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COST-EFFECTIVENESS ANALYSIS OF ANEMIA TREATMENT AMONG CHRONIC KIDNEY DISEASE PATIENTS AT KIEN GIANG GENERAL HOSPITAL

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ABSTRACT

Background: *Anemia due to chronic kidney disease (CKD) is a dangerous complication that causes a burden on the patients and society. However, it can be treated with erythropoietin (EPO). There is a lack of studies evaluating the cost-effectiveness of EPO in Vietnam in treating anemic complications, leading to difficulties in decision-making in terms of prescriptions.*

Objectives: *This studied was undertaken to explore the incremental cost-effectiveness ratio (ICER) of EPO in maintaining different Hb levels when treating anemia in hemodialysis patients due to end-stage CKD at Kien Giang General Hospital, Vietnam, in 2017.*

Methods: *Cost-effectiveness analysis (CEA) was performed based on the decision tree and Markov models. The cost and quality-of-life data was collected via face-to-face interviews using the KDQOL-SF questionnaire. The probability coefficients of the model were sought systemically from the randomised clinical trials.*

Results: *The ICERs indicated that there were no interventions that were cost-effective in relation to gross domestic product (GDP) of Vietnam. However, patients with the target Hb level of >10-11 g/dL were inferred to receive the most benefit from the treatment, as indicated by the corresponding lowest ICER.*

Conclusion: *The findings of this study should be proposed to policy decision makers to set up guidelines for appropriate and cost-effective use of EPO in hospitals in Vietnam.*

Keywords: *CEA, Chronic kidney disease, CKD, Incremental cost-effectiveness ratio, ICER.*

INTRODUCTION

Chronic kidney disease (CKD) is structural or renal dysfunction that lasts more than three months and affects the health of the patients.[1, 2] In more serious cases, CKD involves numerous complications, of which anemia is one of the most common complications and has higher morbidity and mortality rates.[3] Anemia is seen in 43% of patients with stages 1–2 CKD and in 57% of patients with stages 3–5,[4] causing dangerous symptoms, such as visceral bleeding and adverse cardiovascular effects. For every 1 g/dL Hb decrease (in the range of 9–13 g/dL), the risk of death increases three times. 634/5000. Anemia in patients with chronic renal failure is a consequence of decreased red blood cell production and decreased red blood cell life. Additional factors that cause anemia in patients with chronic renal failure include blood loss, hemolysis due to poisoning (in some cases of kidney disease, it is found that complementary activity occurs on red blood cells causing destruction of red blood cells), spleen, malnutrition, lack of hematopoietic factors, bone marrow toxicity, and bone marrow fibrosis. Reduced production of erythrocytes is due to EPO reduction, which is a major cause of anemia in patients with chronic renal failure. Blood deficiency causes increased mortality, increased left ventricular hypertrophy and congestive heart failure, and accelerated progression to end-stage renal failure.[5] Normally, an EPO concentration of 3–30 mU/mL, increases 100 times when Hb drops. This inverse relationship decreases or disappears when MLCT <30–40 mL/p. Some mechanisms that cause relative EPO deficiency include: i) decreased renal adaptation that reduces oxygen consumption, improves oxidative damage in the medulla, and stimulates EPO production; ii) EPO neutralised by soluble EPO receptors (increased production in the presence of intermediates); and iii) EPO inactivated by proteinases (increased activity in high blood urea environment). Even if an adequate amount of EPO reaches intact bone marrow, its activity can still be impaired by the absence of permissible factors (IL-3, calcitriol) and the presence of inhibitory factors (PTH). By 2015, CKD occupied the twelfth position among the leading fatal diseases. In Asia, where 60% of the global population lives, CKD prevalence is reported at one of the highest rates in the world, but knowledge of CKD epidemiology remains limited. In Vietnam, there has been no national scale study on the incidence of CKD; existing research mainly involves the results of epidemiological reports of a specific province or region. According to statistics released during the Artificial Kidneys and Quality in Dialysis Conference in 2009, in Vietnam there are about six million people with CKD, accounting for 6.73% of the population.[6]

