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Mapping the English and Chinese Versions of the Functional Assessment of Cancer Therapy–General to the EQ-5D Utility Index

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ABSTRACT

Objective: This study aims to develop a function for mapping the English and Chinese versions of the Functional Assessment of Cancer Therapy–General (FACT–G) scores to the EuroQoL Group's EQ-5D utility index and to test whether a single function is sufficient for the two language versions.
Methods: A baseline survey of 558 cancer patients in Singapore using the FACT–G and EQ-5D was conducted (308 English and 250 Chinese questionnaires). Regression models were used to predict the EQ-5D utility index values based on the FACT–G scores and thus derive a mapping equation. Data from a follow-up survey of the patients were used to validate the results.
Results: The FACT–G Social/Family scale was not associated with the EQ-5D utility index ($P = 0.701$). There was no interaction between language version and the predictors (each $P > 0.1$). An equation that maps the FACT–G Physical, Emotional, and Functional well-being scales to the EQ-5D utility index was derived. In the validation sample, the mean observed utility values was larger than the mapped by only 0.005 (95% confidence interval [CI] –0.006 to 0.016), but the mean absolute difference was 0.083 (95% CI 0.076 to 0.090).
Conclusions: At the group level, but not individual level, the equation developed can accurately map the English and Chinese versions of the FACT–G scores to the EQ-5D utility index.
Keywords: cancer, EQ-5D, FACT–G, quality of life, utility.

Introduction

Most cancer-specific quality-of-life instruments currently available are based on "psychometric" or "clinometric" principles [1,2]. They were not developed for quantification of the value of a health status or quality-adjusted survival time [3]. The Functional Assessment of Cancer Therapy–General (FACT–G) has been widely used in a variety of cancer clinics and in many parts of the world [4]. Like many other instruments, the FACT–G is an ordinal-level measurement scale: A higher value represents a better quality of life, but the difference between two values cannot be interpreted quantitatively. For example, the difference between the options of "somewhat" and "a little bit" are not the same as the difference between options "a little bit" and "not at all." In contrast, for an interval-level measurement scale, the difference in scores 0.3 and 0.4 is the same as the difference in scores 0.4 and 0.5. A utility value is one such quantitative, interval-level measure that is often needed in cost-utility and quality-adjusted life-year analyses. The EuroQol Group's 5-domain questionnaire, EQ-5D, is a preference-based health-related quality of life (HRQoL) measure which has been tested and used in several disease groups [2]. As opposed to the FACT–G or other ordinal-level measurement scales, the EQ-5D explicitly takes into account the respondents' preferences (or trade-off) between various health states and generates the utility values accordingly. Value sets and algorithms have been developed for transforming the descriptors into a single utility index that has a value not larger than one, where one represents full health [5,6].

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Several noncancer studies have attempted to map HRQoL measures to preference-based utility indices by regression methods, so that the application of one HRQoL measure can achieve the dual purpose of qualitative description of patients' situation and quantification of the utility of patients' health status and survival time [7–10]. The accuracy of mapping can be assessed by using a data set to develop a mapping function, and then applying the mapping function to another data set and comparing the predicted and observed values. A recent study mapped the FACT–Prostate to the EQ-5D utility index [11], but the mean absolute deviation (about 0.15) was substantially larger than what is usually considered a minimal clinically significant difference. This suggests that the mapping was not accurate at the individual level. Alternatively, Kind and Macran [12] and Lamers et al. [13] elicited preference weights for the FACT–Lung health states using visual analog scale (VAS) as the preference measure. The validity of the methodology used has been debated [14,15]. A study of the FACT–G directly elicited time trade-off utility values in a sample of cancer patients and developed an equation for using the FACT–G items to calculate a utility index [16]. The weighting represents patients' preferences although it is generally recommended that economic evaluation should be based on societal preferences [16]. Most of these studies used the English version of the HRQoL instruments; none of them used an Asian language version. In 1995, about 7% and 20% of the world's population used English and Chinese, respectively, as their primary languages [17].

