

Mapping the PHQ-8 to EQ-5D, HUI3 and SF6D in Patients with Depression

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Abstract

There is limited evidence of mapping the clinical instrument to a generic preference-based instrument in an Asian patient population. The current study aims to map the eight-item Patient Health Questionnaire depression scale (PHQ) onto the EuroQol five-dimensional (EQ-5D), the Health Utilities Index Mark 3 (HUI3) and the Short Form-6D SF-36 to inform future in cost-utility analyses for treatment in depression sample. A total of 249 participants who have completed PHQ-8, EQ5D, SF6D and HUI-3 questionnaires were included in the analyses. A beta regression mixture model was used to map the utility scores. The results were compared against two common regression methods including Ordinary Least Square (OLS) and Tobit regression models. The mean age of the sample was 36.2 years (SD=11.1). The mean EQ-5D-3L, EQ-5D-5L, HUI3 and SF-6D utility scores were 0.615, 0.709, 0.461 and 0.607, respectively. The EQ-5D-3L, EQ-5D-5L and SF-6D utility scores were best predicted by the beta mixture regression model consisting of PHQ total scores, PHQ-squared, and covariates including age and gender. The HUI3 was best predicted by the OLS model. The current study provides important evidence to clinicians and researchers about the mapping algorithms that can be used in economics evaluation among patients with depression.

Introduction

Depression is a severe mental disorder that causes substantial impairment to the individual and a significant burden to their family members and society. It is a highly prevalent mental disorder affecting 264 million of the global population. The total direct excess costs of depression per person can range from USD\$124 to USD\$18,174 in adults and between \$2868 and \$2883 in adolescents [1]. The cost of lost productivity in terms of absenteeism and presenteeism varies across countries. It has been reported that the absenteeism costs to be the highest in Japan (\$2674) while the presenteeism costs were \$5524 in the United States and \$5788 in Brazil [2]. Depression has been strongly linked to increased risk of suicide which is the leading cause of death among adolescents [3]. Due to increasing efforts worldwide to develop more effective treatment options and strategies for people with depression, there is a growing need for health technology assessments such as cost-effectiveness analysis (CEA) and cost-utility analysis (CUA).

Measuring health-related quality of life in patients is a crucial component of CEA and CUA for evaluating the benefits of existing or new treatment for depression. The EuroQol Five-Dimension (EQ-5D), Short Form – 36 version (SF-36) and Utilities Index Mark 3 (HUI3) are commonly used generic preference-based instruments to measure health-related quality of life among patients with depression in the literature [4, 5]. These instruments have been widely used to calculate quality-adjusted life-years (QALY) utilities in the CEA and CUA. In the clinical setting, however, these instruments are often not used. Therefore, mapping the clinical instrument to a generic preference-based instrument to produce statistical formula or functions that allow the clinical instruments to estimate utility scores provides an alternative solution to generate QALY for CEA and CUA in clinical studies [5, 6]. The Patient Health Questionnaire (PHQ) depression scale [7] is one of the most widely used clinical instruments to measure symptom severity of depression in a clinical setting. Given that there is limited data on mapping studies using the PHQ among people with depression, the current study

aims to map the PHQ onto the EQ-5D, HUI3 and SF-36 to inform future in cost-utility analyses for treatment in depression sample.

Methods

The study was conducted between August 2016 and November 2017 at a tertiary psychiatric hospital, which serves majority of psychiatric patients in Singapore. Patients were included in the study if they are Singapore citizens or permanent residents, aged 21 years and above, literate in English and having a clinical diagnosis of depressive disorder. A total of 249 participants who have completed PHQ-8, EQ5D, SF6D and HUI-3 questionnaires were included in the analyses.

The study was approved by the relevant institutional ethics review board (National Healthcare Group Domain Specific Review Board (DSRB) (Reference no: 2016/00215). A written informed consent was obtained from all study participants.

Measures

PHQ-8

The eight-item Patient Health Questionnaire depression scale (PHQ-8) is a self-reported questionnaire designed to measure depressive symptom severity in research and clinical care [7]. It assesses how often in the past two weeks participants experienced eight depressive symptoms. Each symptom is rated on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day) with total scores ranging from 0 to 24. The PHQ-8 has been widely used to measure the severity of depressive symptoms in psychiatric patients in Singapore [8, 9].