Cost-effectiveness analysis (CEA) is a comprehensive, high-value method of economic evaluation to be used in the decision-making process. This method may indicate that medical intervention should be considered if it offers more benefits with lower costs or costs equivalent to a reference intervention. The incremental cost-effectiveness ratio (ICER) is a characteristic indicator of this method, wherein the lower the ICER, the more cost-effective the intervention. The advantage of CEA is that it does not require conversion of health outcomes into monetary units, which is a major difficulty in the analysis of health economy.[7, 8] Given the limited number of studies in Vietnam related to cost-effectiveness, and based on disease patterns at Kien Giang General Hospital, this study was conducted to calculate the ICER of EPO to maintain different target hemoglobin (Hb) levels when treating anemia in dialysis patients with CKD at Kien Giang General Hospital in 2017.

MATERIALS AND METHODS

Study design

This study was designed as a cost-effective analysis. This study used two types of models: the decision tree model (Figure 1) and the Markov model (Figure 2). The process is described in Figure 3.

Study location

Kien Giang is a southern province in Vietnam. Kien Giang General Hospital has 900 beds and is responsible for the health care and medical treatment of the people in the province, which has a population of 1.4 million people. The hospital has 820 permanent staff members, including 200 officials and physicians with university and postgraduate qualifications (including 158 doctors) in various specialties. The hospital has medical equipment that is considered relatively complete and modern. The hospital has already implemented 100% of the techniques of the provincial hospitals and more than 90% of the technical level at the central level. High-level techniques have been implemented, including open-heart surgery, cardiovascular interventions, radiotherapy, vascular microsurgery, knee replacement surgery, gastrointestinal surgery, thyroid surgery, obstetrics, replacement of primary blood at birth, super dialysis emergency, partial blood cell separation, biological testing, and immunology.

Study subjects

All patients at Kien Giang General Hospital met the selection and exclusion criteria and criteria.

Selection criteria: i) Diagnosed with CKD according to the N18 international classification code (ICD–10) and being treated with dialysis; ii) Diagnosed with anemia with an ICD-10 code of D63.1 and has been treated with EPO or was assigned to be treated with EPO during the sampling period.

Exclusion criteria: i) Under 18 years of age; ii) Had an appointed blood transfusion within six months of starting EPO treatment; iii) Changed dialysis method; iv) Treatment of anemia changed; v) Had received organ transplant, chemotherapy, or surgery, or had anemia for reasons other than CKD; vi) Was transferred to another facility, left the facility, or did not follow the treatment regimen; vii) Could not answer interview questions or refused to participate in the study.

Model structure

The CEA model was used to compare lifetime costs and health outcomes of HD patients who used EPO for anemia treatment at different Hb levels. Assessment of the health economic model was performed, and input parameters were obtained by systematic reviews of the literature on the clinical and cost-effectiveness of EPO in HD patients.