This study aims to map the FACT–G to the EQ-5D utility index in cancer patients in Singapore, so that clinicians and researchers can obtain both a psychometric description and a quantitative utility summary of a patient's HRQoL from a single assessment using FACT–G. This has the potential of facilitating pharmacoeconomic and other quantitative evaluations without imposing additional assessment burden on patients. Both the

 1098-3015/09/371 371–376

FACT–G and EQ-5D have a Chinese version, and previous studies have suggested that the two language versions of the FACT–G and EQ-5D achieve measurement equivalence [18,19,20]. We have assessed whether a single mapping function can be used for both language versions.

Methods

Design and Recruitment

This is part of a larger study that aimed to confirm the measurement properties of the English and Chinese versions of the EQ-5D in cancer patients [20]. The study was approved by the Ethics Committee of the National Cancer Centre, Singapore. Outpatients who attended the Centre during the period between September 2004 and July 2006 were invited to participate. The patients were approached by a research coordinator while they were in the waiting areas of the specialist outpatient clinics, the ambulatory treatment unit, or the therapeutic radiology department. The inclusion criteria were broad: aged 18 years or older, ability to give written informed consent, and ability to understand Chinese or English. Patients who fulfilled the inclusion criteria and provided written informed consent chose to answer either a Chinese or an English questionnaire package according to their language preference. The packages included the EQ-5D and the FACT–G, as well as questions on demographic characteristics, Eastern Cooperative Oncology Group (ECOG) performance status, and other clinical characteristics. Consented participants were asked to self-administer and return the questionnaires during the same visit. The participants were sent a similar questionnaire package by post in the same language with postage-paid return envelope enclosed approximately 7 days after the baseline interview. Up to two reminders with the questionnaires would be sent at 2-weekly intervals if the questionnaires were not returned.

For the present part of the study, only ethnic Chinese patients, the ethnic majority in Singapore, were included in the analysis. The number of participants from the other ethnic groups was small and the inclusion of the minority ethnic groups would make the test of interaction between language versions (Chinese or English) and predictors uninterpretable. Participants who requested proxy response or interviewer administration were also excluded from the analysis.

Instruments and Variables

The 27-item FACT–G version 4 was used. The FACT–G consists of four domain scales: Physical (GP), Social/Family (GS), Emotional (GE), and Functional (GF) well-being. The validity and reliability of both the English and Chinese versions of the FACT–G as well as their measurement equivalence had been assessed in Singapore in previous studies [19,21]. The five ordinal-level responses to each item were coded as 0, 1, 2, 3, or 4 in such a way that a higher score indicated a better quality of life. The standard "half-rule" was used to impute missing item scores. The total and domain scales are obtained by summing the responses to the individual items they comprise.

A Singaporean English and Chinese version of the EQ-5D questionnaire was administered. The Singaporean English EQ-5D differs from the original English version only in the VAS instructions [18,22]. The Singaporean Chinese EQ-5D had earlier been adapted for use in Singapore, following the EuroQol Group's cultural adaptation guidelines [23]. Measurement equivalence of the two language versions had been confirmed in previous studies [18,20]. The EQ-5D contains five classifiers (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), plus a VAS of overall health status. At the moment, there is no Singaporean scoring function to convert the classifiers to a utility index, although the authors are conducting a study to develop this. The EQ-5D utility index was calculated by using the algorithm from a Japanese study [6], which is the only Asian EQ-5D value set to the best of our knowledge. As a sensitivity analysis, an algorithm from the UK study of Doland was also employed [5]. Both the Japanese and UK algorithms indicate societal preferences, not preferences of patients. In both algorithms, a respondent reporting full health (no problem in all five domains) has a utility value of one. A subtraction is made for 1) having at least one moderate or severe problem; 2) each moderate or severe problem in the five domains; and 3) having at least one severe problem. The two algorithms differ in the amount of subtraction to make.

The ECOG performance status is known to be a strong predictor of quality of life in cancer patients and is an important concern in cancer care [24]. It can be self-administered [25]. ECOG grade 0 refers to a status "Fully active, able to carry on all pre-disease performance without restriction"; grade 3 refers to "Capable of only limited self-care, confined to bed or chair more than 50% of waking hours." Grades 1 and 2 represent intermediate performance status. No respondents had ECOG grade 4 (Completely disabled). In the classification of tumor sites, those with prevalence smaller than 3% in this sample were combined and labeled as "others."

