การวิเคราะห์ต้นทุนอรรถประโยชน์ของการใช้ยาอิริโธรโพอิทินเพื่อรักษาภาวะโลหิตจาง ในผู้ป่วยที่ได้รับการ ฟอกไต ณ โรงพยาบาลศิริราช

นางสาว ฐนิตา ทวีธรรมเจริญ

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาเภสัชศาสตร์สังคมและบริหาร ภาควิชาเภสัชศาสตร์สังคมและบริหาร
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COST UTILITY ANALYSIS OF ERYTHROPOIETIN FOR ANEMIA TREATMENT IN HEMODIALYSIS PATIENTS AT SIRIRAJ HOSPITAL

Miss Tanita Thaweethamcharoen

A Dissertation Submitted in Partial Fulfillment of the Requirements
for the Degree of Doctor of Science Program in Social and Administrative Pharmacy
Department of Social and Administrative Pharmacy
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By	Miss Tanita Thaweethamcharoen
Field of Study	Social and Administrative Pharmacy (International Program)
Thesis Advisor	Assistant Professor Rungpetch Sakulbumrungsil, Ph.D.
Thesis Co-Advisor	Somkiat Vasuvattakul, M.D.

Accepted by the Faculty of Pharmaceutical sciences, Chulalongkorn University in Partial Fulfillment of the Requirements for the Doctoral Degree

..... Dean of the Faculty of Pharmaceutical sciences
(Associate Professor Pintip Pongpech, Ph.D.)

THESIS COMMITTEE

..... Chairman
(Associate Professor Vithaya Kulsomboon, Ph.D.)

..... Thesis Advisor
(Assistant Professor Rungpetch Sakulbumrungsil, Ph.D.)

..... Thesis Co-Advisor
(Somkiat Vasuvattakul, M.D.)

..... Examiner
(Assistant Professor Tanattha Kittisopee, Ph.D.)

..... Examiner
(Assistant Professor Phantipa Sakthong, Ph.D.)

..... External Examiner
(Associate Professor Cherdchai Nopmaneejumruslers, M.D.)

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วัตถุประสงค์ของการศึกษานี้เพื่อประเมินต้นทุนอรรถประโยชน์ของการใช้ยาอิริโธรโพอิทินเพื่อรักษาภาวะโลหิตจางจนได้ระดับฮีโมโกลบินที่แตกต่างกันในผู้ป่วยที่ต้องฟอกเลือดด้วยเครื่องไตเทียม ตัวแปรที่สำคัญในการวิเคราะห์ต้นทุนอรรถประโยชน์ประกอบด้วย 2 ตัวแปรคือต้นทุนและค่าอรรถประโยชน์ของผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมที่ได้รับยาอิริโธรโพอิทิน ทำการสัมภาษณ์แบบตัวต่อตัวโดยใช้แบบสอบถาม KDQOL-SF™ ฉบับภาษาไทย เวอร์ชัน 1.3 (ประกอบด้วย SF-36 และคำถามเกี่ยวกับโรคไต) และแบบสอบถาม EQ-5D ในผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมจำนวน 152 คน ระหว่างเดือนพฤศจิกายนถึงธันวาคม พ.ศ.2552 ค่าเฉลี่ยของค่าอรรถประโยชน์จากเครื่องมือ SF-6D คือ 0.748±0.139 ซึ่งมีค่าสูงกว่าค่าอรรถประโยชน์จาก EQ-5D (0.704±0.341) และ VAS (0.684±0.191) อย่างมีนัยสำคัญ ค่าสัมประสิทธิ์สหสัมพันธ์ (เพียร์สัน) ระหว่างค่าอรรถประโยชน์และค่าคะแนนของแบบสอบถามเฉพาะด้านโรคไตแสดงให้เห็นความสัมพันธ์ที่ดีระหว่างค่าอรรถประโยชน์จากทั้งสามเครื่องมือและคะแนนของคำถามมิติเกี่ยวกับอาการแสดงต่าง ๆ แต่มีความสัมพันธ์ที่ค่อนข้างต่ำกับคะแนนของมิติคำถามเกี่ยวกับภาระจากการเป็นโรคไตและมิติคำถามเกี่ยวกับผลกระทบจากโรคไต เครื่องมือ SF-6D ยังให้ค่าอรรถประโยชน์ที่มีความสอดคล้องกับค่าการวัดเกี่ยวกับโรคไตได้ดีกว่า EQ-5D และ VAS นอกจากนั้นค่าอรรถประโยชน์จาก SF-6D โดยเฉลี่ยของผู้ป่วยที่มีระดับฮีโมโกลบินที่แตกต่างกันจะมีค่าอรรถประโยชน์ที่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p=0.005$) ในขณะที่ค่าอรรถประโยชน์โดยเฉลี่ยจาก EQ-5D และ VAS ของผู้ป่วยที่มีระดับฮีโมโกลบินที่แตกต่างกันไม่ได้ให้ค่าอรรถประโยชน์ที่แตกต่างกันอย่างมีนัยสำคัญ จากผลการทดสอบดังกล่าวแสดงให้เห็นว่า SF-6D เป็นเครื่องมือวัดค่าอรรถประโยชน์เดียวที่สามารถสะท้อนถึงคุณภาพชีวิตทางสุขภาพของผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมและควรใช้เป็นตัวแปรในการวิเคราะห์ต้นทุนอรรถประโยชน์ต่อไป สำหรับค่าตัวแปรอื่นๆ เช่น transitional probability ได้จากการทบทวนวรรณกรรมอย่างเป็นระบบและการวิเคราะห์เชิงอภิมานซึ่งพบว่าการใช้ยาอิริโทรพัวอิตินเพื่อให้ระดับฮีโมโกลบินที่แตกต่างกันไม่ได้เพิ่มอัตราการตายจากภาวะโรคหัวใจหรือจากภาวะอื่นๆ ในผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียม แต่พบว่ามีผลเพิ่มอัตราการตายจากภาวะโรคหัวใจในผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมซึ่งมีภาวะโรคหัวใจอยู่แล้ว ค่าตัวแปรด้านต้นทุนได้แก่ต้นทุนทางตรงทางการแพทย์สามารถคำนวณได้จากอัตราค่าบริการ และราคายาอ้างอิงจากโรงพยาบาล ศิริราช ตัวแปรต้นทุนทางตรงที่ไม่ใช่ทางการแพทย์ได้จากการสัมภาษณ์โดยใช้แบบสอบถาม หลังจากได้ตัวแปรต่างๆ แล้ว จึงใช้แบบจำลองมาร์คอฟเพื่อหาค่าต้นทุนและปีชีวิตที่มีคุณภาพหรือปีสุขภาวะที่เพิ่มขึ้นจากการใช้ยาอิริโธรโพอิทิน เพื่อเพิ่มระดับฮีโมโกลบินจาก ≤9 กรัมต่อเดซิลิตร เป็น >9-10, >10-11, >11-12, และ >12 กรัมต่อเดซิลิตร ทั้งในมุมมองของโรงพยาบาลและมุมมองเชิงสังคมและมีการใช้อัตราปรับลดร้อยละ 3 ต่อปี เมื่อมีการใช้ยาอิริโธรโพอิทินเพื่อให้ระดับฮีโมโกลบินเพิ่มขึ้นจากน้อยกว่า 9 กรัมต่อเดซิลิตร เป็นระดับ >10-11 กรัมต่อเดซิลิตร จะมีต้นทุนส่วนเพิ่มน้อยที่สุดต่อปีสุขภาวะ ทั้งในมุมมองของโรงพยาบาลและของสังคมคือ คือ 492,808.59 และ 609,997.53 บาทต่อปีสุขภาวะ ทำการวิเคราะห์ความไม่แน่นอนโดยใช้ความน่าจะเป็นของตัวแปรที่เกี่ยวข้องกับต้นทุนและประสิทธิผลพบว่าระดับฮีโมโกลบิน >10-11 กรัมต่อเดซิลิตร จะเป็นระดับที่เหมาะสมเมื่อความเต็มใจที่จะจ่ายเป็น 420,000-1,285,000 บาท และ 503,750-1,512,500 บาท โดยมีโอกาสที่จะมีความคุ้มค่าเป็น 31.43-96.17%, และ 29.32-95.94% ในมุมมองของโรงพยาบาลและของสังคมตามลำดับ ผลการศึกษาดังกล่าวจะเป็นข้อมูลที่ช่วยในการพิจารณากำหนดนโยบายและเกณฑ์ในการสั่งใช้ยาและการเบิกจ่ายยาอิริโธรโพอิทินเพื่อให้เกิดการใช้ยาอย่างเหมาะสมและคุ้มค่าต่อไป

ภาควิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่อนิสิต.....

สาขาวิชา เภสัชศาสตร์สังคมและบริหาร ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก.....

ปีการศึกษา 2553 ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์ร่วม .....

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KEYWORDS : COST / UTILITY / HEMODIALYSIS / ERYTHROPOIETIN / HEMOGLOBIN

TANITA THAWEETHAMCHAROEN : COST UTILITY ANALYSIS OF ERYTHROPOIETIN FOR ANEMIA TREATMENT IN HEMODIALYSIS PATIENTS AT SIRIRAJ HOSPITAL. THESIS ADVISOR : ASST. PROF. RUNGPETCH SAKULBUMRUNGSIL, Ph.D., THESIS CO-ADVISOR : SOMKIAT VASUVATTAKUL, M.D. 134 pp.

The purpose of this study was to evaluate the cost utility analysis of EPO for maintaining the different hemoglobin target levels in anemic hemodialysis patients in routine clinical practice. In cost utility analysis (CUA), there were two important variables involved: cost and utility of HD patients using erythropoietin (EPO). Face-to-face interview using KDQOL-SF (SF-36 and kidney disease specific questionnaire) and EQ-5D was conducted during November-December 2009 with 152 hemodialysis patients. The mean SF-6D score was 0.748±0.139 showing significantly higher than EQ-5D (0.704±0.341), and VAS (0.684±0.191) scores. Pearson's correlation coefficients between utility scores with kidney disease specific questionnaires illustrated that all three utility scores were correlated well with the symptoms and problems dimension, but had low association with the burden and effects of kidney disease on daily life dimension. The SF-6D presented better agreement with kidney specific scales than EQ-5D and VAS. The average utility scores of SF-6D were significantly different across Hb levels (ANOVA, $p=0.005$) while other utility scores were not significant different ($p>0.05$). These findings implied that SF-6D could, to a certain extent, reflect HRQoL status of hemodialysis patients and might be used as the input parameter in the analysis. Another input parameter was transitional probabilities that were obtained mainly from a systematic review and meta-analysis. The data showed that using EPO for maintaining the different Hb levels did not indicate a significant effect on increasing cardiovascular (CV) events or CV mortality rate in HD patients without the history of CV events but showed a significant effect on increasing CV mortality rate in HD patients with CV history. The direct medical cost was estimated based on the reference price of the Siriraj hospital and direct non-medical costs were from the structured questionnaire interviews. After derived all input parameters, the Markov model was used to estimate the incremental cost and Quality Adjusted Life Year (QALY) associated with EPO treatment for maintaining hemoglobin levels of >9-10, >10-11, >11-12, and >12 g/dl, comparing with ≤9 g/dl and adopting both the hospital and the societal perspectives. All future costs and outcomes were discounted at the rate of 3% per annum. When providing EPO to raise the Hb level up to >10 to 11 g/dl, up from the initial Hb of less than 9 g/dl, yields the minimum incremental cost per QALY in the hospital and societal perspective about 492,808.59 and 609,997.53 Baht per QALY, respectively. From PSA, Hb level >10 to 11 g/dl was the optimal choice at the willingness to pay (WTP) at 420,000-1,285,000 and 503,750-1,512,500 Baht with the probability of cost effective was 31.43-96.17%, and 29.32-95.94% for the hospital and the societal perspectives, respectively. The findings should be proposed to policy decision makers to set up the guideline for appropriate and cost-effective use of EPO in the hospital as well as to establish the reimbursement criteria for EPO use at the national level.

Academic Year : 2010 Co-Advisor's Signature Somkiat

Department : Social and Administrative Pharmacy Student's Signature Tanita

Field of Study : Social and Administrative Pharmacy Advisor's Signature

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CHAPTER I

INTRODUCTION

Rationale

Anemia is a common clinical problem in patients with chronic kidney disease (CKD) and is associated with increased morbidity and mortality in these patients. Anemia treatment can be managed by either blood transfusion or erythropoietin (EPO). EPO is a hormone synthesized in the kidney responsible for red blood cell maturation in the bone marrow. It is deficient in the majority of patients with advanced kidney disease thereby predisposing to anemia. Several erythropoietin analogues or derivatives are now available. However, there are only a few randomized controlled trials comparing outcomes at pre-specified Hemoglobin (Hb) concentrations. Several unanswered questions remain regarding the optimal use of EPO, including the ideal target Hb level for an individual and a CKD population. The results based on observational data have supported the coincidence of normalization or optimization of Hb with the concept of increasing concentrations to a maximum, and suggested survival advantages, even though trials and meta-analyses clearly pointed in the opposite direction.

Currently a lot of efforts have been invested in developing guidelines on the basis of the strongest possible evidence to be able to justify the recommendations as well as to provide a decision tool for physicians. However, creating and updating evidence-based guidelines is extremely difficult to unity. The nephrological community has been trying to set up a single set of international guidelines under the guidance of Kidney Disease Improving Global Outcomes (KDIGO) and while awaiting the publication of the KDIGO anemia guidelines possibly in 2011.[1] In 2004, the European Dialysis and Transplant Association (EDTA) published the European Best Practice Guidelines or EBPG (at present; EBPG is changed the name to European Renal Best Practice or ERBP) for the treatment of anemia[2] and the US National Kidney Foundation published the evidence-based Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines in 2006. Both guidelines have suggested the treatment target for the anemia of chronic renal failure at hemoglobin (Hb) concentration higher than 11 g/dl (or hematocrit (HCt) at higher than 33%) while United Kingdom Renal Association (RA) have suggested the target Hb in the range 10.5-12.5 g/dl as shown in the table 1.1.[3]

Table 1.1 Summary of current renal anemia guideline.

	RA (2007)	**EBPG (2004)**	**KDOQI (2007)**
Hb, g/dl			
Male	<13	<13.5, <12[a]	<13.5
Female	<13, <12[b]	<11.5	<12
Target Hb, g/dl	10.5-12.5	>11	11-12
Maximum Hb, g/dl	unspecified	14 (HD), 12 (DM)	13 (caution)

a: If>70 yearsold, b: Pre-menopausal.

Source: Courtney AE, Maxwell AP. Critiques of clinical guidelines in nephrology: anaemia. Nephron Clin Pract 2008; 110(2): c115-25.

However, no benefit evidence of using until Hb concentration is 13 g/dl.[4] Nevertheless, the US Food and Drug Administration (FDA) changed the labelling for EPO and added a boxed warning stating that Hb targets of >12 g/dl should be avoided because of the increased risk of death and serious cardiac events, and also noted that EPO should increase Hb only to the lowest level necessary to avoid transfusion in March 2007. Nowsaday, no evidence has shown the best target level of Hb for anemia CKD patients. While it is widely accepted that the renal anemia patients should receive EPO therapy, the appropriate target Hb level is still controversial. Many chronic kidney disease patients receive recombinant human EPO for their anemia as a part of routine therapy. Since EPO is an expensive therapy, it has created economic burden onto the health care system of every country. In 2006, EPO has generated US$10 billion in sales worldwide and $2 billion in the USA from the Medicare program alone. This was increased from $1 billion in 2002[5].

In Thailand, EPO is listed in the National List of Essential Drugs (NLED) under the Jor 2 category and is covered by every health benefit scheme. The use of medicines under the Jor 2 category is subject to the predetermined criteria and requires prescribing authorization. However, any hospital that does not set up the prescribing authority is not qualified for the financial support for EPO from National Health Security Office (NHSO) or under the Universl Health Coverage (UC) scheme. The use of EPO is limited under Social Security Scheme (SSS) and can be reimbursed for 4,000 or 2,000 IU per week in patients with Hb level below 10 or 11 g/dl respectively. The Civil Servant Medical Benefit Scheme (CSMBS) is the only health scheme providing full coverage for EPO. The inequity between 3 public health schemes is inevitably experienced. While patients under CSMBS are provided under minimal cost containment policy, those under UC and SSS have no or inadequate access and if needed, they have to pay out of pocket.

Since the health care spending becomes more stringent, economic evaluation could be a useful tool to assist policy makers in making their decision on alternatives. The health resource allocation policy could then be more efficient and the inequity dilemma could, to a certain extent, be answered.

Top 10 highest expenditures for injectable drugs in 2009 of Siriraj hospital, the largest university hospital (a 2203 bed tertiary care university hospital; Bangkok) in Thailand is shown in table 1.2. Eprex® and Recormon® represent the two highest utilizations with approximately equal share.

Table 1.2 The top 10 of high injectable medicine expenditure at Siriraj Hospital in 2009

Rank	Medicine	Drug expenditure (฿)
1	Eprex®	76,643,691.00
2	Recormon®	74,364,125.00
3	Mabthera®	57,639,988.00
4	Velcade®	53,848,658.00
5	Meropenem®	45,475,890.00
6	Pegasys®	40,532,301.00
7	Gammaraas®	38,881,678.50
8	Gemzar®	37,151,355.50
9	Taxol®	31,425,696.00
10	Enantone®	30,721,290.00

Trend of Erythropoietin expenditure is increasing between 2006 and 2009 as shown as figure 1.1.

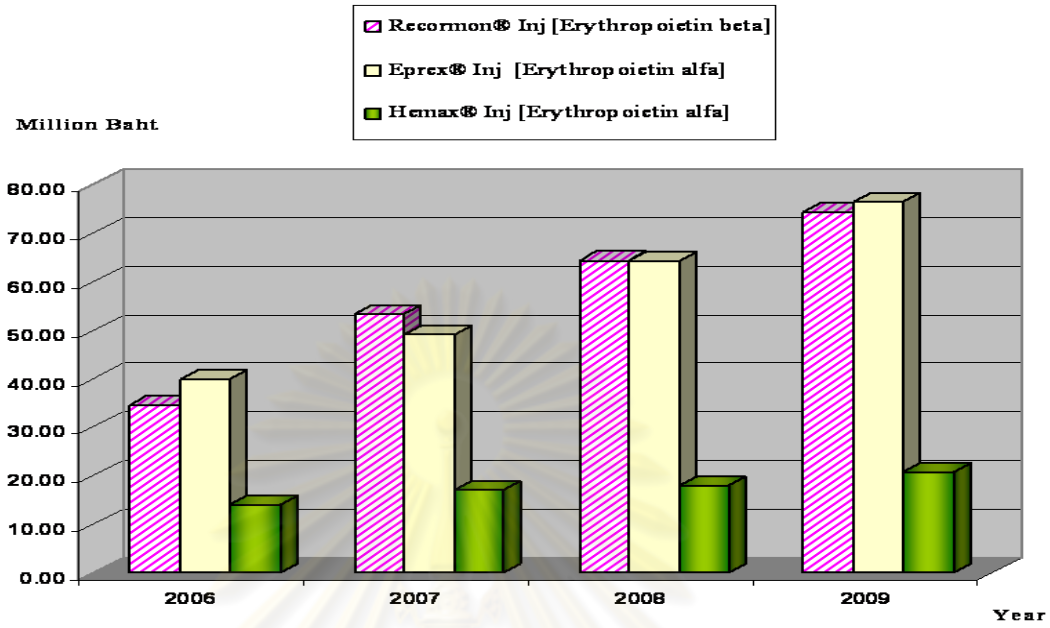

Figure 1.1 Trend of Erythropoietin expenditure (฿) at Siriraj Hospital between 2006-2009

In 2007, overall of EPO expenditure at Siriraj Hospital is 119,597,547 Baht and increased to 171,666,386 Baht in 2009 accounted for approximately 22% increase annually as shown in table 1.3.

Table 1.3 The expenditure (฿) of all Erythropoietin at Siriraj Hospital during 2007 to 2009.

Medicine	2007	2008	2009
Recormon® [Erythropoietin beta]	53,338,161.00	64,571,424.00	74,364,125.00
Eprex® [Erythropoietin alfa]	49,174,078.50	64,268,955.00	76,643,691.00
Hemax® [Erythropoietin alfa]	17,085,307.50	18,068,385.00	20,658,570.00
Total	**119,597,547.00**	**146,908,764.00**	**171,666,386.00**

Although, it is widely accepted that the renal anemia patients should receive EPO therapy, there is controversy regarding the appropriate target hemoglobin level. The problem between containing drug expenditure and managing the anemia in chronic kidney disease (CKD) is the major issue that many studies cannot agree upon the appropriate target Hb level. Thus, the decision to treat anemic chronic kidney disease patients depends on the practice guideline that physicians rely on.

In Thailand, the studies that were conducted to find the most useful target Hb have not included the cost effectiveness and/or cost utility analyses. The level at which quality of life is maximized and risk is minimized would be the optimal target. Dialysis patients carry higher risk of death than general population. Anemia is the

common complication found in dialysis patients that could lead to mortality. Risk of anemia is occurred in HD patients more than CAPD patients because blood loss is less marked and residual renal function maybe better preserved in patients who receive peritoneal dialysis. Also, in HD patients, blood is usually drawn before a dialysis session; as a result, hemoglobin is likely to be partly diluted.[6-14]

Although EPO has been included in the National List of Essential Drugs (NLED) for the treatment of anemia caused by end-stage renal disease for maintaining the target hemoglobin but the cost of EPO is so expensive. The study on cost utility analysis of using EPO for anemia treatment of end-stage renal disease would allow a decision to balance between economic burden of the government and quality of patient life. The cost utility analysis is economic technique for assessing the efficiency of healthcare intervention measuring combined outcomes as the effectiveness, i.e., survival and quality of life in combination as quality adjusted life years (QALYs). At the present, the clinicians and policy makers are recognizing the importance of health-related quality of life (HRQOL). This measure does not only reflect patient perspective it takes into consideration the holistic outcome of care provided. This is a benefit measure at the care giving level by using as a part of planning patient management program and at the policy level for decision making. QALY is the most commonly used as the utility measure. It consists of 2 parts; 1) quantity of life and 2) quality of life. The results obtained from this study will give a better view on the QALY of patients with the different Hb concentration levels. This information will be used as an input for determining the Hb concentration level that would provide the highest QALY and the incremental cost that needs to be paid per an incremental QALY when treating anemic patients from chronic kidney disease with EPO in HD patients. The results would assist in developing the guideline of anemia treatment under Thai clinical care situation.

Research Question

What is the incremental cost effectiveness ratio (ICER) of EPO in maintaining the different hemoglobin target for HD patients?

Research objective

General Objective

To study the cost utility analysis of EPO for maintaining the different hemoglobin target levels in anemic hemodialysis patients in routine clinical practice

Specific Objectives

(1) To assess the utility scores of hemodialysis patients who use erythropoietin to maintain the hemoglobin at different target levels.

(2) To evaluate the cost of erythropoietin for treating anemia in hemodialysis patients.

(3) To analyze the incremental cost-effectiveness ratio (ICER) of erythropoietin at the different hemoglobin target levels in hemodialysis patients in routine clinical practice.

(4) To assess the quality of life of hemodialysis patients who use erythropoietin to maintain the hemoglobin target level.

Expected Benefits:

(1) The utility as well as quality of life scores of hemodialysis patients who use erythropoietin to maintain the hemoglobin level will be determined and could be used as a standard for future utility study.

(2) The cost of erythropoietin for treating anemia in hemodialysis patients in Thailand will be assessed at the hospital and national levels**.**

(3) The compiled results from the study will be used to determine the targeted hemoglobin level for anemic treatment in hemodialysis patients.

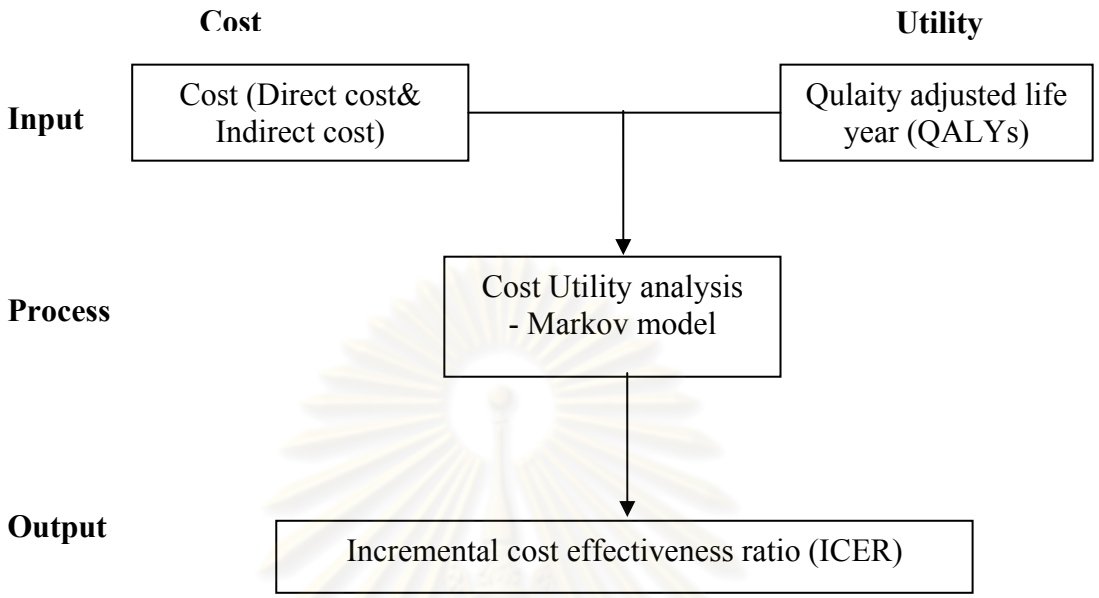

Figure 1.2 Conceptual framework

CHAPTER II

LITERATURE REVIEW

This chapter is divided into 3 major parts. The first part shows the details of anemia in end-stage renal disease (ESRD) which treated by erythropoietin (EPO) and the hypothesis mechanism of EPO for anemia treatment, the adverse events, which are consequences, as well as treatment approaches were conceptually structured in markov models. The second part shows the details of the tools used in measuring utility scores and the kidney specific disease questionnaire. Subsequently, the concept of cost utility analysis is presented including the key structures related to calculation of the incremental cost effectiveness ratio (ICER) by modeling technique.

I. Anemia treatment in end-stage renal disease

1. End-stage renal disease (ESRD)

The National Kidney Foundation of The United States of America defines chronic kidney disease (CKD) as an evidence of kidney damage based on abnormal urinalysis results (e.g, proteinuria, hematuria) or structural abnormalities observed on ultrasound images or an absolute glomerular filtration rate (GFR) of less than 60 ml/min for 3 months or longer. Based on this definition, guidelines are developed by classifying the progression of renal disease into 5 stages. Stage 1, there is an evidence of kidney damage but GFR is preserved (>90 ml/min). Stage 2 is identified by mild kidney damage with GFR 60–90 ml/min. Stage 3 is moderate kidney damage with GFR 30–59 ml/min. Stage 4 is severe kidney damage with GFR 15–29 ml/min while Stage 5 is end-stage renal disease (ESRD) with GFR <15 ml/min. Patients in Stage 5 are often treated with dialysis or kidney transplantation.

At present, the incidence and prevalence of end-stage renal disease (ESRD) patients is increasing both adjusted by age or by race.[15] The ESRD is a worldwide public health problem. In the US alone, the number of patients eventually reaching ESRD is projected to rapidly increase from 354,754 in 2006 to 533,800 patients in 2020.[15] This high prevalence of ESRD, the attendant need for anemia treatment with EPO, and the high costs associated with anemia treatment in ESRD calls for a more structured approach on the use of these agents. These patients at one time will need renal replacement therapy, of which there are 3 available methods, i.e., Continuous Ambulatory Peritoneal Dialysis (CAPD), Hemodialysis (HD), and Renal transplant. Anemia from erythropoietin deficiency is a common complication of chronic kidney disease. It can be treated with EPO administration, red blood cell transfusion (RBCT), or a combination of both.[16] Most patients receiving HD for ESRD currently receive erythropoietin (EPO) or erythropoiesis-stimulating agents (ESAs) for treatment of anemia.

The end-stage renal disease (ESRD) is a chronic health problem and cannot be cured. Furthermore, the management of ESRD is costly, the average dialysis expenditures are 250,000-300,000 baht per person per year.[17] In 2004, the data from the Nephrology Society of Thailand found that there are 12,614 hemodialysis (HD) patients, about 729 Continuous Ambulatory Peritoneal Dialysis (CAPD) patients, and 1,542 renal transplanted patients. All of the data can be summarized that the estimated incidence rate of patients receiving all 3 treatment methods per Thai population is 236 per million while the new patients in 2004 is 7,871 or 125 cases in 1 million population.[18] However, this quantity did not include the patients who could not afford the cost of their disease therapy. This unidentified group is estimated to

have around 3 folds of known cases. The incidence and prevalence of end-stage renal disease (ESRD) patients, who need renal replacement therapy, are increasing.

2. Anemia treatment

Anemia defined as Hb concentration less than 13.0 g/dL for adult males and post-menopausal women, and hemoglobin below 12.0 g/dL for pre-menopausal women (World Health Organization 1968). Anemia is a common clinical problem in patients with chronic kidney disease (CKD) including ESRD and is associated with increased morbidity and mortality in these patients. Erythropoietin is a hormone synthesized in the kidney responsible for red blood cell maturation in the bone marrow.[19] Anemia is a contributing factor in many of the symptoms associated with reduced kidney function. These include fatigue, depression, reduced exercise tolerance and dyspnea. In addition, anemia has direct adverse cardiovascular disease (CV) consequences[20], such as left ventricular hypertrophy (LVH) and left ventricular systolic dysfunction, coronary artery disease, and stroke. Thus, ESRD patients with anemia have the high risk of hospitalization, increased hospital length of stay, reduced quality of life and mortality[21] including the expenditure consequences.[22]

Normally kidneys produce a hormone called erythropoietin (EPO) which stimulates the bone marrow to produce the proper number of red blood cells needed to carry oxygen to vital organs. In ESRD, their kidneys don't make enough EPO. As a result, the bone marrow makes fewer red blood cells. Nevertheless, ESRD who have HD face the severe anemia from blood loss when hemodialysis and low levels of iron and folic acid. These nutrients from food help young red blood cells make hemoglobin, their main oxygen carrying protein. Nevertheless, EPO therapy is associated with increased iron utilization, further leading to iron deficiency. If a person's iron levels are too low, EPO won't help and that person will continue to experience the effects of anemia. Thus, iron deficiency will develop in dialysis patients receiving EPO unless supplemental iron therapy. Some patients are able to take an iron pill, but many studies show that iron pills don't work as well in people with kidney failure as iron given intravenously. Iron can be injected into an arm vein or into the tube that returns blood to the body during hemodialysis. Evaluation of iron stores should include red blood cell indices, reticulocyte count, serum iron, total iron binding capacity, percentage transferrin saturation, serum ferritin, and testing for occult blood in stool. The common evaluate the iron deficiency is serum ferritin level and the transferrin saturation (TSAT) which should higher than 200 ng/ml and 20%, respectively.[19]

Most patients receiving HD for ESRD currently receive erythropoietin (EPO) or erythropoiesis-stimulating agents (ESAs) for treatment of anemia. Anemia from erythropoietin deficiency is a common complication of chronic kidney disease. It can be treated with EPO administration, red blood cell transfusion (RBCT), or a combination of both.[16] But in the widely accepted use in anemia patient is EPO administration. Twenty five years have passed since the first patient received recombinant human erythropoietin in Seattle, November 1985. [23, 24] EPO is effective in reversing anemia of renal failure and all its diverse consequences. A reduction in Hb concentrations in these patients has been shown to be associated with impairment in quality of life, reduced energy, neurocognitive decline, decreased exercise capacity, and increased mortality.[21, 25-27] The cause of anemia in the patients is mainly related to a deficiency in the synthesis of endogenous erythropoietin.[28] Therefore, the use of recombinant human erythropoietin represents a logical and commonly used treatment for this disorder. EPO has been shown to improve quality of life, exercise capacity, cognitive function, sleep disturbances and ameliorates left ventricular hypertrophy, which is a major contributor to cardiac mortality and morbidity in ESRD patients.[29-34]

It is remarkable that the three largest studies, involving 3,268 subjects, have had a very consistent outcome, a 21-48% increased risk for mortality in the higher Hb target group that in each study nearly reached statistical significance. [32, 35-37]

Target hemoglobin

There is no agreement on target Hb. In 2004, the European Dialysis and Transplant Association (EDTA) published the European Best Practice Guidelines or EBPG (at present; EBPG is changed the name to European Renal Best Practice or ERBP) for the treatment of anemia[2] and the US National Kidney Foundation published the evidence-based Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines in 2006. Both guidelines have suggested the treatment target for the anemia of chronic renal failure at hemoglobin (Hb) concentration higher than 11 g/dl (or hematocrit (HCt) at higher than 33%) while United Kingdom Renal Association (RA) have suggested the target Hb in the range 10.5-12.5 g/dl as shown in the table 1.1.[3] Because of EPO cost, target Hb should be individually determined, with near normal levels in active, working patients, and those with heart disease. The most useful information on target Hb requires a study in which a very large group of patients would be randomized to multiple different Hb targets, such as 9,10,11,12, and 13 g/dl.[38] The level at which quality of life was maximized, whereas risk was minimized would be the optimal target. We will explore the major treatment effects that inform the scientific balancing of benefit and risk for Hb target; the tradeoff of quality of life benefit against safety risk. Other factors such as cost should be considered in the cost utility of EPO to maintain the Hb in renal anemia patient.

