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A comparison of Vietnamese, Malaysian, Thai and Indonesian EQ-5D-5L value sets using a Vietnamese sample of HER2 positive breast cancer patients

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ABSTRACT

Background: Vietnamese value set was published in 2019, but so far there has been no assessment comparison of the Vietnamese value set with other value sets. Objectives: To compare the Vietnamese, Malaysian, Thai, Indonesian value sets and evaluate the appropriateness of the Vietnamese value set for Vietnamese people. Methods: A cross-sectional study was conducted on 338 HER2 positive breast cancer patients are treating at 6 hospitals in Vietnam. Data was collected by taking the entire sample from July to December in 2019. The EQ-5D-5L health states ratings were collected through interviews with patients and utility scores were calculated using the Vietnamese, Malaysian, Thai and Indonesian value sets. The difference in the mean values from 4 value sets was verified by the Wilcoxon signed rank test and the consistency between value sets was assessed by using intraclass correlation coefficients (ICCs). Spearman's test was used to evaluate the correlation between the patient's demographic characteristics with EQ-5D score (95% confidence interval). Results: The study was performed on 338 patients with the mean age of 53.870 ± 9.970 and weight of patients of 54.589 ± 7.698 kg. The Thai value set had the highest mean utility score (0.904 ± 0.142), followed by the Indonesian value set (0.881 ± 0.117), Malaysian value set (0.867 ± 0.143) and the Vietnamese value set had the smallest mean utility score (0.863 ± 0.142). There was a very high consistency between the value sets (intraclass correlation coefficients > 0.900). The forecasting model of EQ-5D VAS utility score based on EQ-5D-5L utility score from the Vietnamese value set had the highest R square (R^2 = 0.231). Conclusion: Vietnamese, Malaysian, Thai, Indonesian value sets have an overall high level of correlation and consistency, in which the correlation of Vietnamese and Malaysian value sets is highest. The Vietnamese value set is most suitable for the Vietnamese HER2-positive breast cancer patients, the Malaysian value set is the second-best option to be applied.

Keywords: *HER2 positive breast cancer, EQ-5D-5L, value set comparison*

1. INTRODUCTION

Measures of health-related quality of life (HRQoL) have become more essential in assessing treatment or health-care program outcomes. In many countries, the EuroQoL five-dimensional questionnaire (EQ-5D) is the chosen tool for measuring utility in health technology assessments (HTA). EQ-5D-5L value sets is a set of quality of life (QoL) scales recommended by the National Institutes of Health for Treatment Quality (NICE) to assess the health status of patients, from that estimating quality life years (QALYs) – an important indicator in the economic evaluation of health [1]. The descriptive system classifies health on five dimensions: mobility, self-

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care, usual activities, pain/discomfort and anxiety/depression. Within each dimension, respondents are asked to describe their current health using either three (no problems, some/moderate problems, extreme problems/unable to/confined to bed) or five (no problems, slight problems, moderate problems, severe problems and unable to/extreme problems) levels of severity [2]. Based on the answers, the conversion values of the QoL coefficients are calculated according to a country-specific frame of reference.

Currently, there are 22 countries that have their own value sets, of which Asia has 9 countries with Japan being the first country in the region to have its own value set [2]. In Southeast Asia, there are four countries that have developed and appraised their own value sets: Thailand (2013-2014), Indonesia (2017), Malaysia (2016) and Vietnam (2018-2019) [3]. The application of different value sets will give different utility score results due to differences in design, study methods and population characteristics between countries. The differences in utility scores due to varied valuation will result in different cost-effectiveness ratio results (QALY), so it is necessary to consider choosing an appropriate value set. The Vietnamese value set was published in 2019, but so far there has been no assessment comparison of the Vietnamese value set with other value sets. Therefore, the study compares the Vietnamese, Malaysian, Thai, Indonesian value sets to evaluate the appropriateness of the Vietnamese value set for Vietnamese people. The study provides a comprehensive view of Vietnamese, Malaysian, Thai, Indonesian value sets on HER2 positive cancer patients to help experts make better choices to apply EQ-5D-5L value sets, contributing to creating a selection basis for countries that do not have a value sets separate conversion.

2. MATERIALS AND METHODS

2.1. Material

The study data was collected from medical records and question sheets on QoL of HER2+ breast cancer patients treated at 6 hospitals in Vietnam, which included K Hospital, Oncology Hospital Ho Chi Minh city, Ha Noi Oncology Hospital, Da Nang Oncology Hospital, Cho Ray Hospital and Bach Mai Hospital.

