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Cost-Utility Analysis of Erythropoietin for Anemia Treatment in Thai End-Stage Renal Disease Patients with Hemodialysis

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ABSTRACT

Objective: To compare the cost utility of using erythropoietin (EPO) to maintain different hemoglobin (Hb) target levels in hemodialysis patients from a societal perspective. **Methods:** A Markov model was used to estimate the incremental cost and quality-adjusted life-year of five Hb levels: 9 or less, more than 9 to 10, more than 10 to 11, more than 11 to 12, and more than 12 g/dl. A systematic review of EPO treatment in hemodialysis patients was conducted to estimate transitional probabilities. Cost data were estimated on the basis of the reference price of Siriraj Hospital, the largest university hospital in Thailand. Utility scores were derived from the six-dimensional health state short form (derived from short-form 36 health survey), which were collected from 152 hemodialysis patients receiving EPO at Siriraj hospital. Probabilistic sensitivity analysis was conducted to investigate the effect of uncertain parameters. All future costs and outcomes were discounted at the rate of 3% per annum. **Results:** The incremental cost-effectiveness ratios of Hb levels more than 9 to 10, more than 10 to 11, more than 11 to 12, and more than 12 g/dl compared with the least costly option (Hb $\leq$ 9 g/dl) were US $24,128.03, US $18,789.07, US $22,427.36, and US $28,022.33 per quality-adjusted life-year, respectively. From probabilistic sensitivity analysis, the hemoglobin level of more than 10 to 11 g/dl was appropriate when the willingness to pay was US $15,523.88 to US $46,610.17 and the probability of cost-effective was 29.32% to 95.94%. **Conclusions:** Providing EPO for a hemoglobin level of more than 10 to 11 g/dl had a cost-effectiveness higher than that of doing so for other hemoglobin levels. This finding will be put forward to the policy level to set up the EPO treatment guideline of the hospital for hemodialysis patients.

Keywords: cost-utility analysis, end-stage renal disease, erythropoietin, hemodialysis, Markov model.

Introduction

Twenty-five years have passed since the first patient received recombinant human erythropoietin (EPO) in Seattle in November 1985 [1,2]. EPO is effective in reversing anemia of renal failure and all its diverse consequences. A reduction in hemoglobin (Hb) levels in these patients has been shown to be associated with impairment in quality of life (QOL), reduced energy, neurocognitive decline, decreased exercise capacity, and increased mortality [3–6]. The cause of anemia in the patients is mainly related to a deficiency in the synthesis of endogenous EPO [7]. Therefore, the use of recombinant human EPO represents a logical and commonly used treatment for this disorder. EPO has been shown to improve QOL, exercise capacity, cognitive function, and sleep disturbances and ameliorate left ventricular hypertrophy, which is a major contributor to cardiac mortality and morbidity in patients with end-stage renal disease (ESRD) [8–13]. Most patients receiving hemodialysis (HD) for ESRD currently receive EPO for anemia treatment. Anemia from EPO deficiency is a common complication of chronic kidney disease (CKD). It can be treated with EPO administration, red blood cell transfusion, or a combination of both [14]. But the widely accepted use in patients with anemia is EPO administration. Early studies found that EPO reduced the need for transfusions and improved the QOL in patients with CKD, when compared with not using EPO [15,16]. EPO is routinely used to treat anemia of CKD, especially in patients who need dialysis. The goal of therapy is to achieve specific Hb target levels. Higher doses of EPO, however, are being used to attain higher target levels without evidence of corresponding clinical benefit and possibly resulting in harm. It is remarkable that the three largest studies and a meta-analysis, involving 3268 subjects, have had a very consistent outcome, a 21% to 48% increased risk for mortality in the higher Hb target group, which in each study nearly reached statistical significance [11,17–19]. The Food and Drug Administration in the United States suggests that increasing the hemoglobin level to more