3. Erythropoietin (EPO)

The U.S. Food and Drug Administration (FDA) recommend that patients treated with EPO therapy should achieve the target hemoglobin between 10 and 12 grams per deciliter (g/dL). Recent studies have shown that raising the hemoglobin above 12 g/dL in people who have kidney disease increases the risk of heart attack, heart failure, and stroke.[38] People who take EPO shots should have regular tests to monitor their hemoglobin. If it climbs above 12 g/dL, their doctor should prescribe a lower dose of EPO. The FDA recommends that patients whose hemoglobin does not rise to the target level with normal doses of EPO ask their doctor to check for other causes of anemia. If no other cause for anemia is found, it can be treated with a genetically engineered form of EPO. The EPO is usually injected under the skin two or three times a week. Patients on hemodialysis who can't tolerate EPO shots may receive the hormone intravenously during treatment. The intravenous method, however, requires a larger, more expensive dose and may not be as effective.

Erythropoietin (EPO) is a hormone that produced by the kidney, EPO promotes the formation of red blood cells in the bone marrow. EPO is a glycoprotein (a protein with a sugar attached to it). Human EPO has a molecular weight of 34,000. The kidney cells that make EPO are specialized and are sensitive to low oxygen levels in the blood. These cells release EPO when the oxygen level is low in the kidney then EPO stimulates the bone marrow to produce more red cells and increase the oxygen-carrying capacity of the blood. EPO is the regulator of red blood cell production. Its major functions are to promote the differentiation and development of red blood cells and to initiate the production of hemoglobin, the molecule within red cells that transports oxygen. EPO is produced not only in the kidney but also, to a lesser extent, in the liver. Different DNA sequences flanking the EPO gene act to control kidney versus liver production of EPO. The measurement of EPO in the blood is useful in the study of bone marrow disorders and kidney disease. Normal levels of EPO are 0 to 19 mU/ml (milliunits per milliliter). Elevated levels of EPO can be seen in

polycythemia, a disorder in which there is an excess of red blood cells. Lower than normal levels of EPO are seen in chronic renal failure.

EPO is a glycoprotein hormone. It controls erythropoiesis, or red blood cell production and erythropoietin plays an important role in the brain's response to neuronal injury.[39] EPO is also involved in the wound healing process.[40] Erythropoietin is available as a therapeutic agent produced by recombinant DNA technology in mammalian cell culture. It is used in treating anemia resulting from chronic kidney disease and myelodysplasia, anemia secondary to AZT treatment of AIDS, and anemia from the treatment of cancer (chemotherapy and radiation), and from other critical illnesses (heart failure). EPO have many analogues as the following :

1. **rEPO:** recombinant erythropoietin or epoetin. That classified by epoetin alfa (Recormon®), beta (Eprex®) , omega, delta (Dynepo®), etc.
2. **uEPO:** endogenous erythropoietin (secreted naturally by the athlete's own tissues) as found in the urine.
3. **NESP** (Aranesp®, Amgen)**:** Novel erythropoietin stimulating protein, the erythropoietin analogue known as darbepoietin alfa.
4. **CERA** (Mircera®, Roche)**:** Continuous Erythropoietin Receptor Activator, the methoxy polyethylene glycol-epoetin beta, a derivative of epoetin beta. CERA is available used in Thailand in 2009. CERA or a continuous erythropoietin receptor activated and the price list is around 6,338 Baht per vial. In the view of chemical structure, it is look like EPO but it has polyethylne glycol molecule that gives the drug have a longer lasting effect. CERA has been developed for the treatment of anemia in patients with chronic kidney disease. The different of other EPO, CERA has a longer elimination half-life and slower clearance rate. Thus, CERA can be administered at extended intervals up to once per monthly while the erythropoietin-alfa and beta needed to inject the drug for 2-3 times weekly.[41, 42]

EPO at Siriraj Hospital in 2008 are erythropoietin beta and erythropoietin alfa are available in 3 trade name: Recormon®, Eprex® , Hemax®. In Thailand, erythropoietin has been included in the National List of Essential Drugs (NLED), in subclass 5.2 or category Jor.2 for the treatment anemia that caused by end-stage renal disease for maintain the target hemoglobin. Cost of 3 trade name EPO at Siriraj Hospital in 2010 was shown in the table 2.1.

Table 2.1 EPO brands and average cost per 1,000 unit at Siriraj Hospital in 2010.

Generic name	Trade name	Price (Baht)
Erythropoietin-beta	Recormon Pre-filled Syr. Inj. 1,000 IU.	380
	Recormon Pre-filled Syr. Inj.2,000 IU.	688
	Recormon Prefilled syringe Inj 3,000 IU	1,026
	Recormon Pre-filled Syr. Inj. 5,000 IU.	1,633
	Recormon Pre-filled Syr. Inj. 10,000 IU.	3,239
	Recormon Pre-filled Syr. Inj. 30,000 IU	9,595
Erythropoietin-alfa	Hemax Pre-filled Syr. Inj. 1,000 IU	400
	Hemax Pre-filled Syr. Inj. 2,000 IU	370
	Hemax Pre-filled Syr. Inj. 3,000 IU	685
	Hemax Pre-filled Syr. Inj. 4,000 IU	730
	Hemax Pre-filled Syr. Inj. 10,000 IU	2,235
Erythropoietin-alfa	Eprex Pre-filled Syr. Inj. 2,000 IU	811
	Eprex Pre-filled Syr. Inj. 3,000 IU.	1,179
	Eprex Pre-filled Syr. Inj. 4,000 IU.	1,473
	Eprex Pre-filled Syr. Inj. 10,000 IU	3,984
	Eprex Pre-filled Syr. Inj. 20,000 IU	7,329
	Eprex Pre-filled Syr. Inj. 40,000 IU	13,008
Average cost per 1000 unit		325

* Subclass 5.2: The essential drug for especially patient, this drug is expensive, need to have the experts prescribed, have the trend of misuse, and need to authorized system.

Routes of administration.

Four possible routes of EPO administration exist.

1. Intravenous (i.v.) application was initially used in clinical trials with EPO, because it was easy access in patients on hemodialysis (HD) [43] This is an inconvenient route for outpatients. The adverse effects (flu like syndrome, bone and muscle pain, headaches) seem to occur more frequently than in subcutaneous (s.c.) administration. Patients on HD do have the i.v. route, but s.c. option is thought to be more economical and most patients receive EPO by this way.[44]

2. Subcutaneous (s.c.) administration is the most convenient and cost-effective alternative and preferred route at the present is subcutaneous application. Though bioavailability was low compared with i.v. route, longer plasma half-life and persistence of continuous stimulation is as effective as i.v. given EPO. The studies soon showed that, compared with i.v., the s.c. route allowed a reduction in doses of approximately 30-40% with similar results.[45, 46] However, recent prospective randomized crossover studies show the same elevation of Hb level weather the EPO is given by i.v. or s.c. route. [43] Another advantage is the possibility of self administration. For pre-dialysis and patients on CAPD s.c. application is the only practicable one.

3. Intraperitoneal route is appropriate for patients on peritoneal dialysis, who often do not even demand EPO treatment. Larger doses of EPO are required compared with intravenous (i.v.) or subcutaneous (s.c.) application because bioavailability of hormone is very low.[47]

4. Intradermal injection. Preliminary results with intradermal injection of EPO suggest that it is at least as good as i.v. or s.c. route.[48]

Dosage of EPO

The safest starting dose is not defined. A "low and slow" dosing protocol, common in Europe, means 50-60 U/kg 3 times weakly.[49] The side effects of treatment (hypertension, seizures, vascular access thrombosis) are more likely to occur if the Hb level increases rapidly. When the satisfactory Hb value is reached, the dose of EPO should be titrated down gradually. Individual differences to EPO should be considered. In children[50] and adults[51] with CKD that the same absolute dose of 1,000 IU EPO intravenously is able to increase the Hb level by 0.04 g/dl. The initial EPO dose can be calculated individually, based on the Hb level before treatment, the desired Hb level at steady state. The following formula can be used to calculate the dose (d) which is expected to increase hemoglobin from a pretreatment level (Hb0) to a desired steady state level (HbSS) when given intravenously three times per week:[52]

$$d = 2400 \text{ IU} \ / \ \sqrt{[9.6 / (HbSS - Hb0)]} - 1$$

Controversy of Erythropoietin use

Treatment with EPO has altered the lives of CKD patients, with fewer blood transfusions and improved quality of life. However, randomized trials have suggested that targeting greater hematocrits/hemoglobin levels and exposure to high doses of EPO is associated with a greater risk of cardiovascular complications and mortality. A major critical point in thinking about higher Hb targets was the publication of two large studies in nondialysis CKD in 2006: Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin (CREATE)[35] and Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR).[37] Both studies found trends toward increased mortality risk and for other adverse outcomes as well as a recent meta-analysis in 2007 found that treatment to higher Hb targets resulted in an increasing of risk for mortality. Thus, the hypothesis for the explanation of increased risk with treatment to higher Hb targets was studied that can summarized[38, 53] as Hb can raising by EPO and this increasing of Hb lead to 2 mechanisms: 1) increased blood oxygen carriage; 2) increased viscosity and increase platelet number and aggregation that even the relatively small increases in blood viscosity as Hb rises to 13 g/dl may have the harmful effect on the vascular disease. For the healthy person, the 2 mechanisms is balance together, the body always restores the Hb back to normal when provided with adequate substrates and time. However, individuals with kidney disease differ from those in the healthy state in a number of ways. The tradeoff of blood oxygen carriage and viscosity is optimized at normal Hb levels in this population when compared with those without kidney disease.[54, 55]

The hypothesis of the harmful condition of the higher Hb as follow:

1) High Viscosity

At very high Hb levels, as seen in states of primary or secondary erythrocytosis, this shear stress produces endothelial injury that may result in increased risk for vascular thrombosis[56]

2) Hemoconcentration

The risk related to elevate Hb may be accentuated by HD induced hemoconcentration. Hb levels are measured before the dialysis session in HD patients when the patient is most hemodilute. This results in a spuriously low measured Hb concentration but is the value that is actually used to adjust EPO dosage. Because Hb targets tend to be the same in HD and nondialysis CKD, actual time-averaged Hb levels are actually raised to a greater extent in HD patients. This may be particularly relevant among patients who are large interdialytic weight gainers. Even in moderate weight gainers (up to 2 to 3 L per interdialytic period), the time-averaged Hb averages

approximately 1 g higher than that obtained before dialysis.[57] Changes immediately after dialysis are of cause larger. Those who gain 5 to 9% of their dry weight interdialytically would undergo much larger transients, and with the substantial ultrafiltration that they must undergo, these patients may experience extreme hemoconcentration of 5 to 10 Hct points. Although the Hct in clinical trials or in general practice has usually fallen short of those seen in secondary erythrocytosis, significant hemoconcentration can occur. It may be especially risky to target higher Hb levels in such patients because changes in Hct and in viscosity, producing large changes in shear rate and shear stress, may occur thrombosis. This may partially explain evidence from the studies of increased mortality risk among HD patients with larger interdialytic weight gains. [58, 59]

3) Hypertension

Hypertension is a common and widely known complication of EPO treatment.[55] It is estimated that 20 to 40% of patients who are treated with EPO have new onset or a worsening of BP that requires intensification of antihypertensive therapy.[60, 61] Hypertension is one of the most clearly established independent risk factors for cardiovascular events and death. Cardiac risk reduction is effective treatment with antihypertensive drugs. Increased BP induced by EPO treatment to high Hb targets in CKD population could be especially problematic. In fact, relatively small increases in BP are associated with substantive increases in cardiovascular risk; therefore, it is highly plausible that increased BP could partially explain the increased risk for death in the higher Hb target groups.[36]

4) Higher dose of EPO and higher supplemental iron

We consider the direct effect of Hb level, the potential role of EPO treatment and supplemental iron needed to achieve higher Hb levels. The aspects of EPO treatment that differ from normal biology are the very rapid rise in serum levels after injection, the high peak serum concentration, the rapid decline in levels, and the decline in some patients to very low serum concentrations. [62, 63] The amount of EPO used and/or iron treatment, may play a causative role in increased mortality risk. Most of the Hb target studies in HD used erythropoietin alfa (a first-generation erythropoietin) as the EPO treatment. About iron, the possibility that iron contributes to increased risk was iron must be administered in greater amounts to produce more Hb, Iron increases oxidative stress via the Fenton reaction. In HD patients, treatment with intravenous iron is associated with systemic evidence of increased oxidative stress[64], oxidation of plasma proteins[65], and evidence of vascular injury.[66] In addition, increased concentration of serum ferritin has been associated in some but not all studies with increased risk for death as a result of cardiovascular causes.[67] Among HD patients, treatment with intravenous iron and mortality risk has been reported in some studies to be associated with lead to atherosclerosis[60, 68] and increased risk for death.[69]

II. Utility and the kidney specific disease questionnaire

Utility theory

Utility Theory is based on the Theory of Games and Economic Behavior.[70] In the area of cost utility analysis study, the concept of utility measurement is referred to "expected utility theory or von Neumann-Morgenstern utility theory" which treats utility as an ordinal measure. The utility measurement is not quantified but ranked, and thus the utility rank cannot be added up. A person can say that a new shirt is preferred to a sandwich, but not that it is ten times more preferred to the sandwich. The reason is that the utility of ten sandwiches is not ten times the utility of one sandwich, by the law of diminishing returns. So it is hard to compare the utility of the shirt with "ten times the utility of the sandwich". But Von Neumann and Morgenstern suggested the way of making a comparison like this. Their method of comparison involves considering probabilities. If a person can choose between various randomized events (lotteries), then it is possible to additively compare the shirt and the sandwich. It is possible to compare a sandwich with probability 1, to a shirt with probability p or nothing with probability 1-p. By adjusting p, the point at which the sandwich becomes preferable defines the ratio of the utilities of the two options.[71]

Quality of life (QOL)

Quality of life (QOL) is being used increasingly as an important parameter of health and well-being. QOL is an important outcome representing a person's concerns. QOL also is an important indicator of other outcomes, such as mortality and hospitalization. There are several reasons that QOL study is emerging in patients with end-stage renal disease (ESRD) undergoing hemodialysis (HD). With the increasing prevalence of patients with ESRD treated by HD therapy, which is proven to prolong life, there is a significant reduction in the patient QOL. ESRD is a chronic disease associated with comorbidities and complications that were adversely influence many aspects of QOL in HD patients.

Constructs of QOL consist of several health-related concepts such as physical health, mental health, social health, general health.[72] There are 2 types of instrument used for measuring QOL; 1) generic instrument, 2) disease-specific instrument. Both generic and disease-targeted questionnaires help increasing the understanding of health-related quality of life in patients with disease conditions. General instruments include health profiles and assessments of the overall health state. They can be used to compare the relative burden of illness in the general population and between different diseases. Examples of generic instrument are Nottingham Health Profile, Sickness Impact Profile, McMaster Health Index Questionnaire, EurolQoL (EQ-5D) and Short Form 36 (SF-36).[73] Examples of disease-specific instrument are Condition-specific instruments, Quality of Life after AMI Questionnaire, Quality of Life Index-Cardiac version III, Seattle Angina Questionnaire, Edinburgh Postpartum Depression Scale, Asthma Quality of Life Questionnaire (AQLQ) and The Kidney Disease Quality of Life Short Form (KDQOL-SF). Disease-specific instruments are known to be more sensitive to assess changes within patients, may be more responsive but limited in cases of populations or interventions and do not allow cross condition comparisons.[74-76] Generic instruments are less sensitive to assess intra-individual changes, may not focus adequately on specific area of interest, may not be responsive, are difficulty in determining utility value but are specifically designed to detect differences between individuals from a general population.[76, 77]

Domains measuring disease-related symptoms as well as physical, social, cognitive, and emotional functions that are included in QOL or health-related QOL (HRQOL) instruments vary. Thus, concerns about what dimensions are included to

measure HRQOL/QOL have been raised. QOL and HRQOL are in fact different constructs. QOL is usually described as an overall assessment of well-being across various domains[78]. Whereas QOL includes all aspects of an individual's life (housing, neighborhood, and school), HRQOL only refers to aspects of health.

In HRQOL instruments, many of the domains refer to problems or limitations, such as somatic distress, physical limitation, discomfort from medical treatment, and pain, rather than to wellbeing or positive health. These domains are based on the assumption that the absence of problems (physical, social, or emotional) equals the presence of wellbeing.[79] Those who oppose argue that the optimal effect of negative domains, such as the absence of pain or somatic distress, can only have a neutral effect on QOL, not a positive effect. A further concern with the domains is that many HRQOL instruments measure functioning (e.g. physical functioning, mobility, sensation, self-care, cognitive functioning, and social functioning). Measures of health related quality of life (HRQOL) have become widely used by clinical researchers and can provide useful descriptive information on the effectiveness of health care interventions covering such disparate range of outcomes for HRQOL. However, these measures have not been designed for use in economic evaluation. The limitation of using such instruments in economic evaluation is that they do not explicitly incorporate preferences into their scoring algorithms. The HRQOL scoring systems provide utility (preference) scores on a generic scale where 0 is equivalent to death and 1.00 to full health[80]. Thus, utility is a measurement of the preference for a specific health outcome (HRQOL). The example of multi-attribute utility measurement is SF-6D.[81]

Clinicians and policymakers are recognizing the importance of measuring health-related quality of life (HRQOL) for informed patient management and policy decisions. Questionnaires in the form of self-administration or interviewer administration can be used to measure cross-sectional differences in quality of life between patients at a point of time or longitudinal changes in HRQOL within patients during a period of time (evaluative instruments). Both discriminative and evaluative instruments must be really measuring what they are supposed to measure and have a high reliability and responsiveness, respectively. Reliable discriminative instruments are able to reproducibly differentiate between persons. Responsive evaluative measures are able to detect important changes in HRQOL during a period of time, even if those changes are small. HRQOL measures should also be interpretable; clinicians and policymakers must be able to identify differences in scores that correspond to trivial, small, moderate, and large differences. Two approaches to quality-of-life measurement are available: generic instruments that provide a summary of HRQOL; and specific instruments that focus on problems associated with single disease states, patient groups, or areas of function. Generic instruments include health profiles and instruments that generate health utilities. The approaches are not exclusive. Each approach has the strengths and weaknesses and may be suitable for different circumstances. Investigations in HRQOL have led to instruments suitable for detecting minimally important effects in clinical trials, for measuring the health of populations, and for providing information for policy decisions.[76]

Utility Methods

1. Directly measured Utility Methods
2. Indirectly Measured Utility Methods

1. Directly measured utility methods include:

(1.1) Standard Gamble (SG)

SG is the method for measure the preferences that the individual has for the outcome and the quantitative score represents utility. The respondent considers what probability of painless and immediate death she would risk in order to be restored to perfect health, or better health than the health state under consideration. SG, now known in health applications, is the name by which von Neumann and Morgenstern described the method measuring utilities. In utility elicitation with SG, the respondent is asked to compare a known intermediate state to a gamble, and to choose which of the two is preferable. The gamble has one of two outcomes:

- The best health state under consideration (perfect health), with probability p
- The worst health state under consideration (often "dead"), with probability 1-p.

In decision models, this outcome can be described as any outcomes suitable to the question. In health utility assessments, these outcomes are conventionally set as perfect health, immediate and painless death.

The probability in the gamble is varied until the decision maker is indifferent between the gamble and the intermediate health state. For example, if the subject is willing to take up to a 25% risk of death in exchange for an 75% chance of perfect health rather than accept the intermediate state for certain, then the utility of the intermediate state is 0.75 or 75 percentages.

Developing Expected Utility Theory (EUT), Von Neumann and Morgenstern showed that if a cardinal utility could be expressed as equivalent to a gamble, under certain assumptions, it would be a linear function of the risk involved in the gamble that means the level of risk involved in standard gamble questions is linear in utility. This is the reason lead to regard the SG as the "gold standard" for health status measurement.

(1.2) Time Trade-Off (TTO)

TTO method[82] was developed by Torrance et al. (1972). It measures one's willingness to live a shorter but healthier life. The respondent considers how much of remaining life expectancy he or she would be willing to trade off in order to live in perfect health. The TTO is a direct question about how much life expectancy an individual would trade off to improve quality of life. It attempts to present the respondent with a task that some believe is simpler than the SG task, while preserving an element of trade-off in the assessment.[83] The TTO utility equals one minus the maximum proportion of time that the subject is willing to trade off. For example, if she is willing to give up 1 year from 10 years of her life expectancy in return for perfect health, her utility for the intermediate health state is 1-0.1 = 0.9.

(1.3) Visual Analogue Scale (VAS)

VAS[84, 85] is a psychometric response scale when responding to a VAS item, the respondent answer their level of agreement to a statement by indicating a position at a continuous line between two end-points. Each respondent is asked to rate each item on some response scale. For instance, they could rate each item on a 1-5 response scale where strongly disagree, disagree, undecided, agree, strongly agree. There are variety possible response scales (1-7, 1-9, 0-10). The final score for the respondent on the scale is the sum of their ratings for all of the items. In practice, computer-analysed VAS responses may be measured using discrete values due to the discrete nature of computer displays.

(1.4) Willingness-To-Pay (WTP)

WTP also known as "contingent valuation", the respondent considers how much she would be willing to pay for insurance, to avoid an undesirable health state. WTP can be used as a measurement of the strength of individual's preference or referred to a maximum amount of money that can be paid for receiving the good may be called as compensated variation.[86]

(1.5) Person Trade-Off (PTO)

PTO seeks to equate a certain number of persons with a given health state with an equivalent number of persons with normal health or a different health state. It asks people to say how many outcomes of one kind they consider equivalent in social value to x outcomes of another kind.[87] If treatment type1 costs twice as much as treatment type 2, then two people can be given treatment type 2 for the money needed to give one person treatment type 1. This is the person trade-off in terms of production. While society would want to spend money on two treatment type 2 more than one treatment type 1, depends on the person trade-off in terms of value: Are two treatment type 2 's valued higher by society than one treatment type 1? One way of estimating person trade-offs in terms of social value is to calculate the QALYs gained by different treatments. In this example, if treatment type 1 and treatment type 2 provide 20 and 5 QALYs respectively per person treated, then one treatment type 1 is assumed to be worth 4 folds of treatment type 2. Accordingly, if cost of treatment type 1 is only twice as much as cost of treatment type 2, then money is should to spent on treatment type 1.[88]

From many methods that available for measuring the utility, 2 of the most widely used have been the SG and TTO. SG is the gold standard but based on the uncertainty decision or the patient determined their selected way by trading off the risk while TTO is based on the amount of life expectancy. The utility derived from SG is assumed by a negative function of such a risk whereas that from TTO is assumed by a positive function of life time duration. Generally, SG gives the higher valuation of utility than TTO.[89]

2. The Indirectly measured utility instruments

Indirectly measured utility instruments are multi-domain health status questionnaires completed by patients. These ratings result in a large number of possible health states. The utility of each health state is obtained through a scoring function derived from direct utility assessment of the healthy population. Indirect utilities have the advantage that they can be assessed through self-report questionnaires and are easy to understand.

(2.1) EuroQol-5 Dimensions (EQ-5D)

EQ-5D is a standardized instrument used as a measure of health outcome. Initially the system is developed with six attributes; mobility, self-care, main activity, social relationship, pain, and mood. Then, five attributes, including mobility, self-care, usual activity, pain/discomfort, and anxiety/depression, are selected. The original EQ-5D is EQ-5D-3L. Each attribute has 3 levels: no problem, some problems, and major problems thus generating a total of 3^5 or 243 possible health states. Including 2 more health states on unconsciousness and death, EQ-5D contains total of 245 healths states. At present, the standard 5 levels of EQ-5D (EQ-5D-5L) would improve the descriptive richness and ability of the measure to discriminate among different levels of health. In answering the EQ-5D, the respondent selects his/her health state by ticking in the box against the most appropriate statement in each dimension. Generic utility measure is used to characterize current health states and usually scored by VAS technique. The respondents are asked to evaluate their health state on a “thermometer” calibrated from zero (worst) to 100 (best health state). Based on the answer, the health state can be identified by a five digit number such as 22223 indicating some problems with mobility, self care, usual activities, and pain/discomfort, and extreme problems with anxiety/depression.[90] EQ-5D-3L is a generic health outcome measure which is easily completed and is available to use but

we should ask for permission to use this instrument. This measure was selected because it has been translated officially into Thai and the measure seems to be straightforward to use. A preference based scoring algorithm for estimating EQ-5D index scores was successfully derived from the general population using TTO.[91] The final score could be calculated according to the following algorithm.[92]

Utility = 1 – ∑(coefficient of all dimension) – 0.081 - N3

(Including N3 when the level 3 occurs within at least one dimension)

The coefficient of all dimension (EQ-5D) were shown as the table 2.2.

Table 2.2: Coefficients for TTO tariffs

	Level 2	Level 3
Mobility dimension	0.069	0.314
Self-care dimension	0.104	0.214
Usual activity dimension	0.036	0.094
Pain/ discomfort dimension	0.123	0.386
Anxiety/ depression dimension	0.071	0.236
Constant term = 0.081		
N3 = 0.269		

For example, we can estimate utility score for the health state 11223 as following calculation:

Full health	**= 1**
Constant term	**= -0.081**
Dimension	
Mobility (level 1)	= -0
Self-care (level 1)	= -0
Usual activity (level 2)	= -0.036
Pain/discomfort (level 2)	= -0.123
Anxiety/depression (level 3)	= -0.236
N3 (level 3 occurs within at least one dimension)	**= -0.036**
The estimate utility score of 11223	**= 0.255**

Not only calculation the utility score from the manual method as the above example but we can estimates the EQ-5D utility score from the EQ-5D index calculator program which available from http://www.ahrq.gov/rice/EQ5Dscore.htm. The UK-based preference weights are applied to other populations when country-specific weights are not available. However, the evidence suggests valuations of health states could differ for people in different countries due to differences in demographic backgrounds, social-cultural values, and economic systems.[93, 94] Thus, it is advisable to use country-specific weights in a given country if available. Fortunately, Thai population based preference scores for EQ5D is available now.[95]

(2.2) Short Form 36 (SF-36)

SF-36 is a widely used for a survey of patient health. The SF-36 is commonly used in health economics as a variable to determine the health-related quality of life. SF-36 can be converted to utility and QALYs using Short Form-6 Dimensions (SF-

6D); indirect utility that was developed for the utility measurement. SF-36 consists of multiple item scales measuring the 8 health concepts; physical functioning, bodily pain, vitality, physical role functioning, emotional role functioning, social role functioning, general health perceptions, mental health. Eight domains scores can be summarized to 2 major components, the physical and mental components. SF-36 can be responded by self-administration, 1-4 week recall periods, interviewer-based, computer-based. SF-36 is useful for comparison both general and specific groups, comparing the relative diseases, the different health benefits by the various interventions or treatment. SF-6D consists of 6 dimensions (10 selected questions from the SF-36). These dimensions are (1) physical functioning 2 questions, (2) role limitations 4 questions, (3) bodily pain 1 question, (4) vitality 1 question, (5) social functioning 1 question, and (6) mental health 1 question. The response scales vary for each of the questions. Of the total of 18,000 possible health states, 249 different health states were selected to elicitate utilities. The final utility equation results on a utility value ranging from 0.30 to 1.00.[90] A computer algorithm to automate utility is used for deriving a preference-based index for the SF-6D.[81] The SF-6D is the multi-attribute health status comprising 6 attributes. Each attribute consists of 4-6 levels as presented in table 2.3 and each level possesses scoring algorithm as detailed in table 2.4. By using the SF-6D; 18,000 health states could be differentiated.

Table 2.3 SF-6D classification system

Physical functioning	
PF1	Your health does not limit you in *vigorous activities*.
PF2	Your health limits you a little in *vigorous activities*.
PF3	Your health limits you a little *in moderate activities*.
PF4	Your health limits you a lot in *moderate activities.*
PF5	Your health limits you a little in *bathing and dressing.*
PF6	Your health limits you a lot in *bathing and dressing.*
Role limitations	
RL1	You have no problems with your work or other regular daily activities as a result of your physical health or any emotional problems.
RL2	You are limited in the kind of work or other activities as a result of your physical health.
RL3	You accomplish less than you would like as a result of emotional problems.
RL4	You are limited in the kind of work or other activities as a result of your physical health and accomplish less than you would like as a result of emotional problems.
Social functioning	
SF1	Your health limits your social activities *none of the time.*
SF2	Your health limits your social activities *a little of the time.*
SF3	Your health limits your social activities *some of the time.*
SF4	Your health limits your social activities *most of the time.*
SF5	Your health limits your social activities *all of the time.*
Pain	
PAIN1	You have no pain.
PAIN2	You have pain but it does not interfere with your normal work (both outside the home and housework).
PAIN3	You have pain that interferes with your normal work (both outside the home and housework) *a little bit.*
PAIN4	You have pain that interferes with your normal work (both outside the home and housework) *moderately.*
PAIN5	You have pain that interferes with your normal work (both outside the home and housework) *quite a little bit.*
PAIN6	You have pain that interferes with your normal work (both outside the home and housework) *extremely.*
Mental health	
MH1	You feel tense or downhearted and low *none* of the time.
MH2	You feel tense or downhearted and low *a little bit* of the time.
MH3	You feel tense or downhearted and low *some* of the time.
MH4	You feel tense or downhearted and low *most* of the time.
MH5	You feel tense or downhearted and low *all* of the time.
Vitality	
VIT1	You have a lot of energy *all* of the time.
VIT2	You have a lot of energy *most* of the time.
VIT3	You have a lot of energy *some* of the time.
VIT4	You have a lot of energy *none* of the time.

From Brazier et al. (2002) *The estimation of a preference-based measure of health from the SF-36.*

Table 2.4 SF-6D utility scoring model

General terms	**Term**	C	MOST				
	Score	1	-0.061				
Physical functioning	**Level**	PF1	PF2	PF3	PF4	PF5	PF6
	Score	0	-0.035	-0.035	-0.044	-0.056	-0.117
Role limitations	**Level**	RL1	RL2	RL3	RL4		
	Score	0	-0.053	-0.053	-0.053		
Social functioning	**Level**	SF1	SF2	SF3	SF4	SF5	
	Score	0	-0.057	-0.059	-0.072	-0.087	
Pain	**Level**	PAIN1	PAIN2	PAIN3	PAIN4	PAIN5	PAIN6
	Score	0	-0.042	-0.042	-0.065	-0.102	-0.171
Mental health	**Level**	MH1	MH2	MH3	MH4	MH5	
	Score	0	-0.042	-0.042	-0.1	-0.118	
Vitality	**Level**	VIT1	VIT2	VIT3	VIT4	VIT5	
	Score	0	-0.071	-0.071	-0.071	-0.092	

Where Utility 0-1 dead-healthy scale, C = constant term, PFx = level x on the physical functioning dimension, same for other dimensions, MOST = term to use if any dimension is at its most severe level. From Brazier et al. (2004) The estimation of a preference-based measure of health from the SF-12[81]

The equation for calculate the utility is

Utility = C + PF + RL + SF + PAIN + MH + VIT + MOST

The quality of life data obtained from the questionnaire can be transformed into the utility as the above formula. However, there are SPSS programmes available that produce alternative SF-6D estimates based on rank/ordinal data. Utility scale ranges between 0 and 1, the higher score of utility represents the better health-related quality of life.

(2.3) Quality of Well-being (QWB)

QWB can be classified into 4 attributes such as physical activity (3 steps), social activity (5 steps), mobility (3 steps), and symptom problem complex**.** The score of QWB is a single score and used in general populations, the score range from 0.0 (death) to 1.0 (asymptomatic full function). The QWBs can be used in evaluating programs for a wide range of disease. But QWBs has been criticized for being too long and complex.[90]

(2.4) Health Utility Index (HUI)

HUI is classified into HUI2 and HUI3. For both indices, the scoring formula is based on standard gamble utilities measured on the general public, and the scores range from 0 (death) to 1 (healthy). The utility scores for HUI, derived from a combination of VAS and SG techniques, are based on von Neumann-Morgenstern utility theory. Utility scores are available not only for the overall health state of patients, but also for each attribute independently. HUI2 consists of 7 attributes: sensation (vision, hearing, speech), mobility, emotion, cognition, self-care, pain, and fertility. HUI3 consists of 8 attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. HUI is scored using single- and multi-attribute utility functions. Utilities are preference scores measured under conditions of uncertainty

and utility functions convert descriptive information into utility scores. For application, HUI provides descriptive health profile measures and HRQOL scores on a generic scale. HUI also provides single-attribute scores of morbidity for each attribute. Users are encouraged to report single-attribute scores when applied for the specific health attribute deficits.[96]

What is the different between the multidimensional 36-item Short-Form health survey (SF-36) and EQ-5D.