2.2. Methods

A cross-sectional study was conducted on a breast cancer patient sample. The EQ-5D-5L health states ratings were collected through interviews with patients. Utility scores were calculated using the Vietnamese (Vu Q. M et al., 2020), Malaysian (Yusof F.A et al., 2012), Thai (Pattanaphesaj J. et al., 2021), and Indonesian (Purba F. D. et al., 2018) value sets [4-7]. The difference in the mean values from four value set was verified by the Wilcoxon signed rank test and the consistency between value sets was assessed by using intraclass correlation coefficients (ICCs). In addition, the study also analyzed the correlation between the patient's demographic characteristics with EQ-5D score by Spearman's test and built a linear regression equation to predict EQ-5D VAS score (95% confidence interval).

2.3. Sample

The study conducted sampling by taking the entire sample from July to December in 2019. Then, we recorded 338 HER2+ breast cancer patients meeting fully the selection and exclusion criteria.

The selection criteria

- The patients were diagnosed with HER2+ breast cancer according to the ICD 10 C50 code.
- The patients agreed to participate in the study.
- The patients were able to answer the questions sheet.

The exclusion criteria

- The patients did not complete the survey sheet.
- The patients did not complete treatment due to transfer, death or voluntary appearance.

2.4. Ethical consideration

The study protocol was approved by the Biomedical Research Ethics Council of the University of Medicine and Pharmacy in Ho Chi Minh City, Vietnam.

3. RESULTS

3.1. Sociodemographic and clinical characteristics

Surveying a sample of 338 HER2+ breast cancer

patients treated at 6 hospitals, the study recorded the patient's characteristics presented in table 1.

According to table 1, the study recorded the mean age of patients was 53.870 ± 9.970, mean weight was 54.589 ± 7.698 kg. Most of the participants lived in urban (71.6 %), with under high school (37.9%) and university (27.8%), and with income from no income to over 10 million VND/month. The study found that the majority of patients in the survey sample belonged to the early stage (72.8%), nearly 6.7 times the metastatic stage group (10.9%). Most patients had not metastasized (76.6%), more than 10 times patients who have metastasized (7.1%), the rest were undetermined and do not have access to medical records. Almost 45% of patients had no comorbidities and 39.6% of patients had one comorbidity.

Table 1. Socio-demographic and clinical characteristics of participants

Characteristics		**Mean ± SD (Min – Max)**
Age		53.870 ± 9.970 (28 – 84)
Weight (kg)		54.589 ± 7.698 (32.0 – 81.0)
Characteristics		**Frequency (%)**
Local	Urban	242 (71.6)
	Countryside	88 26.0)
	Mountains/ islands	8 (2.4)
Education	Under high school	128 (37.9)
	High school	76 (22.5)
	Vocational training/ College	30 (8.9)
	University	94 (27.8)
	Postgraduate education	10 (3.0)
Monthly income (VND/ month)	No income	90 (26.6)
	Under 3 million	47 (13.9)
	3-5 million	53 (15.7)
	5-10 million	74 (21.9)
	From 10 million or more	74 (21.9)
Metastasis	No (M0)	259 (76.6)
	Yes (M1)	24 (7.1)
	Undefined (Mx)	29 (8.6)
	No mention	26 (7.1)
Disease stage	Undefined	29 (8.6)
	Early stage	246 (72.8)
	Metastatic	37 (10.9)
	No mention	26 (7.7)
Comorbidities	0	151 (44.7)
	1	134 (39.6)
	2	35 (10.4)
	3	8 (2.4)
	Higher 3	4 (1.2)
	No mention	6 (1.8)

3.2. EQ-5D categories' distribution

The study surveyed 380 patients and collected their utility scores, as presented in Table 2.

According to Table 2, most of the patients were no problems with mobility (81.1%), self care (91.4%), usual activities (75.1%), pain /discomfort (52.4%) and anxiety, depression (52.7%). Besides that, the patients were slight problems of pain/discomfort and anxiety/depression to account for quite a high rate (34.3% and 29.3%, respectively); no patients were unable/extreme problems of self care and pain /discomfort.