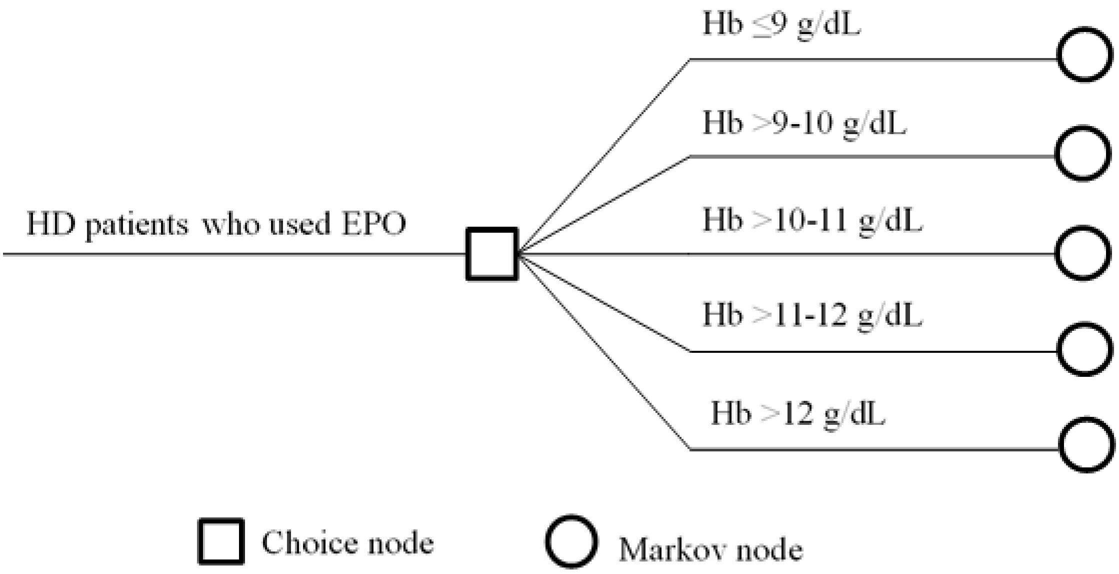
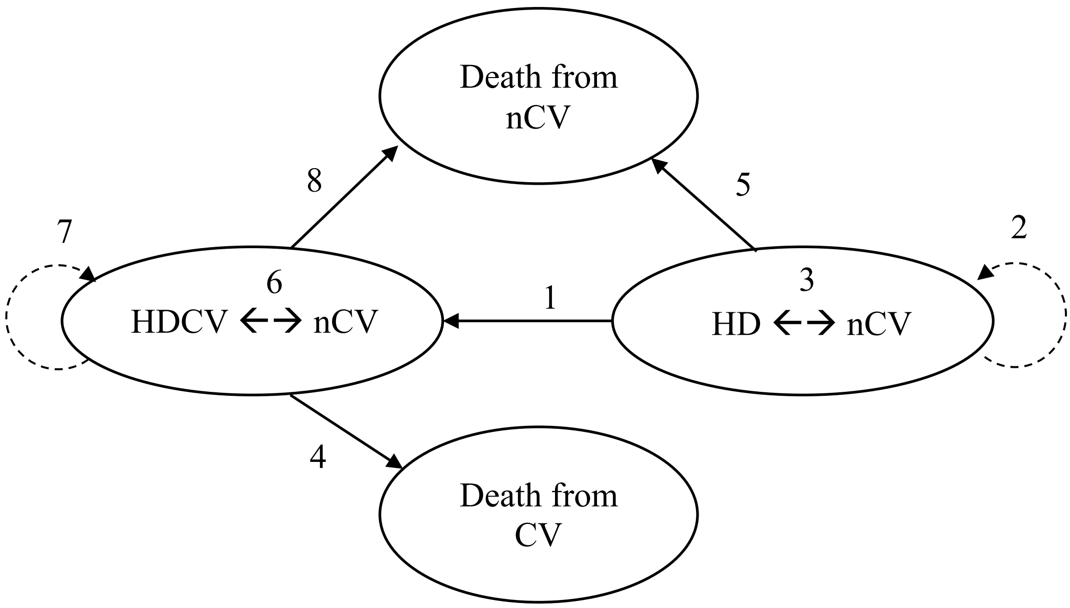


Fig 1: Decision tree model



In Figure 2, the arrows represent the frequency of switching between conditions the patient may have. Hemodialysis frequency can be maintained during the course of the procedure (arrow 2), but once switched to hemodialysis with cardiovascular disease (arrow 1), it is impossible to return to dialysis. The majority of CVD (arrow 7) is because chronic and requires lifelong treatment. If CVD treatment is fails, the patient will likely die of cardiovascular disease (arrow 4). Hemodialysis and hemodialysis with cardiovascular disease can be treated with extra non-cardiovascular diseases (non-CVD). If the non-CVD treatment is successful, the patient can return to dialysis (arrow 3) or dialysis with cardiovascular disease (arrow 6). If the non-CVD treatment is not successful, the patient will likely die of non-cardiovascular disease (arrows 5 and 8).