- The EQ-5D are recorded on a three point scale, which might force responses to the midrange category, as few patients endorse the 'severe' value, and some limitation is often present, which diverts the answer away from the 'no limitation' value. However, EQ-5D could be used more frequently by the dialysis centers in abroad, because it is easy to use, has been translated and validated in many languages, and its five questions and visual analogue scale impose a minimal burden on patients.[97] But the one point of interesting is the disease specific mostly use SF-36 in their questionnaire.
- The SF-36 health survey is a standardized questionnaire used to assess patient health across eight dimensions.[98] SF-36 can detect the health problem and provide more detail than EQ-5D.[99] This is the reason that the disease specific questionnaire such as kidney disease use SF-36 in the part of their question such as KDQOL or CHEQ. It consists of items or questions which present respondents with choices about their perception of their health; the physical functioning dimension. For example, there are 10 items to which the patient can make one of three responses: 'limited a lot', 'limited a little' or 'not limited at all'. These responses are coded 1, 2 and 3, respectively, and the 10 coded responses summed to produce a score from 10 to 30. These raw dimension scores are transformed onto a 0–100 scale, which are not comparable across dimensions. The SF-36 is one of the most widely used generic measures of HRQOL in clinical trials. It has the potential to considerably extend the scope for undertaking economic evaluation in health care using existing and future SF-36 data sets. Measures of health-related quality of life (HRQOL) have become widely used in clinical trials and routine outcome assessment to provide information on the effectiveness of health care. One of the most commonly used measures of HRQOL is the SF-36 which has been reduced to 12 items with minimal loss of information to form the SF-12.[100] Although the psychometric properties of these instruments are well established across many conditions [101-104] but it cannot be used in economic evaluation in its current form. The SF-12 was revised into a 6-dimensional health state classification (SF-6D). Six dimensions with multi-level (n) classifications include physical functioning (6 levels), role limitation (4 levels), social functioning (5 levels), pain (6 levels), mental health (5 levels), vitality (5 levels) and are combined by selecting one level from each dimension to form 18,000 health states. Brazier et al. has estimated the relationship between the SF-6D and SG values using their coefficients, overall fit, and the ability to predict SG values for all health states.[101] Finally, SF-6D data have generated a preference based single index for use in economic.[81]
- SF-6D focused more on social functioning, while EQ-5D gave more weight to physical functioning. Pain and mental health had similar contributions. The scoring range of the EQ-5D was twice the range of the SF-6D.[105] (Range: range of EQ-5D is between - 0.59 to 1.00 while SF-6D is between 0.30 to 1.00)
- SF-6D indices are based on SG exercises and EQ-5D indices are based on TTO exercises so that the score of SF-6D is higher than the score of EQ-5D.[106]

- EQ-5D had a ceiling effect relative to SF-6D, and that SF-6D had a floor effect relative to EQ-5D.[107] For example, more patients who have chronic fatigue syndrome would score at the high end of EQ-5D than low end. This would be difficult to differentiate among patients with better function. Another reason is the different of the valuation methods between TTO and SG. The SG technique usually results in higher values than the TTO. The worst SF-6D states are scored less severe than the worst EQ-5D states thus EQ-5D indices score lower for patients in severe states will be lower than SF-6D indices.[106]

Kidney specific instrument

Several kidney disease–specific HRQOL instruments are available such as Kidney Disease Quality of Life (KDQOL), Kidney Disease Quality of Life short form (KDQOL-SF), Kidney disease questionnaire (KDQ), Dialysis quality of life questionnaire (DIAQOL), Dialysis discontinuation quality of dying (DDQOD), CHOICE Health Experience Questionnaire (CHEQ).[108] The Kidney Disease Quality of Life (KDQOL) instruments were initially developed to evaluate the impact of erythropoietin in HD patients. The first assessment is KDQOL–long form (LF) included 134 questions that spanned 11 kidney disease targeted scales. The long form questionnaire lead to the low responsive. Thus, the KDQOL-SF (short form) was introduced containing questions from the SF-36 plus an additional 43 kidney disease–specific items. A shorter version of this instrument, known as the KDQOL-36 is also available, which consists of the same items as in the generic SF-12 along with an additional 24 questions that are kidney disease specific. The KDQOL-36 is the preferred measurement tool for large-scale assessments in dialysis facilities because of its ease of administration with relatively minimal burden on patients and staffs.[109] The KDQOL has the SF-36 as its generic core and is supplemented with items of relevance to the HRQOL of dialysis patients. Dimensions related to dialysis patients includes symptoms problem, effect of kidney disease on daily life, cognitive function, burden of kidney disease, work status, sexual function, quality of social interaction, and sleep. Other dimensions are the social support, patient satisfaction with care, global rating of health and encouragement from dialysis staff and a global rating of health. Wu and his colleagues developed the CHOICE Health Experience Questionnaire, or CHEQ, to comprehensively measure quality of life of patients on dialysis using patients' reports of the importance they attach to different aspects of their life. CHEQ is the self-reported health-related quality of life. It includes 83 items including the generic measure SF-36, other aspects of life anyone might be concerned about, such as physical and social functioning, and 6 ESRD specific domains (diet, freedom, time, body image, dialysis access, and symptoms). CHEQ is the instrument that is reliable and valid but has not been used by other research group except the the Choices for Healthy Outcomes in Caring for ESKD (CHOICE) study,[110] unlike the KDQOL instrument, which was used by many study groups.[111]

This study use the Kidney Disease Quality of Life - Short Form (KDQOL-SF™1.3) questionnaire with hemodialysis patients. The KDQOL-SF™ was translated into Thai and methodologically validated. This questionnaire was developed in 1994 by the Kidney Disease Quality of Life Working Group (Hays, Kallich, Mapes, Coons, and Carter) as a kidney disease specific measure of HRQOL. This tool summarized the selection of a short-form item set for the kidney disease targeted part. The KDQOL-SF™1.3 includes 36 items of generic core and an overall health-rating item as showed in the appendix 1 as well as 43 disease specific items.

KDQOL-SF™ Kidney Disease-Targeted Scales consists of

1. **Generic core and an overall health-rating item**

The SF-36 Measure of physical component summary or PCS (21 items), mental component summary or MCS (14 items), and overall health rating item

The items are on general health, activity limits, ability to accomplish desired tasks, depression and anxiety, energy level, and social activities

2. **Kidney disease targeted items**

- **Burden of kidney disease (4 items)**

The questions include kidney disease targeted items on how much kidney disease interferes with daily life, takes up time, causes frustration, or makes the respondent feel like a burden.

- **Symptoms and Problems subscale (12 items)**

Items consist of how bothered a respondent feels by sore muscles, cramps, itchy or dry skin, shortness of breath, faintness or dizziness, lack of appetite, feeling washed out or drained, numbness in the hands or feet, nausea, or problems with dialysis access.

- **Effects of kidney disease on daily life subscale (8 items)**

Patients are asked how bothered the respondent feels by fluid limits, diet restrictions, ability to work around the house or travel, feeling dependent on doctors and other medical staff, work status, Sexual function, Sleep, stress or worries and personal appearance.

- **Work status (2 items)**

Respondents answer whether they can work at a paying job and their health keeps them from working at a paying job.

- **Cognitive function (3 items)**

Questions are how much the time that the respondent reacts to the things others said or done, has difficulty concentrating or thinking, has confusion.

- **Quality of social interaction (3 items)**

Items are how much the time that the respondent is isolated from the people, acts irritably toward those around them, gets along well with other people.

- **Sexual function (2 items)**

Questions concern the sexual activity that the respondent has in the past 4 weeks and enjoys sexual activities.

- **Sleep (4 items)**

Items include how the respondent would rate their sleep overall, how often that the respondent is awake during the night, gets the amount of sleep they need, feels trouble staying awake during the day.

3. **Additional quality of life scales** consist of

- **Social support (2 items)**

The scale is on the amount of time that the respondent is able to spend with their family or friends and the support from their family.

- **Dialysis staff encouragement (2 items)**

The respondent is asked about the encouragement that the staffs give to him/her for being as independent as possible and the support to cope with their kidney disease.

- **Patient satisfaction (1 item)**

The question asks the satisfaction on the friendliness and interest from the dialysis staff.

Scoring rules of KDQOL-SF™[112]

The higher value of KDQOL-SF™ reflects a better health state. The raw score of each item is recoded so that a higher score reflects a more favorable health state. Table 2.5 shows the recoding necessary for the majority of the KDQOL-SF™ items.

The first step of the scoring method is transforming the raw precoded numeric values of items to a 0-100 possible range. The higher transformed scores always show better QOL. Each item is put on a 0 to 100 range so that the lowest and highest possible scores for each item are set at 0 and 100, respectively. For example, the 0-4 response scales of an item are transformed into 0-100 as follows: 0=100, 1=75, 2=50, 3=25, and 4=0. A total scale score can also be calculated, so that higher scores indicate better health related quality of life. Four of the KDQOL-SF™ items, which are not listed in table 2.5, need additional instructions. Items 17 and 22 need to be multiplied by 10 to put them on the 0-100 possible ranges. Item 23 is on a 1-7 precoded range. This item is recoded by subtracting 1 (possible minimum) from the precoded value, then dividing the difference by 6 (the difference between the possible maximum and the possible minimum), after that multiplying the result by 100. Item 16 needs to be considered with creating the sexual function scale. In the second and final step in the scoring procedure, items within the same dimension are averaged together to create the scale scores.

Table 2.5 Recode item of KDQOL (Step 1)

Item number	**Original response category → to recode value of**		
4a-d, 5a-c, 21	1 --> 0	2 -->100	
3a-j	1--> 0	2 --> 50	3 -->100
19a, b	1--> 0	2 --> 33.33	3 -->66.66
	4 --> 100		
10, 11a, c, 12a-d	1--> 0	2 --> 25	3 --> 50
	4 --> 75	5 --> 100	
9b, c, f, g, i, 13e, 18b	1--> 0	2 --> 20	3 --> 40
	4 --> 60	5 --> 80	6 --> 100
20	1 --> 100	2 -->0	
1-2, 6, 8, 11b,d, 14a-m,	1--> 100	2 --> 75	3 --> 50
15a-h, 16a-b, 24a-b	4 --> 25	5 --> 0	
7, 9a, d, e, h, 13a-d,f, 18a,c	1--> 100	2 --> 80	3 --> 60
	4 --> 40	5 --> 20	6 --> 0

Note: Item 1 and items 7-8 are scored slightly differently by investigators from the New England Medical Center (cf. Hays et al., 1993). Four of the KDQOL-SF™ items not listed in this table (items 16, 17, 22, 23) require additional instructions

Source: Ron D.Hays et al, Kidney disease quality of life SHORT FORM (KDQOL-SF™), Version 1.3: A Manual for Use and Scoring[112]

Table 2.6 Averaging Items to Form Scales (Step 2)

Scale	Number of Items	After Recoding, Average the following Items
ESRD-targeted Areas		
Symptom/ Problem list	12	14a-k, l (m)*
Effects of Kidney Disease on Daily Life	8	15a-h
Burden of kidney Disease	4	12a-d
Work status	2	20, 21
Cognitive function	3	13b, d, f
Quality of social interaction	3	13a, c, e
Sexual function	2	16a, b
Sleep	4	17, 18a-c
Social support	2	19a, b
Dialysis staff encouragement	2	24a, b
Patient satisfaction	1	23
36-item health survey (SF-36)		
Physical functioning	10	3a-j
Role-physical	4	4a-d
Pain	2	7, 8
General health	5	1, 11a-d
Emotional well being	5	9b, c, d, f, h
Role emotion	3	5a-c
Social functioning	2	6, 10
Energy/fatigue	4	9a, e, g, i

Note: The SF-36 change in health and the 0-10 overall health rating items are scored as single items, 14l is answered by those on hemodialysis; 14m is answered by those peritoneal dialysis

Source: Ron D.Hays et al, Kidney disease quality of life SHORT FORM (KDQOL-SF™), Version 1.3: A Manual for Use and Scoring[112]

Table 2.6 lists the items across each scale. Items that are left blank (missing data) are not taken into account when calculating the scale scores. Thus, the scale scores represent the average of all answered items in the scale. If the answer to item 16 is "no" the sexual function scale score should be coded as missing.

Table 2.7 Central tendency, variability (including floor and ceiling effects), and reliability of KDQOL-SF™scales

Measure	Mean	SD	% Floor	% Ceiling	Internal consistency Reliability
Kidney disease specific					
Symptom/ Problem list	71.21	16.77	0.0	1.2	0.84
Effects of Kidney Disease on Daily Life	57.30	24.53	0.6	5.0	0.82
Burden of kidney Disease	49.62	30.27	6.1	8.0	0.83
Work status	25.26	37.82	63.5	16.4	0.83
Cognitive function	79.11	19.75	0.0	15.9	0.61
Quality of social interaction	76.65	18.71	0.0	15.9	0.61
Sexual function	69.30	36.17	11.6	44.9	0.89
Sleep	60.68	28.61	0.0	7.5	0.90
Social support	64.61	27.73	3.1	16.9	0.89
Dialysis staff encouragement	69.90	23.13	1.3	19.1	0.90
Patient satisfaction	71.38	22.04	0.6	22.0	NA
SF-36					
General health					
RAND scoring	42.88	24.32	3.0	1.8	0.78
SF-36™ scoring	43.87	24.75	3.0	1.8	0.78
Physical functioning	51.83	29.73	3.6	3.6	0.92
Role physical	32.46	39.68	49.4	20.4	0.87
Pain					
RAND scoring	60.40	30.11	3.1	20.2	0.87
SF-36™ scoring	57.60	29.70	3.1	20.2	0.90**
Emotional well being	69.54	20.36	0.6	4.3	0.80
Role emotion	57.76	43.90	29.2	47.2	0.86
Social function	63.57	29.77	4.3	25.0	0.87
Energy/fatigue	45.89	24.06	2.4	1.2	0.90
Overall health rating	59.37	19.54	0.6	5.0	NA

Note: Feedback from international consultants to the Baxter Renal Outcomes Study lead to modifications to the sleep, dialysis staff encouragement, sexual function, cognitive function, and social support items. Results presented here do not reflect these modifications.

* Also includes one item assessing change in health.

** Internal consistency reliability estimate is inflated because scoring of one of the items is conditional on the value of the other. Differnces in RAND and SF-36 scoring of pain and general health perception scores and discussed elsewhere (Hays et al. 1993).

NA: Not applicable for a single-item measure.

Source: Ron D.Hays et al, Kidney disease quality of life SHORT FORM (KDQOL-SF™), Version 1.3: A Manual for Use and Scoring[112]

To use KDQOL-SF™ 1.3 questionnaires, the translation into Thai language (appendix 2) is essential for implement this questionnaire with Thai patients. The researcher was the one of two forward translators from English into Thai language.

The Thai version of KDQOL-SF™ 1.3 questionnaires have been tested for content, validity, and reliabilit.[113] The scaling of convergent and discriminant validity in dialysis patients were 74.17% and 88.81%, Cronbach's alpha (α) in dialysis patients ranging from 0.44 to 0.86 as showed in the table 2.8. Several dimensions showed the internal consistency reliability less than 0.70 including cognitive function (Cronbach's α = 0.59) quality of social interaction (Cronbach's α = 0.44) sleep

(Cronbach's α = 0.68) social support (Cronbach's α = 0.60) and dialysis staff encouragement (Cronbach's α =0.69). Only Cronbach's α of sleep dimension was increasing to 0.73 when deleting an item 18c (have trouble staying awake during the day). Cronbach's α of other dimensions were decreasing when deleting the item-total correlation less than 0.3. The percentage of floor scoring was highest on role-emotional and the % ceiling was highest on role-physical.

Table 2.8 Mean, SD and Reliability of Kidney disease specific in KDQOL-SF™ Thai version scales.[113] (n=64).

Scale	Number of Items	Mean[a]	SD[a]	Reliability[b]
Kidney disease specific				
Symptom/ Problem list	12	81.55	13.99	0.77
Effects of Kidney Disease on Daily Life	8	68.80	21.65	0.74
Burden of kidney Disease	4	44.35	31.44	0.79
Work status	2	56.45	44.80	0.81
Cognitive function	3	82.04	17.60	0.59
Quality of social interaction	3	88.06	11.71	0.44
Sexual function	2	76.25	28.53	0.86
Sleep	4	63.23	21.41	0.68
Social support	2	84.95	19.25	0.60
Dialysis staff encouragement	2	83.26	18.52	0.69
Patient satisfaction	1	69.36	19.37	-

a: the population is the hemodialysis patients (n=62)
b: the population consists of hemodialysis, peritoneal-dialysis and kidney transplant patient (n=126)

About the SF-36 sections in KDQOL-SF™ questionnaire, Cronbach's α of the SF-36 Thai version exceed the 0.7 level (0.72 – 0.86) in all dimensions. Convergent validity was 96.3%. The highest and lowest mean scores were on physical functioning (86.1 ± 13.0) and role-emotional (54.3 ± 40.5). The % Floor was highest on role-emotional and the % ceiling was highest on role-physical. In conclusion, this study has yielded evidence supporting the validity and reliability of Thai version of the SF-36 although caution is recommended in the interpretation of vitality and role-emotional scales.[114]

III. Cost Utility analysis (CUA)

CUA is one of the economic techniques for assessing the effeiciency of healthcare interventions.[115] Health care has different objectives. For instance, the objective of oncologists is on striving to keep their patients alive and being satisfied with a short survival time, the objective of diabetes patient's care is to reduce the complication, whereas primary care providers focus on shortening the cycle of illnesses. All of providers attempt to improve the health of their patients. But they

measure health in a different way since there is no one best way to directly compare the productivity of different providers. This is a reason why many focus on using mortality or life expectancy as the simplest common ground. Mortality allows the comparison between different diseases. We can compare the life expectancy between the cancer and the heart disease. The CUA is considered by dome to be a specific type of cost effectiveness that measures the effectiveness in a utility value or preference adjusted outcome. Utilty is the value on a level of health state or improvement in health status, as measured by the preferences of individual or society. The necessary of measurement the utility is the calculation of quality adjusted life year (QALYs) gained of which the measure combines the quality and quantity of life outcome.[116]

Development of utility measurements and cost utility analysis in healthcare.

The investigation is described for the individual and societal levels. Constructing a 'Robinson Crusoe' society of only a few individuals with different health needs, preferences and willingness to pay is suggested as a method for gaining insight into the problem. The interval property of utilities and QALYs provides the answer to specific concerns on the important requirement that changes of equal magnitude anywhere on the utility scale, or alternatively on the QALY scale, should be measurable. Unfortunately, one of the original restrictions on utility theory states that such comparisons are not permitted by the theory. It is an important new finding, that while this restriction applies in a world of certainty, it does not in a world of uncertainty, such as healthcare. Further research is suggested to investigate this property under both certainty and uncertainty. Other research ideas that are described include: the development of a precise maxim basis for the time trade-off method; the investigation of chaining as a method of preference measurement with the standard gamble or time trade-off; the development and training of a representative panel of the general public to improve the completeful, coherence and consistency of measured preferences; and the investigation, using a model of the conflict between the patient perspective and the societal perspective regarding preferences. Finally, it is suggested that an important area of research would be to work closely with specific decision makers on specific decision problems, to help them solve the problem, provide useful analyses, and to announce these as case studies to give the better understanding of the problems and the essentialness of decision makers.[117]

Quality adjusted life year (QALYs)[118]

In 1968, Herbert Klarman and colleagues introduce the concept of QALYs in their study on chronic renal failure, they use cost per life year gained by the different treatment (kidney transplant and dialysis) but they did not use the word “quality adjusted life year” QALY is advantage for measure the health outcome from reduced morbidity (qualtity of life), and reduced mortality (quantity of life) and combine these into single value. The QALY gained can be calculated using the probabilities to determine the mean, variance, and probability distribution for the QALY gained. The scale of QALY weights must be on the interval scale such as death = 0 and perfect health = 1. Zero is represent in the practical score more than the score that less than zero, zero can be used for death (forever). About one, we use one for perfect health is that the results of 1 QALY that mean 0.5 QALY are the half year in perfect health, and so on.

Life expectancy

Life expectancy in the form of life years gained or saved is the expected number of years of life remaining at a given age. The life expectancy of a group of individuals dependent on the criteria used to select the group. Life expectancy is

usually calculated separately for males and females. Life year gained refers to a single year prolongation of a patient life by means of a certain intervention.

Calculating life expectancies

$$\mathbf{LE = 1/ \mu_C}$$

When; μ_C = Mortality rate derived from the study in the literature

LE = Patients specific life expectancy

From the literature, we derive the compound mortality rate and then we calculate the disease specific mortality rate from DEALE (Declining Exponential Approximation of Life Expectancy).[119, 120] DEALE approach is the approximation of survival by a simple exponential function. This approximation makes it possible to translate data from various literature sources (life expectancy tables, five-year survival rates, survival curves, median survival) into a single, unified mortality scale. In this paper, we use the compound mortality rate to obtain approximations of the disease specific mortality rate from the following formula:

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

When; μ_D: Diseases specific excess mortality rate (fixed rate)

μ_C: Compound mortality rate derived from the study in the literature

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

LE_{ASR} (ASR: age, sex, race adjusted life expectancy) derived from Life table of Vital statistics Thailand 2006 as shown in the table 2.9.

For example, assume CV mortality rate from the clinical trial is 0.202 and the average age of the patient in the trial was 69. What is the diseases specific excess mortality rate*? And what is the* compound mortality rate *when the age of the patient was 79 years old.*

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

$0.202 = \mu_D + 0.065$

$\mu_D = 0.137$

Diseases specific excess mortality rate = 0.137 and μ_D is a fixed rate so that we can calculate the compound mortality rate when the age of the patient was 79 years old from the same formula:

$\mu_C = 0.137+0.105 = 0.242$

Table 2.9 Vital statistics Thailand 2006 (LE_{ASR})

Age (Male)	LE_{ASR} (years)	Mortality rate from age sex race = 1 / LE_{ASR}
55-59	22.34	0.045
60-64	18.69	0.054
65-69	15.31	0.065
70-74	12.26	0.082
75-79	9.54	0.105
80-84	7.22	0.139
85-89	5.36	0.187
90-94	3.92	0.255
95-99	2.86	0.350
100+	2.50	0.400

When we know the mortality rate in the different age, we can convert rate to probability (P) assuming an event occurs at a constant rate (r) over a time period between time zero to some time beyond such as time periods between the first year and the fifth year is 4 (t):

$$\mathbf{P = 1 - \exp\{-rt\}}$$

= probability of an event over the period t

And we can convert probabilities back to rates to exploit their mathematical features (e.g. changing cycle length)[121, 122]:

$$\mathbf{r = -[\ln(1 - P)] / t}$$

For example, assume 596 patients are followed up for 1.85 years after which 33 have had a CV event and death. Assuming a fixed rate with respect to time, what is the failure rate? And what is the transitional probability of dying from CV event.

Rate = -[ln (1 – (33 / 596))] / 1.85 = 0.03079

To convert to a yearly probability (or transitional probability):

Probability = $1 - e^{-0.03079(1)} = 1 - EXP(-0.03079 \times 1) = 0.0303$

Why is CUA appropriate?

CUA may be the most appropriate analysis tool when:[118, 123]

- Quality of life (QOL) is an important outcome when evaluate the outcome associate with the the intervention which related to the patient function and well-being combine with the mortality such as evaluation of the outcome of acute myocardial infarction that the objective is life saved with the quality of life, evalutation the treatment of cancer; chemotherapy may increase survival but decrease quality of life.
- The intervention affect not only mortality but also morbidity and a unit of outcome is desired such as estrogen use by postmenopausal women for reduce mortality from heart disease, improve quality of life from the menopause symptom while estrogen may be increase mortality from uterine cancer.

- The intervention affects the outcome for comparison. For example, when the decision maker allocate limited resources between the intervention that have different objective and resultant benefits such as between providing increased prenatal care or expanding a hypertension screening.
- The analysis need to evaluate the benefit that derived from the different healthcare intervention.
- The goal is comparison the intervention with others that have been evaluated in terms of cost per QALY gained.

Useful of HRQOL in economic evaluations

The use of functional and health status and health-related quality of life measures by clinical nephrologists has begun. That use must grow if health status measurement is to survive as a useful clinical practice. Clinical use of functional and health status measures is being produced, reference values for ESRD patients have been established, and clinical experience with health status outcomes is increasing. All major dialysis chains are examining the use of health status measures and many are moving to implement widespread use as supporting data for quality of care assessment From the Health utility scores meet the criteria for calculating quality-adjusted life years (QALY), and the requirements of published guidelines for economic evaluations of pharmaceutical and other health care services. The formula to calculate the QALY is following[124]

$$\text{QALYs} = \text{Life year gained (years)} \times \text{utility}$$

When utility is value between 0-1

0 = worst health state

1 = perfect health state

Measuring health-state utility is usually based on a definition of utility as the individual's relative preferences between different health states. Normally a scale between 0 and 1 is used, where 0 represents death or the worst-case scenario and 1 represents perfect health. However, utility score can be less than 0 that mean the health state for them is worse than death.[125, 126] QALYs are a commonly accepted measure of the health benefit from a certain intervention.

Utilities in Cost-effectiveness Analysis

Pharmacoeconomics has become an important discipline in the development and marketing of drugs in the 1990s and it will continue to grow in importance in the 21st Century. Pharmaceutical companies are becoming more aware of the need to gain expertise in this area as they start to use these techniques in clinical trials to help get regulatory approvals and more importantly to convince pharmacies of the value of stocking the products. It is the ever increasing cost of medical care that has led manufacturers of medical devices and pharmaceuticals to the recognition of the need to evaluate products in terms of cost versus effectiveness in addition to the usual efficacy and safety criteria that are standard to regulatory approvals. The regulatory authorities in many countries are also seeing the need for these studies.

A cost-effectiveness analysis calculates the ratio of additional net costs of a health care intervention to additional effectiveness (benefits) associated with the intervention compared with the next-best alternative.[88] The health effects may be measured in life-years alone, or may include the quality of life in each year as a weighting factor, yielding quality-adjusted life years (QALYs).

Note that some authors refer to a CEA that uses QALYs as an outcome measure as a "cost-utility analysis." A quality-weighting factor (utility rating) of 1 indicates that a health state is equivalent to full health, while a quality-weighting factor of 0 indicates that a health state is equivalent to being dead. The QALYs associated with an intervention are estimated as the sum of the future expected life years weighted by the quality of life (expected utility) in each time interval. An intervention can increase the number of QALYs by changing the quality weighting (utility) even if it has no effect or a negative effect on survival; an intervention that improves symptoms can increase the expected utility.

The incremental cost-effectiveness ratio is calculated as the ratio between the incremental differences in costs associated with two alternative treatments to the incremental difference in QALYs associated with the alternatives. This ratio is defined only if the more expensive intervention is also more effective, since otherwise one choice would dominate the other. The challenge of incorporating quality of life effects into CEAs arises from the difficulty in measuring the utility associated with the health states. The results of CEAs can be highly sensitive to the methods used to calculate utility. The estimation of the quality weight for a given time period and treatment requires successfully completing two tasks:

- Measuring the impact of the intervention on the distribution of health states, which requires completely characterizing the health states that are influenced by the treatment.
- Assessing the preferences (utilities) for these alternative states of health.

Anemia treatment using EPO in chronic kidney disease has consistently improve HRQOL as demonstrated by 2 meta-analysis[53-54] In conclusion, the use of utilities provides a valuable method for assessing and incorporating quality of life for decision making at the clinical and health policy levels. Utilities provide a common metric that allows comparison across different health states. They can be used as quality weighting factors to estimate quality adjusted life years for cost effectiveness analysis. Chronic kidney diseases that need to have a dialysis, the considerable burden should consider on patients and families. Self-care patient correlated with co morbidities that may worsen the self-care of patient while previous study only interest focused mostly on medical and technical aspects of dialysis care, psychosocial aspects are now increasingly studied, among them quality of life (QOL) and satisfaction with care.

In this study, the change in health status is measured as changes in Hb concentrations and following changes in QOL. During each branch in the model, the Hb level is used to determine the QALY weight. Information about changes in QOL associated with changes in Hb concentrations. Utility levels are measured using the SF-6D instrument.

Costs

1. Direct medical cost includes expenses associated with various levels of physical activities such as medicine, physician visits, costs of in center HD (costs for physician fee, personnel and material), emergency room visits, cost of cardiovascular, non-cardiovascular side effect treatment and hospitalisation per year, home care, supportive care, ICU cost from the event

2. Direct non-medical cost is the out of pocket expenses for the product and service incurred as a result of care which are not medical care, such as cost of informal care (food, accommodation), transportation, paid caregiver time.

3. Indirect cost is the opportunity cost associated with loss of work including the days of hospitalization that are calculated for people employed using the human capital approach, days off work per patient, days for which a caregiver has to

stay away from work to look after the patient, loss of school days or the number of days away from school; these costs are derived from the number days loss work multiplied by the average daily earnings. This is the official figure reported by the National Statistical Office in Economic and social statistics Bureau; the labor force survey in 2010 (206 Baht per day in Bangkok).

Perspective

The study will be performed from the view that appropriate with the objective such as if the researcher's status is the provider, they will handle in the provider perspective. However, societal perspective has been recommended by national health policy experts.[80] This perspective includes a wide range of costs and outcomes. It also provides information applicable for decision making that intergrates all parties involved in the health care system not specific only at patients or hospitals or third parties.

Decision model

Decision analysis (Decision tree) [118, 127, 128]

Decision analysis is a systematic approach to decision making in the condition of uncertainty. Because of decision under the absolute certainty is difficult. Decision analysis can be used to assist the decision maker to

- Identify the available options of their facing.
- Predict the outcomes of each option.
- Assess the probability of the possible outcome.
- Determine the value of outcomes.
- Select the determination options which give the best pay off.

Decision analysis use the decision tree to organize the elements involved in the decision, start with the choice alternatives. A choice node indicate the point in time when decision maker determine to choose the one of the several options, the possible option then originates as branches to the right of the initial choice node. This tree will provide the structure for the cost of study. The branch option with the lower expected cost will be the selected option for the decision. Decision tree model can be applied to the estimates of financial impacts of new drug.

Analysis for a chronic illness is also derived using data from a CEA with the addition of epidemiologic data on the incidence, prevalence, and natural history of the disease of interest. It is assumed that the cost effectiveness model for chronic condition takes a lifetime perspective and tracks the person after treatment with the new drug over their remaining lifetime.

Limitation of decision tree

1. The structure allows progress in one way (left to right), this model can not move back and forth between states. Thus decision tree may not be very suitable for some health conditions where there are recurrent events such as chronic disease.

2. The decision tree does not have a temporal element or every situation happen at a single time point. Thus, if anything happens at other periods of time or sequentially it has to be calculated outside the model and entered in the terminal node stage.

State-transitional model (Markov model) [118, 127, 128]

Markov model is the complex model form. It can categorize to health status with a higher level of detail and divide the model's time perspective into finer intervals more than decision tree. They can reduce the size of decision trees and show the option clearly. This model can represent a series of situations that unfold over time. Markov model defined health state, at the end of each cycle, the patient can

move from one state to another, defined by transition probabilities. Transition probabilities can depend on the current item such as chance of death. The probabilities of moving from one state to all possible state should always add up to 1. There are 7 steps in set up a Markov model

1. Identify the Markov states and the allowable transitions
2. Choose the length of the cycle.
3. Find out and set the initial and transition probabilities
4. Give values (pay off) to the outcomes in the model.
5. Set the stopping rule
6. Decide on the process for analysis
7. Test the validity of the model.

Decision tree is one of the simplest means of modeling uncertainty, they explain or predict short outcomes by addressing choices and uncertainties associated with diagnosis and treatment decisions. Markov model is used to predict long term, more complex outcomes of a treatment. In some cases, the models are complex but give a little benefit over information from RCTs when predict the real practice of outcome.[127] The value from the models lies partly in their ability to predict "real world" cost effectiveness under a variety of assumption. The value can be robusted with the appropriate sensitivity analysis when assumptions and the estimated outcomes are varied.[128]

Both Markov and decision tree model can be used to generate estimates the impact of the new intervention on the outcome of treatment because the model objective or structure or assumptions can be assisted the users with understanding of the analysis and its approach. For health condition definition, the different levels of severity and treatment pathways can be presented. Additionally, the model is programmed to accept various situations. Input parameters such as prevalence, drug costs in this module, the decision models such as Markov or Decision tree can be used to estimate the cost of this study. Finally, analyses using Markov model is appropriate for chronic illness where the new drug slows disease progression. CKD with HD is a chronic disease which should be modeled by using the complex model such as Markov model. HD patient almost have the adverse event such as cardiovascular and non cardiovascular event. Although many study shows that the normalized Hb can defined the benefit of QOL and decrease the cardiovascular event[29-34] such as cardiovascular effects with regression of left ventricular hypertrophy (LVH) but 3 large RCTs[32, 35, 37] found that the opposite results.