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than 12 g/dl may be associated with increased morbidity and mortality and that the benefits of these drugs have not been well documented and this would imply that the Food and Drug Administration asserts an Hb target level of only 10 g/dl because this level is far from the range of demonstrated risk [20] while the cost consequences of using EPO to achieve higher Hb targets is increasing. In 2007, the Food and Drug Administration ruled that minimization of blood transfusions and low red blood cell levels were the predominant indications for EPO in anemic patients with CKD; regarding low red blood cell levels, the recommendation of Hb levels is 10 to 12 g/dl [21]. Nowadays, target Hb levels in CKD remain uncertain because Hb target levels above 13 g/dl have been associated with both benefit (QOL) and harm (cardiovascular events) [22]. Many HD patients receive EPO for their anemia as a part of routine therapy. Because EPO is an expensive therapy, it has created an economic burden onto the health care system of every country including a developing country such as Thailand. The purpose of this study was to evaluate the cost-effectiveness of EPO use for different target Hb levels at the resources of a developing country.

Methods

A Markov model was constructed to estimate the incremental costs and QALY gains associated with EPO treatment for maintaining Hb levels of more than 9 to 10, more than 10 to 11, more than 11 to 12, and more than 12 g/dl compared with 9 g/dl or less. The study adopted a societal perspective. The results were presented in terms of incremental costs (US $), incremental quality-adjusted life-years (QALYs) gained, and incremental cost-effectiveness ratio (ICER). The HD patients may be alive with a cardiovascular (CV) event or a noncardiovascular (nCV) event such as catheter-related infections and then they have a chance of dying from a CV event (death from the CV state) or an nCV event (death from the nCV state). So, the Markov model was viewed as four states: dead from CV, dead from nCV, alive with HD, and alive with hemodialysis and cardiovascular disease (HDCV), as shown in Figure 1. The four health states were defined by the solid line ovals and occurred in each Hb level (five Hb levels such as ≤9, >9–10, >10–11, >11–12, and >12 g/dl). A fixed 1-year cycle length was assigned. The time horizon of the analysis was the lifetime of the patient.

In this Markov model, we classified HD patients into two groups: 1) the patients who were alive with HD (the HD state) and 2) the patients who were alive with HDCV treatment (the HDCV state). When the HD state's patients moved to the HDCV state (arrow no. 1), they could not move back to the HD state because they would be treated CV forever. The HD state's patients, however, stayed in the HD state if no event occurred (dotted-line arrow no. 2) or if they successfully completed the nCV treatment (arrow no. 3). When the nCV treatment was not successful, they moved to the state of death from the nCV event (arrow no. 4). The HDCV patients stayed in the HDCV state when no event occurred (dotted-line arrow no. 5) or they successfully completed the nCV treatment (arrow no. 6). When the nCV or CV treatment was not successful, they moved to the state of death from the nCV event (arrow no. 7) or the CV event (arrow no. 8). It was assumed that once the patients have HD or HDCV, they would continue to hemodialyse until dead (absorbing health state). Costs and QALYs gained were calculated as patients went through the model. The moving of any state was assumed to be independent of their moving Hb level. The movement between each state was determined by probabilities that were obtained from randomized controlled trials (RCTs) and systematic reviews.

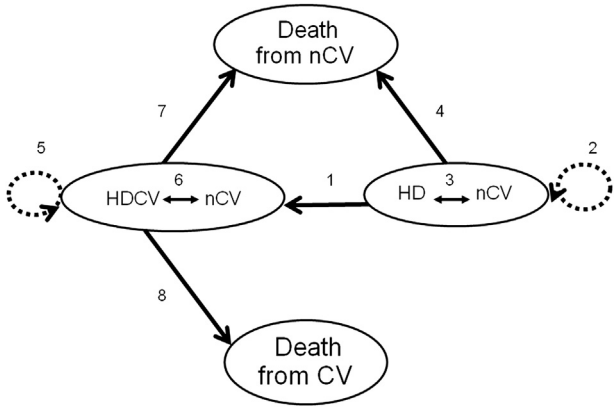

Fig. 1 – Schematic representation of Markov model. CV, cardiovascular; nCV, noncardiovascular; HD, hemodialysis; HDCV, hemodialysis and cardiovascular disease.

