu, \sigma) &= \sum_{i=1}^N \ln \left(\sum_{j=1}^{m+1} \alpha_{ij} [F(T_j) - F(T_{j-1})] \right) \\ &= \sum_{i=1}^N \ln \left(\sum_{j=1}^{m+1} \alpha_{ij} \left[\exp \left\{ - \exp \left(\frac{\ln T_j - \mu}{\sigma} \right) \right\} - \exp \left\{ - \exp \left(\frac{\ln T_{j-1} - \mu}{\sigma} \right) \right\} \right] \right) \end{aligned}$$

Parameters were estimated by maximizing the likelihood function, and the integration of the estimated Weibull curve was equal to the WTP.

$$\begin{aligned} \text{WTP} &= \int_0^{T_m} \exp \left\{ - \exp \left(\frac{\ln T - \hat{\mu}}{\hat{\sigma}} \right) \right\} dT \\ \text{WTP}_{\text{median}} &= \exp(\hat{\mu}) \cdot (-\ln 0.5)^{\hat{\sigma}} \end{aligned}$$

The upper limit of integration was T_m , and therefore 15 million JPY (US\$ 150 000) and 50 million JPY (US\$ 500 000) were adopted.

The confidence interval was determined by the bootstrap method.

2.3.3. Bidding game. As opposed to dichotomous choice, which only determines a range, the bidding game elicits an individual's maximum WTP for each question. The result of the bidding game is shown as a simple mean. An exploratory analysis of multiple regression in each country was performed to investigate the relationship between WTP and the demographic characteristics of the respondents.

The variables examined were (a) the degree of satisfaction with medical care (x_1 , $0 \leq x_1 \leq 5$), (b) the degree of satisfaction with the medical system (x_2 , $0 \leq x_2 \leq 5$), (c) gender of respondent (dummy variables: x_{3i} , $i = 1, 2$), (d) age of respondent (dummy variables: x_{4i} , $i = 1, 2, 3$), (e) household income (x_5), (f) education level (dummy variables: x_{6i} , $i = 1, 2$), (g) hospitalization in the last 5 years (dummy variables: x_{7i} , $i = 1, 2$), (h) hospitalization of any household member in the last 5 years (dummy variables: x_{8i} , $i = 1, 2$), (i) specific occupation (dummy variables: x_{9i} , $i = 1, \dots, 6$), (j) occupation as medical professional (dummy variables: x_{10i} , $i = 1, 2$), (k) type of residential area (dummy variables: x_{11i} , $i = 1, 2$).

The linear model is

$$\ln(\text{WTP}_{\text{sel}} + 1) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \sum_{i=1}^2 \beta_{3i} x_{3i} + \sum_{i=1}^3 \beta_{4i} x_{4i} + \beta_5 \log(x_5) + \sum_{i=1}^2 \beta_{6i} x_{6i} + \sum_{i=1}^2 \beta_{7i} x_{7i} \\ + \sum_{i=1}^2 \beta_{7i} x_{7i} + \sum_{i=1}^2 \beta_{8i} x_{8i} + \sum_{i=1}^6 \beta_{9i} x_{9i} + \sum_{i=1}^2 \beta_{10i} x_{10i} + \sum_{i=1}^2 \beta_{11i} x_{11i}$$

and we tested the null hypothesis, $\beta = 0$ as an exploratory analysis.

3. RESULTS

Of the 5520 respondents who participated in this study, 1114 respondents from Japan, 1000 from the ROK, 504 from Taiwan, 1002 from the UK, 1000 from Australia, and 1000 from the US were surveyed via the Internet. The demographic characteristics of the respondents are shown in Table II.

Table III (a) compares the WTP per an additional QALY, as estimated by the nonparametric Turnbull method (WTP_{Turn}) and the implicit discount rates across the different countries. The estimated WTP is JPY 5.0 million in Japan, KWN 68 million in the ROK, NT\$ 2.1 million in Taiwan, £23 000 in the UK, AU\$ 64 000 in Australia and US\$ 62 000 in the US. The implicit discount rate is 6.8% in Japan, 3.7% in the ROK, 1.6% in Taiwan, 2.8% in the UK, 1.9% in Australia, and 3.2% in the US. Table III (b) shows the WTP data from different countries adjusted by comparative price levels (CPL), as defined as the ratios of purchasing power parity (OECD, 2008).