Sensitivity Analysis[118, 123, 129]

All output in the study have the variation (uncertainty) from many reasons such as the different sources of variation in the input of a model such as pooled data sets, meta-analyses, unverifiable assumptions. Sensititvity analysis is a technique for systematically changing parameters in a model to determine the effects of such changes. Uncertainty and sensitivity analyses investigate the robustness of a study when the study includes some form of the modelling. Sensitivity analysis can be support decision making or the development of recommendations for decision makers, making recommendations or compelling or persuasive from modellers to decision makers. Nevertheless, sensitivity analysis increased understanding relationships between input and output variables and model development such as searching for errors in the model. While uncertainty analysis studies the overall uncertainty in the conclusions of the study, sensitivity analysis is a tool to ensure the quality of the assessment and sensitivity analysis tries to identify what source of uncertainty weights more on the study's conclusions. The term sensitivity analysis

encompasses several techniques and it is useful to distinguish three approaches as following:

1. One way sensitivity analysis examines the impact of each variable in the study by varying it across a reasonable range of values while other variables still holding constant at their estimate value.

2. Extreme sensitivity analysis involves setting each variable at the same time to take the most optimistic or pessimistic value in order to generate the best or worst case scenario. In real life, of course, the components of an evaluation do not vary in loneliness, and nor are they perfectly correlated, so one way sensitivity analyses will probably underestimate, and extreme sensitivity analysis overestimate.

3. Probabilistic sensitivity analysis examines the effect on the results of an evaluation when the fundamental variables are allowed to vary all together across a plausible range according to predefined distributions. These probabilistic analyses may be expected to produce a more realistic interval. Probability analysis derived from a large number of Monte Carlo simulations.

Discounting

In health economic analysis, costs and outcomes are considered over a period that longer than 1 year. Discounting allows two different treatment alternatives in which costs and benefits of a particular reference point generally occur at different times to be compared. Discounting is a financial mechanism for a defined period of time, in exchange for a charge on the truth situation that the value of $1 today is not equal $1 in the future. The discount or charge is the difference value between the original amount owed in the present and the amount that has to be paid in the future to settle the debt. The Task Force suggests that the discount rate is often 3-5 %[128] and non monetary outcomes should be discounted in a separate calculation.

CHAPTER III

METHODOLOGY

This chapter started with explaining components of the study and followed by the research design and method. In cost utility analysis (CUA), there were two important variables involved: cost and utility of HD patients who used erythropoietin (EPO). Number of use and the estimation of possible costs of drug and the treatment were done and illustrated in this part. The Markov model was applied to this study. Details of modeling technique used included how the model was constructed by type and data inputs. The study adopted the societal perspectives. The results were presented in terms of incremental cost, incremental Quality Adjusted Life Years (QALYs) gained and incremental cost-effectiveness ratio (ICER) in Baht per QALY.

I. Components of the study

To conduct cost utility analysis, three components are required as followed:

1) Cost is the direct or indirect expense incurred as a part of treating anemia with EPO such as cost of adverse event treatment, cost of hemodialysis, cost of EPO, direct non medical costs and indirect costs.

2) Probability is the chance that each clinical incidence will be occurred. For example, the probability of cardiovascular event, non cardiovascular event, probability of death from cardiovascular disease and non cardiovascular disease.

3) Utility scores of hemodialysis patients who use erythropoietin to maintain the hemoglobin target level**,** specifically quality adjusted life year (QALY)**,** is a measure of the relative satisfaction, desirability, consumption of various goods and services. The individual's relative preferences between different health states. Normally a scale between 0 and 1 is used, where 0 represents death or the worst case scenario and 1 represents perfect health. However, utility score can be less than 0 that mean the health state for them is worse than death.

II. Research Design

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

(1.1) Model structure

This study combined both the decision tree and the Markov models. The decision tree model was used to optimize the maintenance of the different hemoglobin targets in HD patients in routine clinical practice using EPO for anemia treatment portfolio. In developing the decision tree, 5 maintaining Hb levels, i.e., Hb ≤ 9, >9 to 10, >10 to 11, >11 to 12, >12 g/dl were displayed as choice node as shown in the figure 3.1 Connected to each choice node was one Markov model which ran after the decision of Hb target, as shown in the figure 3.2.

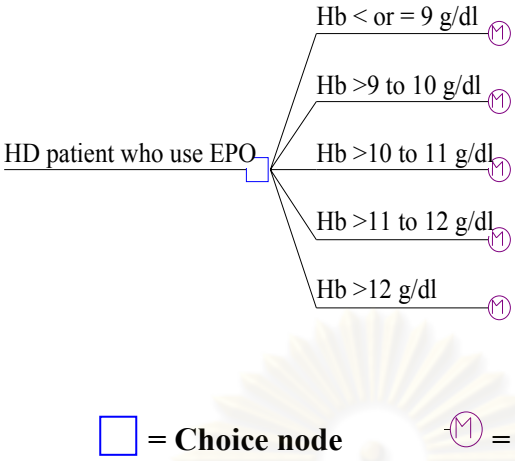

Figure 3.1 Decision tree models of 5 maintaining Hb levels decision

Four possible outcomes of HD patients were alive with the cardiovascular conditions (CV), alive with non-cardiovascular condition (nCV) such as catheter-related infections, or without any complication, dead from CV conditions (death from CV state), and dead from nCV conditions (death from nCV state). Thus the Markov model was composed of 4 states, i.e., death from CV, death from nCV, hemodialysis (HD) with nCV, hemodialysis with cardiovascular disease (HDCV) as figure 3.2. The Markov model encompassed these 4 clinical consequences were identified as chance nodes after the physicians decide to treat the anemia event in HD patient. Four health states were denoted in the solid line ovals. An arrow indicated the probability of moving from one state to another. It was determined by transitional probabilistic parameters. A fixed 1 year cycle length was assigned. The time horizon of the analysis was the life time of a patient. Costs and QALYs gained were calculated as patients went through the model. Patients were characterized by their hemoglobin level with the aim of health state determination for enter.

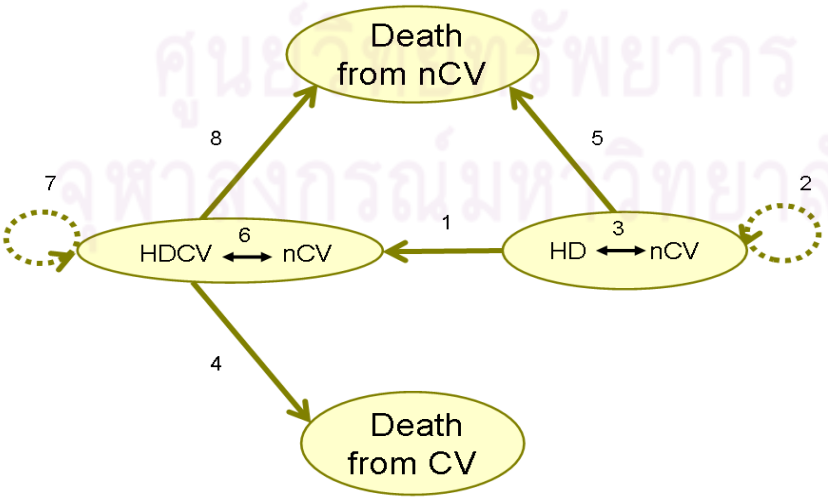

Figure 3.2 Schematic diagram of the Markov model

In this Markov model, we classified hemodialysis patients for 2 groups; 1) the patients who were alive with hemodialysis (HD state) and 2) the patient who were alive with hemodialysis and required cardiovascular treatment (HDCV state). When the HD state's patients moved to the HDCV state (the arrow no.1), they could not move back to the HD state (dotted-line arrow no.7) because CV disease was the chronic condition that once attacked, required medical treatment until death. They could stay on the HDCV state with or without nCV events (the arrow no.6). HDCV, if with nCV, would be treated and returned to HDCV which would finally move to the absorbing state, death from CV state (the arrow no.4). If the nCV treatment was fail, they would move on to another absorbing state, death from nCV state (the arrow no.8). No event in the first cycle was allowed, which implied no event within the first year after treatment. At the HD state, patients could stay on (dotted-line arrow no.2) with or without nCV events (the arrow no.3). Patients could then move to the death from nCV state (arrows no.5) which was the absorbing state. It was assumed that once the patients have HD or HDCV, they would continue with HD until death (absorbing health state). The moving to any state was assumed to be independent of their changing hemoglobin levels and dose escalation was not considered in this model. The movement between each state is determined by probabilities that were obtained from randomized control trial and systematic reviews.

Case scenario

Male patient, 59 years old, diagnostic as ESRD and anemia (Hb = 8 g/dl) so that he need to hemodialysis and use EPO. The question of this situation: what is the appropriate maintaining Hb target that is the lowest incremental cost effectiveness were choosed. In this model, patient started to receive EPO for anemia treatment when hemoglobin level fell at 8 g/dl. And the physicians decide to increase his Hb level to higher Hb. For example, Hb level target is11 g/dl so EPO dose for him is 4,854.24 IU/ time, 3 times weekly until he has any event that attack his life. Assume that all patient response immediately at the end of the cycle but lasting for only one cycle. If he have the CV event in this cycle, he still have CV treatment with HD forever (HDCV) until he die but in the next cycle he has the probability to have nCV event or CV event attack again and he has to treat, then he has a probability to dead or alive. If he alive, he has the probability of any event again. He still alive with HDCV state and continue move to other state (except HD state) or stable at the HDCV state in the cycle until dead. The movement between each state is determined by probabilities that were obtained from randomized control trial and systematic reviews which are clarified in section 1.2

(1.2) Input parameters

i) Transitional probabilities

Transitional probabilities used in this study were obtained mainly from a systematic review of the literature using the PubMed database, the National Coordinating Centre for Health Technology Assessment (NCCHTA), the Cochrane library, and the ClinicalTrials.gov website. Searching was conducted during 1 January 1966 and 31 December 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. The inclusion criteria and exclusion criteria were as follow;

Inclusion criteria

1. The studies of efficacy of EPO (e.g. erythropoietin beta, and alfa).

2. The methodology of the studies was randomized controlled trials, meta-analysis of RCTs, which assessed the effects of targeting different Hb concentrations when treating patients with anemia caused by CKD with EPO. Potential therapies used to achieve target hemoglobin concentrations were erythropoietin beta, Erythropoietin alfa.

3. The studies were targeted patients aged greater than 18 years.

4. The studies of hemodialysis patients.

Exclusion criteria

1. Non-randomised trials or RCTs which were the evaluating other interventions such as subcutaneous versus intravenous EPO treatment for anemia of CKD, the outcomes were reported such as blood viscosity, hematopoietic progenitor cell assays.

From the clinical trial, we derive the compound mortality rate and then we calculate the disease specific mortality rate from the following formula:

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

when, μ_D: Diseases specific excess mortality rate (fixed rate)

μ_C: Compound mortality rate derived from the study in the literature

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

LE_{ASR} (ASR: age, sex, race adjusted life expectancy) is life expectancy of the Thai general population classified by age group (derived from Life table of Vital statistics Thailand 2006) as shown in the table 2.7

For example, assume CV mortality rate from the clinical trial is 0.202 and the average age of the patient in the trial was 69. What is the diseases specific excess mortality rate*? And what is the* compound mortality rate *when the age of the patient was 79 years old.*

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

$0.202 = \mu_D + 0.065$

$\mu_D = 0.137$

Diseases specific excess mortality rate = 0.137 and μ_D is a fixed rate so that we can calculate the compound mortality rate when the age of the patient was 79 years old from the same formular;

$\mu_C = 0.137+0.105 = 0.242$

When we know the mortality rate in the different age, we can convert rate to probability(P) assuming an event occurs at a constant rate (r) over a time period between time zero to some time beyond such as time periods between the first year and the fifth year is 4 (t):

$$P = 1 - \exp\{-rt\}$$

= probability of an event over the period t

And we can convert probabilities back to rates to exploit their mathematical features (e.g. changing cycle length)[121, 122]:

$$r = -[\ln(1 - P)] / t$$

For example, assume 596 patients are followed up for 1.85 years after which 33 have had a CV event and death. Assuming a fixed rate with respect to time, what is the failure rate? And what is the transitional probability of dying from CV event.

Rate = -[ln (1 – (33 / 596))] / 1.85 = 0.03079

To convert to a yearly probability (or transitional probability):

Probability = 1 - $e^{-0.03079(1)}$ = 1 – EXP (-0.03079 x 1) = 0.0303

Model parameters, data sources and values of transitional probability used in the model are presented in the results.

ii) Utility score

Utility score is derived from the SF-6D of which items were drawn from the SF-36 instruments. The utility score represented the quality of life of patients during the interview as the input parameter in the model. Thus, the Hb level identified was the Hb of the patient collected during the lastest visit before the questionnaire interview. The questionnaire of this study included KDQOL-SF™ 1.3 in Thai language version[113] that contained questions from the SF-36 plus an additional 43 kidney disease–specific items and EQ-5D questionnaire. One hundred and fifty two patients were enrolled from 5 hemodialysis sites of Nephrology Unit at Siriraj Hospital that was the university hospital where the patients came from throughout Thailand. Microsoft Excel spreadsheet version 2003 and SPSS version 14 were used for utility analysis.

Inclusion Criteria

Patients use EPO at least 6 months with titration of EPO therapy is permitted.

Exclusion Criteria

- Patients under 18 years old.
- Patients who have blood transfusion for anemic treatment within 6 months before EPO treatment and before the study starts
- Patients who change the modality of dialysis
- Patients who switch to other anemia treatment method between the study
- Patients who cannot answer the questionnaire and are not willing to participate in the study

Face-to-face interviews were conducted during November-December 2009 after patients signed informed consent. The ethics approval was obtained from Siriraj Institutional Review Board Ethics Committee. The patient specific information regarding demographics, health care scheme, clinical laboratory, prescriptions were collected at baseline and at the time when face to face interview was conducted. Demographic data were obtained included age, gender, marital status, duration of hemodialysis, hemodialysis frequency per week, underlying disease such as diabetes, hypertension, or myocardial infarction. The clinical lab data of patients were included in the retrospective chart review, data were collected for the one year period since starting the face to face interview and this study separated Hb levels of 152 patients to 5 levels such as Hb ≤ 9, >9 to 10, >10 to 11, >11 to 12, >12 g/dl.

The quality of life data obtained from the questionnaire can be transformed into the utility. About the utility, EuroQol were used to calculate the EQ-5D utility based on the scoring function that was derived from a UK and Thai (TH) population utility[92, 95]. The visual analog scale (VAS) of the EuroQol was used as the direct well-being score. From the SF-36, the SF-6D utility was calculated by applying the scoring method that was also derived from a UK preference scores by using the computer algorithm.[81] Pearson's correlation coefficient was used for statistical testing of correlation between EQ-5D, SF-6D, VAS and Hb level. The utility which are highly

correlated with Hb level could be use as the utility parameter in the model of this study and then, the utility score of 5 group levels were examined for cost utility analysis.

iii) Costs

Cost data in the model consists of;

(1) Direct medical costs, the cost of HD treatment, cost of EPO use, cost of treating CV and nCV events (nCV event including other event except cardiovascular event resulting in hospitalization for 24 hours or more or prolongation of hospitalization); CV event including myocardial infarction, stroke, heart failure, revascularization (percutaneous transluminal coronary angioplasty, or coronary-artery bypass grafting) resulting in hospitalization for 24 hours or more or prolongation of hospitalization.

a) The costs of HD treatment were calculated by the number of HD per year multiplying by HD cost (Baht/HD visit).
   *Annual cost of HD = Number of HD per year * HD cost (Baht/HD visit)*
b) Costs of CV treatment were calculated by the number of in-patient visit per year because CV event multiplying by its CV treatment cost (Baht/in-patient visit)
   *Annual cost of CV treatment = Number of in-patient visit per year*treatment cost per visit*
c) Costs of nCV treatment were calculated by the number of in-patient visit per year because nCV event multiplying by its nCV treatment cost (Baht/in-patient visit)
   *Annual cost of nCV treatment = Number of in-patient visit per year*treatment cost per visit*
d) Annual EPO cost per patient, it should be calculated from the unit cost (the societal perspective; unit cost = selling price = 0.325 Baht while the hospital perspective; unit cost = acquisition cost = 0.262 Baht) multiplied by the amount of use per year. The average unit cost for EPO is calculated based on the drug price list in 2009 at Siriraj hospital concerning the consumption of erythropoietin (Recormon®, Hemax® and Eprex®). The amount of EPO dose should be calculated as the formular, the dose per time (D) which is expected to increase hemoglobin from a pretreatment level (Hb0) to a desired steady state level (HbSS) when given intravenously three times per week for 11 weaks.[52]

   $$D = 2400 \text{ IU} / \sqrt{[9.6 / (HbSS - Hb0)] - 1}$$

The treatment costs which incurred at inpatient department were estimated based on the actual costs of the event treatment (the event that classified by the Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10) as table 3.1) at Siriraj hospital in 2009 and calculated using the average cost method.

Table 3.1 Classification of CV events that including in the study by ICD-10.

Code (ICD 10)	Disease
I20	ANGINA PECTORIS
I21	ACUTE MYOCARDIAL INFARCTION
I22	SUBSEQUENT MYOCARDIAL INFARCTION
I23	CERTAIN CURRENT COMPLICATIONS FOLLOWING ACUTE MYOCARDIAL INFARCTION
I24	OTHER ACUTE ISCHAEMIC HEART DISEASES
I25	CHRONIC ISCHAEMIC HEART DISEASE
I42	CARDIOMYOPATHY
I46	CARDIAC ARREST
I47	PAROXYSMAL TACHYCARDIA
I48	ATRIAL FIBRILLATION AND FLUTTER
I49	OTHER CARDIAC ARRHYTHMIAS
I50	HEART FAILURE
I60	SUBARACHNOID HAEMORRHAGE
I61	INTRACEREBRAL HAEMORRHAGE
I62	OTHER NONTRAUMATIC INTRACRANIAL HAEMORRHAGE
I63	CEREBRAL INFARCTION
I64	STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION
I65	OCCLUSION AND STENOSIS OF PRECEREBRAL ARTERIES, NOT RESULTING IN CEREBRAL INFARCTION
I66	OCCLUSION AND STENOSIS OF CEREBRAL ARTERIES, NOT RESULTING IN CEREBRAL INFARCTION
I70	ATHEROSCLEROSIS
I73	OTHER PERIPHERAL VASCULAR DISEASES
I74	ARTERIAL EMBOLISM AND THROMBOSIS
I77	OTHER DISORDERS OF ARTERIES AND ARTERIOLES

For this model, EPO were given when the hemoglobin level start at 8 g/dl. The target results were that the patient's hemoglobin level reached to the Hb level as the choice node. The amount of EPO use for increasing the Hb levels to the different Hb level per patient per week was shown as the table 3.2.

After the Hb level reach to the target level, the maintenance dose of EPO is still in these dose until the patients have any situation which attack their symptom such as the operation or bleeding, then the physician have to adjust the EPO dose.

Table 3.2 Amount of EPO per patient per week for increasing the Hb levels to the different target level.

Hb level	Dose EPO per week (IU)
Hb level from 8 to 9 g/dl	2,455.18
Hb level from 8 to 10 g/dl	3,693.52
Hb level from 8 to 11 g/dl	4,854.24
Hb level from 8 to 12 g/dl	6,085.11
Hb level from 8 to 13 g/dl	7,506.52

Annual cost of EPO =Unit cost * amount of use per year

For example, annual cost of EPO for the patient who have the start Hb at 8 g/dl and she use EPO for increasing Hb to 10, she need EPO 3,693.52 IU per week as Table 3.2 and one year = 52 weeks, EPO selling price = 0.325 Baht/unit

*Annual cost of EPO = 0.325*3,693.52*52 Baht*

(2) Direct non medical costs

Direct non medical costs (e.g., food cost, travelling costs and accomodation for patients and their caregiver) derived from the structured questionnaire interviews (as showed in the appendix 3 and the example of filling data were showed in the appendix 4) from 152 patients receiving treatment for HD at Siriraj hospital between November and December 2009.

(3) Indirect non medical costs such as inco,me lost as a result of sick leave or hospital visits. It should be calculated from the minimum wage in 2010 (206 Baht/day) multiplied by the length of stay from \the sick leave or providing informal care (days). While mortarity costs were excluded to avoid double-counting since helath outcome as QALYs had already been taken into account the mortality effects.[130]

All costs were included when the societal perspective was considered but only cost item (1) was included for the hospital or health care provider's perspective. For inter-country comparisons, costs can be converted into $US using the purchasing power parity exchange rate of $US1 = 32.45 (April 2010) Thai Baht. The values used in the model are presented in the results section.

(1.3) Perspective

This study was conducted based on societal and hospital perpectives.

(1.4) Time horizon

This study was chosen to model cost and treatment effect for lifetime period.

(1.5) Treatment alternatives

In this pharmacoeconomic evaluation, four Hb level such as >9 to 10, >10 to 11, >11 to 12, and >12 g/dl, which are the possible Hb level in HD patient after treated with EPO for anemia treatment in Thailand were compared to the lowest Hb level (≤9 g/dl).

(1.6) Sensitivity Analysis

i) One way sensitivity analysis was conducted on rate of having CV and stay on HD from RCTs (rate = 0.194). And we consider the changing of net health benefit (NHB) when providing this rate between 0.1 to 0.9

ii) Probabilistic sensitivity analysis was performed by Monte Carlo simulation. It was carried out using TreeAge™ Software. Monte-Carlo simulation was used by involving random sampling of each variable under the specified probability distribution within the model to produce more than one thousands of iterations. All input parameters were assigned probability distributions according to their feature to reflect the feasible range of values that each input parameter could attain. Gamma-distribution, which ensures positive values, was modeled for all costs parameters and Beta-distribution was chosen for the probability and utility parameters, which were bounded zero-one. We calculated the alpha and beta value for push in the specified distribution from the following formula:

Gamma distribution; $\text{alpha} = (\text{mean}/\text{SE})^2$

$\text{beta} = \text{mean}/(\text{SE}^2)$

Beta distribution; $\text{alpha} = \text{mean}^2((1-\text{mean}) / (\text{SE}^2))$

$\text{beta} = [\text{mean}(1-\text{mean})/\text{SE}^2]-\text{alpha}$

The simulation drew one value from each distribution simultaneously and calculated cost and effectiveness pairs. A Monte-Carlo simulation was repeated 10,000 times to provide a range of possible values given the specified probability distribution, each time using different randomly all selected values. The results were expressed as average value of all costs, QALYs and ICER in the Results section. And we calculate

1.6 Discounting rate

Discounting was performed since the time horizon was longer than one year. Discounting allows two different treatment alternatives in which costs and benefits of a particular reference point generally occur at different times to be compared. Discounting of costs and effects at 3% per annum by following WHO guide to cost effectiveness analysis.

1.7 Determine incremental cost effectiveness ratio (ICER)

The incremental cost effectiveness ratio (ICER) was calculated by incremental cost divided by incremental effecetiveness.

$$ICER = (C_I - C_N) / (E_I - E_N)$$

When; C_I = Intervention cost

C_N = Null cost

E_I = Intervention effectiveness

E_N = Null effectiveness

1.8 Determine net health benefit (NHB)

NHB is the alternative approach is to measure cost-effectiveness. The NHB was calculated by the following formular;

$$NHB = (E_A - E_B) - [(C_A - C_B) / WTP]$$

When; E_A = Effectiveness of strategy A
E_B = Effectiveness of strategy B
C_A = Cost of strategy A
C_B = Cost of strategy B
WTP = Williness to pay

The strategy A is appropriate when the NHB values is more than 0 and the high NHB is better than the low NHB

CHAPTER IV
RESULTS

To conduct the cost utility analysis of erythropoietin (EPO) for maintaining the different hemoglobin (Hb) target levels in anemic hemodialysis (HD) patients in routine clinical practice, the following six key elements are required; 1) general characteristics of the patients who answering the KDQOL questionnaire from face to face interview, 2) utility and quality of life, 3) probability of cardiovascular event, non cardiovascular event, probability of dead from cardiovascular disease and non cardiovascular disease, 4) costs, 5) cost utility analysis and 6) probabilistic sensitivity analysis. This chapter provides the details of each element in sequence.

I. General characteristics

Face-to-face interviews questionnaire of the study was KDQOL-SF™ 1.3 that included questions from the SF-36 plus an additional 43 kidney disease–specific items and EQ-5D questionnaire. One hundred and fifty two patients were enrolled from 5 hemodialysis sites of Nephrology Unit at Siriraj Hospital and their general characteristic data were shown in the Table 4.1

Table 4.1 General characteristic of 152 hemodialysis patients

Characteristic	Value
Age (yrs, Mean ± SD)	57.32±14.52
Gender (%)	
Male	47.40%
Female	52.60%
Marital status (%)	
Single	41.45%
Couple	58.55%
Underlying disease (%, n)	
Diabetes	27.63%
Hypertension	76.97%
Myocardial infarction	14.47%
Other	9.21%
Frequency of hemodialysis	
2 times per week (%)	41.45%
3 times per week (%)	58.55%
Length of HD (yrs, mean ± sd)	7.66 ± 4.87
Clinical laboratory	
Hb (g/dl)	10.75 ± 1.64
Albumin (g/dl)	3.96 ± 0.37
Creatinine (mg/dL)	11.21 ± 5.49
BUN (mg/dL)	69.37 ± 16.77

Patients were grouped into 5 Hb levels, i.e., Hb ≤ 9, >9 to 10, >10 to 11, >11 to 12, >12 g/dl because these levels were approximately targeted in the real practice in the institute. The difference of 1 g/dl Hb was the level which allowed clinical symptoms and the evidence of mortality rate to be differentiated. The basic

demographic data by Hb level of the 152 patients included in this study were shown in the Table 4.2

Table 4.2 Basic characteristic by Hb level

Parameter	≤ 9 (n = 26)	>9-10 (n = 18)	>10-11 (n = 40)	>11-12 (n = 35)	>12 (n = 33)	p-value
Age (yrs)						0.096 [a]
Mean	50.88	55.06	58.45	59	60.48	
SD	14.15	18.07	13.57	14.16	13.29	
Gender						**0.006** [b]
Male (%)	38.46	16.67	60	62.86	39.39	
Female (%)	61.54	83.33	40	37.14	60.61	
Marital status (%)						0.110 [b]
Single*	65.38	38.89	37.5	34.29	36.36	
Couple	34.62	61.11	62.5	65.71	63.64	
Underlying disease (%)						
Diabetes	34.62	33.33	22.5	25.71	27.27	0.823 [b]
Hypertension	73.08	94.44	75	77.14	72.73	0.441 [b]
MI	11.54	11.11	22.5	5.71	18.18	0.581 [b]
Other	3.85	5.56	10	14.29	9.09	0.682 [b]
Length of HD (yrs)						0.622 [a]
Mean	8.73	7.64	7.61	7.87	6.68	
SD	5.62	4.28	5.69	3.77	4.59	
Frequency of HD per week						0.110 [b]
2 times (%)	65.38	38.89	37.5	34.29	36.36	
3 times (%)	34.62	61.11	62.5	65.71	63.64	

a: ANOVA test
b: Chi-square test
* Including single, widow, divorce

Mean Hb for all patients were 10.75 g/dl. Mean Hb levels were 8.06 in the ≤ 9 group, 9.62 in the > 9 to 10 group, 10.58 in the >10 to 11 group, 11.60 in the >11 to 12 group, and 12.79 in the > 12 group (P <0.001) as shown in the Table 4.2.Albumin, creatinine, and blood urea nitrogen (BUN) levels were not different in the five Hb levels (P> 0.05); these mean of albumin, creatinine and BUN values were similar in all five Hb levels (Table 4.3).

Table 4.3 Clinical laboratory by Hb level (Mean ± SD)

Parameter	≤ 9 (n = 26)	>9-10 (n = 18)	>10-11 (n = 40)	>11-12 (n = 35)	>12 (n = 33)	p-value
Hb (g/dl)						**0.000**
Mean	8.06	9.62	10.58	11.6	12.79	
SD	0.74	0.33	0.29	0.32	0.55	
Albumin (g/dl)						0.700
Mean	3.91	3.99	3.98	4.02	3.91	
SD	0.43	0.42	0.37	0.29	0.39	
Creatinine (mg/dL)						0.766
Mean	10.5	10.7	10.89	11.32	10.43	
SD	2.94	2.99	3.34	2.95	2.89	
BUN (mg/dL)						0.201
Mean	68.58	71.23	69.99	73.46	63.87	
SD	18.6	17.26	17.93	15.93	13.6	

II. Utility and quality of life

2.1 Quality of life

The score of quality of life in KDQOL questionnaire were transformed onto 0 to 100 scale range shown as the Table 4.4 between symptom/problem, effects of kidney disease, burden of kidney disease, work status, cognitive function, quality of social interaction, sexual function, sleep, social support, dialysis staff encouragement, patient satisfaction. The better status patients were indicated with the higher score. The internal consistency reliability estimates of the KDQOL-SF^{TM} scale, mean and SD of the questionnaire in 152 hemodialysis patients were shown in the table 4.4**.**

Table 4.4 Mean, SD and Reliability of Kidney disease specific disease scales

Scale	Number of Items	Mean	SD	Reliability
Kidney disease specific				
Symptom/ Problem list	12	77.45	15.05	0.780
Effects of Kidney Disease on Daily Life	8	61.29	22.98	0.772
Burden of kidney Disease	4	44.08	30.01	**0.687**
Work status	2	49.01	39.23	0.783
Cognitive function	3	83.33	17.75	**0.579**
Quality of social interaction	3	86.54	14.89	**0.484**
Sexual function	2	73.91	30.37	0.883
Sleep	4	61.63	23.24	**0.623**
Social support	2	87.83	19.46	0.735
Dialysis staff encouragement	2	88.24	18.32	0.789
Patient satisfaction	1	75.99	20.28	NA

Mean values for the kidney disease targeted scales ranged from 44.08 (Burden of kidney Disease, SD = 30.01) to 88.24 (Dialysis staff encouragement, SD = 18.32) on the percent of total possible (0-100) scores. Internal consistency reliability of the six scales in kidney disease scale (the Symptom/ Problem list, Effects of Kidney Disease on Daily Life, Work status, Sexual function, Social support and Dialysis staff encouragement) was good (Cronbach's α = 0.735–0.883). However, internal consistency reliability estimates for the KDQOL-SF™ targeted scales less than 0.700 with four dimensions (0.687 for Burden of kidney Disease, 0.579 for cognitive function, 0.484 for quality of social interaction and 0.687 for sleep). Only Cronbach's α of sleep dimension was increasing more than 0.700 (Cronbach's α = 0.716) when deleting an item 12D (I feel like a burden on my family). While Cronbach's α of Quality of social interaction and Sleep dimension was increasing but stil less than 0.700 (Cronbach's α = 0.534, 0.648, respectively) when deleting an item 13C (Did you act irritable toward those around you?) and 18C (have trouble staying awake during the day) as showed in the appendix 5.

For our hemodialysis patients, we compare the quality of life measures in the patients 5 groups as Hb level ≤9, >9-10 g/dl, >10-11 g/dl, >11–12 g/dl and >12 g/dl. The results of KDQOL questionnaire were shown as the table 4.5.

Table 4.5 Kidney Disease Quality of Life Short Form Questionnaire scores and hemoglobin levels.

Parameter	≤ 9 (n = 26)	> 9 to 10 (n = 18)	>10 to 11 (n = 40)	>11 to 12 (n = 35)	> 12 (n = 33)	P-value
Kidney disease specific						
Symptom/ problem list	74.8	78.6	76.6	77.3	80.1	0.723
Effects of kidney disease	49.0	68.1	62.0	64.2	63.3	**0.042**
Burden of kidney disease	34.9	43.4	41.7	51.6	46.6	0.274
Work status	51.9	50.0	47.5	54.3	42.4	0.781
Cognitive function	80.0	84.8	82.2	83.2	86.7	0.671
Quality of social interaction	85.1	88.9	82.7	87.2	90.3	0.234
Sexual function	60.0	68.8	72.5	83.9	78.1	0.779
Sleep	58.6	60.8	59.3	60.5	68.6	0.422
Social support	86.5	89.8	84.6	91.4	87.9	0.630
Dialysis staff encouragement	88.9	86.8	88.8	87.1	89.0	0.986
Patient satisfaction	64.6	69.4	63.5	67.4	72.7	0.213
SF-36						
General health	29.8	45.8	35.4	43.1	44.2	**0.023**
Physical functioning	60.2	57.8	60.0	63.6	67.1	0.836
Role physical	65.4	66.7	87.5	79.3	82.6	0.060
Pain	58.0	69.4	71.5	73.9	74.7	0.162
Emotional well being	72.9	75.3	71.2	80.2	84.1	0.106
Role emotion	59.0	79.6	85.8	79.0	84.8	**0.015**
Social function	79.8	83.3	93.8	96.1	93.2	**0.008**
Energy/fatigue	58.7	56.7	59.9	60.9	71.4	0.173
Physical component summary	40.9	41.8	43.9	44.1	45.0	0.397
Mental component summary	48.1	50.9	51.1	53.7	55.9	**0.039**
Overall health	64.6	69.3	63.6	67.5	72.7	0.235

About kidney disease specific, only effects of kidney disease scores was significantly difference between Hb levels (p= 0.042). For SF-36, almost of physical domains was not significantly difference except general health component which were significantly difference in the difference of Hb level (p=0.023) as the table 4.5. For mental domains, the difference between 5 groups of Hb levels were not significant in a variety of quality of life domains but the difference was statistically significant in role emotion scores and social functioning scores; p-value = 0.015 and 0.008 respectively.