Statistical Analysis

The baseline survey data were used to develop the mapping function. The EQ-5D utility index was regressed upon the FACT–G total score or its GP, GE, GS, and GF scores. Previous studies have suggested that because of the ceiling effect in EQ-5D, regression methods that take into account right censoring such as Tobit and censored least absolute deviations (CLAD) methods are preferred to the ordinary least squares (OLS) method [8,9]. Because the Tobit method is sensitive to assumptions of normality and homoscedasticity, the CLAD is a logical choice [8]. We performed both CLAD and OLS for comparison purposes. The Wald test was used to assess the statistical significance of predictors and interaction between predictors and questionnaire language. The ECOG performance score was used as a criterion of validity to examine and compare the performance of the observed and predicted EQ-5D utility values. Goodness-of-fit is further examined by R^2, mean absolute deviation, and graphical assessment of residuals. Because OLS minimizes the R^2 whereas CLAD minimizes the sum of absolute deviation, one should bear in mind that the R^2s is an index that tends to favor the OLS, and vice versa.

We then used the follow-up data to validate the findings from the baseline data. The signed-rank test was used to assess the difference between observed and each of the two regression-based predicted EQ-5D utility index values. In the analysis of follow-up data, it was also used to assess the difference in the predicted values based on mapping function developed from baseline data and those based on mapping function developed from the follow-up data. Student's *t*-test was used to obtain mean values and their 95% confidence intervals. All statistical analyses were performed in Stata version 10 (StatCrop, College Station, TX). CLAD models were estimated by using a Stata macro [26].

Results

Descriptive Summary

Five hundred seventy-two ethnic Chinese patients who self-administered the questionnaires were eligible in the analyses,

Table 1 Characteristics of patients completing English or Chinese questionnaires (n = 558)

Characteristics	% or mean*
Age (years)	49.3
Gender	
Male	37.1
ECOG performance	
0	32.8
1	40.3
2	23.5
3	3.4
On chemo/radiotherapy	
Yes	54.7
Tumor site	
Breast	37.1
Head & neck (inc. nasopharyngeal cancer)	18.6
Colorectal	10.9
Lung	6.1
Gynecological	6.1
Lymphoma	4.1
Prostate	3.1
Others	14.0
Questionnaire language	
English	55.2

*Mean for age and % for categorical variables.
ECOG, Eastern Cooperative Oncology Group.

among whom, 257 (44.9%) chose to answer a Chinese questionnaire. Ten patients were excluded because of missing FACT–G values beyond imputation by the half-rule. Four patients were excluded because of missing EQ-5D utility scores. As such, a total of 558 patients, of whom 250 used the Chinese language, were available for analysis.

Table 1 shows the mean age and the percentage distribution of characteristics of the participants. The participants were heterogeneous in terms of type of tumor and performance status. About half of them were receiving chemotherapy or radiotherapy.

Table 2 describes the distribution of the FACT–G scores and EQ-5D utility index values. The mean FACT–G total score was 81.1. GE, GS, and GF reached the floor score (score zero), but the GP and the total score did not. All the FACT–G scores reached their ceiling levels (24 for GE, 28 for the other three domain scales, and 108 for the total score). The EQ-5D utility index based on the Japanese and UK algorithms were highly correlated (Spearman's correlation = 0.99). They gave similar mean and median values, and both reached the ceiling level (value = 1) but not the floor.

Regression and Prediction

Table 3 shows the regression analysis results based on the Japanese algorithm. OLS regression of the EQ-5D utility index using the FACT–G total score as the predictor gave an R^2 of 0.345 and mean absolute deviation of 0.106 (model I). Using all four domain scores as the predictors gave an R^2 of 0.451 and mean absolute deviation of 0.097 (model II). GS, however, was not statistically significantly associated with EQ-5D utility index ($P = 0.467$). Furthermore, the negative (–0.001) regression coefficient did not make sense. Model III dropped GS from the regression equation. The R^2 and mean absolute deviation were practically unchanged. Table 3 also shows the CLAD regression results. Model III, which used GP, GE, and GF as predictors of utility values, gave a fit not worse than models I and II did. The R^2 values were lower than those of the OLS models, e.g., 0.450 versus 0.417 for model III, but the mean absolute deviations were also smaller, e.g., 0.097 versus 0.095 for model III.