In terms of US\$ adjusted by CPL, ROK, and Taiwan WTP values were higher than most other countries surveyed, despite their lower gross domestic product (GDP) per capita. No relationship was observed between WTP per QALY and GDP per capita. In all countries examined, WTP_{sel} exceeded $\text{WTP}_{5\text{sel}}$, which suggests the existence of a time preference for outcomes.

With the exception of Taiwan, WTP_{sel} was found to be lower than WTP_{soc} and WTP_{fam} . ROK had the highest WTP_{fam} , which likely reflects the high commitment to familial responsibility as a societal value in the ROK.

Median WTP_{sel} (WTP_{med}), mean WTP_{sel} (WTP_{par} : T_m is 15 million JPY), and extrapolated WTP_{sel} (WTP_{ext} : T_m is 50 million JPY) in different countries, as estimated by parametric method, are displayed in Table IV. WTP_{par} was nearly equal to WTP_{Turn} . Estimated WTP_{med} was JPY 3.1 million in Japan, KWN 46 million in the ROK, NT\$ 1.4 million in Taiwan, £12 000 in the UK, AU\$ 36 000 in Australia

Table II. Demographics of respondents

Country	Japan	ROK	Taiwan	UK	AU	US
Total # of respondents	1114	1000	504	1002	1000	1000
<i>Gender</i>						
Male	579 (52%)	500 (50%)	251 (50%)	500 (50%)	500 (50%)	500 (50%)
Female	535 (48%)	500 (50%)	253 (50%)	502 (50%)	500 (50%)	500 (50%)
<i>Age</i>						
20–29	266 (24%)	250 (25%)	125 (25%)	245 (24%)	250 (25%)	250 (25%)
30–39	266 (24%)	250 (25%)	125 (25%)	253 (25%)	250 (25%)	250 (25%)
40–49	268 (24%)	250 (25%)	130 (26%)	253 (25%)	250 (25%)	250 (25%)
50–59	314 (28%)	250 (25%)	124 (24%)	251 (25%)	250 (25%)	250 (25%)
<i>Household income (US\$ 1000)</i>						
< 10	42 (4%)	31 (3%)	45 (9%)	13 (1%)	29 (3%)	30 (3%)
10 ≤ < 30	141 (13%)	304 (30%)	172 (34%)	93 (9%)	135 (14%)	105 (11%)
30 ≤ < 50	226 (20%)	383 (38%)	150 (30%)	120 (12%)	201 (20%)	158 (16%)
50 ≤ < 70	222 (20%)	167 (17%)	52 (10%)	141 (14%)	169 (17%)	150 (15%)
70 ≤ < 100	219 (20%)	73 (7%)	27 (5%)	206 (21%)	280 (28%)	179 (18%)
100 ≤ < 150	127 (11%)	19 (2%)	8 (2%)	166 (17%)	124 (12%)	157 (16%)
150 ≤	37 (3%)	6 (1%)	15 (3%)	116 (12%)	44 (4%)	132 (13%)
Unknown	100 (9%)	17 (2%)	35 (7%)	147 (15%)	96 (10%)	89 (9%)
<i>Education</i>						
Graduation from 4-year college or university	624 (56%)	411 (41%)	254 (50%)	319 (32%)	284 (28%)	342 (34%)
Other	490 (44%)	589 (59%)	250 (50%)	683 (68%)	716 (72%)	658 (66%)
<i>Hospitalization (within the last 5 years)</i>						
Yes	208 (19%)	209 (21%)	87 (18%)	278 (28%)	489 (49%)	289 (29%)
No	906 (81%)	791 (79%)	417 (83%)	724 (72%)	511 (51%)	711 (71%)
<i>Hospitalization of any member of household (within the last 5 years)</i>						
Yes	489 (44%)	531 (53%)	313 (62%)	444 (44%)	607 (61%)	467 (47%)
No	625 (56%)	469 (47%)	191 (38%)	558 (56%)	393 (39%)	533 (53%)
<i>Occupation</i>						
Company- or self-employed worker	490 (44%)	517 (57%)	216 (43%)	488 (49%)	346 (35%)	576 (58%)
Contract or temporary worker	64 (6%)	73 (7%)	69 (14%)	35 (3%)	56 (6%)	11 (1%)
Part-time worker	168 (15%)	34 (3%)	28 (6%)	106 (11%)	146 (15%)	70 (7%)
Homemaker	172 (15%)	186 (19%)	45 (9%)	94 (9%)	173 (17%)	67 (7%)
Unemployed	57 (5%)	34 (3%)	29 (6%)	69 (7%)	50 (5%)	57 (6%)
Retired	6 (1%)	186 (19%)	27 (5%)	38 (4%)	64 (6%)	34 (3%)
Other work status	157	150	90	172	165	185