Post-hoc analysis was conduct for the multiple comparisons, the significant difference of pairwise from ANOVA tests can be detected by LSD more than Bonferroni as the table 4.6.

Table 4.6 Post-hoc analysis

Hb level comparison		General health	Role emotional	Social function	SF-12 Mental	Effects of kidney disease
LSD						
1. ≤9	2. >9 to10	**0.013**	**0.039**	0.564	0.359	**0.007**
	3. >10 to 11	0.289	**0.001**	**0.006**	0.239	**0.023**
	4. >11 to 12	**0.014**	**0.018**	**0.002**	**0.032**	**0.010**
	5. >12	**0.009**	**0.003**	**0.011**	**0.004**	**0.017**
2. >9 to10	1. ≤9	**0.013**	**0.039**	0.564	0.359	**0.007**
	3. >10 to 11	0.078	0.501	0.067	0.956	0.347
	4. >11 to 12	0.656	0.951	**0.029**	0.337	0.556
	5. >12	0.794	0.584	0.093	0.095	0.468
3. >10 to 11	1. ≤9	0.289	**0.001**	**0.006**	0.239	**0.023**
	2. >9 to10	0.078	0.501	0.067	0.956	0.347
	4. >11 to 12	0.108	0.367	0.615	0.256	0.678
	5. >12	0.072	0.897	0.903	**0.045**	0.817
4. >11 to 12	1. ≤9	**0.014**	**0.018**	**0.002**	**0.032**	**0.010**
	2. >9 to10	0.656	0.951	**0.029**	0.337	0.556
	3. >10 to 11	0.108	0.367	0.615	0.256	0.678
	5. >12	0.828	0.462	0.550	0.383	0.864
5. >12	1. ≤9	**0.009**	**0.003**	**0.011**	**0.004**	**0.017**
	2. >9 to10	0.794	0.584	0.093	0.095	0.468
	3. >10 to 11	0.072	0.897	0.903	**0.045**	0.817
	4. >11 to 12	0.828	0.462	0.550	0.383	0.864
Bonferroni						
1. ≤9	2. >9 to10	0.130	0.394	1.000	1.000	0.066
	3. >10 to 11	1.000	**0.013**	0.061	1.000	0.234
	4. >11 to 12	0.143	0.180	**0.019**	0.318	0.103
	5. >12	0.090	**0.028**	0.113	**0.037**	0.173
2. >9 to10	1. ≤9	0.130	0.394	1.000	1.000	0.066
	3. >10 to 11	0.782	1.000	0.669	1.000	1.000
	4. >11 to 12	1.000	1.000	0.287	1.000	1.000
	5. >12	1.000	1.000	0.930	0.954	1.000
3. >10 to 11	1. ≤9	1.000	**0.013**	0.061	1.000	0.234
	2. >9 to10	0.782	1.000	0.669	1.000	1.000
	4. >11 to 12	1.000	1.000	1.000	1.000	1.000
	5. >12	0.716	1.000	1.000	0.447	1.000
4. >11 to 12	1. ≤9	0.143	0.180	0.019	0.318	0.103
	2. >9 to10	1.000	1.000	0.287	1.000	1.000
	3. >10 to 11	1.000	1.000	1.000	1.000	1.000
	5. >12	1.000	1.000	1.000	1.000	1.000
5. >12	1. ≤9	0.090	**0.028**	0.113	**0.037**	0.173
	2. >9 to10	1.000	1.000	0.930	0.954	1.000
	3. >10 to 11	0.716	1.000	1.000	0.447	1.000
	4. >11 to 12	1.000	1.000	1.000	1.000	1.000

Because of the LSD test is a two-step test. First the ANOVA test is performed. If it is significant at level alpha, then all pairwise t-tests are carried out, each at level alpha. If the ANOVA test is not significant, then the procedure terminates. The LSD test does not control the set of comparisons while the Bonferroni multiple comparison test is a conservative test, that is, the set of comparisons is not exactly equal to alpha,

but is less than alpha in most situations. Even though the Bonferroni test controls the set of comparisons rate, in many situations it may be too conservative and not have enough power to detect significant differences.[131, 132] About SF-36, the least significant difference (LSD) test showed that the role-emotional scores of the Hb level ≤9 were significantly lower than those derived from Hb >9 to 10 group (p=0.039), Hb >10 to 11 group (p=0.001), Hb >11 to 12 group (p=0.018), and the >12 group (p=0.003). The general health scores of the Hb level ≤9 were significantly lower than 3 Hb level such as Hb level >9 to 10 (p=0.013), Hb level >11 to 12 group (p=0.014), and Hb level >12 (p=0.009). The social function scores of the Hb level ≤9 were significantly lower than 3 Hb level such as Hb level >10 to 11 (p=0.006), >11 to 12 group (p=0.002), and the >12 group (p=0.011) but the score of Hb level >9 to 10 was significantly lower than Hb level >11 to 12 (p=0.029). While the SF-12 mental component summary scores of Hb level ≤9 were significantly lower than 2 Hb level such as Hb level >11 to 12 (p=0.032), and Hb level >12 (p=0.004) but the score of Hb level >10 to 11 was significantly lower than Hb level >12 (p=0.045). However, Bonferroni multiple comparison shown that the role emotion scores of the ≤9 group were significantly lower than those derived from the >10 to 11 group (p=0.013) and the >12 group (p=0.028). The difference of post-hoc analysis results between LSD and Bonferroni comparison can be explained that the LSD test is a two-step test. First the ANOVA test is performed. If it is significant at level alpha, then all pairwise t-tests are carried out, each at level alpha. If the ANOVA test is not significant, then the procedure terminates. The LSD test does not control the set of comparisons while the Bonferroni multiple comparison test is a conservative test, that is, the set of comparisons is not exactly equal to alpha, but is less than alpha in most situations. Even though the Bonferroni test controls the set of comparisons rate, in many situations it may be too conservative and not have enough power to detect significant differences. The social function scores of Hb level ≤9 were significantly lower than Hb level >11 to 12 (p=0.019) and the mental component summary scores of the ≤9 group were significantly lower than Hb level >12 (p=0.037) as showed in the table 4.6. From the results, the LSD test is largely different to the Bonferroni test, and yields the p-value highly significant difference when compared with the p-value from Bonferroni multiple comparisons as showed in the table 4.6.

About kidney disease specific dimension, the significantly difference from Post-hoc analysis (LSD multiple comparison) showed that the Effects of kidney disease on daily life scores role-emotional scores of the Hb level ≤9 were significantly lower than those derived from Hb >9 to 10 group (p=0.007), Hb >10 to 11 group (p=0.023), Hb >11 to 12 group (p=0.001), and the >12 group (p=0.017). However, Bonferroni multiple comparison showed that no significantly difference between Hb level as showed in the table 4.6

Pearson's correlation coefficients of kidney specific disease dimension and SF-36 were shown in Table 4.7.

Table 4.7 Correlation of kidney disease specific dimension and SF-36

Dimension	Physical functioning	Role physical	Pain	General health	Emotional well being	Role emotion	Social function	Energy/ fatigue	SF-12 Physical	SF-12 Mental	Overall health
Symptom/ problem list	**0.385***	0.122	**0.475***	**0.408***	**0.595***	**0.361***	**0.238****	**0.580***	**0.351***	**0.511***	**0.352***
Effects of kidney disease	0.031	0.078	**0.264***	**0.409***	**0.445***	**0.275***	**0.321***	**0.301***	0.184***	**0.404***	**0.381***
Burden of kidney disease	0.147	-0.039	**0.211***	**0.422***	**0.420***	0.128	0.126	**0.402***	0.167	**0.324***	**0.389***
Work status	**0.345***	-0.022	0.143	0.110	0.079	-0.033	-0.001	0.208***	**0.287***	-0.030	0.144
Cognitive function	**0.279***	0.186***	**0.346***	**0.302***	**0.455***	**0.282***	0.122	**0.433***	**0.304***	**0.345***	**0.450***
Quality of social interaction	0.096	0.146	**0.235***	**0.293***	**0.512***	**0.323***	**0.227***	**0.332***	0.164	**0.400***	**0.220****
Sexual function	0.005	-0.055	-0.204	**0.441**	0.273	0.038	0.237	0.165	-0.004	0.177	0.376
Sleep	**0.232***	0.085	**0.411***	**0.373***	**0.523***	**0.252***	0.173	**0.493***	**0.240****	**0.487***	**0.310***
***Social support**	0.097	-0.087	0.007	**0.294***	**0.364***	0.114	0.017	**0.277***	-0.038	**0.337***	**0.266***
Dialysis staff encouragement	-0.064	0.038	-0.024	-0.093	0.072	0.039	0.071	0.019	-0.057	0.135	-0.065
Patient satisfaction	-0.145	-0.052	0.060	-0.006	0.101	-0.031	0.057	0.034	-0.043	0.097	0.027

*Note: * p-value* < 0.001, ** *p-value* < 0.01, *** *p-value* < 0.05

Many dimensions of kidney specific disease were correlated with SF-36 dimensions such as symptoms and problems, effects of kidney disease, burden of kidney disease, cognitive function, quality of social interaction and Sleep dimensions. These findings implied that this SF-36 dimension could reflect HRQoL status of hemodialysis patients and might be used as the measurement tool for hemodialysis patients. Especially the symptoms and problems dimension revealed the highest relationship with all SF-36 scores except role-physical dimension. Follow by sleep and cognitive function dimension which revealed the relationship with all SF-36 dimensions except Role-physical and Social function as showed in the table 4.7. The Effects of kidney disease and quality of social interaction revealed the relationship with all SF-36 scores except physical functioning, role physical and SF-12 physical components. Burden of kidney disease dimension have relationship with some SF-36 dimension such as pain, general health, emotional well being, energy/fatigue, SF-12 mental components and overall health.

These findings implied that symptoms and problems, effects of kidney disease, burden of kidney disease, cognitive function, quality of social interaction and sleep scores of kidney disease dimensions could reflect HRQoL status of hemodialysis patients and might be used as the only kidney disease questionnaire instrument for patient care to avoid patients' burden on answering multiple questionnaires

2.2 Utility

Utility of 3 tools, the average of utility score in HD patient was highest from SF-6D (0.748) while the utility from EQ-5D (UK) and VAS were 0.704 and 0.684, respectively. The average and range of utility score from Thai algorithm was less than UK algorithm as shown in the table 4.8. SF-6D indices a much narrower range compared to EQ-5D indices has a floor effect with SF-6D near the lowest possible value being associated with a wider range of EQ-5D values. Conversely, EQ-5D indices a much wider range compared to SF-6D indices has a ceiling effect with EQ-5D near the highest possible value being associated with a narrower range of SF-6D values as shown in the table 4.8. This is a reason that the EQ-5D differentiates less in the better health states. It should be emphasized that the utility score of EQ-5D or SF-6D or VAS, which are not simply interchangeably to measure the utility in HD patients.

Table 4.8 Summary utility of SF-6D, EQ-5D, and VAS questionnaires in 152 HD patients.

Value	SF-6D	EQ-5D (UK)	EQ-5D (TH)	VAS
Mean	0.748	0.704	0.654	0.684
Median	0.758	0.796	0.693	0.700
SD	0.139	0.341	0.312	0.191
Range	0.605	1.594	1.454	1.000
Minimum	0.395	-0.594	-0.454	0.000
Maximum	1.000	1.000	1.000	1.000

Ceiling effects were observed in the EQ-5D both UK and Thai preference weight as the table 4.9. 25.6% of respondents reporting the perfect health (11111) on

the EQ-5D, mean utility scores were 0.800 on the VAS (range 0.40–1.00) and 0.856 on the SF-6D (range 0.556–1.00). While only 1.32% of respondents reporting the perfect health (645655) on SF-6D and 3.29% on VAS. About floor effect were not observed in any instrument tools.

Table 4.9 Percentage of respondent reporting perfect and worst health state

Instrument	% of respondent reporting	
	Perfect state	Worst state
SF-6D	1.32	0.00
EQ-5D (UK)	25.66	0.66
EQ-5D (TH)	25.66	0.66
VAS	3.29	1.32

From the respondent who reporting perfect health, 8 from 39 of respondents (20.51%) and 17 from 39 of respondents (43.60%) reporting on the Effect of kidney on daily life dimension and Burden of kidney disease dimension scores less than 50, respectively. For VAS, only 1 from 6 respondents (16.67%) 2 from 6 respondents (33.33%) reporting on the Symptoms and Problems and the Effect of kidney on daily life dimension less than 50, respectively. While measured with the SF-6D, no respondents reported perfect health reporting the Kidney disease score less than 50 as showed in the table 4.10

Table 4.10 Percentage of respondent reporting perfect health in utility score but reporting Kidney disease score less than 50

Instrument	% (n) of respondent reporting		
	Symptoms and Problems	Effects of Kidney Disease	Burden of kidney disease
SF-6D	0% (0 from 2)	0% (0 from 2)	0% (0 from 2)
EQ-5D (UK)	0% (0 from 39)	20.51% (8 from 39)	43.60% (17 from 39)
EQ-5D (TH)	0% (0 from 39)	20.51% (8 from 39)	43.60% (17 from 39)
VAS	20% (1 from 5)	0% (0 from 5)	20% (1 from 5)

Correlation coefficients of utility scores from SF-6D, EQ-5D, VAS and kidney disease specific disease scores were shown in Table 4.11. All three specific dimensions were better correlated with SF-6D than EQ-5D and VAS scores. The Symptoms and Problems dimension revealed the highest relationship with the utility measures.

Table 4.11 Correlation coefficients of utility score from SF-6D, EQ-5D, VAS and 3 kidney disease scores.

Kidney disease-targeted Scales	SF6D	EQ-5D (UK)	VAS
Symptoms and Problems	0.518**	0.480**	0.304*
Effects of Kidney Disease on Daily Life	0.363**	0.150 (NS)	0.244*
Burden of kidney disease	0.311**	0.240**	0.201*

Note: ** *p-value* < 0.001, **p* < 0.005, and NS = not significant.

The mean and SD of utility scores from SF-6D, EQ-5D (UK, Thai algorithm) and VAS in the different Hb level were shown as the table 4.12. The average utility scores of SF-6D were significantly different across Hb levels (ANOVA, p=0.005) while other utility scores were not significant different (p>0.05).

Table 4.12 Mean±SD of utility scores and Hemoglobin levels

Hb level		SF-6D	EQ-5D* (UK)	EQ-5D* (TH)	VAS
≤ 9	**(n = 26)**	0.67±0.16	0.66±0.33	0.61±0.25	0.65±0.19
> 9 to 10	**(n = 18)**	0.71±0.13	0.69±0.39	0.63±0.38	0.73±0.17
>10 to 11	**(n = 40)**	0.75±0.12	0.65±0.41	0.62±0.37	0.66±0.20
>11 to 12	**(n = 35)**	0.77±0.14	0.78±0.23	0.72±0.23	0.67±0.18
> 12	**(n = 33)**	0.80±0.12	0.72±0.34	0.67±0.32	0.73±0.21
p-value		0.005	0.516	0.635	0.312

**EQ-5D utility based on the scoring function that was derived from a UK and Thai (TH) population utility*

Rank correlation of utility score from SF-6D, EQ-5D (UK, Thai algorithm), VAS and Hb level were shown in the table 4.13; only SF-6D correlated with Hb level and this correlation was statistically significant (p<0.001). These findings implied that SF-6D could, to a certain extent, reflect Hb level of hemodialysis patients and be use as the only utility parameter in the model.

Table 4.13 Correlation coefficients of utility score from SF-6D, EQ-5D (UK, Thai algorithm), VAS and Hb level.

Utility	Correlation coefficients	p-value
SF6D	0.330	0.000
EQ-5D (UK)	0.082	0.313
EQ-5D (TH)	0.091	0.265
VAS	0.081	0.321

2.3 Utility for Markov modelling

We use SF-6D score as the utility in the model and this model need to have the utility of HDCV, HD patient. Table 4.14 show the SF-6D scores of all HD patients, HD patients who have the history of CV event (HDCV) and HD patient who don't have the history of CV event (HD_nCV) were 0.74±0.14, 0.70±0.14 and 0.76±0.14, respectively.

Table 4.14 Mean± SD of SF-6D score of HD, HDCVand HD_nCV patient

SF-6D score	All HD (n = 152)	HDCV (n = 22)	HD_nCV (n = 130)
Mean ± SD	0.74±0.14	0.70±0.14	0.76±0.14

The utility of HD_nCV and HDCVpatient were estimated approximately 101.00% and 94.10% of all HD patients, respectively. The utility parameters in the model were shown as the table 4.15.

Table 4.15 Mean and standard error (SE) of utility parameter

Utility	Parameter distribution	Mean	SE	Resource
Utility of HDCV patient				Average utility of HDCV patient is 94.10% of average utility of all HD patients. (Face to face interview HD patient at Siriraj Hospital)
≤ 9	Beta	0.633	0.030	
> 9 to 10	Beta	0.667	0.029	
>10 to 11	Beta	0.709	0.018	
>11 to 12	Beta	0.724	0.022	
> 12	Beta	0.754	0.020	
Utility for HD patient without CV event				Average utility of HD_nCV patient is 101.00% of average utility of all HD patients. (Face to face interview HD patient at Siriraj Hospital)
≤ 9	Beta	0.680	0.032	
> 9 to 10	Beta	0.716	0.031	
>10 to 11	Beta	0.761	0.020	
>11 to 12	Beta	0.777	0.024	
> 12	Beta	0.809	0.022	

III. Probability data

We identified 277 potentially eligible articles, 204 of which were excluded because these were not RCTs. Seventy three RCTs were consisted of 22 studies assessed dose and route of administration, fifteen hematological and haemodynamic effects studies and twenty one other intervention studies i.e., nutritional supplement. Thirteen RCTs and 2 meta-analysis of RCTs of EPO in CKD were English full papers but only 4 RCTs[32, 33, 133, 134] met the specified criteria (figure 4.1). These studies were conducted in the Canada and Europe. There was no study conducted in Thailand or Asia. Table 4.16 shows the description of included clinical trials. Briefly, the trials differed in terms of the population studied, and duration of intervention.

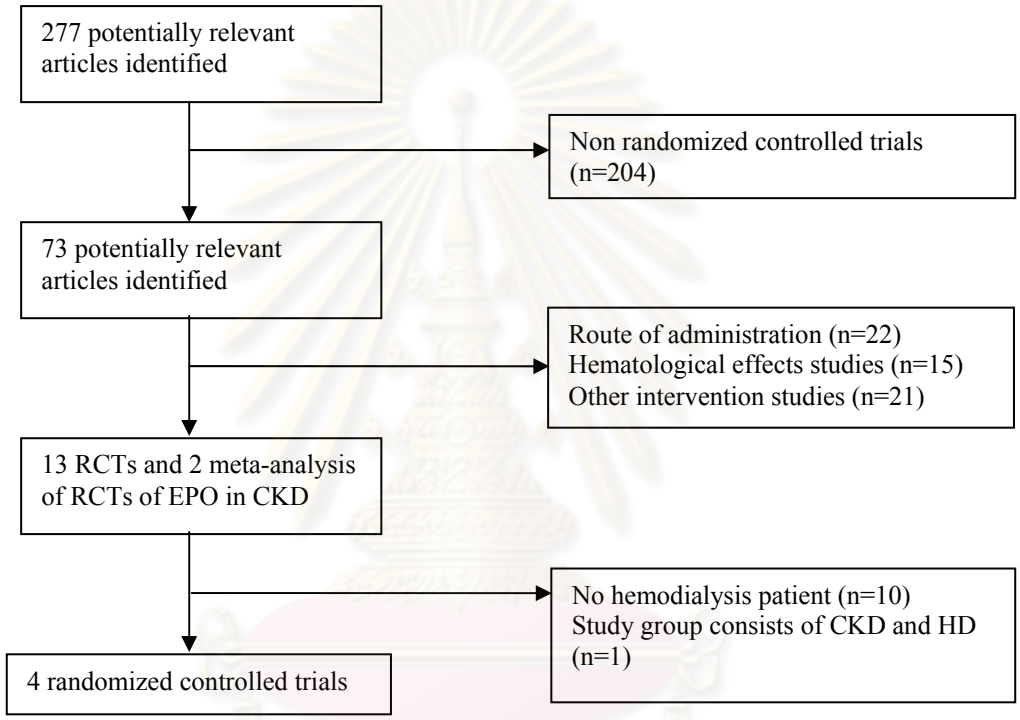

Figure 4.1 Flow chart of the search strategy and selection of trials

From 4 randomized controlled trials, the average age of study population was 59 years. Average age should be calculated from the following formular;

$$\mathbf{age_t = age_1(n_1) + age_2(n_2) + age(n_3) + age_4(n_4) / (n_1+n_2+n_3+n_4)}$$

when; age_t = Average age of all patients in the model of this study
age_1 = Average age of patients in the first randomized control trial
age_2 = Average age of patients in the second randomized control trial
age_3 = Average age of patients in the third randomized control trial
age_4 = Average age of patients in the fourth randomized control trial
n_1 = number of patient in the first randomized control trial
n_2 = number of patient in the second randomized control trial
n_3 = number of patient in the third randomized control trial
n_4 = number of patient in the fourth randomized control trial

Table 4.16 The description of included 4 randomized control trials

Author, year		Parfrey, 2005	Foley, 2000	CESG, 1990	Besarab, 1998
Years of follow-up		1.85	0.92	0.5	2.42
Number of patient		596	146	78	1233
Mean age (yr)		50	61	45	65
%male	**High**	60%	79%	68%	50%
	Low	60%	76%	48%	52%
Number of patient	**High**	296	73	38	618
	Low	300	73	40	615
Hb start (g/dl)		8.0-12.0	9.0-11.0	< 9.0	9.0-11.0
Hb target (g/dl)	**High**	13.5-14.5	13.0-14.0	115-130	13.0-15.0
	Low	9.5-11.5	9.5-10.5	90-110	9.0-10.0
Type of EPO		alfa	alfa	alfa	alfa
Route of EPO		sc or iv	sc	iv	sc or iv
Country		Europe, Canada	Canada	Canada	Canada
%Cardiovascular disease*		0	0	0	100

* Patients with clinical evidence of congestive heart failure or ischemic heart disease.

From the 4 clinical trials, they group the patient as the low Hb and the high Hb group thus we imply to group the patient for 2 group such as the ≤12 g/dl and >12 g/dl group for deriving the probability of the model. About HD patient who don't have cardiovascular disease (nCV), three trials [33, 133, 134] (n=820) reported non cardiovascular mortality (Figure 4.2). The relative risk (RR) of non cardiovascular death was not statistically significant difference between groups [RR: 0.747 (95% CI: 0.403; 1.383)] and no heterogeneity (I^2=0%). Only study by Parfrey and colleagues show the results of cardiovascular event, cardiovascular mortality, and hospitalization. The cardiovascular mortality, cardiovascular event, and hospitalization were similar in both target groups (p>0.05). About the HD patients who have cardiovascular disease, we included only study of Besarab and colleague[32]. The probability of CV event, CV mortality of the >12 group were significantly higher than other group (P<0.01). From all study, we received the rate of probability and can be calculated to the transitional probability. The transitional probability for all parameters was shown as the table 4.17.

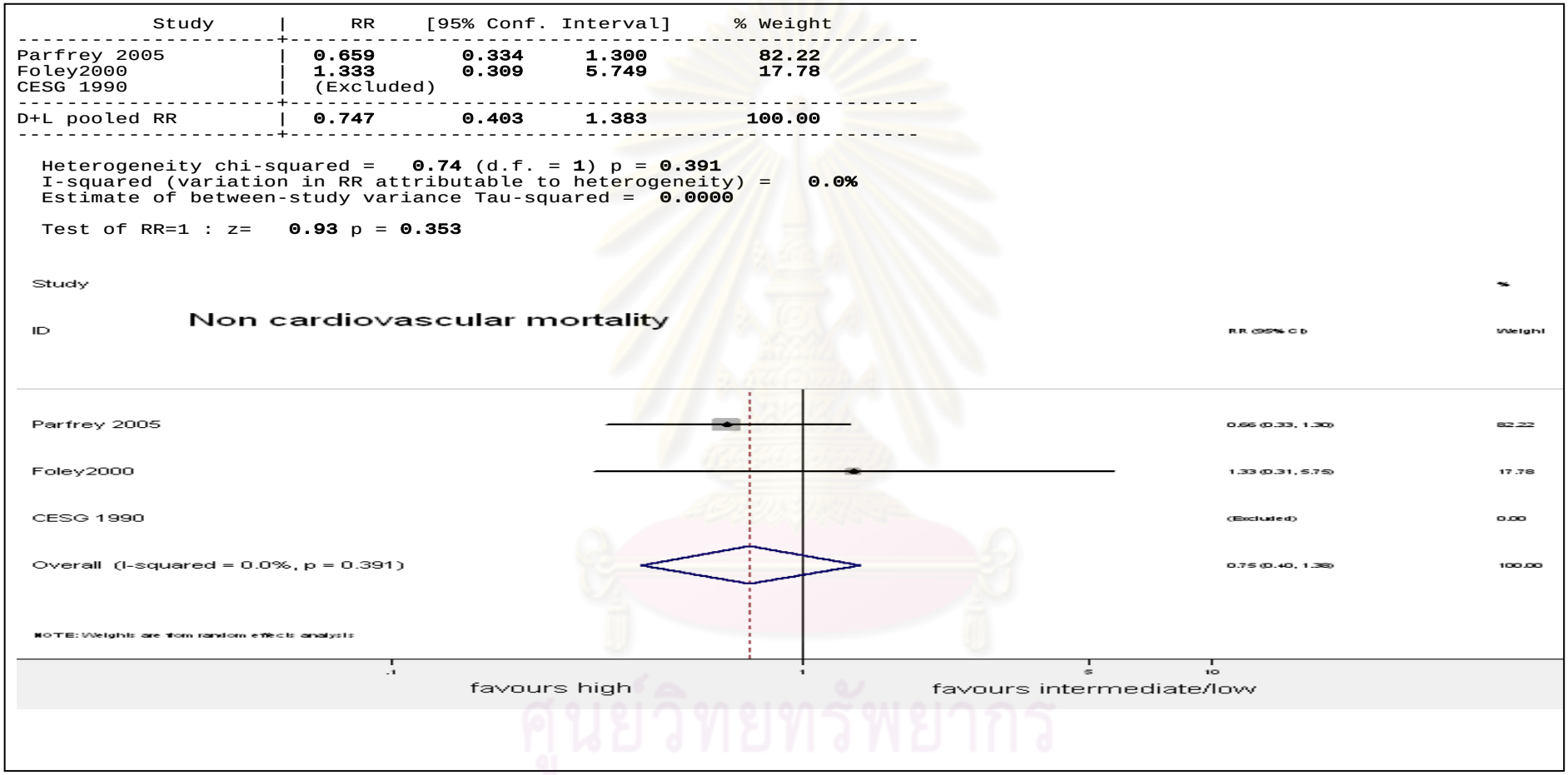

Figure 4.2 Non cardiovascular mortality of HD patient : High and intermediate/ low target Hb protocols

Table 4.17 Mean and standard error (SE) of transitional probability parameters

Parameter	Parameter distribution	Mean	SE	Reference
Transitional probability of adverse event among HD patients received EPO	Beta	0.79800	0.004	Parfrey et.al. 2005
Transitional probability of CV event among HD patients received EPO	Beta	0.11000	0.026	
Transitional probability of nCV event among HD patients received EPO	Beta	0.89000	0.006	
Transitional probability of CV event and dying among HD patients received EPO (All Hb)	Beta	0.03000	0.029	
Transitional probability of CV event and still alive among HD patients received EPO (All Hb)	Beta	0.97000	0.002	
Transitional probability of no adverse event among HD patients received EPO (All Hb)	Beta	0.20200	0.070	
Transitional probability of adverse event among HDCVpatients received EPO	Beta	0.39700	0.009	Besarab et.al. 1998
Transitional probability of no adverse event among HDCVpatients received EPO	Beta	0.60300	0.022	
Transitional probability of CV event among HDCVpatients received EPO	Beta	0.13200	0.021	

Table 4.17 Mean and standard error (SE) of transitional probability parameters (continue)

Parameter	Parameter distribution	Mean	SE	Reference
Transitional probability of dying from CV event among HDCVpatients received EPO (all Hb, except Hb>12)	Beta	0.08000	0.023	
Transitional probability of alive after have CV event among HDCVpatients received EPO (all Hb, except Hb>12)	Beta	0.92000	0.005	
Transitional probability of nCV event among HDCVpatients received EPO (all Hb, except Hb>12)	Beta	0.86800	0.009	
Transitional probability of dying from nCV event among HDCVpatients received EPO (all Hb, except Hb>12)	Beta	0.03300	0.025	
Transitional probability of alive after have nCV event among HDCVpatients received EPO (all Hb, except Hb>12)	Beta	0.96700	0.002	
Transitional probability of dying from nCV event among HD patients received EPO (all Hb, except Hb>12)	Beta	0.02700	0.025	Parfrey et. al. 2005, Foley et.al. 2000, CESG 1990
Transitional probability of alive after have nCV event among HD patients received EPO (all Hb, except Hb>12)	Beta	0.97300	0.001	Besarab et.al. 1998
Transitional probability of dying from CV event among HDCVpatients received EPO (only the Hb>12)	Beta	0.09000	0.023	
Transitional probability of alive after have CV event among HDCVpatients received EPO (only the Hb>12)	Beta	0.91000	0.005	

Table 4.17 Mean and standard error (SE) of transitional probability parameters (continue)

Parameter	Parameter distribution	Mean	SE	Reference
Transitional probability of dying from nCV event among HDCVpatients received EPO (only the Hb>12)	Beta	0.04900	0.024	
Transitional probability of alive after have nCV event among HD CV patients received EPO (all Hb, except Hb>12)	Beta	0.95100	0.002	
Transitional probability of dying from CV event among HD patients received EPO (only the Hb>12)	Beta	0.13500	0.024	
Transitional prob of alive after have CV event among HD patients received EPO (only the Hb>12)	Beta	0.86500	0.024	

IV. Cost

Cost data in the Markov model consisted of (1) direct medical costs,e.g., the cost of HD treatment, cost of EPO use, cost of treating CV and nCV events (nCV event including other event except cardiovascular event resulting in hospitalization for 24 hours or more or prolongation of hospitalization); CV event including myocardial infarction, stroke, heart failure, revascularization (percutaneous transluminal coronary angioplasty, or coronary-artery bypass grafting) resulting in hospitalization for 24 hours or more or prolongation of hospitalization in the Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10) as table 3.1; (2) direct non medical costs, e.g., food cost, travelling costs and accomodation for patients and their caregiver; and (3) indirect non medical costs such as income lost as a result of sick leave or hospital visits. For this model, EPO cost were calculated from the unit cost (0.325 Baht per unit for societal perspective and 0.262 Baht per unit for hospital perspective) multiplied by the amount of use for maintaining the different target Hb level (amount of use were calculated from the EPO dose for reaching and maintaining to the target Hb level when the initial Hb was 8 g/dl). The average treatment costs were estimated based on the actual charges recorded in database of Siriraj Hospital in 2009 and present as the annual cost as shown in the table 4.18.