Both in OLS and CLAD models, there was no significant interaction between language version and GP, GE, and GF (each $P > 0.10$).

Table 4 describes the distributions of the observed (Japanese algorithm) and two predicted EQ-5D utility indices. A signed-rank test showed no statistically significant differences between the distribution of the observed and the OLS predicted values ($P = 0.788$) or the CALD predicted values ($P = 0.104$). Although the mean and median predicted scores based on OLS followed the observed mean and median more closely than those based on CLAD, the spread of the OLS predicted score was limited: The standard deviation (SD) was only about two-thirds of the observed SD, and the minimum and maximum scores thus calculated were 0.459 and 0.951, respectively. In contrast, the CLAD prediction gave an SD, minimum, 10th percentile, 90th percentile, and maximum closer to the observed values. The maximum was 0.999, which was practically reaching the full health level which is scored at one.

The left-hand side of Table 5 describes the mean observed (Japanese algorithm) and predicted utility values by ECOG performance status in the baseline survey. The OLS prediction tended to underestimate EQ-5D utility index in the group with ECOG score 0 ($P = 0.002$) and overestimate in the group with ECOG score 2 ($P = 0.001$). The CLAD prediction followed the group-specific means more closely, although it overestimated the mean by 0.019 in the group with ECOG score 2 ($P = 0.015$). Assuming a linear trend, the observed EQ-5D utility index decreased by 0.094 per grade, which was worse on the ECOG scale. The corresponding figures for OLS- and CLAD-based utility values were 0.067 and 0.082.

Validation

We used the follow-up data to validate findings from the baseline data. Three hundred sixty patients returned the follow-up questionnaire (65%). The mean changes (95% CI) in FACT–G total and EQ-5D utility scores from baseline to follow-up were –2.0

Table 2 Distribution of FACT–G and EQ-5D scores

Scores	Mean	Min	Median	Max	% at floor	% at ceiling
FACT–G						
Physical	21.9	3.0	23.0	28.0	0.0	15.1
Emotional	18.2	0.0	19.0	24.0	0.2	9.7
Social	21.7	0.0	23.0	28.0	1.1	12.2
Functional	19.3	0.0	20.0	28.0	0.1	12.2
Total	81.1	18.0	83.0	108.0	0.0	1.4
EQ-5D utility index						
Japanese value set	0.80	0.25	0.77	1.00	0.0	33.3
UK value set	0.81	–0.13	0.80	1.00	0.0	33.3

FACT–G, Functional Assessment of Cancer Therapy–General.

Table 3 Regression of EQ-5D utility index upon FACT–G scores by ordinary least squares (OLS) and censored least absolute deviation (CLAD)

	OLS			CLAD		
Scores	Model I	Model II	Model III	Model I	Model II	Model III
Physical		0.013*	0.013*		0.014*	0.014*
Emotional		0.005*	0.004*		0.006**	0.006*
Social		–0.001			–0.002	
Functional		0.005*	0.005*		0.009*	0.008*
FACT–G Total	0.006*			0.007*		
Constant	0.350*	0.352*	0.341*	0.229*	0.254*	0.238*
R^2	0.345	0.451	0.450	0.317	0.409	0.417
Mean absolute deviation	0.106	0.097	0.097	0.104	0.095	0.095

*$P < 0.001$; **$P < 0.01$.
FACT–G, Functional Assessment of Cancer Therapy–General.

(–3.2 to –0.8) and –0.004 (–0.017 to 0.009), respectively. Using the follow-up data, we again found that the regression predictions based on GP, GE, and GF were better than those based on the FACT–G total scores in terms of R^2 and absolute deviation, the GS scale was not significantly associated with the utility index, and the GP, GE, and GF scales did not interact with questionnaire language in making the prediction (details not shown). Furthermore, the regression coefficients estimated using the validation data were comparable to those from the baseline. For example, in the CLAD model III, the intercept (95% CI) was 0.244 (0.171 to 0.316) and the coefficients for GP, GE, and GF were 0.013 (0.009 to 0.017), 0.008 (0.004 to 0.012), and 0.008 (0.005 to 0.011), respectively.