Table II. *Continued*

Country	Japan	ROK	Taiwan	UK	AU	US
Total # of respondents	1114	1000	504	1002	1000	1000
	(14%)	(15%)	(18%)	(17%)	(17%)	(19%)
<i>Medical professional</i>						
Yes	58	34	16	54	52	82
	(5%)	(3%)	(3%)	(5%)	(5%)	(8%)
No	1056	966	488	948	948	918
	(95%)	(97%)	(97%)	(95%)	(95%)	(92%)
<i>Residential area</i>						
Urban or metropolitan area	723	566	68	565	718	641
	(65%)	(57%)	(13%)	(56%)	(72%)	(64%)
Regional or rural area	391	434	436	437	282	359
	(35%)	(43%)	(87%)	(44%)	(28%)	(36%)

Table III. (a) Results of WTP per QALY, as estimated by Turnbull method and discount rates of outcome and (b) results of WTP per QALY, as estimated by Turnbull method and expressed as comparative price level (CPL)

Country	Unit	WTP _{sel} 95%CI		WTP _{5sel} 95%CI		WTP _{fam} 95%CI		WTP _{soc} 95%CI		Implicit Discount rate
(a)										
Japan	JPY 1 mil	5.0		3.5		6.4		5.4		6.8%
		4.7	5.4	3.2	3.9	6.0	6.8	5.0	5.8	
ROK	KWN 1 mil	68		56		79		69		3.7%
		64	73	52	60	75	83	65	73	
Taiwan	NT\$ 1 mil	2.1		1.9		1.9		1.8		1.6%
		1.9	2.3	1.7	2.1	1.7	2.1	1.6	1.9	
UK	£1000	23		20		26		38		2.8%
		22	25	19	22	24	28	36	39	
AU	AUS 1000	64		58		78		89		1.9%
		60	68	54	62	73	82	85	93	
US	US\$ 1000	62		52		69		96		3.2%
		57	66	48	56	65	74	92	101	
(b)										
Country	Unit	WTP _{sel} 95%CI		WTP _{5sel} 95%CI		WTP _{fam} 95%CI		WTP _{soc} 95%CI		Exchange rate (1 US\$)
Japan	US\$ 1000	41		28		52		44		123
		38	44	26	32	49	55	41	47	
ROK	US\$ 1000	74		61		86		75		920
		70	79	57	65	82	90	71	79	
Taiwan	US\$ 1000	77		70		70		66		29.7
		70	84	62	77	62	77	59	70	
UK	US\$ 1000	36		31		41		60		0.635
		35	39	30	35	38	44	57	61	
AU	US\$ 1000	47		43		57		66		1.35
		44	50	40	46	54	60	63	68	
US	US\$ 1000	62		52		69		96		1
		57	66	48	56	57	66	48	56	

and US\$ 31 000 in the US. Estimated WTP_{ext} was JPY 7.7 million in Japan, KWN 117 million in the ROK, NT\$ 3.5 million in Taiwan, £39 000 in the UK, AUS 118 000 in Australia and US\$ 115 000 in the US.

Estimated WTP_{sel}, as determined by the bidding game was JPY 5.8 million in Japan, KWN 103 million in the ROK, NT\$ 2.3 million in Taiwan, £26 000 in the UK, AUS 79 000 in Australia and US\$ 88 000 in the US. With the exception of ROK, WTP_{sel} values were nearly equal to WTP_{Turn} in all countries examined.