Table 4.18 Mean and standard error (SE) of cost parameters

Parameter	Parameter distribution	Mean	SE	Reference
Cost of EPO calculated from acquisition cost (Hospital perspective)				
Annual cost of EPO to reach Hb level 8-9 g/dl	Gamma	4,925.68	512.77	Dose of EPO from Port et al. and acquisition cost of EPO from Siriraj hospital in 2010
Annual cost of EPO to reach Hb level 9-10 g/dl	Gamma	9,084.96	337.53	
Annual cost of EPO to reach Hb level 10-11 g/dl	Gamma	12,481.85	319.87	
Annual cost of EPO to reach Hb level 11-12 g/dl	Gamma	15,910.81	340.92	
Annual cost of EPO to reach Hb level >12 g/dl	Gamma	22,039.83	614.20	
Annual cost of EPO to maintain Hb level 8-9 g/dl	Gamma	23,285.04	2,423.98	Dose of EPO from Port et al. and expert opinion, acquisition cost of EPO from Siriraj hospital in 2010
Annual cost of EPO to maintain Hb level 9-10 g/dl	Gamma	42,947.06	1,595.58	
Annual cost of EPO to maintain Hb level 10-11 g/dl	Gamma	59,005.12	1,512.09	
Annual cost of EPO to maintain Hb level 11-12 g/dl	Gamma	75,214.76	1,611.60	
Annual cost of EPO to maintain Hb level >12 g/dl	Gamma	104,188.29	2,903.50	
Cost of EPO calculated from selling price (Societal perspective)				
Annual cost of EPO to reach Hb level 8-9 g/dl	Gamma	6,110.10	636.06	Dose of EPO from Port et al. and selling price of EPO from Siriraj hospital in 2010
Annual cost of EPO to reach Hb level 9-10 g/dl	Gamma	11,269.51	418.69	

Table 4.18 Mean and standard error (SE) of cost parameters (continue)

Parameter	Parameter distribution	Mean	SE	Reference
Annual cost of EPO to reach Hb level 10-11 g/dl	Gamma	15,483.21	396.78	
Annual cost of EPO to reach Hb level 11-12 g/dl	Gamma	19,736.70	422.89	
Annual cost of EPO to reach Hb level >12 g/dl	Gamma	27,339.48	761.89	
Annual cost of EPO to maintain Hb level 8-9 g/dl	Gamma	28,884.11	3,006.85	Dose of EPO from Port et al. and expert opinion, selling price of EPO from Siriraj hospital in 2010
Annual cost of EPO to maintain Hb level 9-10 g/dl	Gamma	53,274.03	1,979.25	
Annual cost of EPO to maintain Hb level 10-11 g/dl	Gamma	73,193.38	1,875.69	
Annual cost of EPO to maintain Hb level 11-12 g/dl	Gamma	93,300.75	1,999.12	
Annual cost of EPO to maintain Hb level >12 g/dl	Gamma	129,241.19	3,601.66	
Direct medical care costs				
Annual cost of CV treatment for HD patient when admit at the hospital, but finally dead	Gamma	263,372.32	50,203.00	Survey from Siriraj hospital
Annual cost of CV for HD patient when admit at the hospital and alive	Gamma	173,573.22	15,057.70	
Annual cost of nCV treatment for HD patient when admit at the hospital but finally dead	Gamma	315,127.77	37,393.80	
Annual cost of nCV treatment for HD patient when admit at the hospital and alive	Gamma	84,566.17	5,548.15	

Table 4.18 Mean and standard error (SE) of cost parameters (continue)

Parameter	Parameter distribution	Mean	SE	Reference
Annual cost of hemodialysis for HD patient	Gamma	268,894.74	4,169.33	
Annual cost of CV treatment for HDCVpatient when admit at the hospital, but finally dead	Gamma	328,696.25	74,510.50	
Annual cost of CV treatment for HDCVpatient when admit at the hospital and alive	Gamma	183,570.46	27,004.70	
Annual cost of nCV treatment for HDCVpatient when admit at the hospital, but finally dead	Gamma	220,246.75	61,376.00	
Annual cost of nCV treatment for HDCVpatient when admit at the hospital and alive	Gamma	162,776.31	17,083.20	
Annual cost of no adverse event for HDCVpatient	Gamma	152,613.65	24,721.30	
Direct non-medical care cost i.e. travel costs, foods, caregiver, and accommodation				
Total cost of direct non-medical cost when admit from CV event (per time)	Gamma	14,388.66	3,023.47	Survey from HD patient at Siriraj hospital
Total cost of direct non-medical cost when admit from nCV event (per time)	Gamma	13,688.91	2,876.43	
Number of in-patient visit for treating of nCV event	Normal	1.32	0.030	Survey from Siriraj hospital
Length of stay when admits for treating of nCV event	Normal	15.65	0.877	
Number of in-patient visit for treating of CV event	Normal	1.07	0.025	
Length of stay when admits for treating of CV event	Normal	16.45	1.530	

Table 4.18 Mean and standard error (SE) of cost parameters (continue)

Parameter	Parameter distribution	Mean	SE	Reference
Indirect non-medical cost i.e. income loss from sick leave or providing informal care (income loss from sick leave is a major part, accounting from minimum wage per day in Bangkok)				
Income loss from CV event leave	Gamma	3,502.00	3,502.00	Minimum wage (206 Baht x Length of stay from CV event)
Income loss from nCV event leave	Gamma	3,296.00	3,296.00	Minimum wage (206 Baht x Length of stay from nCV event)

V. Cost utility analysis

Based on the hospital and societal perspective, compared with Hb level ≤ 9 g/dl, the total costs and QALYs gained from each treatment options, and the incremental costs per QALY gained from providing EPO in comparison to the different Hb level, were shown in the table 4.19. Based on hospital perspective, the incremental costs for patients at the Hb >9 to 10 g/dl, >10 to 11 g/dl, >11 to 12 g/dl and >12 g/dl compared with the Hb ≤ 9 g/dl were 227,428.40, 418,887.30, 612,275.70, and 766,353.70 Baht, respectively while the incremental QALYs gained were 0.36, 0.85, 1.04 and 1.08, respectively. The minimum ICERs was the ICER of Hb level >10 to 11 g/dl (ICER= 492,808.59 Baht per QALY). Thus, providing EPO for the Hb level >10 to 11 g/dl had less cost at a higher effectiveness than other Hb levels.

Table 4.19 Cost-effectiveness results (probabilistic results)

Hb level (g/dl)	Total cost (Baht)	Total effectiveness (QALYs)	Incremental cost (Baht)	Incremental effectiveness (QALYs)	ICER (Baht/QALY)
Hospital perspective Calculates all incrementals relative to the *least costly* option**:** Hb level ≤ 9 g/dl)					
≤ 9	4,344,652.70	7.39			
>9 to 10	4,572,081.10	7.75	227,428.40	0.36	631,745.56
>10 to 11	4,763,540.00	8.24	418,887.30	0.85	492,808.59
>11 to 12	4,956,928.40	8.43	612,275.70	1.04	588,726.63
>12	5,111,006.40	8.47	766,353.70	1.08	709,586.76
Calculates all incrementals relative to the *next least costly* option.					
≤ 9	4,344,652.70	7.39			
>9 to 10	4,572,081.10	7.75	227,428.40	0.36	631,745.56
>10 to 11	4,763,540.00	8.24	191,458.90	0.49	390,732.45
>11 to 12	4,956,928.40	8.43	193,388.40	0.19	1,017,833.68
>12	5,111,006.40	8.47	154,078.00	0.04	3,851,950.00

Table 4.19 Cost-effectiveness results (probabilistic results (continue)

Hb level (g/dl)	Total cost (Baht)	Total effectiveness (QALYs)	Incremental cost (Baht)	Incremental effectiveness (QALYs)	ICER (Baht/QALY)
Societal perspective Calculates all incrementals relative to the *least costly* option**:** Hb level ≤ 9 g/dl)					
≤ 9	4,416,875.10	7.39			
>9 to 10	4,698,738.70	7.75	281,863.60	0.36	782,954.44
>10 to 11	4,935,373.00	8.24	518,497.90	0.85	609,997.53
>11 to 12	5,173,753.40	8.43	756,878.30	1.04	727,767.60
>12	5,398,945.70	8.47	982,070.60	1.08	909,324.63
Calculates all incrementals relative to the *next least costly* option.					
≤ 9	4,416,875.10	7.39			
>9 to 10	4,698,738.70	7.75	281,863.60	0.36	782,954.44
>10 to 11	4,935,373.00	8.24	236,634.30	0.49	482,927.14
>11 to 12	5,173,753.40	8.43	238,380.40	0.19	1,254,633.68
>12	5,398,945.70	8.47	225,192.30	0.04	5,629,807.50

From societal perspective, the incremental costs for patients with Hb ≤ 9 g/dl compared to >9 to 10 g/dl, >10 to 11 g/dl, >11 to 12 g/dl and >12 g/dl were 281,863.60, 518,497.90, 756,878.30, and 982,070.60 Baht, respectively while the incremental QALYs gained were 0.36, 0.85, 1.04 and 1.08, respectively. The minimum ICERs was the ICER of Hb level >10 to 11 (ICER=609,997.53 Baht per QALY). Hb level >10 to 11 appears more cost-effective than other Hb levels.

The incremental costs per QALY between different Hb levels were shown in figure 4.3 for the hospital perspective. The ICER for patients at the Hb >9 to 10 g/dl when compared with ≤ 9 g/dl was 631,745.56 Baht per QALY (a), at the Hb >10 to 11 g/dl when compared with >9 to 10 g/dl was 390,732.45 Baht per QALY (b), Hb > 11 to 12 g/dl when compared with >10 to 11 g/dl was 1,017,833.68 Baht per QALY (c), and the Hb >12 g/dl when compared with > 11 to 12 g/dl was 3,851,950.00 Baht per QALY (d).

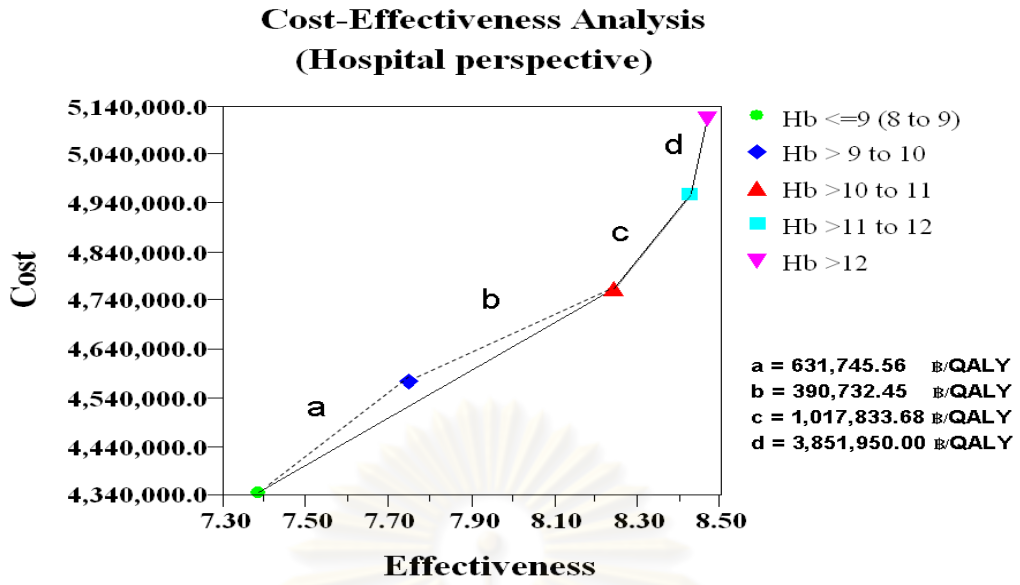

Figure 4.3 Cost-effectiveness EPO treatment target Hb levels between ≤ 9 versus >9 to 10, >9 to 10 versus >10 to 11, and >11 to 12 versus >12 g/dl (Hospital perspective)

The incremental costs per QALY between different Hb levels in the societal perspective were shown in figure 4.4. The ICER for patients at the Hb >9 to 10 g/dl when compared with ≤ 9 g/dl was 761,793.51 Baht per QALY (a), at the Hb >10 to 11 g/dl when compared with >9 to 10 g/dl was 482,927.35 Baht per QALY (b), Hb > 11 to 12 g/dl when compared with >10 to 11 g/dl was 1,324,335.00 Baht per QALY (c), and the Hb >12 g/dl when compared with > 11 to 12 g/dl was 5,629,810.00 Baht per QALY (d).

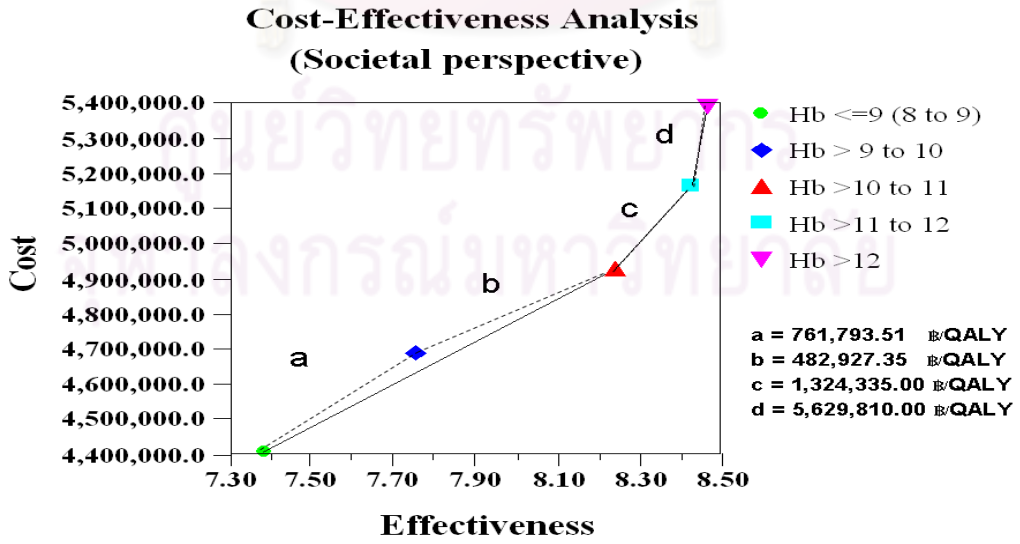

Figure 4.4 Cost-effectiveness EPO treatment target Hb levels between ≤ 9 versus >9 to 10, >9 to 10 versus >10 to 11, and >11 to 12 versus >12 g/dl (Societal perspective)

In Thailand, many hemodialysis patients receive recombinant human EPO for their anemia as a part of routine therapy but the problem between containing drug expenditure and managing the anemia in hemodialysis patient is the major issue that many studies cannot agree on the appropriate target Hb level. As the results, the higher Hb yield the higher QALYs and cost of EPO thus the optimal strategy should be consider from the lowest ICER. When the initial Hb of HD patient was less than 9 g/dl, providing EPO for the Hb level >10 to 11 g/dl was the less cost at a higher effectiveness than other Hb levels. Practicing an EPO treatment target Hb-level of >10 to 11 g/dl yields the incremental cost per QALY in the hospital and societal perspective about 492,808.59 and 609,997.53 Baht per QALY, respectively. In 2009, Thai Gross Domestic Product (GDP) per capita was 135,073.138 Baht.[135] The recommendations made by the Macroeconomics and Health Committee, it was suggested that technology is considered to be cost effective if its ICER is lower than three times of the GDP per capita,[136] this imply a ceiling threshold of 400,000 Baht per QALY in Thailand. As above results and based on the recommendations, all strategy were considered cost-ineffectiveness. However, the results of this study clearly indicated that maintaining the Hb level about >10-11 g/dl by using EPO is the most cost effective for treating anemia with EPO among HD patients when compared with other Hb level. For instance, the QALY increases the medium quantity for a shift from Hb levels ≤ 9 to Hb level >10-11 g/dl was 0.85 QALYs, and the incremental cost increasing for a shift from Hb levels ≤ 9 to >10-11 g/dl was 418,887.30 Baht thus ICER of Hb level >10-11 g/dl was 492,808.59 Baht per QALY while it increases the most QALY for a move from Hb level ≤ 9 to >12 g/dl was 1.08 QALYs, but the incremental cost increasing for a shift from Hb levels ≤ 9 to >12 g/dl was 766,353.70 Baht thus ICER of Hb level ≤ 9 to >12 g/dl was 709,586.76 Baht per QALY. These findings support the need to allocate the available resource to cover more people with the cost-effective Hb level (10-11 g/dl) for anemia treatment and their quality of life. The results of this evaluation indicated that providing Hb level >12 g/dl is associated with unfavorable cost-effectiveness ratios based on both perspective, which like to previous study.[137]

VI. Sensitivity analysis

<u>One way sensitivity analysis based on hospital perspective</u>

One way sensitivity analyses are displayed in a tornado diagram of the most influential variables. In this diagram, each bar represents the impact of uncertainty in an individual variable on the NHB. At the WTP 400,000 Baht/QALY gained, when altering the value of each parameter (95% CI for cost, ±10% for rate and probability), cost of nCV treatment for HDCV patient when admit at the hospital and still alive was the most sensitive compared to other cost (95% CI). On the other hand, rate of having CV and stay on HD (±10%) was the least sensitive compared to other variables based on both hospital perspective (figure 4.5) and societal perspective (figure 4.6)

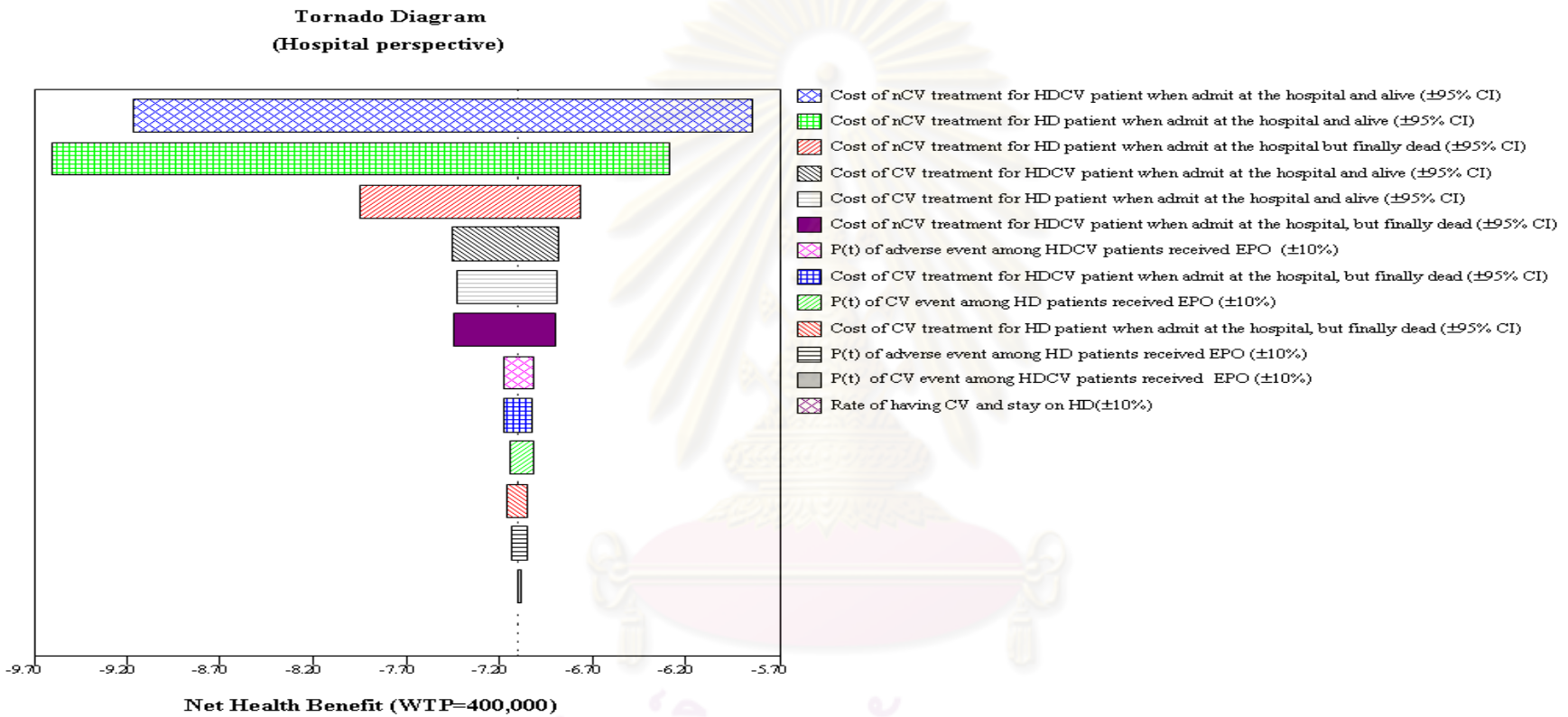

Figure 4.5 Tornado diagram showing the sensitivity of NHB to plausible ranges of parameter (hospital perspective, WTP = 400,000 Baht)

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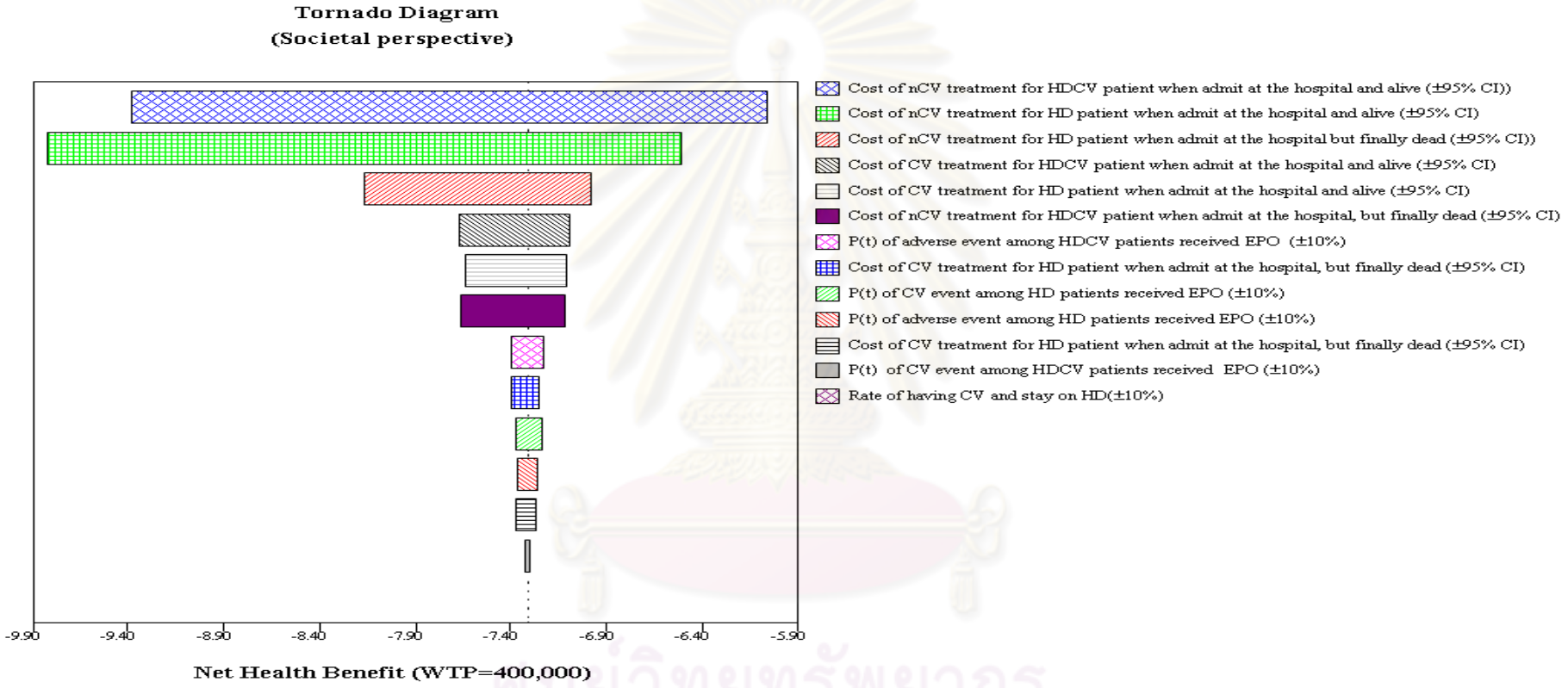

Figure 4.6 Tornado diagram showing the sensitivity of NHB to plausible ranges of parameter (societal perspective, WTP = 400,000 Baht)

Probabilistic sensitivity analysis

For sensitivity analysis, probabilistic sensitivity analysis (PSA) was performed using Monte Carlo simulation. It was carried out using TreeAge Pro 2009. All input parameters were assigned probability distributions according to their attribute to reflect the feasible range of values that each input parameter could attain as show in table 4.15, 4.17 and 4.18. Cost-effectiveness acceptability curves were presented using PSA based on societal perspective in order to inform the probability of multiple treatment options being cost effectiveness at the different levels of willingness to pay (WTP) per QALY gained. In developing countries, WHO recommended the ICER per QALY gained of medical interventions below one time of Gross Domestic Product (GDP) per capita was cost effectiveness maximum, between 1 and 3 times of GDP per capita was cost effectiveness, and more than 3 times might be not cost effectiveness. The results of the probabilistic sensitivity analysis are presented in terms of cost-effectiveness acceptability curves from hospital perspective and societal perspective as shown in the figure 4.7 and figure 4.8, respectively. Table 4.20 shown that if the policy makers were willing to pay at 100,000 Baht per QALY gained, no strategy Hb level was considered cost effective. Furthermore, at the WTP of 400,000 Baht per QALY gained, the probabilities that providing Hb level >9 to 10, >10 to 11, >11 to 12 g/dl and >12 g/dl would be cost effective when compared with the level ≤ 9 g/dl were 28.77%, 25.87%, 6.21% and 0.48%, respectively. Figure 4.7 shown that the level >9 to 10 g/dl was appropriate when the willingness to pay (WTP) was less than 420,000 Baht (a) while level >10 to 11 g/dl was the optimal choice at the WTP was between 420,000 (a) and 1,285,000 Baht (b) and the probability of cost effective was between 31.43% and 96.17%. However, at Hb level 11-12 g/dl was an optimal choice when WTP was more than 1,285,000 Baht.

Table 4.20 Probability of favouring the different Hb level compared with the Hb level ≤ 9 g/dl and WTP in the hospital perspective

Willingness to Pay	> 9 to 10	>10 to 11	>11 to 12	>12
100,000	0	0	0	0
110,000	0.0003	0	0	0
120,000	0.0006	0	0	0
130,000	0.0009	0	0	0
140,000	0.0016	0	0	0
150,000	0.0023	0	0	0
160,000	0.0042	0	0	0
170,000	0.0067	0	0	0
180,000	0.0088	0	0	0
190,000	0.0128	0	0	0
200,000	0.0198	0.0001	0	0
210,000	0.0268	0.0001	0	0
220,000	0.0351	0.0006	0	0
230,000	0.0445	0.0015	0	0
240,000	0.0556	0.0029	0	0
250,000	0.0701	0.0050	0.0001	0
260,000	0.0832	0.0087	0.0001	0
270,000	0.0952	0.0134	0.0002	0
280,000	0.1104	0.0200	0.0002	0
290,000	0.1240	0.0290	0.0007	0
300,000	0.1385	0.0389	0.0013	0
310,000	0.1554	0.0511	0.0022	0
320,000	0.1689	0.0670	0.0044	0
330,000	0.1817	0.0876	0.0068	0.0003
340,000	0.2001	0.1069	0.0106	0.0005

Table 4.20 Probability of favouring the different Hb level compared with the Hb level ≤ 9 g/dl and WTP in the hospital perspective (continue)

Willingness to Pay	> 9 to 10	>10 to 11	>11 to 12	>12
350,000	0.2164	0.1312	0.0163	0.0006
360,000	0.2311	0.1555	0.0230	0.0011
370,000	0.2449	0.1800	0.0314	0.0014
380,000	0.2601	0.2083	0.0407	0.0019
390,000	0.2750	0.2338	0.0514	0.0026
400,000	0.2877	0.2587	0.0621	0.0048
410,000	0.3010	0.2867	0.0770	0.0067

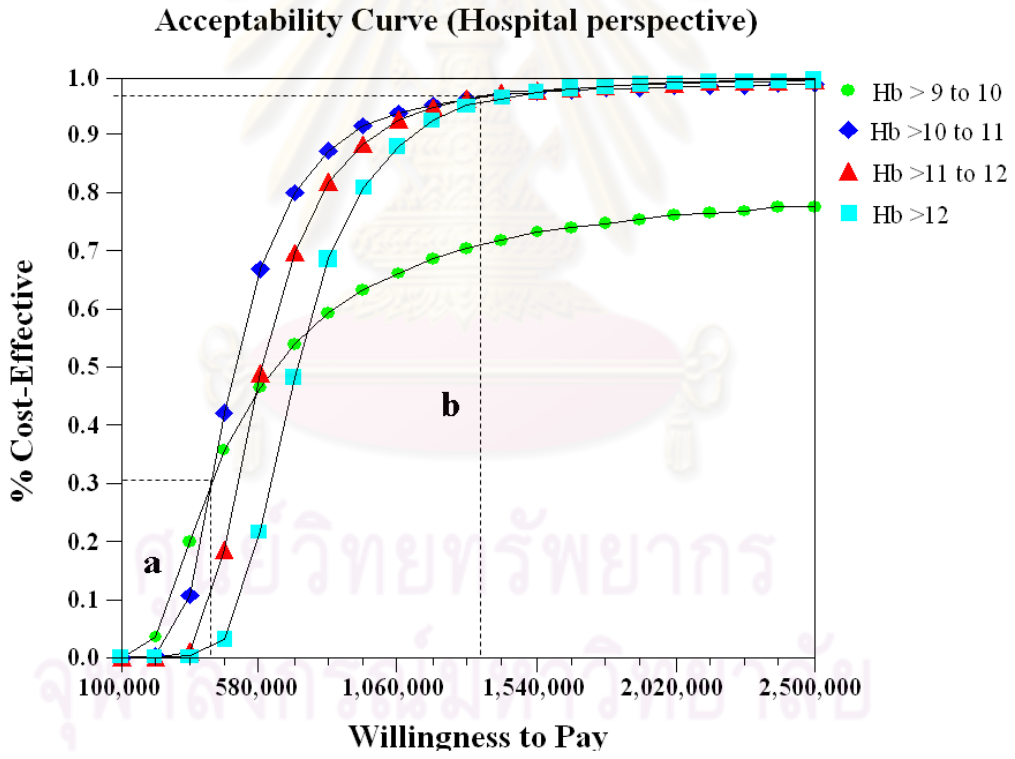

Figure 4.7 Cost-effectiveness acceptability curve of the different Hb level compared with the Hb level ≤ 9 g/dl (Hospital perspective)

About Societal perspective, table 4.21 shown that if the policy makers were willing to pay at 100,000 Baht per QALY gained, no strategy Hb level was considered cost effective. At the WTP of 400,000 Baht per QALY gained, the probabilities that providing Hb level >9 to 10, >10 to 11 g/dl, >11 to 12 g/dl and >12 g/dl would be cost

effective when compared with the level ≤ 9 g/dl were 17.55%, 7.76%, 0.60% and 0.01%, respectively. Figure 4.8 shown that the level >9 to 10 g/dl was appropriate when the willingness to pay (WTP) was less than 503,750 Baht (a) while level >10 to 11 g/dl was the optimal choice at the WTP was between 503,750 (a) and 1,512,500 Baht (b) and the probability of cost effective was betwen 29.32% and 95.94%. The results of PSA for providing EPO at the Hb level >10-11 g/dl confirmed the robustness of the model.