Transitional Probability Data

Transitional probabilities used in this study were obtained mainly from systematic review of the literature using the PubMed database, the National Coordinating Centre for Health Technology Assessment, the Cochrane library, and the ClinicalTrials.gov Web site. Search dates were between January 1, 1966, and December 31, 2009. All searches included the keywords and corresponding MeSH terms for erythropoietin, kidney disease, renal disease, hemodialysis, randomized controlled trial (RCTs), meta-analysis, and practice guideline. These studies included the studies of efficacy of EPO (e.g., erythropoietin beta, and alfa); the methodology of the studies was RCTs, meta-analysis of RCTs, which assessed the effects of targeting different Hb concentrations when treating patients with anemia caused by CKD with EPO, and the targeted patients were older than 18 years. These studies excluded nonrandomized trials or RCTs that were evaluating other interventions such as subcutaneous versus intravenous EPO treatment for anemia of CKD; outcomes such as blood viscosity and hematopoietic progenitor cell assays were reported.

We identified 277 potentially eligible articles, 204 of which were excluded because these were not RCTs. Seventy-three RCTs consisted of 22 studies that assessed the dose and route of administration, 15 hematological and hemodynamic effects studies, and 21 other intervention studies, that is, nutritional supplement. Thirteen RCTs and 2 meta-analyses of RCTs of EPO in CKD were full articles but only 4 RCTs [11,12,23,24] met the specified inclusion criteria. These studies were conducted in Canada and Europe. There was no study conducted in Thailand or Asia. From the clinical trial, we derived the compound mortality rate and then we calculated the disease-specific mortality rate using the following formula:

$$\mu_C = \mu_D + \mu_{ASR}$$

where μ_D is the disease-specific excess mortality rate (fixed rate), μ_C is the compound mortality rate derived from the study in the literature, and μ_{ASR} is the age-, sex-, race-adjusted mortality rate.

$$\mu_{ASR} = 1/LE_{ASR}$$

where LE_{ASR} (ASR is the age-, sex-, race-adjusted life expectancy) is the life expectancy of the Thai general population classified by age group (derived from Life Table of Vital Statistics Thailand 2006 [25]).

When we knew the mortality rate for different ages, we converted the rate to probability (P), assuming that an event occurs at a constant rate (r) over a time period between time zero to sometime beyond, such as the time period between the first year and the fifth year is 4 (t):

$$P = 1\text{–}e^{-\text{rate}}$$

Utility Parameter

Utility in this study used the six-dimensional health state short form (calculated from the short-form 36 survey) (SF-6D) and derived from the previous study during November-December 2009 with 152 HD patients (22 HD patients with a history of a CV event and 130 HD patients without a history of a CV event) at Siriraj Hospital where the patients come from throughout Thailand [26]. From the short-form 36 survey score in the previous study, the SF-6D utility was calculated by applying the scoring method that was also derived from UK preference scores by using the computer algorithm [27] because preference weights of the SF-6D for Thai people were not available.

QALY Calculation

QALYs were calculated as the number of additional years of life gained from an intervention multiplied by a utility judgment of the QOL. The QALYs gained can be calculated using the probabilities to determine the mean, variance, and probability distribution for the QALYs gained. It was carried out using TreeAgePro 2009 (TreeAge Software, Inc., Williamstown, MA).

Cost Parameter

Direct medical costs were estimated on the basis of the reference price of the hospital. The treatment costs incurred at the inpatient department were estimated on the basis of the actual treatment costs of HD, CV event including myocardial infarction, stroke, heart failure, or revascularization (percutaneous transluminal coronary angioplasty or coronary-artery bypass grafting) resulting in hospitalization for 24 hours or more or prolongation of hospitalization, and nCV events including other events except the CV event resulting in hospitalization for 24 hours or more or prolongation of hospitalization. The events were classified by using the *International Statistical Classification of Diseases, Tenth Revision*, in 2009 and the event costs such as CV, nCV events that occurred in HD patients were calculated using the average cost method. Direct nonmedical costs (e.g., food cost, traveling costs, and accommodation costs for patients and their caregivers) were derived from structured questionnaire interviews from 152 patients receiving HD between November and December 2009. Indirect nonmedical cost such as income lost as a result of sick leave or hospital visits was calculated by multiplying the minimum wage in 2010 (US $6.35 per day) with the length of stay from the sick leave or providing informal care (days). Mortality costs were excluded to avoid double counting because health outcomes such as QALYs had already taken into account the effects of mortality [28].