In the validation data, the observed mean EQ-5D utility index value was 0.808. The mean of the predicted values based on OLS and CLAD were 0.774 and 0.803 ($P < 0.001$ and $P = 0.281$, respectively, in signed-rank tests against observed values). The right-hand side of Table 5 shows the analysis in relation to ECOG performance status. The differences between mean observed and CLAD predicted utility values ranged from 0.003 (ECOG 1) to 0.017 (ECOG 0) in the four groups. The CLAD and the observed EQ-5D values had more similar gradients in relation to ECOG, with estimated linear trends of 0.129 and 0.123, respectively, per grade worsening in ECOG, than in the baseline survey.

Figure 1 shows the residuals calculated for OLS and CLAD model III in the validation data. Two features are clearly visible. First, at the individual level, the degree of variability in the residuals was substantial. The mean, first quartile, median, and third quartile of the absolute deviation were, respectively, 0.083, 0.030, 0.067, and 0.117. Second, there was a trend in the residuals. At high values of observed EQ-5D utility index, there was a tendency for both regression methods to underestimate, whereas at low values, the tendency was to overestimate. Also, the prediction using CLAD was more accurate than the prediction by OLS.

Using the UK algorithm gave similar results (details not shown).

Discussion

A utility index is important in the studies of cost-utility and quality-adjusted survival time. Presently, most cancer-specific HRQoL measures do not feature such an interpretation. The Functional Assessment of Chronic Illness Therapy measurement system is an important set of measurement tools in oncology care and research. Recently, several studies have attempted to provide a utility index for the FACT–G [16], FACT-L [12,13], and FACT-P [11]. The methodological issues in using VAS to map the FACT-L to a utility index have been controversial

Table 4 Descriptive summary of utility indices derived from observed EQ-5D data and regression models

Utility index	Mean	SD	Minimum	P10	Median	P90	Maximum
Observed	0.803	0.156	0.246	0.628	0.769	1.000	1.000
OLS Model III	0.803	0.105	0.459	0.659	0.813	0.926	0.951
CLAD model III	0.811	0.130	0.393	0.633	0.822	0.969	0.999

CLAD, censored least absolute deviation; OLS, ordinary least squares; SD, standard deviation; P10 and P90, 10th and 90th percentiles.

Table 5 Utility values by ECOG performance scores at baseline and follow-up survey

	Baseline			Follow-up		
ECOG	Observed	OLS Model III	CLAD Model III	Observed	OLS Model III	CLAD Model III
0†	0.899	0.869*	0.8921	0.921	0.853*	0.904**
1	0.791	0.797	0.803	0.773	0.754**	0.776
2	0.718	0.744*	0.737**	0.678	0.668	0.666
3	0.596	0.644	0.616	0.530	0.560	0.526
Linear trend‡	–0.094*	–0.067*	–0.082*	–0.129*	–0.095*	–0.123*

*$P < 0.01$ and **$P < 0.05$.
†Signed-rank test for difference between observed and each predicted utility values within each ECOG category.
‡Test for linear trend in (observed or predicted) utility values across ECOG categories.
CLAD, censored least absolute deviation; ECOG, Eastern Cooperative Oncology Group; OLS, ordinary least squares.