EQ-5D

The EQ-5D is a generic preference-based measure for subjectively describing and valuing health-related quality of life that has been developed by the EuroQol Group [10]. It comprises of two versions – EQ-5D-3L and EQ-5D-5L. The EQ-5D-3L included five questions on mobility, self-care, pain, usual activities, and psychological status with three possible answers for each item (1=no problem, 2=moderate problem, 3=severe problem). The utility scores of EQ-5D-3L were calculated using the scoring algorithm developed in Singapore (Luo et al., 2014). The EQ-5D-5L is a new version of the EQ-5D comprised of five questions on mobility, self-care, pain, usual activities, and psychological status with five possible responses for each item (1=no problem, 2=slight problems, 3=moderate problems, 4=severe problems, 5=extreme problems). The utility scores of EQ-5D-5L were developed by van Hout et al. using a crosswalk project that maps EQ-5D-5L utility scores from the EQ-5D-3L [11].

HUI3

The HUI3 is a generic comprehensive health status classification instrument (Feeny et al., 1995). It generates utility scores using a utility scoring function derived from a representative sample of the general Canadian population based on the Standard Gamble and visual analogue scale methods (Horsman et al., 2003). The utility score ranged between -0.36 and 1. The HUI3 comprised of eight domains: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain, with 5 to 6 levels per attribute derived from 15-multiple choice questions. The utility scores obtained from Chinese and Malay versions of the HUI3 have been demonstrated to be equivalent and valid in Singapore (Luo et al., 2007).

SF-36

The SF-36 is a generic instrument that can be used to generate SF-6D utility scores using a utility scoring function derived from a representative sample of the general UK population (Brazier et al., 2002). The utility score ranged between 0.29 and 1. It has six domains: physical functioning, role limitation, social functioning, pain, mental health, and vitality, with 4–6 levels for each domain. The utility scores derived from Chinese and English versions of the SF-6D have been demonstrated to be equivalent and valid in Singapore (Wee et al., 2004).

Statistical analyses

Statistical analyses were carried out using the STATA software version 13 (StataCorp LP, College Station, TX). Since the distribution of utility scores derived from generic preference-based measures such as EQ-5D are often not normally distributed and had higher ceiling effect at a value of 1 [12], we used a beta regression mixture model (betamix) to map the utility scores. The results were compared against two common regression methods including Ordinary Least Square (OLS) and Tobit [13]. The beta regression mixture model is a two-part model that incorporates a multinomial logit model and a beta mixture model in their algorithms. Studies have increasingly suggested that this regression method outperforms linear regression model [14-16]. In order to determine the best performance of the prediction model, three main different model specifications were included in each regression methods. The first model included only PHQ total scores as a main predictor for the utility score; the second model included PHQ total scores, age and gender, and the third model included PHQ total scores, PHQ-squared, age and gender. The performance of regression methods was assessed using the following criteria. Both mean absolute error (MAE) and root mean square error (RMSE) were used as a main criterion to compare the performance of regression methods. Values from both indices were ranked and summed to get an average ranking. The regression model with the lowest average ranking values was considered to be the best prediction model [6, 16, 17].

Results

Descriptive statistics

The descriptive statistics are presented in Table 1. The sample included 249 participants with depression. The mean age of the overall sample was 36.2 years (SD = 11.1), 69.6% were Chinese, 13.7% were Malays,

14.5% were Indians, and 2% belonged to other ethnicities. The EQ-5D-3L showed a mean (SD) index score of 0.615 (0.317) with minimum and maximum scores of -0.2999 and 1 while the mean (SD) EQ-5D-5L index was 0.709 (0.212) with minimum and maximum scores of -0.027 and 1, respectively. The mean (SD) HUI3 index score was 0.461 (0.331) with minimum and maximum scores of -0.289 and 1, while the mean SF-6D was 0.607 (0.105) with minimum and maximum scores of 0.385 and 0.958, respectively. An inspection of the distribution of the EQ-5D-3L, EQ-5D-5L and HUI3 utilities showed a skew substantially to the right, that is, toward a better quality of life (Fig. 1). The mean (SD) PHQ total score was 11.526 (6.590) with minimum and maximum scores of 0 and 24, respectively.

Table 1
Characteristics of the sample

N (%)	
Demographic profiles	
Age, Mean (SD)	36.2 (11.1)
Gender	
Female	118 (47.4)
Male	131 (52.6)
Ethnicity	
Chinese	174 (69.9)
Malay	34 (13.7)
Indian	36 (14.5)
Others	5 (2.0)
Utilities	
EQ-5D-3L, Mean (SD)	0.615 (0.317)
EQ-5D-5L, Mean (SD)	0.709 (0.212)
HUI3, Mean (SD)	0.461 (0.331)
SF6D, Mean (SD)	0.607 (0.105)

Mapping on EQ-5D-3L

Table 2 shows the performance of beta mixture regression model versus other regression methods (OLS and Tobit) for mapping PHQ8 to the EQ-5D-3L utility scores. Three regression methods with 18 model specifications were tested. Among the three regression methods, beta mixture regression method with two components, probability mass at the full health (1) and the truncation point (0.8538) using Model 3d specification produce the smallest average ranking of MAE (0.1765) and RMSE (0.2326) values than other

model specifications. The model, which consists of the PHQ total scores, PHQ-squared, age and gender as predictor variables revealed that PHQ-squared scores were significantly and negatively associated with higher EQ-5D-3L's first component utility scores. We also found that the PHQ total scores and PHQ-squared were negatively and positively associated with the full health (Supplementary Table 1).