Table IV. Results of median WTP_{sel} (WTP_{med}), parametric mean WTP_{sel} (WTP_{par}), and parametric extrapolated WTP_{sel} (WTP_{ext})

Country	Unit	WTP_{med}		WTP_{par}		WTP_{ext}	
		95% CI*		95% CI*		95% CI*	
Japan	JPY 1 mil	3.1		5.8		7.7	
		2.6	3.7	5.3	6.2	6.5	9.1
ROK	KWN 1 mil	46		67		117	
		39	54	63	72	101	134
Taiwan	NT\$ 1 mil	1.4		2		3.5	
		1.1	1.8	1.8	2.2	2.9	4.3
UK	£1000	12		5.8		39	
		11	15	5.3	6.2	33	45
AU	AUS 1000	36		67		118	
		29	43	63	72	102	134
US	US\$ 1000	31		60		115	
		25	37	56	64	97	131

*95% CI, 95% confidence interval.

Table V. Relationship between WTP_{sel} by bidding game and main respondent demographics

Country	Coefficient					
	Japan	ROK	Taiwan	UK	AU	US
<i>Parameter</i>						
Degree of satisfaction with medical care	-0.113	-0.133	-0.040	0.062	0.165	-0.020
Degree of satisfaction with medical system	0.093	0.207**	0.160	-0.083	-0.021	0.110
Gender	0.088	-0.242	-0.263	-0.197	-0.123	-0.094
Age ≥ 30	0.117	0.325	0.308	0.169	0.373	0.426
Age ≥ 40	-0.197	0.049	0.114	0.196	0.232	-0.086
Age ≥ 50	0.147	0.287	-0.528*	0.376	0.124	0.168
Household income	0.365**	0.527**	0.690**	0.768**	0.726**	1.021**
Graduation from 4-year college or university	0.712**	0.384**	0.397*	0.344**	0.472**	0.339*
Company employee or self-employed worker	0.138	-0.153	-0.568*	0.098	-0.473*	-0.034
Contract or temporary worker	0.519	-0.080	-0.546	0.305	0.048	0.025
Part-time worker	0.381	0.107	0.137	-0.216	-0.451	-0.387
Homemaker	0.388	-0.300	-0.447	0.305	-0.583*	0.080
Unemployed	0.422	0.487	-0.111	0.285	-0.380	0.162
Retired	-0.780	0.486	-0.124	-0.188	-0.390	-0.341

* $p < 0.05$; ** $p < 0.01$.

Table V displays the relationship between demographic characteristics of respondents in different countries and WTP_{sel} determined by the bidding game, as determined by explanatory regression analysis. Household income often influenced WTP values in the countries examined. The coefficient for household income was the largest in the US and smallest in Japan. Education level of respondents also commonly influenced WTP values. With the exception of ROK, no significant correlation was observed between WTP and satisfaction with medical care or medical system in any of the countries examined.

Figure 2 illustrates the relation between private health expenditure and WTP among the countries. According to the health data from the Organization for Economic Co-operation and Development (OECD) published in 2007 (OECD, 2007), private expenditure as a percentage of total expenditure on health in Japan (18.3%) and the UK (13.7%) in 2004 was much less than that in the ROK (47.4%) and the US (55.3%). Private expenditure in Australia (32.5%) is halfway between the lower level in Japan and the UK, and the higher level in the ROK and the US. According to estimates by the Department of Health in Taiwan, private expenditure represents approximately 35% of total expenditures on health in Taiwan. WTP per QALY seems to be associated with the extent of private expenditure on health.

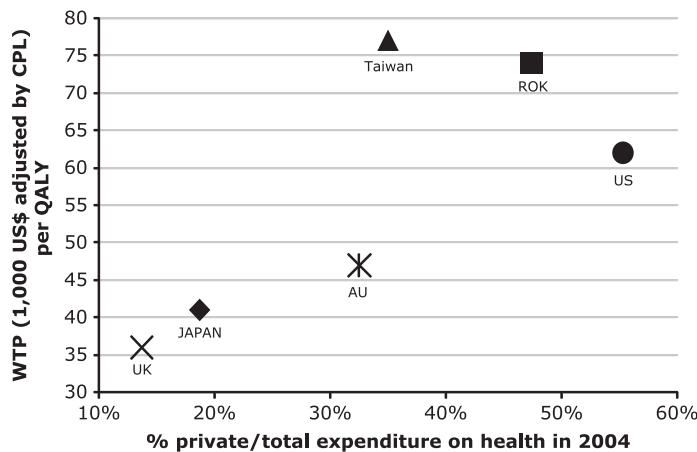


Figure 2. Relationship between WTP (adjusted by CPL*) per QALY and the proportion of private expenditure on health in different countries in 2004. *CPL: Comparative price levels, defined as the ratios of purchasing power parity (PPP)