Annual EPO costs were derived from the unit cost of EPO multiplied by the amount of use per year. The unit cost of EPO was calculated from the average unit cost of EPO, that is, the reference price of multiple brands at the largest university hospital in Thailand in 2010 (unit cost = US $0.010). For this model, EPO was given when the Hb level start at 8 g/dl. The EPO dose was calculated by using the following formula:

$$D = 2400\ \text{IU}/\sqrt{[9.6/(\text{Hb}_{SS}-\text{Hb}_0)]-1}$$

The dose per time (D) was expected to increase the Hb level from a pretreatment level (Hb_0) to a desired steady state level (Hb_{SS}) when given intravenously three times per week [29].

Sensitivity Analysis

Probabilistic sensitivity analysis was performed by using Monte-Carlo simulation. Monte-Carlo simulation was used by involving random sampling of each variable under the specified probability distribution within the model to produce more than 1000 iterations. All input parameters were assigned probability

Table 1 – Mean and standard error (SE) of transitional probability parameters.

Parameter	Parameter distribution	Mean	SE	Source
P(t) among HD (no CV) patients received EPO				
P(t) of adverse event	Beta	0.798	0.004	[12]
P(t) of CV event	Beta	0.110	0.026	[12]
P(t) of nCV event	Beta	0.890	0.006	[12]
P(t) of CV event and dying (all Hb levels)	Beta	0.030	0.029	[12]
P(t) of CV event and still alive (all Hb levels)	Beta	0.970	0.002	[12]
P(t) of no adverse event (all Hb levels)	Beta	0.202	0.070	[12]
P(t) of dying from nCV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.027	0.025	[11–13]
P(t) of alive after having nCV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.973	0.001	[12]
P(t) of dying from CV event (only Hb > 12 g/dl)	Beta	0.135	0.024	[12]
P(t) of alive after having CV event (only Hb > 12 g/dl)	Beta	0.865	0.024	[12]
P(t) among HDCV patients received EPO				
P(t) of adverse event	Beta	0.397	0.009	[6]
P(t) of no adverse event	Beta	0.603	0.022	[6]
P(t) of CV event	Beta	0.132	0.021	[6]
P(t) of dying from CV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.080	0.023	[6]
P(t) of alive after having CV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.920	0.005	[6]
P(t) of nCV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.868	0.009	[6]
P(t) of dying from nCV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.033	0.025	[6]
P(t) of alive after having nCV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.967	0.002	[6]
P(t) of dying from CV event (only Hb > 12 g/dl)	Beta	0.090	0.023	[6]
P(t) of alive after having CV event (only Hb > 12 g/dl)	Beta	0.910	0.005	[6]
P(t) of dying from nCV event (only Hb > 12 g/dl)	Beta	0.049	0.024	[6]
P(t) of alive after having nCV event (all Hb levels, except Hb > 12 g/dl)	Beta	0.951	0.002	[6]

CV, cardiovascular; EPO, erythropoietin; Hb, hemoglobin; HD, hemodialysis; HDCV, hemodialysis and cardiovascular disease; nCV, noncardiovascular.

Table 2 – Mean and standard error (SE) of utility parameter.