Table 4.21 Probability of favouring the different Hb level strategy compared with the Hb level ≤ 9 g/dl and WTP in the societal perspective

Willingness to Pay	> 9 to 10	>10 to 11	>11 to 12	>12
100,000	0	0	0	0
110,000	0	0	0	0
120,000	0	0	0	0
130,000	0	0	0	0
140,000	0	0	0	0
150,000	0.0004	0	0	0
160,000	0.0008	0	0	0
170,000	0.0015	0	0	0
180,000	0.0023	0	0	0
190,000	0.0037	0	0	0
200,000	0.0048	0	0	0
210,000	0.0066	0	0	0
220,000	0.0099	0	0	0
230,000	0.0131	0	0	0
240,000	0.0178	0	0	0
250,000	0.0235	0.0002	0	0
260,000	0.0298	0.0003	0	0
270,000	0.0375	0.0009	0	0
280,000	0.0448	0.0015	0	0
290,000	0.0530	0.0025	0	0
300,000	0.0623	0.0040	0	0
310,000	0.0709	0.0062	0	0

Table 4.21 Probability of favouring the different Hb level strategy compared with the Hb level ≤ 9 g/dl and WTP in the societal perspective (continue)

Willingness to Pay	> 9 to 10	>10 to 11	>11 to 12	>12
320,000	0.0795	0.0082	0	0
330,000	0.0909	0.0126	0.0001	0
340,000	0.1027	0.0175	0.0004	0
350,000	0.1136	0.0231	0.0006	0
360,000	0.1263	0.0316	0.0010	0
370,000	0.1379	0.0403	0.0018	0
380,000	0.1499	0.0520	0.0030	0
390,000	0.1627	0.0649	0.0040	0.0001
400,000	0.1755	0.0776	0.0060	0.0001
410,000	0.1890	0.0943	0.0079	0.0001

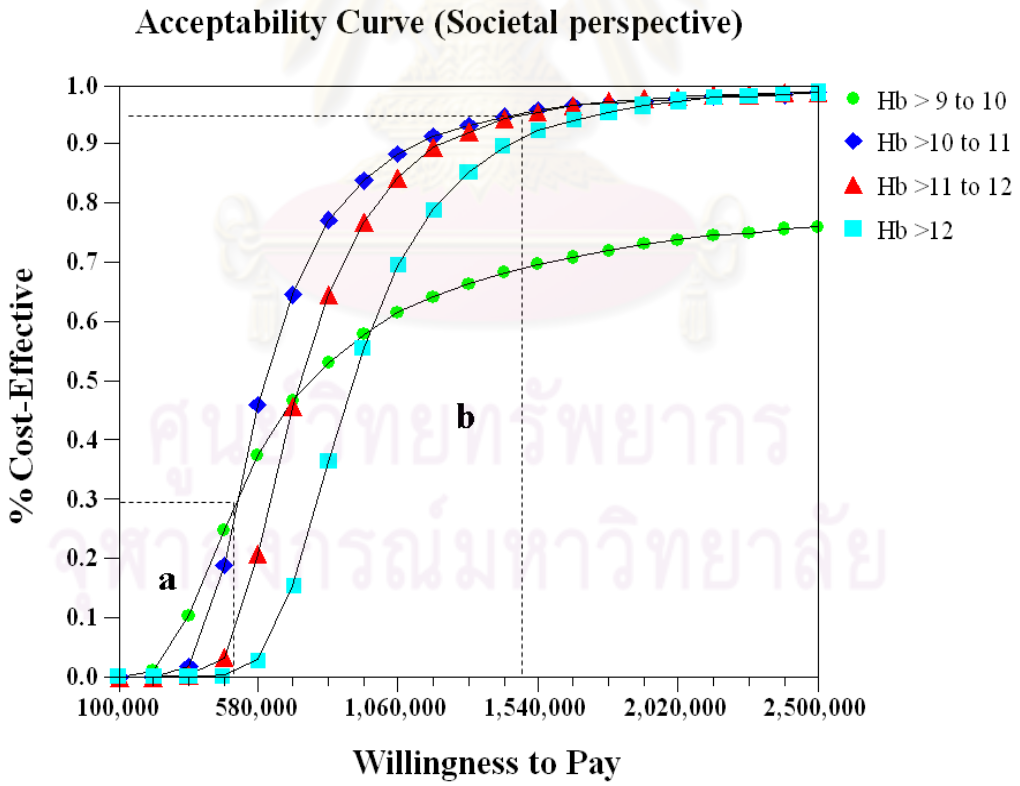

Figure 4.8 Cost-effectiveness acceptability curve of the different Hb l compared with the Hb level ≤ 9 g/dl (Societal perspective)

CHAPTER V
DISCUSSION AND CONCLUSION

Discussion

At present, the committee for development of the National List of Essential Drugs (NLED) has decided to include erythropoietin for the treatment of anemia among HD patients from the NLED because it proved cost-effective but the cost effectiveness of maintaining Hb level is not proved in Thailand. Thus, the decision to treat anemic chronic kidney disease patients depends on the practice guideline that physicians rely on. The recent treatment trials reported that a maximum dose of erythropoietin was associated with decreased survival, especially when EPO was used to maintain hemoglobin at a level higher than 12 g/dl.[32, 35, 37] Thus, the purpose of this study was to evaluate the cost utility analysis of EPO for maintaining the different hemoglobin target levels in anemic hemodialysis patient in routine clinical practice. In Cost utility analysis (CUA), there are two important variables involved: cost and utility of HD patient who use erythropoietin (EPO). Face-to-face interview included KDQOL-SF v. 1.3 (SF-36 and kidney disease specific questionnaire) and EQ-5D was conducted during November-December 2009 with 152 hemodialysis patients. The mean SF-6D score was 0.748±0.139 showing significantly higher than EQ-5D (0.704±0.341), and VAS (0.684±0.191) scores. Pearson's correlation coefficients between utility scores with kidney disease specific questionnaires illustrated that all three utility scores correlated well with Symptoms and Problems dimension, but were low associated with Burden and Effects of Kidney Disease on Daily Life dimensions. The SF-6D presented better agreement with kidney specific scales than EQ-5D and VAS. Nevertheless, the average utility scores of SF-6D were significantly different across Hb levels (ANOVA, $p=0.005$) while other utility scores were not significant different ($p>0.05$). These findings implied that SF-6D could, to a certain extent, reflect HRQoL status of hemodialysis patients and might be used as the input parameter in the analysis. The results of systematic review and meta-analysis of this study showed that using EPO for maintaining the different Hb level did not indicate a significant effect on increasing CV event or CV mortality rate in HD patients who don't have the history of CV events but show a significant effect on increasing CV mortality rate in HD patient who have the CV history. As the results of cost utility analysis, the higher Hb yield the higher QALYs and higher cost of EPO thus the optimal strategy should be consider from the lowest ICER. When the initial Hb of HD patient was less than 9 g/dl, providing EPO for the Hb level >10-11 g/dl was the less cost at a higher effectiveness than other Hb levels. Practicing an EPO treatment target Hb level >10-11 g/dl yields the incremental cost per QALY about 609,997.53 Baht per QALY. In 2009, Thai Gross Domestic Product (GDP) per capita was 135,073.138 Baht.[135] World Health Organization (WHO) recommended the ICER per QALY gained of medical interventions below one time of Gross Domestic Product (GDP) per capita being cost-effectiveness maximum, between 1 and 3 times of GDP per capita being cost effectiveness, and more than 3 times might be not cost effectiveness.[138] These imply a ceiling threshold of 400,000 Baht per QALY in Thailand. As above results and based on the recommendations, all strategy were considered cost-ineffectiveness. However, the results of this study clearly indicated that the ICER increases the least for a shift from Hb levels ≤ 9 g/dl to >10-11 g/dl, while it increases the most for a move from Hb level ≤ 9 g/dl to >12 g/dl. For instance, the QALY increases the medium quantity for a shift from Hb levels ≤ 9 to >10-11 g/dl was 0.85 QALYs, and the incremental cost increasing for a shift from Hb

levels ≤ 9 to >10-11 g/dl was 518,497.90 Baht thus ICER of Hb level >10-11 g/dl was 609,997.53 Baht per QALY while it increases the most QALY for a move from Hb level ≤ 9 to >12 g/dl was 1.08 QALYs, but the incremental cost increasing for a shift from Hb levels ≤ 9 to >12 g/dl was 982,070.60 Baht thus ICER of Hb level ≤ 9 to >12 g/dl was 909,324.63 Baht per QALY based on societal perspective. These findings support the need to allocate the available resource to cover more people with the cost effective Hb level >10-11 g/dl for anemia treatment and their quality of life. Although Hb level 11-12 g/dl is the recommendation for anemia treatment in the guideline[139], providing EPO for patients with Hb>11-12 g/dl was considered cost-effectiveness less than Hb>10-11 g/dl in the developing country as Thailand. And Hb>12 g/dl was the least cost-effectiveness option when compare with other Hb levels. In sensitivity analysis, the level >9-10 g/dl was appropriate when the willingness to pay (WTP) was less than 503,750 Baht while Hb level >10-11 g/dl was the optimal choice at the WTP was between 503,750-1,512,500 Baht and the probability of cost effective was between 29.32% and 95.94%.

Conclusion

Most ESRD patients with hemodialysis currently receive erythropoietin (EPO) for anemia treatment but no evidence has shown the cost-effectiveness of target hemoglobin level in Thailand. Markov model was used to estimate the incremental cost and Quality Adjusted Life Year (QALY) gains associated with EPO treatment for maintaining hemoglobin levels of >9-10, >10-11, >11-12, and >12 g/dl, comparing with ≤9 g/dl and adopting both hospital and societal perspective. Systematic review of EPO for anemia treatment associated with hemodialysis was used to estimate QALY gains associated with changes in hemoglobin concentrations. Direct medical cost was estimated based on the reference price of the Siriraj hospital and direct non medical costs derived from the structured questionnaire interviews. Probabilistic sensitivity analysis (PSA) was conducted to investigate the effect of parameter uncertainty. All future costs and outcomes were discounted at the rate of 3% per annum. The finding of this study showed that if the WTP 100,000 to 400,000 Baht (1 to 3 times of GDP per capita in Thailand) per QALY gained, providing all Hb level might be cost-ineffective strategy for anemia treatment with EPO in HD patient both hospital and societal perspective but practicing an EPO treatment target Hb-level of >10 to 11 g/dl yields the minimum incremental cost per QALY in the hospital and societal perspective about 492,808.59 and 609,997.53 Baht per QALY, respectively. From PSA, Hb level >10 to 11 g/dl was the optimal choice at the willingness to pay (WTP) was 420,000-1,285,000 Baht, and 503,750-1,512,500 Baht with the probability of cost effective was 31.43-96.17%, and 29.32-95.94% in hospital and societal perspective, respectively. The findings should be proposed to the Pharmacy and Therapeutic Committee to improve the guidelines for appropriate and cost-effective use of EPO in the hospital that imply to the decision of reimbursement system for more people and also increases the use of health care resources more efficiently in Thai health care setting.

Limitations of the study

This study assessed the cost utility of EPO for maintaining the different Hb level. The limitations of this cost utility analysis were as following;

1) This study was no information on some epidemiological parameters such as mortarity rate of CV event in HDCV or HD patient that related to the Hb level studies in Thailand. For this study, it was derived from the RCTs of other countries that might be different from race.

2) This study was to estimate the mortarity rate of CV and nCV for each Hb level from the systemetric review that there were only 4 RCTs related to these events which only one RCT related to these events among HD patient who have CV event. However, the sensitivity analysis was performed to ensure the quality of the assessment and to produce a more realistic interval on the study's conclusions. While 3 RCTs related to these events among HD patient who don't have CV event. Therefore, meta-analysis of mortarity rate in the different Hb level due to using EPO was performed.

3) EPO dose of each Hb level was defined from the formula[52] that is the nearest practice for approximation of EPO dose in the real practice. The initial dose for reaching to the target Hb was equal as the maintaining dose (from the expert opinion). It was assumed that people with different CV risk or other characteristics would receive a fixed dose of each Hb level target. However, titration to a higher or lower dose of EPO might be found in the realistic clinical practice.

4) Disease treatment costs per annum of CV event and nCV event were calculated by the summation of service quantities received multiplying by its average cost. Quantities of service and the average cost received were derived from the realistic data in HD patient of Siriraj Hospital but the generalized to other settings would be considered.

5) The cost of out-patient visit for adverse drug event treatment was excluded in this study because the incidence and severity of adverse drug events were not available to include in the evaluation.

6) The limitation of this study is a non-randomized, unselected cohort study involving 152 hemodialysis patients were performed for represent the utility of HD Thai patient in the different Hb level of Siriraj Hospital. Thus, the utility of HD patient were estimated from the cohort which is not randomized group and we can not know the utility of patient when they face the CV or nCV event until admission because we can not interview them at that time thus we assume the utility of HD patient who have CV events (HDCV) from the HD patient who ever admit from CV event and then we use the weight approximation technique[140] for calculation the utility of HDCV and HD patient and imply to the utility of different Hb level in any health state (HD and HDCV health state). Besides, the utility score from the SF-6D represent the quality of life of HD patient during the past 4 weeks before interview and the Hb level is mostly stable at least one month. Thus, the utility of patient from SF-6D can represent the utility of different Hb level. Moreover, SF-6D utility is the highest correlation with Hb level of the HD patient when compared with EQ-5D (UK and Thai algorithm) and VAS. However, the utility score was estimate further study should be done in longitudinal data.

Generalization

All costs of EPO from the price of generic product and original product that available at Siriraj Hospital, which was different from generic product in other settings. Costs of CV treatment, nCV treatment and HD cost in HD patient were

obtained from the treatment costs that occurred in the realistic situation at Siriraj Hospital in only 1 year (2009) because the treatment cost of Siriraj Hospital in 2009 were revised and increase from 2008 about 20-30% so that the treatment costs before 2009 were excluded in this analysis. However, we performed the sensitivity analysis for all parameters

Finally, a systematic review and meta-analysis of RCTs were also performed in this study, which minimized the biased and improved transparent and realiability. Nevertheless, PSA were performed to ensure the quality of the assessment and to minimize the variation.

In summary, based on the experiences and perspective of caregivers and nurses in hemodialysis unit, it was suggest that HD patient was an unfortunately life and their kidney disease is a much burden on patients both financially and personally. The early diagnosis and provision the chronic kidney disease patients to access to the healthcare system would assist the delay of disease progression until dialysis or kidney transplant. Also the health care system should support HD patients and their caregivers in order to maintain the best long term condition of HD patients. Finaaly, the environment (their family, friend and health care personnel) of HD patient is important for their encouragement to survive in the real world.

Recommendations to the further study

(1) The data of new available EPO such as CERA (Mircera®**:** Continuous Erythropoietin Receptor Activator) were excluded from this study because the data of this product has not been available, CERA using in Thailand has not yet been available for every hospital and the objective of this study was to compare the cost utility of EPO for maintaining the different Hb level, thus the EPO which should be included in this study might be the similar frequency of administration and pharmacokinetic information. CERA differed from other EPO, CERA has a longer elimination half-life and slower clearance rate. Thus, CERA can be administered at extended intervals up to once per monthly while the erythropoietin-alpha and beta needed to inject the drug for 2-3 times. However, EPO beta and alfa are available when the study of epidemiology of any events and the comparison study between CERA. These datas should be included in meta-analysis and economic evaluations to compare the cost effectiveness of the different type of EPO using in Thailand.

(2) In this study, there was no information on some parameter such as the mortarity rate of HD Thai patient who use EPO that related to the different Hb level. In addition, study related to epidemiology of these criteria in Thailand would be useful for future analysis.

Recommendations for policy maker

These findings supported the need to allocate the available resource to cover more people with the Hb level 10-11 g/dl for anemia treatment and their quality of life that is the nearest criteria of EPO reimbursement for SSS patient, which the EPO using can be reimbursed for 4,000 or 2,000 IU per week in patients with Hb level below 10 or 11 g/dl, respectively thus out-of-pocket rather than those will occur when the patient need to use EPO more than the criterion dose. However, the amount of EPO dose should be revised for the real treatment that this EPO dose can increase the Hb to the target Hb; should not be limit as the fixed dose. At the present, there is no official restriction of using EPO, based on the historical dispensing pattern and personal communication with physicians, EPO is tentatively used in patients with CSMBS (Civil Servant Medical Benefit Scheme). Note that the official utilization

policy should be set up for all health scheme; patients who became to be EPO users should be meet either clinical-related criterion or setting-specific policy. This evaluation was conducted based on economic model. The model was based on the important assumption that efficacy of generic EPO was considered to be equal to that of original EPO. The results of economic evaluation were based on this assumption. Thus, there was bioequivalence of generic product of generic product compared with original product for registration of medicine but this criteria was except for injectable drug so therapeutic equivalence should be consider. In addition, the quality assurance on generic product should be developed. Comparison between the long half life EPO (CERA) and the conventional EPO (EPO alfa and beta) should be conduct for the cost effectiveness that imply to the decision of reimbursement system for more people and also increases the use of health care resources more efficiently in the Thai health care setting where the insufficiency of health care resources is increasingly causing concerned. In the view of patient care, KDQOL questionnaire can be used for health related quality of life in routine practice and can be imply to the consideration of the maintaining Hb level. For example, if the score of the symptom and problem of kidney disease dimension is lower than 50, the maintaining Hb level should be consider again and maybe it is reasonable to use EPO for increasing the Hb level more than >11 g/dl. However, if the score is not lower than 50, the maintaing Hb level >10-11 g/dl is the reasonable and cost-effective level as the results of cost utility analysis.

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APPENDICES

Appendix A

Kidney Disease and Quality of Life Short-Form™ (KDQOL-SF™) Version 1.3

Study of quality of life for patients on dialysis

What is the purpose of the study?

This study is being carried out in cooperation with physicians and their patients. The purpose is to assess the quality of life of patients with kidney disease.

What will I be asked to do?

For this study, we want you to complete a survey today about your health, how you feel and your background.

Confidentiality of information?

We do not ask for your name. Your answers will be combined with those of other participants in reporting the findings of the study. Any information that would permit identification of you will be regarded as strictly confidential. In addition, all information collected will be used only for purposes of the study, and will not be disclosed or released for any other purpose without your prior consent.

How will participation benefit me?

The information you provide will tell us how you feel about your care and further understanding about the effects of medical care on the health of patients. This information will help to evaluate the care delivered.

Do I have to take part?

You do not have to fill out the survey and you can refuse to answer any question. Your decision to participate will not affect your opportunity to receive care.

Instructions for filling out survey

A. This survey asks for your view about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

B. This survey includes a wide variety of questions about your health and your life. We are interested in how you feel about each of these issues.

C. Please answer the questions by circling the appropriate number or by filling in the answer as requested.

Example:

During the past four weeks, how much back pain have you had?

(Circle One Number)

None …… (1)

Very mild …….. 2

Mild …….. 3

Moderate ……..... 4

Severe …… 5

D. Several items in the survey ask about the effect of kidney disease on your life. Some items will ask about limitations related to your kidney disease, and some items will ask about your well-being. Some questions may look like others, but each one is different. Please answer every question as honestly as possible. If you are unsure about answer the question, Please give the best answer you can. This will allow us to have an accurate picture of the different experiences of individuals with kidney disease.

Thank you for completing the survey

YOUR HEALTH

1. In general, would you say your health is:
(Circle One Number)

Excellent…….1

Very good…….....2

Good……3

Fair……...4

Poor…….…….5

2. Compared to one year ago, how would you rate your health in general now?

(Circle One Number)

Much better now than one year ago……...……..1

Somewhat better now than one year ago……..2

About the same as one year ago……...…3

Somewhat worse now than one year ago…….4

Much worse now than one year ago……...……..5

3. The following items are about activities you might do during a typical day. **Dose your health now limit** you in these activities? If so, how much? **(Circle One Number on Each Line)**

	Yes, Limited **a Lot**	Yes, Limited **a Little**	No, Not Limited **at All**
a. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing **several** flights of stairs	1	2	3
e. Climbing **one f**ight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking **more than a mile**	1	2	3
h. Walking **several blocks**	1	2	3
i. Walking **one block**	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the **past 4 weeks**, have you had any of the following problems with your work or other regular activities **as a result of your physical health**?

(Circle One Number on Each Line)

	Yes	**No**
a. Cut down **the amount of time** you spent on work or other activities?	1	2
b. **Accomplished less** than you would have liked?	1	2
c. Were limited in the **kind** of work or other activities?	1	2
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)?	1	2

5. During the **past 4 weeks**, have you had any of the following problems with your work or other regular activities **as a result of any** emotional problem (such as feeling depressed or anxious)

(Circle One Number on Each Line)

	Yes	**No**
a. Cut down the **amount of time** you spent on work or other activities?	1	2
b. **Accomplished less** than you would have liked?	1	2
c. Didn't do work other activities **as carefully as usual?**	1	2

6. During the **past 4 weeks**, to what **extent** have your **physical health or emotional problem** interfered with your normal social activities with family, friends, neighbors, or groups?

(Circle One Number)

Not at all……1

Slightly……..……2

Moderately…….3

Quite a bit……..4

Extremely……..5

7. How much **bodily pain** have you had during the past 4 weeks?

(Circle One Number)

None…..……..1

Very mild……2

Mild……....3

Moderate……..……...4

Severe…….……....5

Very severe…….……6

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

(Circle One Number)

Not at all……1

A little bit……2

Moderately……..……3

Quite a bit……..4

Extremely……..……5

9. These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closet to the way you have been felling. How much of the time during the past 4 weeks **(Circle One Number on Each Line)**

	All of the time	**Most of the time**	**A good bit of the time**	**Some of the time**	**A little of the time**	**None of the time**
a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt came and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
H. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time have your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(Circle One Number)

All of the time……1

Most of the time…….....2

Some of the time…….…...3

A little of the time……..4

None of the time……..…5

11. Please choose the answer that best describes how TRUE or FALSE each of the following statements is for you.

(Circle One Number on Each Line)

	Definitely True	**Mostly True**	**Don't Know**	**Mostly True**	**Definitely True**
a. I seem to get sick a little easier than other people.	1	2	3	4	5
b. I am as healthy as anybody I know.	1	2	3	4	5
c. I expect my health to get worse.	1	2	3	4	5
d. My health is excellent.	1	2	3	4	5

YOUR KIDNEY DISEASE

12. How **TRUE** or **FALSE** is each of the following statements for you?
(Circle One Number on Each Line)

	Definitely True	**Mostly True**	**Don't Know**	**Mostly True**	**Definitely True**
a. My kidney disease interferes too much with my life.	1	2	3	4	5
b. Too much of my time is spent dealing with my kidney disease.	1	2	3	4	5
c. I feel frustrated dealing with my kidney disease	1	2	3	4	5
d. I feel like a burden on my family	1	2	3	4	5

13. These questions are about how you feel and how things have been going during the **past 4 weeks.** For each question, Please give the one answer that comes closet to the way you have been feeling. How much of the time during the **past 4 weeks.**

(Circle One Number on Each Line)

	None of the time	**A little of the time**	**Some of the time**	**A good bit of the time**	**Most of the time**	**All of the time**
a. Did you isolated yourself from people around you?	1	2	3	4	5	6
b. Did you react slowly to things that were said or done	1	2	3	4	5	6
c. Did you act irritable toward those around you?	1	2	3	4	5	6
d. Did you have difficulty concentrating or thinking	1	2	3	4	5	6
e. Did you get along well with other people?	1	2	3	4	5	6
f. Did you become confused?	1	2	3	4	5	6

14. During the **past 4 weeks,** to what extent were you bothered by each of the following? **(Circle One Number on Each Line)**

	Not at all bother	**Somewhat bother**	**Moderately bother**	**Very much bother**	**Extremely bother**
a. Soreness in your muscles?	1	2	3	4	5
b. Chest pain?	1	2	3	4	5
c. Cramps?	1	2	3	4	5
d. Itchy skin?	1	2	3	4	5
e. Dry skin?	1	2	3	4	5
f. Shortness of breath?	1	2	3	4	5
g. Faintness or dizziness?	1	2	3	4	5
h. Lack of appetite?	1	2	3	4	5
i. Washed out or drained?	1	2	3	4	5
j. Numbness in hands or feet?	1	2	3	4	5
k. Nausea or upset stomach?	1	2	3	4	5
Hemodialysis patient only l. Problems with your access site?	1	2	3	4	5
Peritoneal patient only m. Problems with your catheter site?	1	2	3	4	5

EFFECTS OF KIDNEY DISEASE ON YOUR DAILY LIFE

15. Some people are bothered by the effects of kidney disease on their daily life, while others are not. How much dose kidney disease **bother** you in each of the following areas?

(Circle One Number on Each Line)

	Not at all bother	**Somewhat bother**	**Moderately bother**	**Very much bother**	**Extremely bother**
a. Fluid restriction?	1	2	3	4	5
b. Dietary restriction?	1	2	3	4	5
c. Your ability to work around the house?	1	2	3	4	5
d. Your ability to travel?	1	2	3	4	5
e. Being dependent on doctors and other medical staff?	1	2	3	4	5
f. Stress or worries caused by kidney disease?	1	2	3	4	5
g. Your sex life?	1	2	3	4	5
h. Your personal appearance?	1	2	3	4	5

The next three questions are personal and relate to your sexual activity, but your answers are important in understanding how kidney disease impacts on people's lives.

16. Have you had any sexual activity in the **past 4 weeks**?

(Circle One Number)

No……..… 1 → Please skip to Question 17

Yes……..… 2

↓

How much of a problem was each of the following in the **past 4 weeks**?

(Circle One Number on Each Line)

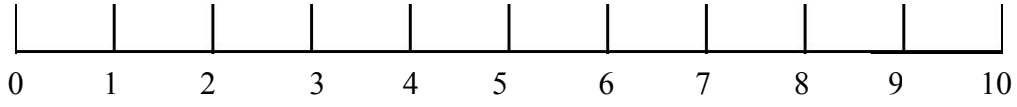
	Not a problem	**A little problem**	**Somewhat A problem**	**Very much a problem**	**Severe problem**
a. Enjoying sex?	1	2	3	4	5
b. Becoming sexually aroused?	1	2	3	4	5

For the following question, please rate your sleep using a scale ranging from 0 **representing "very bad" to 10 representing "very good."**
If you think your sleep is half-way between "very bad" and "very good" please circle 5. **If you think your sleep is one level better than 5, circle 6. If you think your sleep is one level worse than 5, circle 4 (and so on)**.

17. On a scale from 0 to 10, how would you rate your sleep overall?

(Circle One Number)

(Circle One Number)



Very Bad Very Good

18. How often during the **past 4 weeks** did you….

(Circle One Number on Each Line)

	None of the time	**A little of the time**	**Some of the time**	**A good bit of the time**	**Most of the time**	**All of the time**
a. Awaken during the night and have trouble falling asleep again?	1	2	3	4	5	6
b. Get the amount of sleep you need?	1	2	3	4	5	6
c. Have trouble staying awake during the day?	1	2	3	4	5	6

19. Concerning your **family and friends**, how satisfied are you with…

(Circle One Number on Each Line)

	Very Dissatisfied	**Somewhat Dissatisfied**	**Somewhat Satisfied**	**Very Satisfied**
a. The amount of time you are able to spend with your family and friends?	1	2	3	4
b. The support you receive from your family and friends?	1	2	3	4

20. During the **past 4 weeks**, did you work at a paying job?

(Circle One Number)

Yes…….. 1

No…… 2

21. Does your health keep you from working at a paying job?

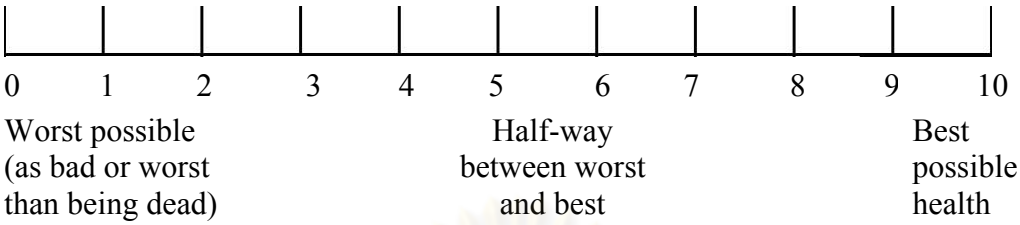
(Circle One Number)

Yes…….. 1

No…… 2

22. Overall, how would you rate your health?

(Circle One Number)



SATISFACTION WITH CARE

23. Think about the care you receive for kidney dialysis. In terms of your satisfaction, how would you rate the friendliness and interest shown in you as a person?

(Circle One Number)

Very Poor…….. ..1

Poor……. 2

Fair……...3

Good…….4

Very Good……..……. 5

Excellent……..…… 6

24. How **TRUE** or **FALSE** is each of the following statements for you?

(Circle One Number on Each Line)

	Definitely True	**Mostly True**	**Don't Know**	**Mostly True**	**Definitely True**
a. Dialysis staff encourage me to be as independent as possible.	1	2	3	4	5
b. Dialysis staff support me in coping with my kidney disease	1	2	3	4	5

Appendix B

แบบสอบถาม "โรคไตกับคุณภาพชีวิต"
การศึกษาคุณภาพชีวิตของผู้ป่วยล้างไต

คำแนะนำในการตอบแบบสำรวจ

ก. แบบสำรวจนี้ประกอบด้วยแบบสอบถาม 2 ชุด โดยเป็นการถามความคิดเห็นของท่านเกี่ยวกับสุขภาพของท่านเอง

ข้อมูลนี้จะช่วยให้สามารถติดตาม ว่าท่านรู้สึกอย่างไรและท่านสามารถทำกิจกรรมต่างๆ ตามปกติได้ดีเพียงใด

ข. แบบสำรวจนี้รวมข้อคำถามเกี่ยวกับสุขภาพและการดำเนินชีวิตของท่านในหลายลักษณะว่าท่านรู้สึกอย่างไรเกี่ยวกับประเด็นต่างๆ เหล่านี้

ค. กรุณาตอบคำถามโดยวงกลมล้อมรอบตัวเลขที่เหมาะสม หรือเติมคำตอบที่ระบุไว้

ตัวอย่างเช่น

ในช่วง 1 เดือนที่ผ่านมา ท่านมีอาการปวดหลังมากเพียงใด (วงกลมหนึ่งคำตอบ)

ไม่มีอาการเลย	มีอาการน้อยมาก	มีอาการเล็กน้อย	มีอาการปานกลาง	มีอาการรุนแรง
1	2	(3)	4	5

ง. หลายคำถามในแบบสำรวจนี้ถามเกี่ยวกับผลกระทบของโรคไตต่อชีวิตของท่าน คำถามบางข้อถามเกี่ยวกับข้อจำกัดที่เกี่ยวเนื่องกับโรคไต และบางข้อถามเกี่ยวกับความเป็นอยู่ของท่าน ***บางคำถามอาจดูคล้ายกัน แต่คำถามแต่ละข้อแตกต่างกัน*** กรุณาตอบคำถามทุกข้อตามความเป็นจริงเท่าที่จะทำได้ ถ้าท่านไม่แน่ใจในคำตอบ โปรดเลือกคำตอบที่ดีที่สุดที่ท่านจะให้ได้ วิธีนี้ช่วยให้เราเห็นภาพประสบการณ์ที่แตกต่างกันของผู้ป่วยโรคไตแต่ละคนอย่างชัดเจน

กรุณาทำเครื่องหมาย x ในช่องสี่เหลี่ยม ☐ ของคำถามแต่ละข้อที่ตรงกับสภาวะสุขภาพของท่าน **ในวันนี้** มากที่สุดเพียงข้อเดียว

1. การเคลื่อนไหว

ข้าพเจ้าไม่มีปัญหาในการเดิน ☐

ข้าพเจ้ามีปัญหาในการเดินบ้าง ☐

ข้าพเจ้าไม่สามารถไปไหนได้ และจำเป็นต้องอยู่บนเตียง ☐

2. การดูแลตนเอง

ข้าพเจ้าไม่มีปัญหาในการดูแลตนเอง ☐

ข้าพเจ้ามีปัญหาในการอาบน้ำหรือแต่งตัวบ้าง ☐

ข้าพเจ้าไม่สามารถอาบน้ำหรือแต่งตัวด้วยตนเองได้ ☐

3. กิจกรรมที่ทำเป็นประจำ (เช่น การทำงาน การเรียนหนังสือ การทำงานบ้าน การทำกิจกรรมในครอบครัว หรือการทำกิจกรรมยามว่าง)

ข้าพเจ้าไม่มีปัญหาในการทำกิจกรรมที่ทำเป็นประจำ ☐

ข้าพเจ้ามีปัญหาในการทำกิจกรรมที่ทำเป็นประจำอยู่บ้าง ☐

ข้าพเจ้าไม่สามารถทำกิจกรรมที่ทำเป็นประจำได้ ☐

4. ความเจ็บปวด ไม่สุขสบาย

ข้าพเจ้าไม่มีอาการเจ็บปวดหรืออาการไม่สุขสบาย ☐

ข้าพเจ้ามีอาการเจ็บปวดหรืออาการไม่สุขสบายปานกลาง ☐

ข้าพเจ้ามีอาการเจ็บปวดหรืออาการไม่สุขสบายมากที่สุด ☐

5. ความวิตกกังวล ซึมเศร้า

ข้าพเจ้าไม่รู้สึกวิตกกังวลหรือซึมเศร้า ☐

ข้าพเจ้ารู้สึกวิตกกังวลหรือซึมเศร้าปานกลาง ☐

ข้าพเจ้ารู้สึกวิตกกังวลหรือซึมเศร้ามากที่สุด ☐

ถ้ากำหนดให้คะแนนมีค่าตั้งแต่ 0 ถึง 100 ท่านให้คะแนนสุขภาพของท่านที่ระดับใด กรุณาทำเครื่องหมาย x ในมาตรวัดคะแนนที่ตรงกับสภาวะสุขภาพของท่านในปัจจุบันมากที่สุด

แบบสอบถามฉบับนี้สำรวจความเห็นของท่านเกี่ยวกับสุขภาพของท่านเอง ข้อมูลนี้จะช่วยติดตามดูว่าท่านรู้สึกอย่างไรและท่านสามารถทำกิจกรรมปกติต่าง ๆ ของท่านได้ดีเพียงใด โปรดตอบคำถามทุกคำถามโดยวงกลมตัวเลือกในแต่ละข้อ หากไม่แน่ใจว่าจะตอบอย่างไรดีให้เลือกคำตอบที่ท่านคิดว่าใกล้เคียงที่สุดเพียงข้อเดียว

1. โดยทั่วไปแล้ว ท่านพูดได้ว่า สุขภาพของท่านเป็นอย่างไร **(วงกลมหนึ่งคำตอบ)**

ดีเลิศ	ดีมาก	ดี	พอใช้ได้	ไม่ดี
1	2	3	4	5

2. เปรียบเทียบกับเมื่อ 1 ปี ที่แล้ว ท่านพูดได้ว่าสุขภาพของท่านโดยทั่วไปตอนนี้เป็นอย่างไร
(วงกลมหนึ่งคำตอบ)

ดีกว่าเมื่อ 1 ปี ที่แล้วมาก	ดีกว่าเมื่อ 1 ปี ที่แล้วบ้างเล็กน้อย	ไม่ต่างกับ เมื่อปีที่แล้ว	แย่กว่าเมื่อ 1 ปี ที่แล้วบ้างเล็กน้อย	แย่กว่าเมื่อ 1 ปี ที่แล้วมาก
1	2	3	4	5