Fig 2: Markov model

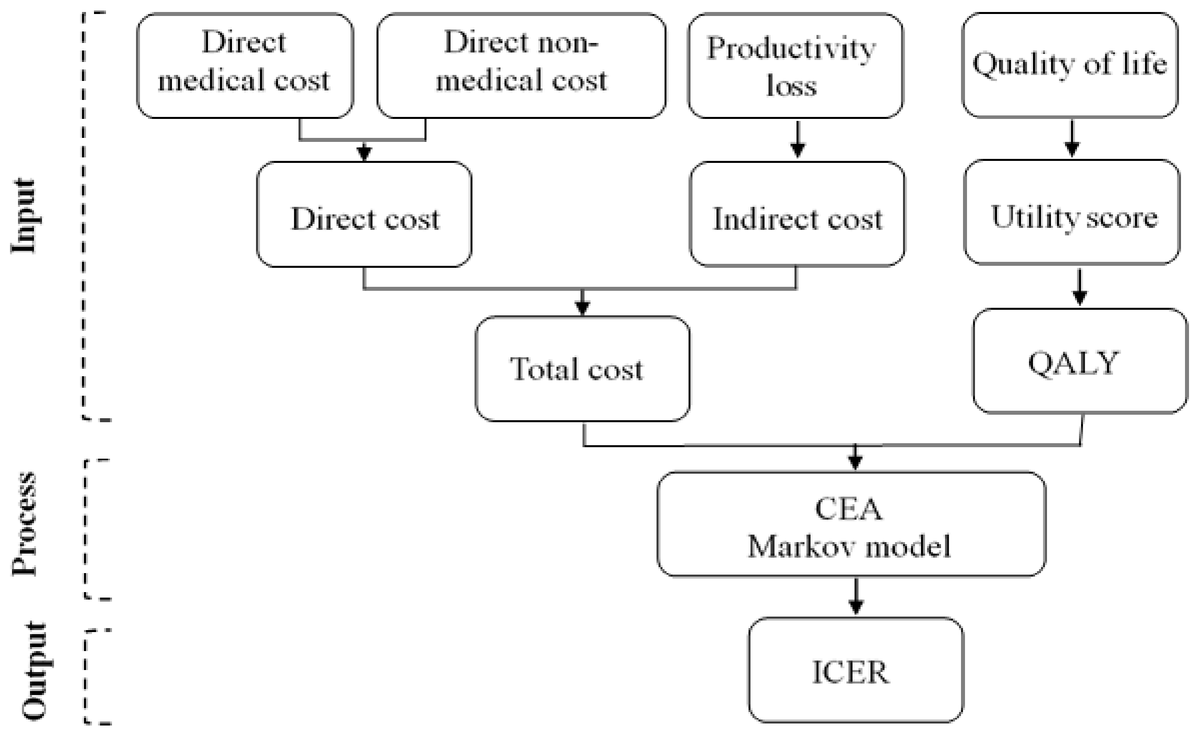


Fig 3: Process of cost-effectiveness analysis

All switching frequencies used in the Markov model were screened from randomised controlled trials (RCT) through a literature review (Table 1). Assuming the patient will undergo dialysis until the end of life, the model is designed for one year of treatment. After one year, the patient's condition is re-evaluated and the model is repeated in a circular pattern until the patient dies.

Data analysis

Input data included cost and quality of life (QoL). Cost data was collected through medical records, medical bills, and interviews with patients. Data on QoL was collected through interviews using a revised and reliable KDQOL-SF questionnaire. Microsoft Excel 2016 and SPSS 20.0 software were used to calculate the ICER index. The ICER index was calculated by the ICER = $(C_y - C_x)/(E_y - E_x)$ formula according to two aspects: comparing EPO cost-effectiveness between Hb>9 levels and Hb≤9 and comparing between low Hb and higher consecutive Hb, where y>x. Cost when treating with EPO with the goal of Hb x was represented by C_x; C_y represented cost when treating with EPO with the goal of Hb medical; E_x represented the effect (QALY) when treating with EPO with the goal of Hb x; E_y represented the effect (QALY) when treating with EPO with the goal of Hb y. After being calculated, the ICER ratio was compared to the gross domestic income (GDP) to assess the cost-effectiveness of the treatment. Specifically, if ICER<GDP, the medical intervention was considered absolutely cost-effective, if ICER was between one and three times GDP, the health intervention was considered relatively cost-effective, and if ICER was three times or higher than GDP, the intervention was not considered cost-effective. According to the General Statistics Office of Vietnam, Vietnam's GDP in 2017 was 50,792,040 VND.