Table 2. EQ-5D categories' distribution

	Mobility	Self care	Usual activities	Pain/Discomfort	Anxiety, Depression
No problems (%)	81.1	91.4	75.1	52.4	52.7
Slight problems (%)	12.4	6.5	16.9	34.3	29.3
Moderate problems (%)	4.7	1.2	6.5	11.2	13.0
Severe problems (%)	0.9	0.9	0.9	2.1	3.8
Unable/Extreme problems (%)	0.9	0	0.6	0	1.2

3.3. Comparison of Mean EQ-5D Index Scores

The study recorded utility scores from value sets of Vietnam, Thailand, Malaysia, and Indonesia presented in Table 3.

According to Table 3, the study found that the mean utility scores from four value sets were almost similar with the difference in mean utility scores being very low from 0.037 to 0.096 points. In which, the Thai value set had the highest mean utility score with 0.904 ± 0.142 and the Vietnamese value set had the smallest mean utility score of 0.863 ± 0.142. There was a statistically significant difference in EQ-5D utility scores in most value sets, except for Vietnamese - Indonesian value set. Consistency between the utility scores obtained between Vietnam and Thailand/Malaysia/Indonesia using intraclass correlation coefficient (ICC), the results presented in Table 4 show that all ICCs were above 0.9 and were statistically significant ($p < 0.001$), which means that there was a very high consistency between the value sets. The ICCs of the value sets did not differ much, in which, the Vietnamese and Malaysian value sets had the most consistency (ICC = 0.992), Vietnamese and Thai value sets (ICC = 0.975); and the lowest was Vietnamese and Indonesian value sets (ICC = 0.913).

Table 3. Utility scores calculated using the value sets of Vietnam, Thailand, Malaysia, Indonesia

Value set	Mean*± SD	Median	Min	Max
Vietnam	0.863 ± 0.142	0.915	0.105	1.000
Thailand	0.904 ± 0.125	0.944	0.114	1.000
Malaysia	0.867 ± 0.143	0.919	0.054	1.000
Indonesia	0.881 ± 0.117	0.914	0.347	1.000

Note: Wilcoxon signed rank test between Vietnam and Thailand/Malaysia: P < 0.001; Vietnam and Indonesia: P = 0.097.

Table 4. Intraclass correlation coefficient of EQ-5D utility scores between Vietnam and Thailand/ Malaysia/Indonesia

Value set	ICC
Thailand	0.975*

Value set	ICC
Malaysia	0.992*
Indonesia	0.913*

*Note: ICC: intraclass correlation coefficient; *p < 0.005*

3.4. Sociodemographic and clinical Factors Associated to EQ-5D Mean Scores

The study showed that the data of utility scores derived from the four value sets were not normally distributed, so the study applied the Spearman's test to analyze the correlation of factors affecting the utility scores from the Vietnamese, Thai, Malaysian and Indonesian value sets. After performing Spearman's test for the factors with 95% confidence intervals, the study obtained results in Table 5.

According to Table 5, the study recorded the factors of education level, monthly income, disease stage and comorbidities affected utility scores from the four value sets. All the regression models showed a statistically significant association between EQ-5D index scores and education level ($r_{Vietnam}$ = 0.133; $r_{Thailand}$ = 0.151; $r_{Malaysia}$ = 0.135; $r_{Indonesia}$ = 0.119), monthly income ($r_{Vietnam}$ = 0.181; $r_{Thailand}$ = 0.196; $r_{Malaysia}$ = 0.186; r_{Japan} = 0.165), disease stage ($r_{Vietnam}$ = -0,111; $r_{Thailand}$ = -0.110; $r_{Malaysia}$= -0,111; $r_{Indonesia}$ = -0.107) , comorbidities ($r_{Vietnam}$ = -0.160; $r_{Thailand}$ = -0.152; $r_{Malaysia}$ = -0.155; $r_{Indonesia}$= -0.165): EQ-5D index scores increased when education level, monthly income increased; EQ-5D index scores increased when disease stage, comorbidities decreased. The age factor ($r_{Thailand}$ = -0.124; $r_{Malaysia}$ = -0.114; $r_{Indonesia}$ = -0.126) affected the utility scores of three countries Thailand, Malaysia, Indonesia with negative correlation. The factor of metastasis only affected utility score from Indonesian value set with negative correlation (r = -0.116). Despite the significant association between EQ-5D index scores and education level, monthly income, disease stage, and comorbidities, the overall strength of the association was weak, as indicated by the relatively low correlation coefficients (r<0.02).