Table 2

Model performance of three regression methods for mapping the PHQ-8 to the EQ-5D-3L utility scores

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
1	BETAMIX M1a	1 component without truncation	Probability mass at full health	0.0904	0.2014	0.2621	18	18	18
2	BETAMIX M1b	2 components without truncation	Probability mass at full health	0.0130	0.1868	0.2381	15	11	13
3	BETAMIX M1c	2 components with truncation	Probability mass at full health	-0.0043	0.1839	0.2370	12	9	11
4	BETAMIX M1d	2 components with truncation	Probability mass at full health and truncation point	-0.0024	0.1861	0.2390	13	13	13
5	BETAMIX M2a	1 component without truncation	Probability mass at full health	0.0866	0.1962	0.2607	17	17	17
6	BETAMIX M2b	2 components without truncation	Probability mass at full health	0.0101	0.1825	0.2349	8	7	8
7	BETAMIX M2c	2 components with truncation	Probability mass at full health	-0.0038	0.1806	0.2341	6	5	6
8	BETAMIX M2d	2 components with truncation	Probability mass at full health and truncation point	-0.0013	0.1813	0.2355	7	8	8
9	BETAMIX M3a	1 component without truncation	Probability mass at full health	0.0659	0.1864	0.2504	14	16	15
10	BETAMIX M3b	2 components without truncation	Probability mass at full health	0.0119	0.1800	0.2321	5	1	3

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
11	BETAMIX M3c	2 with truncation point	Probability mass at full health	0.0020	0.1774	0.2328	2	3	3
12	BETAMIX M3d	2 components with truncation point	Probability mass at full health and truncation point	0.0057	0.1765	0.2326	1	2	2
13	OLS M1			0.0000	0.1837	0.2374	11	10	11
14	OLS M2			0.0000	0.1798	0.2347	4	6	5
15	OLS M3			0.0000	0.1784	0.2331	3	4	4
16	TOBIT M1			-0.0263	0.1870	0.2413	16	15	16
17	TOBIT M2			-0.0264	0.1834	0.2389	9	12	11
18	TOBIT M3			-0.0264	0.1836	0.2390	10	14	12
NOTE: ME = Mean error, MAE = Mean absolute error, RMSE = Root mean square error									
M1 = Regression model including PHQ as explanatory variable									
M2 = Regression model including PHQ, age, gender as explanatory variables									
M3 = Regression model including PHQ, PHQ-squared, age, gender as explanatory variables									

Mapping on EQ-5D-5L

Among the three regression methods and 18 model specifications (Table 3), we found that model 3d specification from the beta mixture regression model consisting of the PHQ total scores, PHQ-squared, age and gender as predictors produced the best prediction performance index (MAE = 0.1208 and RMSE = 0.1620). In this model (Supplementary Table 2), age was inversely associated with the EQ-5D-5L utility scores in the first component utility scores. In contrast, PHQ-squared was significantly and negatively associated with the EQ-5D-5L utility scores in the second component. We also found that the PHQ-squared and age were inversely associated with the full health (Supplementary Table 2).

Table 3

Model performance of three regression methods for mapping the PHQ-8 to the EQ-5D-5L utility scores

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
1	BETAMIX M1a	1 component without truncation	Probability mass at full health	0.0354	0.1374	0.1720	18	18	18
2	BETAMIX M1b	2 components without truncation	Probability mass at full health	0.0010	0.1296	0.1708	15	17	16
3	BETAMIX M1c	2 components with truncation	Probability mass at full health	-0.0007	0.1274	0.1687	11	14	13
4	BETAMIX M1d	2 components with truncation	Probability mass at full health and truncation point	0.0031	0.1293	0.1696	14	16	15
5	BETAMIX M2a	1 component without truncation	Probability mass at full health	0.0355	0.1338	0.1691	17	15	16
6	BETAMIX M2b	2 components without truncation	Probability mass at full health	-0.0018	0.1254	0.1670	7	11	9
7	BETAMIX M2c	2 components with truncation	Probability mass at full health	0.0002	0.1243	0.1656	5	8	7
8	BETAMIX M2d	2 components with truncation	Probability mass at full health and truncation point	0.0051	0.1258	0.1657	10	9	10
9	BETAMIX M3a	1 component without truncation	Probability mass at full health	0.0357	0.1297	0.1663	16	10	13
10	BETAMIX M3b	2 components without truncation	Probability mass at full health	-0.0011	0.1213	0.1631	3	2	3