4. DISCUSSION

In the current study, we examined the WTP for an additional QALY. Based on nonparametric estimates, the UK and US thresholds we determined were similar to previously reported thresholds in these countries (£20 000–£30 000 per QALY in the UK, or US\$ 50 000–100 000 per QALY in the US). Except for Japan, Taiwan and Australia, the 3% (Siegel *et al.*, 1996) or 3.5% (NICE, 2004) discount rate of outcome, which is widely used, seems to be a reasonable assumption. Japan has the highest implicit discount rate (6.8%), whereas Taiwan and Australia have discount rates under 3%. Although the implicit discount rates vary between the countries studied, the difference is not very large. From the viewpoint of international standardization, adoption of a 3 or 3.5% discount rate and sensitivity analysis from 0 to 7% are recommended for analyses.

The fact that WTP_{fam} was higher than WTP_{sel} suggests that altruistic utility (Basu and Meltzer, 2005) is larger than the respondent's perceived value of one QALY gained for themselves, at least in the case of health care for a family member. The fact that WTP_{soc} exceeded WTP_{sel} may be explained by 'free ride' on healthcare system or altruistic motivation in people who were led to offer a healthcare payment to individuals in need.

When the four types of WTP in Japan and the ROK were examined, the findings were that $WTP_{5sel} < WTP_{sel} < WTP_{soc} < WTP_{fam}$. In contrast, in Australia, the UK, and the US, $WTP_{5sel} < WTP_{sel} < WTP_{fam} < WTP_{soc}$. WTP_{fam} was higher than WTP_{soc} in the two Asian countries studied, whereas the inverse relationship was observed in the three countries with predominantly Western culture. This finding represents an interesting cultural difference between Asian and Western-based countries. We believe that because family plays a more important role in life, including in medical care, people in certain East Asian countries, think that patients should be cared for by family, rather than by society. In Taiwan, however, little difference between the four types of WTP was observed; the hierarchy of the types of WTP was $WTP_{soc} < WTP_{5sel} \approx WTP_{fam} < WTP_{sel}$, which was not seen in the other countries studied.

One limitation of our survey is that WTP for a QALY was considered to be the WTP value for one additional life year in perfect health. Other ways to present QALY gain include that outlined by Gyrd-Hansen (2003) and King *et al.* (2005). Both of these reports treat QALY gain as a gain in quality of life with no effect on life expectancy. As WTP per QALY values are dependent on the presentation of

QALY gain, WTP per QALY values obtained in the current study may reflect the state of a life-limiting illness such as metastatic cancer. It is possible, however, that WTP per QALY values with no effect on life expectancy translate into the monetary value of QALY in the case of chronic disease. These two types of WTP per QALY values represent something different. WTP per QALY values as determined by Gyrd-Hansen (2003) and King *et al.* (2005) were DKK 88 000 (US\$ 15 000) and US\$ 12 500 to US\$ 32 200, respectively, both of which are lower than our estimated WTP per QALY. Different threshold or criteria may be necessary for decisions made regarding medication for chronic diseases as opposed to life-limiting diseases. We believe that it is natural for WTP values to change when people are faced with death.

This research was Web-based, and respondents were sampled from Internet panels, rather than by random sampling from the population in each country. Compared with paper-based survey research, Web-based survey research has some advantages. Web-based surveys can avoid the bias that occurs when respondents choose a bid value following reading or answering previous questions or after bid values are seen. In properly constructed, Web-based research, respondents cannot see the next questions, unless they click the answer to the current question, and the respondents cannot return to the previous questions.