Target hemoglobin	Parameter distribution	Mean	SE
HDCV patient with hemoglobin level (g/dl)			
≤9	Beta	0.633	0.030
>9–10	Beta	0.667	0.029
>10–11	Beta	0.709	0.018
>11–12	Beta	0.724	0.022
>12	Beta	0.754	0.020
HD (no CV) patient with hemoglobin level (g/dl)			
≤9	Beta	0.680	0.032
>9–10	Beta	0.716	0.031
>10–11	Beta	0.761	0.020
>11–12	Beta	0.777	0.024
>12	Beta	0.809	0.022

CV, cardiovascular event; HDCV, hemodialysis and cardiovascular disease.

distributions according to their feature to reflect the feasible range of values that each input parameter could attain. All cost parameters were assigned to use gamma distribution and the probability and utility parameters, which were bounded zero-one, used beta distribution.

Discounting

All future costs and future outcomes were discounted at the rate of 3% per annum.

Results

Transitional Probability Data

Transitional probability parameters are shown in Table 1.

Utility Data

We found that the average utility score of HD patients treated to Hb levels of less than 9, more than 9 to 10, more than 10 to 11, more than 11 to 12, and more than 12 g/dl was 0.672 ± 0.161, 0.709 ± 0.132, 0.753 ± 0.124, 0.769 ± 0.139, and 0.801 ± 0.122, respectively. The utility scores of SF-6D were significantly different across Hb levels ($P = 0.005$). This model assumed that the utility scores of HDCV patients were lower by 5.9% when compared with all HD patients and lower by 6.9% when compared with HD (no CV) patients [26]. Thus, the utility scores of five group levels were examined for cost-utility analysis, as shown in Table 2.

Cost Data

The cost parameters in the model are shown in Table 3. For intercountry comparisons, cost parameters were converted to US $ using the purchasing power parity exchange rate of US $1 = 32.45 (April 2010) Thai baht.

Cost-Effectiveness Analysis

Total cost of the least costly option (Hb ≤ 9 g/dl) was US $136,113.25 for 7.39 QALYs. The incremental costs of patients with an Hb level of 9 g/dl or less compared with more than 9 to 10 g/dl, more than 10 to 11 g/dl, more than 11 to 12 g/dl, and more than 12 g/dl were US $8,686.09, US $15,978.36, US $23,324.45, and US $30,264.12, respectively, while the incremental QALYs gained were 0.36, 0.85, 1.04, and 1.08, respectively. The ICER of Hb levels more than 9 to 10, more than 10 to 11, more than 11 to 12, and more than 12 g/dl compared with the least costly option (Hb ≤ 9 g/dl) was US $24,128.03, US $18,789.07, US $22,427.36, and US $28,022.33 per QALY, respectively. The minimum ICER was the ICER of Hb level more than 10 to 11 g/dl. Hb level of more than 10 to 11 g/dl appeared more cost-effective than other Hb levels. When the ICER was calculated from all incremental costs and QALYs, it was confirmed that Hb level of more than 10 to 11 g/dl was still the cost-effective option, as shown in Table 4. (The ICER of patients at Hb level of more than 10 to 11 g/dl when compared with Hb level of more than 9 to 10 g/dl was US $14,882.19 per QALY.)

Probabilistic Sensitivity Analysis

The results of the probabilistic sensitivity analysis were presented in terms of cost-effectiveness acceptability curves, as

Table 3 – Mean and standard error (SE) of annual cost parameters.

Parameter	Parameter distribution	Mean	SE
Cost of EPO (US $) to maintain Hb level (g/dl)			
8–9 (1,711.75 units per week)	Gamma	890.11	92.66
9–10 (3,157.17 units per week)	Gamma	1,641.73	60.99
10–11 (4,337.64 units per week)	Gamma	2,255.57	57.80
11–12 (5,529.26 units per week)	Gamma	2,875.22	61.61
>12 (7,659.19 units per week)	Gamma	3,982.78	110.99
Cost of HD (US $)	Gamma	8,286.43	128.48
Cost for HD patient (US $)			
CV treatment but finally dead	Gamma	8,116.25	1,547.09
CV treatment and alive	Gamma	5,348.94	464.03
nCV treatment but finally dead	Gamma	9,711.18	1,152.35
nCV treatment and alive	Gamma	2,606.05	170.98
Cost for HDCV patient (US $)			
CV treatment but finally dead	Gamma	10,129.31	2,296.16
CV treatment and alive	Gamma	5,657.02	832.19
nCV treatment but finally dead	Gamma	6,787.27	1,891.40
nCV treatment and alive	Gamma	5,016.22	526.45
Cost of direct nonmedical cost for treatment (US $)			
CV event (per time)	Gamma	443.41	93.17
nCV event (per time)	Gamma	421.85	88.64
Length of stay when admits for treating (d)			
nCV event	Gamma	15.65	0.877
CV event	Gamma	16.45	1.53
Income loss from CV event leave (US $)	Gamma	107.92	107.92
Income loss from nCV event leave (US $)	Gamma	101.57	101.57