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
11	BETAMIX M3c	2 components with truncation	Probability mass at full health	0.0031	0.1212	0.1632	2	4	3
12	BETAMIX M3d	2 components with truncation	Probability mass at full health and truncation point	0.0023	0.1208	0.1620	1	1	1
13	OLS M1			0.0000	0.1279	0.1673	13	12	13
14	OLS M2			0.0000	0.1255	0.1642	8	5	7
15	OLS M3			0.0000	0.1238	0.1631	4	3	4
16	TOBIT M1			-0.0098	0.1278	0.1681	12	13	13
17	TOBIT M2			-0.0101	0.1256	0.1653	9	7	8
18	TOBIT M3			-0.0098	0.1245	0.1644	6	6	6

Mapping on HUI3

We found the OLS method with model 3 specification consisting of the PHQ total scores, PHQ-squared, age and gender as predictors produce the best prediction performance index (MAE = 0.1584 and RMSE = 0.2024) (Table 4). In this regression model, those with lower PHQ total scores and of younger age were significantly associated with higher HUI3 scores (Supplementary Table 3).

Table 4

Model performance of three regression methods for mapping the PHQ-8 to the HUI3 utility scores

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
1	BETAMIX M1a	1 component without truncation	Probability mass at full health	-0.2680	0.2844	0.3644	17	17	34
2	BETAMIX M1b	2 components without truncation	Probability mass at full health	-0.0013	0.1664	0.2077	13	13	26
3	BETAMIX M1c	2 components with truncation	Probability mass at full health	-0.0001	0.1666	0.2082	14	14	28
4	BETAMIX M1d	2 components with truncation	Probability mass at full health and truncation point	-0.0007	0.1662	0.2074	12	12	24
5	BETAMIX M2a	1 component without truncation	Probability mass at full health	-0.2682	0.2842	0.3624	16	16	32
6	BETAMIX M2b	2 components without truncation	Probability mass at full health	.	.	.			
7	BETAMIX M2c	2 components with truncation	Probability mass at full health	-0.0010	0.1607	0.2023	7	1	8
8	BETAMIX M2d	2 components with truncation	Probability mass at full health and truncation point	0.0002	0.1606	0.2025	6	6	12
9	BETAMIX M3a	1 component without truncation	Probability mass at full health	-0.2679	0.2839	0.3623	15	15	30

∴ the analysis is not converge

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
10	BETAMIX M3b	2 components without truncation	Probability mass at full health	-0.0048	0.1602	0.2027	5	7	12
11	BETAMIX M3c	2 components with truncation	Probability mass at full health	-0.0026	0.1612	0.2028	8	8	16
12	BETAMIX M3d	2 components with truncation	Probability mass at full health and truncation point	-0.0158	0.1634	0.2048	11	9	20
13	OLS M1			0.0000	0.1630	0.2066	10	10	20
14	OLS M2			0.0000	0.1584	0.2024	3	3	6
15	OLS M3			0.0000	0.1584	0.2024	4	2	6
16	TOBIT M1			-0.0011	0.1627	0.2066	9	11	20
17	TOBIT M2			-0.0012	0.1579	0.2024	2	4	6
18	TOBIT M3			-0.0012	0.1579	0.2024	1	5	6
∴ the analysis is not converge									

Mapping on SF-6D

We found beta mixture regression method with two components without truncation and probability mass at the full health (1) using Model 3b specification produced the best prediction performance index (MAE = 0.0519 and RMSE = 0.0683) (Table 5). The model which consists of the PHQ total scores, PHQ-squared, age and gender as predictor variables revealed that PHQ total scores, age and female were significantly and negatively associated with higher utility scores in the first component. In comparison, the PHQ total scores and age were significantly and negatively associated with higher utility scores in the second component (Supplementary Table 4).