Our data collection has some limitations, however, although face-to-face interviews are perhaps more desirable as a methodology, the sample size would be smaller than that of a Web-based survey conducted under the same conditions and budget. In planning our study, we expected that the potential inter-respondents' variance in WTP would be very large. Because we judged that it was more important to recruit many respondents than to conduct face-to-face interviews, we chose an Internet survey as the methodology.

Although we recruited respondents stratified by age and gender in each country, it is possible that the characteristics of respondents or responses to the questions were different than from a survey conducted among the general population. In addition, it is difficult to assume that respondents sampled from the Internet panel would be either more or less inclined to pay for the healthcare intervention than would the general population. Future surveys based on the more rigorous method of random sampling from the general population, however, may be needed.

Because the distribution of WTP is broad, it was difficult to determine the precise parameter for the cut-off value from this study. The options were the median WTP and the mean WTP. Median WTP is simply justified by the principle of democracy, a majority vote, however it cannot consider right-skewed distribution of WTP.

In our study, we had to decide whether or not to parametrically extrapolate the data. We adopted the nonparametric Turnbull method for primary analysis. This method is free from the assumption of a survival curve. A nonparametric Turnbull method, however, cannot consider the WTP value as higher than the maximum bid value of 15 million JPY. Nevertheless, the acceptance rate actually was not 0 in the range > 15 million JPY. The mean WTP estimated by the Turnbull method is thought to be rather modest.

A parametric analysis was used in conjunction with the nonparametric method. The curve was extrapolated to estimate the acceptance rate for a cost higher than JPY 15 million. When we extrapolated the curve, it was difficult to decide on the upper limit of integration. If the parametric curve is integrated from 0 to infinity, WTP may be overestimated. This is because the area of the high WTP value, the payment of which is unrealistic, would be included in the integral range. We believe that the upper limit of integration, rather than infinity, should be used. However, it is highly likely that this extrapolated WTP is overestimated, because we think that almost no one pays US\$ 500 000 for medical costs in the real world. JPY 50 million or US\$ 500 000 for actual medical care costs was considered too high to pay.

Devlin and Parkin (2004) pointed out that there is no single threshold value for WTP. It is not considered appropriate or realistic decision making that if the cost per QALY exceeds the cut-off value,

payment is rejected. Nor is it considered appropriate or realistic that if the cost per QALY does not exceed the cut-off value, payment automatically is accepted. In practice, the threshold for WTP is not clearly defined. Instead, the threshold for WTP should be treated as a range of cost. The probability of rejection of payment approaches 1 when the cost per QALY is at the upper limit of the threshold range. In contrast, the probability of rejection approaches 0 when the cost per QALY is at the lower limit of the threshold range.

Our recommendation for the threshold for WTP is based on Devlin and Parkin's concept. We think the probability of rejection should be determined based on the estimated acceptance curve. First, we suggest that the cost-effectiveness plane be divided into six domains by the three different kinds of WTP value, as depicted in Figure 3. The rationale of these criteria is shown in discussion section. Second, we suggest that new healthcare technologies be treated differently, depending on the domain in which they exist. The six domains (Figure 3) are defined as follows:

- Domain A: Incremental cost < 0 , and incremental effectiveness > 0 (dominant).
- Domain B: $0 < \text{cost per QALY} \leq \text{WTP}_{\text{med}}$.
- Domain C: $\text{WTP}_{\text{med}} < \text{cost per QALY} \leq \text{WTP}_{\text{Turn}}$.
- Domain D: $\text{WTP}_{\text{Turn}} < \text{cost per QALY} \leq \text{WTP}_{\text{ext}}$.
- Domain E: $\text{WTP}_{\text{ext}} < \text{cost per QALY}$.
- Domain F: Incremental cost > 0 , and incremental effectiveness < 0 (dominated).

The boundary values estimated by this study are shown in Table VI. Figure 4 can be used to illustrate examples of application of our classification in reimbursement decision-making or recommended for adoption by health service.

- (a) Healthcare technology in domain A: Reimbursed.
- (b) Healthcare technology in domain B: Reimbursed in principle.
- (c) Healthcare technology in domain C: Many technologies are reimbursed except those with limitations such as a therapeutic having only marginal efficacy, being indicated for a condition that has a small unmet need (e.g. if currently available drugs are sufficient), or having a major impact on budget.