Table 1: Probabilities used for Markov models extracted from RCTs

Probabilities	Object	Mean	SD
Cardiovascular events in dialysis patients when using EPO	All Hb levels	0.110	0.026
Cardiovascular events in dialysis people when using EPO (live)	All Hb levels	0.970	0.002
Cardiovascular events in dialysis people when using EPO (death)	All Hb levels	0.030	0.029
Cardiovascular events in dialysis patients with CVD when using EPO	All Hb levels	0.132	0.021
Cardiovascular events in dialysis patients with CVD when using EPO (live)	All Hb levels, except Hb> 12	0.920	0.005
	Hb>12	0.910	0.005
Cardiovascular events in dialysis patients with CVD when using EPO (death)	All Hb levels, except Hb> 12	0.080	0.023
	Hb>12	0.090	0.023
Non-CVD in dialysis patients when using EPO	All Hb levels	0.890	0.006
Non-CVD in dialysis patients when using EPO (live)	All Hb levels, except Hb> 12	0.973	0.001
	Hb>12	0.772	0.004
Non-CVD in dialysis patients when using EPO (death)	All Hb levels, except Hb> 12	0.027	0.025
	Hb>12	0.031	0.014
Non-CVD in dialysis patients with CVD when using EPO	All Hb levels, except Hb> 12	0.868	0.009
	Hb>12	0.752	0.003
Non-CVD in dialysis patients with CVD when using EPO (live)	All Hb levels, except Hb> 12	0.967	0.002
	Hb>12	0.951	0.002

Non-CVD in dialysis patients with CVD when using EPO (death)	All Hb levels, except Hb> 12	0.033	0.025
	Hb>12	0.049	0.024

RESULTS

Demographic characteristics

The average age of the 304 patients in the study was 57.32±14.52. Most of were female patients (52.60%), married (58.55%), and suffered from hypertension (76.97%). On average, patients had undergone dialysis for 7.66±4.87 years, in which the number of dialysis patients in one week accounted for a higher rate (58.55%). Research on biochemical indicators showed that the average albumin concentration was 3.96±0.37 g/dL, the average creatinine concentration was 11.21±5.49 mg/dL, and the average BUN index was 69.37±16.77 mg/dL.

Cost-effective analysis

Treatment *costs*

Research showed that the higher the Hb target, the higher the cost of EPO used in the early stages of treatment. Specifically, the cost increased from 3,645,003 VND to 379,450 VND for the target of Hb 8-9 g/dL to 16,309,474±454,508 VND for the target of Hb>12 g/dL. In terms of direct medical costs, for patients without cardiovascular history, the average cost of treating cardiovascular events was 128–195 million VND/year and the average cost of treating of non-CVD was 62–233 million VND/year. For patients with cardiovascular history, the average cost of treating cardiovascular events was 135–243 VND million/year and the average cost of treating non-CVD was 120–162 million VND/year. The average direct out-of-medical cost when hospitalised for cardiovascular events was about 10.6 million VND/year; when the patients were hospitalised for cardiovascular events the cost was about 10.1 million VND/year. The average indirect cost due to cardiovascular events was about 2.6 million VND/year, and the average indirect cost due to cardiovascular disease was about 2.4 million VND/year.