CV, cardiovascular event; EPO, erythropoietin; Hb, hemoglobin; HD, hemodialysis; HDCV, hemodialysis and cardiovascular disease; nCV, noncardiovascular event.

Table 4 – Cost-effectiveness results obtained from the analysis.

Comparator strategies	Incremental cost (US $)	Incremental QALY (QALY)	ICER (US $/QALY)
All incremental relative to the lowest cost option (Hb ≤ 9 g/dl)			
>9–10 g/dl vs. ≤9 g/dl	8,686.09	0.36	24,128.03
>10–11 g/dl vs. ≤9 g/dl	15,978.36	0.85	18,789.07
>11–12 g/dl vs. ≤9 g/dl	23,324.45	1.04	22,427.36
>12 g/dl vs. ≤9 g/dl	30,264.12	1.08	28,022.33
All incremental relative to the next Hb level			
>9–10 g/dl vs. ≤9 g/dl	8,686.09	0.36	24,128.03
>10–11 g/dl vs. >9–10 g/dl	7,292.27	0.49	14,882.19
>11–12 g/dl vs. >10–11 g/dl	7,346.08	0.19	38,663.60
>12 g/dl vs. >11-–12 g/dl	6,939.67	0.04	173,491.76

Hb, hemoglobin; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

shown in Figure 2. Providing EPO for patients with an Hb level of more than 9 to 10 g/dl was appropriate when the willingness to pay (WTP) was less than US $15,523.88, while the Hb level of more than 10 to 11 g/dl was the optimal choice if the WTP was between US $15,523.88 and US $46,610.17 and the probability of being cost-effective was between 29.32% and 95.94%.

Discussion

Higher Hb levels yielded higher QALYs and higher cost of EPO; thus, the optimal strategy should be considered from the lowest ICER. When the initial Hb level of an HD patient was less than 9 g/dl, providing EPO for the Hb level of more than 10 to 11 g/dl was less costly at a higher effectiveness than doing so for other Hb levels. Practicing an EPO treatment target Hb level of more than 10 to 11 g/dl yielded an incremental cost per QALY of about US $18,789.07. In 2009, Thai gross domestic product (GDP) per capita was US $4,162.50 [30]. The World Health Organization recommended the ICER per QALY gained of medical interventions below one time of GDP per capita as maximum cost-effective, between 1 and 3 times of GDP per capita as cost-effective, and more than 3 times of GDP per capita as not cost-effective [31]. These implied a ceiling threshold of US $12,327 per QALY in Thailand. As per the above results and based on the recommendations, all strategies were considered cost-ineffective. The results of this study clearly indicated that the lowest ICER was for the Hb level of more than 10 to 11 g/dl while the highest ICER was for the Hb level of more than 12 g/dl on comparing each Hb level with Hb levels of 9 g/dl or less. These findings supported the need to allocate the available resources to cover more people with an Hb level of more than 10 to 11 g/dl for anemia treatment and improve their QOL. The results of this evaluation indicated that providing EPO for an Hb level of more than 12 g/dl was associated with unfavorable cost-effectiveness ratios based on the societal perspective of a developing country such as Thailand. In sensitivity analysis, the level of more than 9 to 10 g/dl was appropriate when the WTP was less than US $15,523.88 while the Hb level of more than 10 to 11 g/dl was the optimal choice if the WTP was between US $15,523.88 and US $46,610.17 and the probability of being cost-effective was between 29.32% and 95.94%.