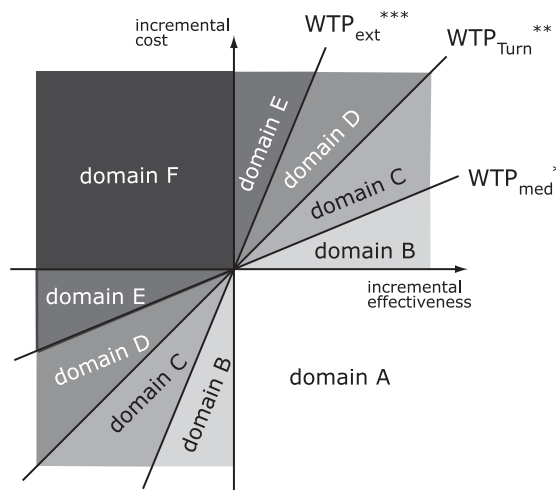


Figure 3. Domains on the cost-effectiveness plane. $\text{WTP}_{\text{med}}^*$: median WTP; $\text{WTP}_{\text{Turn}}^{**}$: WTP calculated by the nonparametric Turnbull method; $\text{WTP}_{\text{ext}}^{***}$: parametric extrapolated WTP

Table VI. Boundary values of suggested classification

		WTP_{med}^*	WTP_{Turn}^{**}	WTP_{exp}^{***}
Japan	JPY 1 mil	2.5	5.0	8.0
ROK	KWN 1 mil	45	70	120
Taiwan	NT\$ 1 mil	1.5	2.5	3.5
UK	£1000	10	25	40
AU	AUS 1000	35	65	120
US	US\$ 1000	30	60	120

WTP_{med}^* : median WTP; WTP_{Turn}^{**} : WTP calculated by the nonparametric Turnbull method; WTP_{ext}^{***} : parametric extrapolated WTP.

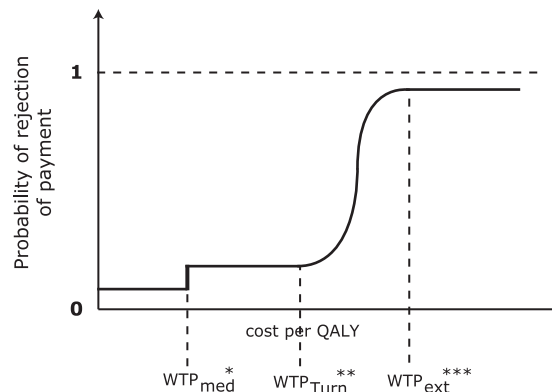


Figure 4. Cost-effectiveness threshold, based on our criteria. WTP_{med}^* : median WTP; WTP_{Turn}^{**} : WTP calculated by the nonparametric Turnbull method; WTP_{ext}^{***} : parametric extrapolated WTP

- (d) Healthcare technology in domain D: Some technologies are reimbursed, whereas others are not. For this 'gray' area, we recommend that the probability of rejection of payment should be based on a logistic-like curve. In that way, even if WTP_{Turn}^{**} is underestimated, or WTP_{ext}^{***} is overestimated, the social loss caused by wrong decision making would be small.
- (e) Healthcare technology in domain E: Not reimbursed in principle, except for products such as orphan drugs.
- (f) Healthcare technology in domain F: Not reimbursed.

The probability of payment rejection should be determined by groups such as decision-making health care payer sectors in each country. The boundary value results, however, may have reflected the type of question we asked. Future work should use different types of questions, and our suggested boundary values should be adjusted as other results emerge. This threshold may decrease for cases such as medication for chronic diseases, as discussed above.

Our study shows that WTP_{sel} generally is less than WTP_{fam} across the countries studied, and altruistic utility in health care is valued more than the respondent's utility achieved by the same gain of one additional QALY. Nevertheless, there is no consensus about how altruistic utility should be reflected in healthcare decision making. In addition, some difficulties remain, such as the possible perception of a lower WTP threshold for health care of single individuals than for married people in some cultures. Allowing differing attitudes on social status to affect payment for health care cannot be justified from the perspective of equality. Currently, our classification scheme does not consider altruistic utility. Development of a methodology to address altruistic utility appropriately is one of our challenges in future research.