Table 5. Correlation between patient's characteristics and utility scores from four value sets

Characteristics	Correlation coefficients			
	Vietnam	Thailand	Malaysia	Indonesia
Age	-0.103	-0.124*	-0.114*	-0.126*
Education level	0.133*	0.151*	0.135*	0.119*
Monthly income	0.181*	0.196*	0.186*	0.165*
Degree of metastasis	-0.097	-0.091	-0.095	-0.116*
Disease stage	-0.111*	-0.110*	-0.111*	-0.107*
Comorbidities	-0.160*	-0.152*	-0.155*	-0.165*

**p < 0.005*

3.5. Linear regression

After selecting the variables to be included in the model, the study recorded linear regression models from Vietnamese, Thai, Malaysian and Indonesian value sets. The results were presented in Table 6.

According to Table 6, the study found that the forecasting model of EQ-5D VAS utility score base on EQ-5D-5L utility score from the Vietnamese value set had the highest R square (R^2 = 0.231), followed by the Malaysian value set with R^2 = 0.204, the Thai value set with R^2 = 0.191 and the Indonesian value set with the lowest R^2 value of 0.161.

Table 6. EQ-5D VAS utility score regression results

Dependent variable	Independent variable	Unstandardized Coefficients	Constant	R^2	P - value
EQ-5D VAS	Vietnam	47.334	37.892	0.231	<0.001
	Age	-0.201			
	Thailand	50.579	32.915	0.191	<0.001
	Age	-0.199			
	Malaysia	46.093	38.546	0.204	<0.001
	Age	-0.197			
	Indonesia	48.74	35.725	0.161	<0.001
	Age	-0.002			

4. DISCUSSIONS

The study compared the EQ-5D value set between Vietnam and Southeast Asia countries (Thailand, Malaysia, Indonesia) using a sample of breast cancer patients being treated at six hospitals: Bach Mai Hospital, Oncology Hospital Hanoi, Da Nang Oncology Hospital, Ho Chi Minh City Oncology Hospital, Cho Ray Hospital and K Hospital. The ratings for the EQ-5D-5L health states were obtained through patient interviews and utility scores were calculated using the Vietnamese, Malaysian, Thai and Indonesian value sets.

Except for Vietnam and Indonesia, the study found a statistically significant difference in patient utility scores between Vietnam and Thailand/Malaysia. As a result, it's clear that employing different value sets will result in different utility ratings, which will have an impact on the HTA study's conclusions, notably the cost-effectiveness analysis. This disparity can be explained by the use of diverse approaches by countries in constructing value sets, as well as the economic and cultural situations of each country [8]. The mean utility scores from the four value sets were nearly identical, with the Thai value set having the highest utility scores because the coefficients of all aspects were lower than those of the other countries, and the Vietnamese value set having the lowest utility scores because the coefficients of the dimensions were higher than those of the other three countries [4-7]. The study also showed that the utility scores from the four value sets had high consistency, the results from Dwi Endarti's study gave similar results when comparing the EQ-5D-3L value set of Thailand, Malaysia, and Singapore in Indonesian patients [9]. The greater the education and income level, the higher the utility scores from the four value groups, according to the study's findings. Patients with a higher income would have the financial capability and understanding to obtain better therapies, better living situations, less anxiety, and greater peace of mind. Jilia Roick (2019) found that income was a predictor of quality of life in cancer patients, with patients with low income having lower physical, emotional, and functional roles [10]. In all value sets, the disease stage and comorbidities were inversely connected with utility scores, which was consistent with Dwi Endarti's findings when comparing EQ-5D-3L utility scores [9]. In general, the influence of factors on utility scores from four value sets was quite similar, however, there were some factor differences. Age factor was negatively correlated with utility scores from other value sets except the Vietnamese value set while the degree of metastasis was only negatively correlated with the utility scores from the Indonesian value set. A linear regression model predicted EQ-5D-VAS scores in Vietnamese HER2-positive breast cancer patients. Among the four value sets evaluated, the Vietnamese value set demonstrated the highest R^2 value of 0.231, indicating the most suitable fit for this patient population. The study suggests that the Malaysian value set is the second-best option to be applied for the following reasons: the

mean utility scores of the two value sets were equivalent (Vietnam: 0.863 ± 0.142; Malaysia: 0.867 ± 0.143), the ICC of the Malaysian value set compared to Vietnamese value set reached the highest value, the factors affecting the utility scores from the two value sets had many similarities; the EQ-5D VAS utility score prediction model had the second highest R square (only after the model of the Vietnamese value set).