The findings of this study have shown that if policymakers were willing to pay at US $12,327 (3 times of GDP per capita in Thailand) per QALY gained, providing EPO for anemia treatment for all Hb levels may be deemed a cost-ineffective strategy for all HD patients but practicing an EPO treatment target Hb level of more than 10 to 11 g/dl yielded minimum incremental cost per QALY. Although the Hb level of 11 to 12 g/dl was the recommendation for anemia treatment in many guidelines, providing EPO for patients with an Hb level of more than 11 to 12 g/dl was considered less cost-effective than providing EPO for patients with an Hb level of more than 10 to 11 g/dl in a developing

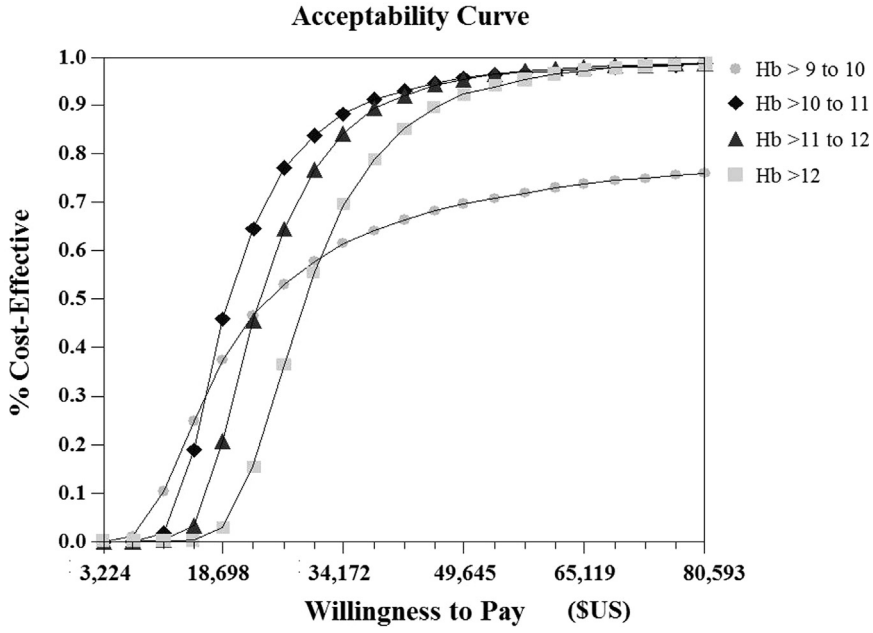

Fig. 2 – Cost-effectiveness acceptability curve of the different Hb levels compared with the Hb levels <9 g/dl. Hb, hemoglobin.

country such as Thailand. The Hb level of more than 12 g/dl was the least cost-effective option when compared with other Hb levels.

Limitations of the Study

This study had no information on some epidemiological parameters such as the mortality rate of a CV event in HDCV or HD patients that related to the Hb level studies in Thailand. For this study, it was derived from RCTs or systematic review. There were only four RCTs related to these events among HD patients of other countries, which might be different from the Thai race. The sensitivity analysis, however, was performed to ensure the quality of the assessment and to produce a more realistic interval on the study's conclusions. The EPO dose of each Hb level was defined from the formula [29] that was the nearest practice for the approximation of the EPO dose in real practice. It was assumed that people with different CV risks or other characteristics would receive a fixed dose for each Hb level target. Titration to a higher or lower dose of EPO, however, might be found in realistic clinical practice. Disease treatment costs per annum of a CV event and an nCV event were calculated by the summation of service quantities received multiplied by its average cost. Quantities of service and the average cost received were derived from realistic data in HD patients of Siriraj Hospital but whether these can be generalized to other settings needs to be considered. The SF-6D utility was calculated by applying the scoring method that was derived from a UK preference score (Thai preference score was not available), which might be different from that for the Thai race, but the sensitivity analysis was performed to ensure the quality of the assessment. The utility score, however, was estimated; further study should be done in longitudinal data.

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