Quality of life and utility scores

Table 2: Utility scores of included cases

Mức Hb mục tiêu (g/dL)	HDCV (n=44)	HDnCV (n=260)
≤ 9 (n=52)	0,633 ± 0,030	0,680 ± 0,032
> 9-10 (n=36)	0,633 ± 0,030	0,680 ± 0,032
> 10-11 (n=80)	0,709 ± 0,018	0,761 ± 0,020
> 11-12 (n=70)	0,724 ± 0,022	0,777 ± 0,024
>12 (n=66)	***0,754 ± 0,020***	***0,809 ± 0,022***
Tổng	0,700 ± 0,140	0,760 ± 0,140
	0,740 ± 0,140	

For general QoL scores (SF-36), patients answered 36 questions in the questionnaire. The results showed that there was only a difference in ‘mental health’ among groups of patients. The average ‘physical health’ score was 43.4±13.7, and the average ‘general health’ score was 67.3±20.4.

For kidney disease–related quality of life scores, patients answered 43 detailed questions related to kidney disease; the results showed only differences in ‘the effect of kidney disease on daily life.’ The highest QoL score was related to ‘social interaction’ with an average QoL score of 86.6±14.9.

Regarding the other factors affecting QoL, the study showed the no difference in QoL scores among groups of patients. Specifically, the average ‘social support’ score was 87.8±19.5, the ‘encouragement from health workers’ average was 88.2±18.3, and score for ‘satisfaction of patients’ was an average of 76.0±20.3.

Utility points were calculated based on the SF-6D toolkit. The results showed that the average utility score among 44 dialysis patients who had a history of CVD was 0.700±0.140, which was not significantly different from the group without CVD history (0.760±0.140). The group of patients with target Hb>12 g/dL had the highest utility score, with 0.754±0.020 (cardiovascular history) and 0.809±0.022 (no cardiovascular history).

ICER index

Table 3: ICER index comparing cost-effectiveness between Hb> 9 levels with Hb≤9 level

Target Hb level (g/dL)	Cost (VND)	Effectiveness (QALY)	Incrementalc osts (VND)	Incremental efficiency (QALY)	ICER (VND/QALY)
≤9	3,268,487,574	7.39	-	-	-
>9-10	3,477,066,638	7.75	208,579,064	0.36	579,386,289
>10-11	3,652,176,020	8.24	383,688,446	0.85	451,398,172
>11-12	3,828,577,516	8.43	560,089,942	1.04	538,548,021
>12	3,995,219,818	8.47	726,732,244	1.08	672,900,226

Table 4: ICER index comparing cost-effectiveness between low Hb level and consecutive higher Hb level

Target Hb level (g/dL)	Cost (VND)	Effectiveness (QALY)	Incrementalc osts (VND)	Incremental efficiency (QALY)	ICER (VND/QALY)
≤9	3,268,487,574	7.39	-	-	-
>9-10	3,477,066,638	7.75	208,579,064	0.36	579,386,289
>10-11	3,652,176,020	8.24	175,109,382	0.49	357,366,086
>11-12	3,828,577,516	8.43	176,401,496	0.19	928,428,926
>12	3,995,219,818	8.47	166,642,302	0.04	4,166,057,550

The ICER index was calculated according to two aspects: between Hb>9 levels with Hb≤9 (Table 3) and between Hb levels with lower and higher consecutive Hb levels (Table 4). For cost-effectiveness between Hb levels>9 with Hb≤9 and a QALY unit increase, the cost was an additional 673 million VND. The highest cost-effective Hb level (lowest ICER) was Hb>10–11 g/dL for about 451 million VND/QALY. For cost-effectiveness between low Hb with higher consecutive Hb, the target Hb>10–11 g/dL had the highest cost-effectiveness (lowest ICER) with a 357 million VND/QALY increase compared to Hb>9–10 g/dL. Compared to the Hb group>11–12 g/dL, the Hb group>12 g/dL was very cost effective, up to about 4.2 billion VND for each QALY increase.