Table 5

Model performance of three regression methods for mapping the PHQ-8 to the SF-6D utility scores

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
1	BETAMIX M1a	1 component without truncation	Probability mass at full health	0.0008	0.0587	0.0746	10	9	10
2	BETAMIX M1b	2 components without truncation	Probability mass at full health	0.0060	0.0575	0.0749	9	10	10
3	BETAMIX M1c	2 components with truncation	Probability mass at full health	N/A	N/A	N/A	N/A	N/A	N/A
4	BETAMIX M1d	2 components with truncation	Probability mass at full health and truncation point	N/A	N/A	N/A	N/A	N/A	N/A
5	BETAMIX M2a	1 component without truncation	Probability mass at full health	0.0013	0.0539	0.0695	6	6	6
6	BETAMIX M2b	2 components without truncation	Probability mass at full health	0.0055	0.0527	0.0693	2	5	4
7	BETAMIX M2c	2 components with truncation	Probability mass at full health	N/A	N/A	N/A	N/A	N/A	N/A
8	BETAMIX M2d	2 components with truncation	Probability mass at full health and truncation point	N/A	N/A	N/A	N/A	N/A	N/A
9	BETAMIX M3a	1 component without truncation	Probability mass at full health	0.0020	0.0533	0.0683	5	2	4
10	BETAMIX M3b	2 components without truncation	Probability mass at full health	0.0057	0.0519	0.0683	1	1	1

No	Mapping method	Number of components and truncation	Specification	ME	MAE	RMSE	MAE rank	RMSE rank	Final rank
11	BETAMIX M3c	2 components with truncation	Probability mass at full health	N/A	N/A	N/A	N/A	N/A	N/A
12	BETAMIX M3d	2 components with truncation	Probability mass at full health and truncation point	N/A	N/A	N/A	N/A	N/A	N/A
13	OLS M1			0.0000	0.0587	0.0754	11	11	11
14	OLS M2			0.0000	0.0545	0.0710	7	7	7
15	OLS M3			0.0000	0.0532	0.0686	3	3	3
16	TOBIT M1			0.0000	0.0587	0.0754	12	12	12
17	TOBIT M2			0.0000	0.0545	0.0710	8	8	8
18	TOBIT M3			0.0000	0.0532	0.0686	4	4	4

Discussion

This is one of few studies that have been conducted to map PHQ-8 scores on three common utility scores, the EQ-5D-3L, EQ-5D-5L, HUI3 and SF-6D among people with depression in a multiethnic Asian population. By doing so, we facilitate the calculation of utility scores for health economic evaluation of clinical trials and studies which collect PHQ-8 scores. In the current study, three different regression methods with 18 model specifications were explored to develop mapping functions for PHQ-8. The findings provide evidence that different predictive models should be used for mapping EQ-5D-3L, EQ-5D-5L, HUI3 and SF-6D in our sample. Our analyses showed that both versions of the EQ-5D utility scores were best predicted by the beta mixture regression model which is consistently reported in other studies [14–16]. Our mapping algorithm for the HUI3 was best predicted by model 3 using ordinary least square model. This model produces minimal MSE and MAE. We found PHQ total scores, PHQ-squared scores, as well as age and gender to play a significant role in mapping the utility scores with the expected direction in depression sample. For example, lower the PHQ total scores more the likelihood of the EQ-5D-3L, EQ-5D-5L, HUI3 and SF6D scores to increase significantly. It is important to note that the primary intention of the study is to develop mapping function that best predicts utility scores derived from EQ-5D-3L, EQ-5D-5L, HUI3 and SF-6D, so whether the regression coefficients are statistically significant is of secondary consideration [18]. In the current study, model selection was primarily determined by the MAE and MSE. In order to avoid bias, the choice of the best model was based on the average ranking of both indices instead of focusing exclusively on one fit index.

Several limitations should be acknowledged in the current study. Firstly, the utility values for EQ-5D-5L were based on a crosswalk project that maps EQ-5D-5L utility scores from the EQ-5D-3L. Secondly, due to the small sample size, we are unable to test whether the model works equally well in sub-samples of the overall sample. However, a recent guideline by the ISPOR Good Practice for Outcomes Research Task Force has not recommended splitting the sample to validate results on part of the sample [19]. Hence, further validation of the current mapping findings using external dataset is recommended. Nonetheless, to our knowledge this is the first study to use beta mixture regression model against the Tobit and linear regression methods to map PHQ-8 scale onto widely used generic preference-based measures specifically for depression patients.

In conclusion, we have provided the algorithm for converting PHQ-8 scores into utility scores that are easily applicable in the clinical setting when the EQ-5D-3L, EQ-5D-5L, HUI3 and SF-6D data were not available. The current study provides important evidence to clinicians and researchers about the mapping algorithms that can be used in economics evaluation among patients with depression.

Declarations

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Declaration of conflicting interests

The authors do not have any Conflict of Interest to declare.

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