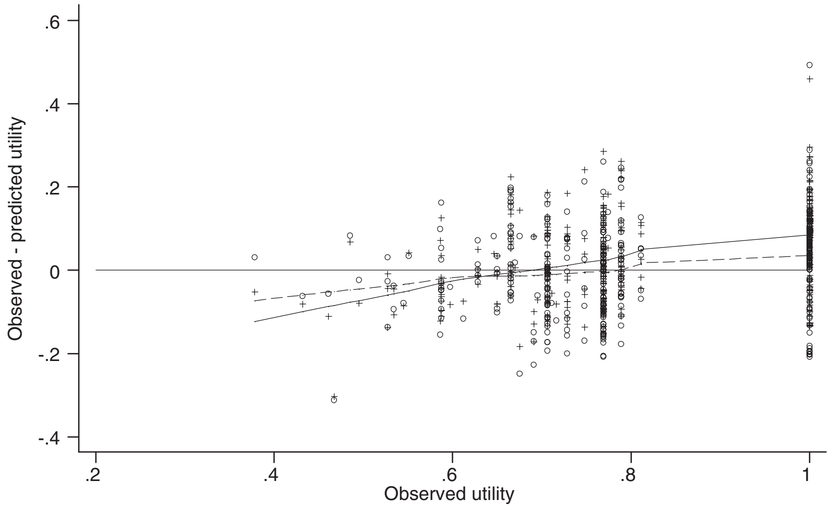

Figure 1 Plot of residuals from regression models against observed EQ-5D utility index in validation sample: + and o for residuals from ordinary least squares (OLS) and censored least absolute deviations (CLAD) regression models, respectively; solid and broken lines are locally weighted regression smooth mean values for OLS and CLAD regression models, respectively. A horizontal reference line of zero is superimposed.

[14,15]. Directly eliciting time trade-off values from cancer patients for the FACT–G has been successful at the group level, but the accuracy is limited at the individual level [16]. A function for converting the FACT-P to the EQ-5D utility index has been developed [11], but the absolute deviation is substantial and further information on its performance at the individual level is needed.

Following previous researchers' recommendations, we have estimated and compared OLS and CLAD regression models. In our opinion, the solution given by CLAD more closely describes the variation of health utilities in the present sample. The FACT Social/Family scale was not associated with EQ-5D utility index. This is not surprising because the EQ-5D does not include a classifier on this aspect of quality of life. Furthermore, items on social aspects of quality of life tend to differ in focus even among cancer-specific HRQoL measures [24]. This highlights the need of future research to consider further the utility value of social aspects of HRQoL and how to measure it. In both our study and the previous study of the FACT-P [11], the regression coefficient for the Social/Family scale was negative. It is not sensible to expect that a better social well-being would reduce one's health utility. Unlike the previous study, we have excluded the GS scale from the mapping function. Data from a follow-up survey confirmed and validated the findings based on the baseline survey. The analyses were not sensitive to the choice between Japanese and UK scoring functions.

At the group level, the CLAD regression equation

$$\text{EQ-5D utility index} = 0.238 + 0.014 \times \text{GP} + 0.006 \times \text{GE} + 0.008 \times \text{GF} \qquad (1)$$

was successful in predicting the observed EQ-5D utility index values. This reflects societal preferences as the Japanese and UK algorithms employed in this mapping exercise were both based on population value sets. The mean and median absolute deviations were smaller than those in the previous study mapping the FACT-P to the EQ-5D [11]. In the development and validation samples, the overall differences in mean between the CLAD-based and the observed utility index values were 0.008 and 0.005, respectively. They are far smaller than the previously suggested definitions of a minimal clinically important difference (MCID; 0.03 to 0.05) [16,18]. The equation also accurately provided estimates of the mean utility index values in patients with different performance status in the validation sample. The difference within each ECOG group was again smaller than the strict definition of MCID (0.03). The trend in CLAD-based utility values in relation to ECOG was very similar to that based on the observed EQ-5D utility values (–0.123 vs. –0.129), suggesting their equivalence also in studies of association.

The equation is easy to use and allows clinicians and researchers who only have FACT–G data to obtain a health utility value. The predictors did not interact with language version. Hence, a single equation can be applied to both the English and Chinese versions of the FACT–G. The English and Chinese languages are two of the world's most spoken languages [17]. The findings here will be useful to many people and cancer centers.

At the individual level, however, graphical examination of residuals showed a considerable level of inaccuracy, as well as a systematic pattern of underestimation in those with large and overestimation among those with small utility values. This pattern is similar to that found in the time trade-off study of Dobrez et al. [16]. As such, we would like to repeat the cautionary note that the use of mapped utility index values may not be appropriate for application at the individual level [10,16]. Other approaches to obtain health utilities in individual cancer patients need further research. Cost-utility studies, however, typically use group means instead of individual-level data [16]. Therefore, the present findings remain useful.

In conclusion, our study offers an equation for calculating a health utility index at the group level based on the English or Chinese versions of the FACT–G. This should add to the armamentarium of measures for use in cost-utility and quality-adjusted survival time studies in cancer research.

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