This study is the first in Vietnam to compare the EQ-5D-5L value set between Vietnam and other countries in Southeast Asia. The study provides an objective view of the four value sets, helps experts make the choice to apply the value set to better evaluate the HTA study. The study has certain limitations that should be considered. Firstly, the focus on HER2-positive breast cancer patients may limit the generalizability of the results to other types of breast cancer or to broader populations of cancer patients. The specific clinical characteristics and treatment responses of HER2-positive patients may not fully represent the experiences and needs of those with other breast cancer subtypes. Additionally, the study sample was relatively small, and the patients included may not be representative of the entire population of patients with this diagnosis.

5. CONCLUSION

The study offers an objective analysis of the value sets from Vietnam, Thailand, Malaysia, and Indonesia, providing valuable insights for experts in selecting appropriate value sets for a more accurate evaluation of HTA studies concerning breast cancer patients. The findings indicate a high overall correlation and consistency among the four value sets, with the Vietnamese and Malaysian value sets showing the strongest correlation. Among these, the Vietnamese value set is the most suitable, while the Malaysian value set is considered the second-best option for application in HER2-positive breast cancer patients in Vietnam. However, due to these countries' demographic, cultural, and economic differences, careful consideration is necessary when applying these value sets.

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So sánh các bộ giá trị EQ-5D-5L Việt Nam, Malaysia, Thái Lan và Indonesia sử dụng mẫu bệnh nhân ung thư vú HER2 dương tính tại Việt Nam

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TÓM TẮT

Mục tiêu: Bộ giá trị của Việt Nam được công bố vào năm 2019, tuy nhiên đến nay chưa có đánh giá so sánh nào giữa bộ giá trị của Việt Nam và các bộ giá trị khác. Nghiên cứu này nhằm so sánh các bộ giá trị của Việt Nam, Malaysia, Thái Lan và Indonesia, đồng thời đánh giá sự phù hợp của bộ giá trị Việt Nam đối với người Việt. Phương pháp: Một nghiên cứu cắt ngang được thực hiện trên 338 bệnh nhân ung thư vú HER2 dương tính đang điều trị tại 6 bệnh viện ở Việt Nam. Dữ liệu được thu thập từ tháng 7 đến tháng 12 năm 2019. Các trạng thái sức khỏe EQ-5D-5L được thu thập thông qua các cuộc phỏng vấn với bệnh nhân và điểm tiện ích được tính toán sử dụng các bộ giá trị của Việt Nam, Malaysia, Thái Lan và Indonesia. Sự khác biệt trong giá trị trung bình của 4 bộ giá trị được xác minh bằng phép kiểm định Wilcoxon và sự nhất quán giữa các bộ giá trị được đánh giá bằng hệ số tương quan nội bộ (ICCs). Phép kiểm định Spearman được sử dụng để đánh giá mối tương quan giữa các đặc điểm nhân khẩu học của bệnh nhân với điểm EQ-5D (khoảng tin cậy 95%). Kết quả: Nghiên cứu được thực hiện trên 338 bệnh nhân với độ tuổi trung bình là 53,870 ± 9,970 và cân nặng trung bình là 54,589 ± 7,698 kg. Bộ giá trị của Thái Lan có điểm tiện ích trung bình cao nhất (0,904 ± 0,142), tiếp theo là bộ giá trị của Indonesia (0,881 ± 0,117), bộ giá trị của Malaysia (0,867 ± 0,143) và bộ giá trị của Việt Nam có điểm tiện ích trung bình thấp nhất (0,863 ± 0,142). Có sự nhất quán rất cao giữa các bộ giá trị (hệ số tương quan nội bộ > 0,9). Mô hình dự báo điểm tiện ích EQ-5D VAS dựa trên điểm tiện ích EQ-5D-5L từ bộ giá trị của Việt Nam có R bình phương cao nhất (R2 = 0,231). Kết luận: Các bộ giá trị của Việt Nam, Malaysia, Thái Lan và Indonesia có mức độ tương quan và nhất quán cao, trong đó tương quan giữa bộ giá trị của Việt Nam và Malaysia là cao nhất. Bộ giá trị của Việt Nam là phù hợp nhất cho người bệnh ung thư vú HER2 dương tính ở Việt Nam, bộ giá trị của Malaysia là lựa chọn thay thế tốt thứ hai có thể áp dụng.

Từ khóa: *ung thư vú HER2 dương tính, EQ-5D-5L, so sánh bộ giá trị*

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