DISCUSSION

This study conducted a cost-effective analysis of the use of EPO to treat anemia in dialysis patients due to end-stage CKD. Most dialysis patients with end-stage renal disease experience anemia and EPO designation. However, the results of this study indicate that there was no real evidence at Kien Giang General Hospital that the use of EPO in patients with end-stage renal disease was cost-effective. Specifically, when comparing ICER with Vietnam's GDP in 2017 (50,792,040 VND/person), all eight ICER indexes calculated were more than three times the GDP (152,376,120 VND). This showed that the treatment of EPO anemia in dialysis was a burden in terms of cost for Kien Giang General Hospital in particular, as well as for society in general. This results also helped provide the hospital with a basis for advising the Department of Health and the Provincial People's Committee on the issue of additional funding for public hospitals with dialysis. Thereby, it was revealed that it is necessary to orient some district hospitals in Kien Giang province to establish kidney dialysis in the context of the hospital's revenues as increasingly narrow and the state's obligation to implement financial autonomy.

When comparing ICER between different target Hb levels, we found that ICER of the target Hb level>10–11 g/dL always had the highest cost-effectiveness (lowest ICER). The target level of Hb>12 g/dL recorded the highest QALY index with 8.47 points. However, compared to the adjacent lower Hb level of >11–12 g/dL, this figure did not increase significantly (only 0.04). Despite a modest increase in the QALY index, the cost for treatment with target Hb>12 g/dL was more than Hb>11–12 g/dL to 167 million VND. This led to a tremendous increase in the ICER index between these two goals (4.2 billion VND for 1 QALY increase). Even when comparing Hb target>12 g/dL with target Hb<9 g/dL, patients had to pay up to 727 million VND only to get 1.08 QALY points. Meanwhile, with an increase in QALY of 1.04 points compared to Hb<9 g/dL, patients only needed to pay an additional 560 million VND to achieve Hb>11–12 g/dL.

Based on a review of the literature, the study recorded ICER calculations in hemodialysis patients treated with EPO. The research in Thailand conducted in 2014 on the same subject as this research at Kien Giang General Hospital was the only comparable study. The ICER index of this study was similar to that in Vietnam.[9] Research in the United States in 2015 noted that when treated with EPO, patients spent 751,397,400 VND to achieve one year of quality life compared to the target of 10.0 g/dL. The target Hb 10.5 g/dL was more cost-effective with ICER = 759,915,000 VND/QALY.[10] Also in 2015, a study in Morocco that compared the cost-effectiveness between CERA EPO type with a long-acting one-time-use CERA three times per week showed that the conversion from the effect type should be considered short- to long-acting with a level of 151,105,500 VND for one year of quality life.[11] A 2016 study in Egypt conducted a cost-effective analysis between the use of Darberythropoietin Alfa and Erythropoietin Alfa, resulting in lower treatment costs with Darberythropoietin Alfa but more effective treatment with Erythropoietin Alfa therapy.[12]

This study also noted certain limitations that need to be overcome. This study used the frequency shift indicated in RCTs in the literature review. However, the data in the literature was collected in countries outside Vietnam, so may not be suitable for the ethnic characteristics of the Vietnamese people. This study was performed only on the inpatient population; nevertheless, outpatients also contributed to the burden of the disease not included in this study. The output is the ICER index compared with GDP. This was a basic comparison, but the comparison will be much more meaningful if based on the willingness to pay (WTP) of a patient with CKD instead of GDP. WTP more accurately reflects the ability of patients to pay to improve CLCS. Therefore, it is necessary to investigate the payment threshold of kidney patients in the territory of Vietnam for the treatment of chronic kidney disease as well as complications of CKD in order to achieve a closer basis for the comparison of cost-effectiveness.

CONCLUSIONS

No EPO medical intervention was cost-effective when compared to Vietnam's GDP in 2017. Target Hb level >10–11 g/dL had the lowest ICER score with the highest cost-effectiveness. The results of this study provide important information for policy activists in drafting guidelines for treatment using EPO in hospitals and for providing appropriate co-payment limits for medical insurance for the use of EPO in treating anemia in BTM.

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CONFLICTS OF INTERESTS

The authors have no conflicts of interests to declare.

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