For a long time, the threshold of cost effectiveness was based merely on conventional value, and was criticized due to lack of scientific evidence. Inability to judge whether or not a medical technology is cost effective from cost per QALY data was a serious problem in the past. In the current study, we used double-bound dichotomous choice to measure the WTP per QALY and to recommend classification based on a cost-effectiveness plane. Our estimated WTP_{sel} by Turnbull method (JPY 5.0 million in Japan, KWN 68 million in the ROK, NT\$ 2.1 million in Taiwan, £23 000 in the UK, AUS 64 000 in Australia and US\$ 62 000 in the US) is nearly equal to the conventional values (£20 000–£30 000 per QALY in the UK, or US\$ 50 000–100 000 per QALY in the US) and the rationale for threshold ranges has been clarified.

Increasing medical costs are becoming a major issue in developed countries. Making decisions that consider cost effectiveness, in addition to efficacy and safety, of healthcare interventions has become increasingly important. Our results provide a rationale for a threshold range of WTP, as well as contribute to more rigorous scientific decision making about healthcare technology for the future.

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APPENDIX A

Questionnaire for Japanese and British is shown below:

(1) WTP for their own additional QALY: WTP_{sel} .

Imagine that you are stricken with a serious illness that immediately threatens your life. Now, please assume that Medication A has been developed to treat your illness and if you take it your life will be extended for 1 full year and you will be completely healthy (without being confined to bed) for 1 full year.

Please assume, however, that Medication A will not be covered by health insurance [NHS (National Health Service) or private medical insurance (*in the British version*)] and you will have to pay the full amount to receive the product, which will cost JPY xxxx [£ xxxx] (*bid value*).

In this case, would you purchase the product?

(2) WTP for their own additional QALY 5 years later: WTP_{5sel} .

Imagine that you are stricken with an illness that leaves you with only 5 years to live. Now, please assume that Medication B has been developed to treat your illness and if you take it now you will live for 6 full years. Medication B will increase your life expectancy by 1 year and you will be completely healthy (without being confined to bed) for an additional 1 year (6 years in total).

Please assume, however, that Medication B will not be covered by health insurance [NHS (National Health Service) or private medical insurance (*in the British version*)] and you will have to pay the full amount to receive the product, which will cost JPY xxxx [£ xxxx] (*bid value*) (*bid value*).

In this case, would you purchase the product?

(3) WTP for their family's additional one QALY: WTP_{fam} .

Imagine that a member of your immediate family is stricken with a serious illness that immediately threatens their life. Now, please assume that Medication C has been developed to treat their illness and if they take it their life will be extended for 1 full year and they will be completely healthy (without being confined to bed) for 1 full year.

Please assume, however, that Medication C will not be covered by health insurance [NHS (National Health Service) or private medical insurance (*in the British version*)] and you will have to pay the full amount to receive the product, which will cost JPY xxxx [£ xxxx] (*bid value*).

In this case, would you purchase the product?

(4) The amount they think society should pay for someone's additional one QALY: WTP_{soc} .

Imagine that someone in your society is stricken with a serious illness that immediately threatens their life. Now, please assume that Medication D has been developed to treat the illness and if it is taken the patient's life will be extended for 1 full year and they will be completely healthy (without being confined to bed) for 1 full year. Currently Medication D is to be covered through health insurance [NHS (National Health Service) (*in the British version*)], which would cause an increase in taxes.

If the cost of Medication D is JPY xxxx [£ xxxx] (*bid value*), do you think it should be covered under publicly funded health insurance.

GLOSSARY

WTP_{sel} : WTP for the respondent's additional QALY.

WTP_{5sel} : WTP for the respondent's additional QALY 5 years later.

WTP_{fam} : WTP for an additional QALY for a family member.

WTP_{soc} : the cost that the respondent thinks that society should pay for someone's additional QALY.

WTP_{med} : median WTP estimated using the parametric method.

WTP_{Turn} : means WTP estimated using the nonparametric Turnbull method.

WTP_{par} : parametric mean WTP using the parametric method.

WTP_{ext} : parametric extrapolated WTP using the parametric method.

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