3. คำถามต่อไปนี้เป็นคำถามเกี่ยวกับกิจกรรมที่ท่านปฏิบัติในแต่ละวัน ท่านคิดว่าสุขภาพของท่านตอนนี้มีผลทำให้ท่านไม่สามารถทำกิจกรรมต่อไปนี้ได้อย่างเต็มที่หรือไม่ ถ้ามี มีแค่ไหน
(วงกลมเลือกคำตอบในแต่ละบรรทัด)

กิจกรรม	ทำได้ น้อยลงมาก	ทำได้บ้าง	ทำได้เต็มที่
ก. กิจกรรมที่ต้องใช้แรงมาก เช่น การวิ่ง ยกของหนัก การร่วมเล่นกีฬาที่ต้องออกแรงมาก	1	2	3
ข. กิจกรรมที่ต้องใช้แรงพอสมควร เช่น ย้ายโต๊ะ ถูบ้านด้วยไม้ถูพื้น เดินเร็วๆ หรือเดินเล่นไกลๆ	1	2	3
ค. ยกหรือถือของเมื่อไปจ่ายตลาด	1	2	3
ง. ขึ้นบันไดหลายๆ ชั้น	1	2	3
จ. ขึ้นบันไดชั้นเดียว	1	2	3
ฉ. ก้ม คุกเข่า หรือโก้งโค้ง	1	2	3
ช. เดินมากกว่าหนึ่งกิโลเมตร	1	2	3
ซ. เดินครึ่งกิโลเมตร	1	2	3
ฌ. เดินหนึ่งร้อยเมตร	1	2	3
ญ. อาบน้ำหรือแต่งตัวสวมเสื้อผ้าเอง	1	2	3

4. ในช่วงหนึ่งเดือนที่ผ่านมา**สุขภาพกาย**ของท่านทำให้ท่านมีปัญหาต่อไปนี้ ในการทำงานหรือทำกิจวัตรประจำวันต่าง ๆ ของท่าน หรือไม่ **(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)**

กิจกรรม	**มี**	**ไม่มี**
ก. ทำงานหรือทำกิจกรรมต่างๆ ได้ไม่นานเท่าที่เคย	1	2
ข. ทำงานเสร็จได้น้อยกว่าที่อยากจะทำ	1	2
ค. ไม่สามารถทำงานหรือกิจกรรมบางอย่างได้อย่างที่เคยทำ	1	2
ง. ทำงานหรือกิจกรรมต่างๆ ได้ด้วยความลำบาก (เช่น ต้องใช้ความพยายามมากขึ้น)	1	2

5. ในช่วงหนึ่งเดือนที่ผ่านมา ปัญหาทางอารมณ์ของท่าน (เช่น รู้สึกหดหู่ หรือวิตกกังวล) ทำให้ท่านมีปัญหาในการทำงานหรือกิจกรรมปกติประจำวัน หรือไม่
(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

กิจกรรม	**มี**	**ไม่มี**
ก. ทำงานหรือทำกิจกรรมต่างๆ ได้**ไม่นาน**เท่าที่เคย	1	2
ข. ทำงาน**เสร็จได้น้อยกว่า**ที่อยากจะทำ	1	2
ค. ทำงานหรือกิจกรรมต่างๆ โดย**ไม่ระมัดระวัง**อย่างที่เคยทำ	1	2

6. ในช่วงหนึ่งเดือนที่ผ่านมา สุขภาพกายหรือปัญหาทางอารมณ์ของท่าน รบกวนการทำกิจกรรมทางสังคมตามปกติ ของท่าน เช่น การพบปะสังสรรค์กับครอบครัว เพื่อนฝูง หรือเพื่อนบ้าน มากน้อยเพียงใด **(วงกลมหนึ่งคำตอบ)**

ไม่เลย	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากอย่างยิ่ง**
1	2	3	4	5

7. ในช่วงหนึ่งเดือนที่ผ่านมา ท่านมีอาการปวดตามร่างกาย รุนแรงเพียงใด **(วงกลมหนึ่งคำตอบ)**

ไม่มีอาการเลย	**มีอาการ เล็กน้อยมาก**	**มีอาการ เล็กน้อย**	**มีอาการ ปานกลาง**	**มีอาการ มาก**	**มีอาการ รุนแรงมาก**
1	2	3	4	5	6

8. ในช่วงหนึ่งเดือนที่ผ่านมาอาการปวดตามร่างกายของท่าน รบกวนการทำงานตามปกติของท่าน (ทั้งงานที่ทำงานและงานบ้าน) เพียงใด **(วงกลมหนึ่งคำตอบ)**

ไม่เลย	**เล็กน้อย**	**ปานกลาง**	**ค่อนข้างมาก**	**มากอย่างยิ่ง**
1	2	3	4	5

9. คำถามต่อไปนี้เกี่ยวกับว่า ท่านรู้สึกอย่างไร และท่านเป็นอย่างไรในช่วงหนึ่งเดือนที่ผ่านมาโปรดตอบคำถามแต่ละข้อ โดยให้คำตอบที่ใกล้เคียงกับความรู้สึกของท่านมากที่สุด

ในช่วงหนึ่งเดือนที่ผ่านมา ท่านมีความรู้สึกต่อไปนี้ บ่อยแค่ไหน

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

กิจกรรม	ตลอดเวลา	เกือบตลอดเวลา	บางครั้ง	นาน ๆ ครั้ง	นานๆ ครั้ง	ไม่เลย
ก. ท่านรู้สึกมีชีวิตชีวา กระปรี้กระเปร่าหรือไม่	1	2	3	4	5	6
ข. ท่านรู้สึกวิตกกังวลหรือไม่	1	2	3	4	5	6
ค. ท่านรู้สึกหดหู่ซึมเศร้ามากจนไม่มีอะไรทำให้รู้สึกดีขึ้นหรือไม่	1	2	3	4	5	6
ง. ท่านรู้สึกสงบสบายหรือไม่	1	2	3	4	5	6
จ. ท่านมีพลังมากมายหรือไม่	1	2	3	4	5	6
ฉ. ท่านรู้สึกท้อแท้ และหดหู่ใจหรือไม่	1	2	3	4	5	6
ช. ท่านรู้สึกหมดเรี่ยวแรงหรือไม่	1	2	3	4	5	6
ซ. ท่านเป็นคนที่มีความสุขหรือไม่	1	2	3	4	5	6
ฌ. ท่านรู้สึกเหนื่อยหรือไม่	1	2	3	4	5	6

10. ในช่วงหนึ่งเดือนที่ผ่านมา สุขภาพกายหรือปัญหาทางอารมณ์ของท่าน รบกวนการทำกิจกรรมทางสังคมตามปกติของท่าน เช่น การพบปะสังสรรค์กับครอบครัว เพื่อนฝูง หรือเพื่อนบ้าน บ่อยครั้งแค่ไหน

(วงกลมหนึ่งคำตอบ)

ตลอดเวลา	เกือบตลอดเวลา	บางครั้ง	นาน ๆ ครั้ง	ไม่เลย
1	2	3	4	5

11. ข้อความแต่ละข้อความต่อไปนี้ **ถูกต้อง**หรือ**ไม่ถูกต้อง** มากน้อยแค่ไหนสำหรับท่าน

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่ถูกต้องอย่างยิ่ง	ค่อนข้างไม่ถูกต้อง	ไม่แน่ใจ	ค่อนข้างถูกต้อง	ถูกต้องอย่างยิ่ง
ก. ฉันดูเหมือนจะไม่สบายง่ายกว่าคนอื่น	1	2	3	4	5
ข. ฉันมีสุขภาพแข็งแรงดีพอๆ กับคนอื่นๆ ที่ฉันรู้จัก	1	2	3	4	5
ค. ฉันคิดว่าสุขภาพของตัวเองจะแย่ลง	1	2	3	4	5
ง. สุขภาพของฉันดีเยี่ยม	1	2	3	4	5

โรคไตของคุณ

12. ข้อความแต่ละข้อความต่อไปนี้ ถูกต้องหรือไม่ถูกต้อง มากน้อยเพียงใดสำหรับท่าน

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่จริงอย่างยิ่ง	ไม่จริงอย่างมาก	ไม่แน่ใจ	จริงอย่างมาก	จริงอย่างยิ่ง
ก. โรคไตรบกวนชีวิตของท่านมากเกินไป	1	2	3	4	5
ข. เวลาของท่านหมดไปกับการรักษาโรคไตมากเกินไป	1	2	3	4	5
ค. ท่านรู้สึกวุ่นวายใจกับการรักษาโรคไต	1	2	3	4	5
ง. ท่านรู้สึกเป็นภาระของครอบครัว	1	2	3	4	5

13. คำถามต่อไปนี้ถามเกี่ยวกับ ความรู้สึกและสิ่งต่างๆในการดำเนินชีวิตในช่วงหนึ่งเดือนที่ผ่านมา กรุณาเลือกเพียงหนึ่งคำตอบที่ใกล้เคียงกับความรู้สึกของท่านมากที่สุด

ในช่วงหนึ่งเดือนที่ผ่านมา ท่านมีความรู้สึกต่อไปนี้ บ่อยแค่ไหน

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่เลย	นานๆครั้ง	บางครั้ง	บ่อยๆ	ค่อนข้างบ่อย	บ่อยมาก
ก. ท่านแยกตัวเองออกจากคนรอบข้าง	1	2	3	4	5	6
ข. ท่านตอบสนองช้า ต่อสิ่งที่ได้ยินหรือสิ่งที่เกิดขึ้น	1	2	3	4	5	6
ค. ท่านแสดงอาการหงุดหงิดต่อคนรอบข้าง	1	2	3	4	5	6
ง. ท่านลำบากในการใช้สมาธิหรือใช้ความคิด	1	2	3	4	5	6
จ. ท่านเข้ากับผู้อื่นได้ดี	1	2	3	4	5	6
ฉ. ท่านรู้สึกสับสนหรือมึนงง	1	2	3	4	5	6

14. ในช่วงหนึ่งเดือนที่ผ่านมา ท่านถูกรบกวนโดยอาการเหล่านี้มากน้อยเพียงใด

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่รบกวนเลย	รบกวนเล็กน้อย	รบกวนปานกลาง	รบกวนมาก	รบกวนมากที่สุด
ก. ปวดเมื่อยกล้ามเนื้อ	1	2	3	4	5
ข. เจ็บหน้าอก	1	2	3	4	5
ค. เป็นตะคริว	1	2	3	4	5
ง. คันตามผิวหนัง	1	2	3	4	5
จ. ผิวแห้ง	1	2	3	4	5
ฉ. หายใจได้ไม่เต็มที่ หรือหายใจเหนื่อย	1	2	3	4	5
ช. เป็นลมหน้ามืด หรือวิงเวียนศีรษะ	1	2	3	4	5
ซ. เบื่ออาหาร	1	2	3	4	5
ฌ. อ่อนแรง หรือหมดกำลัง	1	2	3	4	5
ญ. มือหรือเท้าชา	1	2	3	4	5
ฎ. คลื่นไส้หรือไม่สบายท้อง	1	2	3	4	5
สำหรับผู้ป่วยที่ล้างไตโดยการฟอกเลือดด้วยเครื่องไตเทียมเท่านั้น					
ฏ. ปัญหาเกี่ยวกับบริเวณที่แทงเข็มหรือทางออกของสายฟอกเลือด	1	2	3	4	5
สำหรับผู้ป่วยที่ล้างไตทางช่องท้องเท่านั้น					
ฐ. ปัญหาเกี่ยวกับบริเวณแผลทางออกของสายล้างไตทางหน้าท้อง	1	2	3	4	5

ผลกระทบของโรคไตต่อชีวิตประจำวัน

15. ชีวิตประจำวันของบางคนได้รับผลกระทบจากโรคไตในขณะที่ผู้อื่นไม่ได้รับผลกระทบ โรคไต รบกวนท่านมากน้อยเพียงใด ในเรื่องต่อไปนี้

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่เลย	เล็กน้อย	ปานกลาง	มาก	มากที่สุด
ก. การจำกัดน้ำดื่ม	1	2	3	4	5
ข. การจำกัดอาหาร	1	2	3	4	5
ค. ความสามารถในการทำงานบ้าน	1	2	3	4	5
ง. ความสามารถในการเดินทางไปที่ต่าง ๆ	1	2	3	4	5
จ. การต้องพึ่งพาแพทย์และบุคลากรทางการแพทย์อื่นๆ	1	2	3	4	5
ฉ. ความเครียดหรือความวิตกกังวลจากโรคไต	1	2	3	4	5
ช. การมีเพศสัมพันธ์	1	2	3	4	5
ซ. ลักษณะรูปร่างภายนอกของท่าน	1	2	3	4	5

คำถาม 3 ข้อ ต่อไปนี้ถามเรื่องส่วนตัวและเกี่ยวข้องกับกิจกรรมทางเพศแต่คำตอบของท่านมีความสำคัญต่อการช่วยให้เข้าใจว่าโรคไตมีผลกระทบต่อการใช้ชีวิตของคนทั่วไปอย่างไร

16. ในช่วงหนึ่งเดือนที่ผ่านมาท่านมีกิจกรรมทางเพศหรือไม่

(วงกลมหนึ่งคำตอบ)

ไม่มี	1 ⇨	(หากเลือกข้อนี้ ให้ข้ามไปตอบคำถามข้อ 17 ต่อ)
มี	2	(ให้ทำข้อต่อไป)

ท่านมีปัญหาเหล่านี้มากน้อยเพียงใด ในช่วงหนึ่งเดือนที่ผ่านมา

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่มีปัญหา	มีปัญหาเล็กน้อย	มีปัญหาปานกลาง	มีปัญหามาก	มีปัญหามากที่สุด
ก. มีความสุขในการมีเพศสัมพันธ์	1	2	3	4	5
ข. ตอบสนองต่อการกระตุ้นทางเพศ	1	2	3	4	5

สำหรับคำถามต่อไปนี้ กรุณาให้คะแนน การนอนหลับของท่าน จาก 0 ถึง 10 (0 คะแนน คือ แย่มาก และ 10 คะแนน คือดีมาก) ถ้าท่านคิดว่าการนอนหลับของท่านอยู่กึ่งกลางระหว่าง แย่มาก กับ ดีมาก กรุณาให้คะแนน โดยวงกลมเลข 5 ถ้าท่านคิดว่าอยู่ในระดับที่ดีกว่า 5 หนึ่งระดับ ให้วงกลมเลข 6 ถ้าแย่กว่า 5 หนึ่งระดับให้วงกลมเลข 4 (เช่นนี้ต่อไป)

17. จากคะแนน 0 ถึง 10 โดยรวมแล้ว ท่านให้คะแนนการนอนหลับของท่านที่ระดับใด

(วงกลมหนึ่งคำตอบ)

แย่มาก **ดีมาก**

18. ในช่วงหนึ่งเดือนที่ผ่าน มีสิ่งเหล่านี้เกิดขึ้นกับท่านบ่อยครั้งเพียงใด

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่เลย	นานๆ ครั้ง	บางครั้ง	บ่อยๆ	ค่อนข้างบ่อย	บ่อยมาก
ก. ตื่นกลางดึกและนอนหลับต่อได้ยาก	1	2	3	4	5	6
ข. นอนได้เพียงพอตามต้องการ	1	2	3	4	5	6
ค. ง่วงนอนระหว่างวัน	1	2	3	4	5	6

19. เกี่ยวกับครอบครัว และเพื่อนของท่าน ท่านรู้สึกพอใจเพียงใด ในประเด็นต่อไปนี้

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ไม่พอใจมาก	**ค่อนข้างไม่พอใจ**	**พอใจบ้าง**	**พอใจมาก**
ก. เวลาที่ท่านมีให้กับครอบครัวและเพื่อน	1	2	3	4
ข. ความช่วยเหลือและกำลังใจที่ได้รับจากครอบครัวและเพื่อน	1	2	3	4

ข้อ 20-21 ให้วงกลมรอบตัวเลขที่เป็นคำตอบ **(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)**

	ใช่	**ไม่ใช่**
20. ในช่วงหนึ่งเดือนที่ผ่านมา ท่านทำงานที่ได้รับค่าตอบแทนหรือไม่	1	2
21. สุขภาพของท่านทำให้ท่านไม่สามารถทำงานที่ได้รับค่าตอบแทนหรือไม่	1	2

22.โดยรวมแล้วท่านให้คะแนนสุขภาพของท่านที่ระดับใด

(วงกลมหนึ่งคำตอบ)

แย่ที่สุดเท่าที่เป็นไปได้ (แย่เท่ากับหรือแย่กว่าการตาย)

ครึ่งทางระหว่างแย่ที่สุดกับดีที่สุด

ดีที่สุดเท่าที่เป็นไปได้

ความพึงพอใจต่อการดูแลรักษา

23.ให้ท่านคิดถึงการดูแลรักษาเกี่ยวกับการล้างไตที่ท่านได้รับจากเจ้าหน้าที่หน่วยล้างไต ในเรื่องของความพึงพอใจ ท่านให้คะแนนความเป็นกันเองและความเอาใจใส่ที่ได้รับอย่างไร

(วงกลมหนึ่งคำตอบ)

แย่ที่สุด	แย่	ปานกลาง	ดี	ดีมาก	ดีเยี่ยม	ดีที่สุด
1	2	3	4	5	6	7

24. ข้อความแต่ละข้อความต่อไปนี้ ถูกต้องหรือไม่ถูกต้อง มากน้อยเพียงใดสำหรับท่าน

(วงกลมรอบตัวเลขที่เป็นคำตอบในแต่ละบรรทัด)

	ถูกต้องอย่างยิ่ง	ถูกต้องค่อนข้างมาก	ไม่ทราบ	ถูกต้องค่อนข้างน้อย	ไม่ถูกต้องเลย
ก. เจ้าหน้าที่หน่วยล้างไตช่วยเหลือและสนับสนุนให้ท่านพึ่งตนเองให้มากที่สุดเท่าที่ทำได้	1	2	3	4	5
ข. เจ้าหน้าที่หน่วยล้างไตช่วยเหลือให้ท่านต่อสู้กับโรคไตได้	1	2	3	4	5

*** ขอขอบพระคุณทุกท่านที่กรุณาให้ความร่วมมือในการตอบแบบสอบถาม ***

Appendix C

วันที่ส่งแบบบันทึก……..วันที่รับแบบบันทึกคืน…….. วันที่ส่งเพื่อปรับปรุง……วันที่รับหลังปรับปรุง…….

ชื่อผู้บันทึก .....วัน เดือน ปี ที่บันทึก ……..…..…

Case record form

การบันทึกข้อมูลทั่วไปของผู้ป่วยซึ่งเป็นข้อมูลจากการเปิดแฟ้มประวัติของผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมตั้งแต่ ปีพ.ศ. 2547 ถึง พ.ศ. 2552

ส่วนที่ 1 ข้อมูลทั่วไป (ใช้จากเวชระเบียนและแฟ้มประวัติที่หน่วยฟอกไต)

	Question	Code
1.1	เพศ ☐ 1. ชาย ☐ 2. หญิง	Sex……
1.2	สถานภาพ ☐ 1. โสด ☐ 2. สมรส ☐ 3. หย่าร้าง ☐ 4. คู่สมรสเสียชีวิตแล้ว	Marital……..
1.3	สาเหตุที่ทำให้ผู้ป่วยต้องบำบัดทดแทนไต (End-Stage Renal Disease) ☐ 1. Hypertension ☐ 2. Diabetes nephopathy ☐ 3. Ischemic nephropathy ☐ 4. Renal artery stenosis ☐ 5. Glomerulonephritis ☐ 6. ADPKD ☐ 7. Unknown ☐ 8. อื่นๆ (โปรดระบุ)	CauRF……..
1.4	Underlying disease ที่ผู้ป่วยเป็นอยู่ในปัจจุบัน ☐ 1. Hypertension ☐ 2. Diabetes mellitus ☐ 3. Ischemic nephropathy ☐ 4. Renal artery stenosis ☐ 5. Myocardial infarction ☐ 6. อื่นๆ (โปรดระบุ)	Comorb…….
1.5	สิทธิการเบิกจ่ายของผู้ป่วย ☐ 1. ประกันสุขภาพถ้วนหน้า ☐ 2. ข้าราชการ/ รัฐวิสาหกิจ ☐ 3. ประกันสังคม ☐ 4. ผู้ป่วยทั่วไป (จ่ายเงินเอง) ☐ 5. อื่นๆ (โปรดระบุ)	Scheme……
1.6	ปัจจุบันผู้ป่วย ☐ 1. เสียชีวิตแล้ว ☐ 2. ยังคงฟอกไตอยู่ที่ร.พ.ศิริราช (ข้ามไปข้อ 1.8) ☐ 3. ย้ายไปรักษาตัวที่อื่น ☐ 4. อื่นๆ(โปรดระบุ)	Pstatus……..

	Question		Code
1.7	กรณีที่ผู้ป่วยเสียชีวิตแล้ว สาเหตุของการเสียชีวิตคือ		
	1. CARDIOVASCULAR	**2. NONCARDIOVASCULAR**	**CVofD.....**
	☐ 1. Myocardial/Cerebral infarction ☐ 2. Hemorrhage ☐ 3. Thrombosis ☐ 4. Arrhythmia ☐ 5. อื่นๆ (โปรดระบุ)	☐ 6. Sepsis ☐ 7. Pneumonia ☐ 8. อื่นๆ (โปรดระบุ)	**CofD.....**
1.8	ผู้ป่วยเคยมีการให้เลือดในช่วง 6 เดือน ที่ผ่านมา **หรือ** ช่วง 6 เดือน ก่อนเสียชีวิต หรือไม่ ☐ 1. ไม่มี ☐ 2. มี เมื่อ วัน/เดือน/ปี		Bldate _ _/_ _/_ _ _ _
1.9	จำนวนครั้งที่ทำ HD .....ครั้ง / สัปดาห์		HDTm.....
1.10	ผู้ป่วยเคยทำการรักษาดังนี้ (อดีต → ปัจจุบัน) ☐ 1. เริ่มที่ HD และทำ HD จนถึงปัจจุบัน ☐ 2. PD → HD (เคยทำ PD ล่าสุดเมื่อวัน/เดือน/ปี .....) ☐ 3. RT → HD (เคยทำ RT ล่าสุดเมื่อวัน/เดือน/ปี ..... ☐ 4. RT → PD → HD (เคยทำ RT ล่าสุดเมื่อวัน/เดือน/ปี .....PD ล่าสุดเมื่อวัน/เดือน/ปี .....)		HofD.....
1.11	ผู้ป่วยทำ HD มานานเพียงใด..... ปี.....เดือน ผู้ป่วยทำ HD ครั้งแรกเมื่อ วัน/เดือน/ปี พ.ศ. .....(ถ้าสามารถระบุวันเดือนปีที่เริ่มใช้ได้ กรุณาระบุ)		LOHD..... HDStD _ _/_ _/_ _ _ _
1.12	ผู้ป่วยมีการใช้ยา EPO หรือไม่ ☐ 1. ไม่มี ☐ 2. ใช้ น้อยกว่า 6 เดือน ☐ 3. ใช้ 6-12 เดือน ☐ 4. ใช้ มากกว่า 12 เดือน วันเดือนปีที่เริ่มใช้ EPO .....(ถ้าสามารถระบุวันเดือนปีที่เริ่มใช้ได้ กรุณาระบุ)		LOEPO.....EP OStD _ _/_ _/_ _ _ _
1.13	ผู้ป่วยเคยสูบบุหรี่หรือไม่ ถ้าเคย ปัจจุบันยังสูบอยู่หรือไม่ ☐ 1. ไม่เคยสูบ ☐ 2. เคยสูบและเลิกแล้วมากกว่า 5 ปี ☐ 3. เคยสูบและเลิกแล้วน้อยกว่า 5 ปี ☐ 4. ยังสูบอยู่		Smok..... LOSm.....

ส่วนที่ 2 ผลการตรวจทางห้องปฏิบัติการ <u>ในช่วงเวลา 1 ปี ที่ผ่านมา</u> *(กรณีที่ผู้ป่วยเสียชีวิตแล้วใช้ข้อมูลก่อนเสียชีวิต 1 ปี)* <u>แต่ละเดือน</u>ผู้ป่วยมีค่าผล Lab มีการใช้ยาฉีด EPO อย่างไร (กรณีมีค่า lab นั้นๆ หลายครั้งใน 1 เดือน กรุณากรอกทุกค่าที่มีผลในแฟ้มประวัติ โดยกรอกข้อมูลจาก เดือนที่เริ่มบันทึก (ปัจจุบัน) → เดือนที่ผ่านๆ มา (อดีต)

เดือน / ปี		…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...
2.1	**Hb (g/dl)**	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……
2.2	**Hct %**	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……	1. ……2…… 3… …4…… 5……
2.3	KTV												
2.4	Albumin (g/dl)												
2.5	Creatinine (Cr)												
2.6	BUN												
2.7	GFR (ml/min)												
2.8	Ferritin (ng/ml)												
2.9	TSAT												
2.10	dose EPO / **ครั้ง**	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……	1……2……
2.11	EPOครั้ง / **week**												
2.12	ยี่ห้อ EPO ที่ใช้ 1= Eprex 2= Recormon 3= Hemax 4= Other												
2.13	วิธีการฉีด EPO 1 = SC 2 = IV 3 = Other												
2.14	ยา HTN <u>ก่อน</u> HD												
2.15	BP **ก่อน/ หลัง** HD	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….

ให้หาข้อมูลย้อนหลัง เริ่ม ณ วันที่ผู้ป่วยมีระดับ Hb เริ่มต้นที่ 7-8 g/dl และบันทึกต่อเนื่องไปอีก 1 ปี แต่ละเดือนผู้ป่วยมีค่าผล Lab, ใช้ ยาฉีด EPO อย่างไร (กรณีมีค่า lab นั้นๆ หลายครั้งใน 1 เดือน กรุณากรอกทุกค่าที่มีผลในแฟ้มประวัติ) โดยกรอกข้อมูลจาก เดือนที่เริ่มมี Hb 7-8 g/dl , Hct 21-24 % ติดตามต่อเนื่องไปข้างหน้าจนครบ 12 เดือน (Historical cohort)

เดือน / ปี		…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...	…../…...
2.1	**Hb (g/dl)**	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……
2.2	**Hct %**	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……	1. ……2…….. 3… …4…….. 5……
2.3	KTV												
2.4	Albumin (g/dl)												
2.5	Creatinine (Cr)												
2.6	BUN												
2.7	GFR (ml/min)												
2.8	Ferritin (ng/ml)												
2.9	TSAT												
2.10	dose EPO / **ครั้ง**	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...	1……2…...
2.11	EPOครั้ง / **week**												
2.12	ยี่ห้อ EPO ที่ใช้ 1= Eprex 2= Recormon 3= Hemax 4= Other												
2.13	วิธีการฉีด EPO 1 = SC 2 = IV 3 = Other												
2.14	ยา HTN ก่อน HD												
2.15	BP **ก่อน/ หลัง** HD	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….	……./…….

ส่วนที่ 3 ข้อมูล Event และยาที่ผู้ป่วยต้องใช้ **<u>ระบุชื่อยา, วิธีใช้ยา, ระยะเวลาที่ใช้</u>** **เช่น ยาลดความดันที่ต้องกินเพิ่มขึ้นจากปกติ, ยาฆ่าเชื้อ ในช่วงปี 2547-2552 นี้ ที่<u>ไม่ใช่กรณีอุบัติเหตุ</u> และคาดว่ามีความสัมพันธ์กับภาวะโรคไตที่เป็นอยู่** ***Event*** *<u>ใช้รหัส CV1=MI, CV2= stroke, CV3=HF, CV4= revascularization (percutaneous transluminal coronary angioplasty, or coronary-artery bypass grafting), CV5=other CV SE</u> (ระบุรายละเอียด), <u>NCV1=infection, NCV2=headache, NCV3=dizziness, NCV4=GT disorders, NCV5=other NCV SE</u> (ระบุรายละเอียด)*

	ครั้งที่	1		2		3		4		5		6	
3.	Event <u>เกี่ยวกับ</u> <u>วดป ที่เกิด</u>	…………………………… ☐ EPO ☐ อื่น ๆ ……………………… ☐ 1. OPD ☐ 2. IPD		…………………………… ☐ EPO ☐ อื่น ๆ ……………………… ☐ 1. OPD ☐ 2. IPD		…………………………… ☐ EPO ☐ อื่น ๆ ……………………… ☐ 1. OPD ☐ 2. IPD		…………………………… ☐ EPO ☐ อื่น ๆ ……………………… ☐ 1. OPD ☐ 2. IPD		…………………………… ☐ EPO ☐ อื่น ๆ ……………………… ☐ 1. OPD ☐ 2. IPD		…………………………… ☐ EPO ☐ อื่น ๆ ……………………… ☐ 1. OPD ☐ 2. IPD	
	ยาที่ใช้รักษา วิธี ระยะเวลา	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..
	ยาที่ใช้รักษา วิธี ระยะเวลา	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..
	ยาที่ใช้รักษา วิธี ระยะเวลา	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..	……….. ……….. ………..	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..	……… ……… ………	……….. ……….. ………..
	Hb / Hct ย้อนหลัง 6 เดือน	1. ……..2……...3……...…4….. ......5....…...6…….... 7. ……..8……...9……….10... ......11..……12……...		1. ……..2……...3……...…4….. ......5....…...6…….... 7. ……..8……...9……….10... ......11..……12……...		1. ……..2……...3……...…4….. ......5....…...6…….... 7. ……..8……...9……….10... ......11..……12……...		1. ……..2……...3……...…4….. ......5....…...6…….... 7. ……..8……...9……….10... ......11..……12……...		1. ……..2……...3……...…4….. ......5....…...6…….... 7. ……..8……...9……….10... ......11..……12……...		1. ……..2……...3……...…4….. ......5....…...6…….... 7. ……..8……...9……….10... ......11..……12……...	

โครงการวิจัยการวิเคราะห์ต้นทุนอรรถประโยชน์ของการใช้ยา erythropoietin เพื่อรักษาภาวะโลหิตจางในผู้ป่วยที่ฟอกไต

	Question
1.	ระดับการศึกษาขั้นสูงสุดหรือที่กำลังศึกษาอยู่ ☐ 1. ไม่ได้เรียน ☐ 2. ประถมศึกษา ☐ 3. มัธยมศึกษา/ ปวช. ☐ 4. ปวส./ อนุปริญญา หรือเทียบเท่า ☐ 5. ปริญญาตรี หรือเทียบเท่า ☐ 6. สูงกว่าปริญญาตรี ☐ 7. อื่นๆ (ระบุ) .....
2.	ผู้ป่วยสามารถฟังและตอบแบบสอบถามได้หรือไม่ ☐ 1. ไม่ได้ ☐ 2. ได้
3.	อายุ……ปี
4.	อาชีพหลัก ☐ 1. นักเรียน/ นักศึกษา ☐ 2. ข้าราชการ/ รัฐวิสาหกิจ ☐ 3. แม่บ้าน ☐ 4. ค้าขาย/ เจ้าของกิจการ ☐ 5. พนักงานบริษัทเอกชน ☐ 6. เกษียณ ☐ 7. เกษตรกรรม (ทำนา, ไร่, สวน) ☐ 8. ไม่ได้ประกอบอาชีพ ☐ 9. อื่นๆ .....
5.	รายได้จากอาชีพเฉลี่ย .....บาทต่อเดือน (ทั้งอาชีพหลักและอาชีพเสริม กรณีไม่มีรายได้ให้เติมศูนย์)
6.	ผู้ป่วยได้รับการสนับสนุนค่าใช้จ่ายจากผู้อื่นหรือไม่ ☐ 1. ไม่มี ☐ 2. ได้รับจาก.....เป็นเงิน.....บาทต่อเดือน
7.	ที่อยู่ เลขที่ ……ถนน…… แขวง……... เขต……จังหวัด…….
ข้อมูลของต้นทุนทางตรงที่ไม่เกี่ยวข้องทางการแพทย์	
8.	ส่วนใหญ่ผู้ป่วยและหรือญาติ เดินทางไป-กลับเพื่อรักษาตัวหรือฟอกเลือดโดยวิธี ☐ แท็กซี่ (……บาท) ☐ รถโดยสาร (……บาท) ☐ รถส่วนตัว (ค่าน้ำมัน……บาท) เฉลี่ยค่าเดินทางสำหรับผู้ป่วยและญาติหรือผู้ดูแล……..บาท / ครั้ง (ถ้าไม่มีให้ใส่ศูนย์)
9.	ผู้ป่วยมีญาติ/ผู้ดูแลหรือไม่ ☐ 1. ไม่มี ☐ 2. มี
10.	ค่าอาหารและค่าที่พักสำหรับผู้ป่วย……..……บาท/ครั้ง ญาติ/ ผู้ดูแล……..บาท/ครั้ง
11.	จำนวนครั้งที่ต้องฟอกเลือด ……ครั้ง / สัปดาห์ (รวมที่ฟอกที่ร.พ.อื่นด้วย)
12.	ผู้ป่วยมีค่าใช้จ่ายในการจ้างผู้ดูแล เป็นเงิน……..…บาท (ต่อเดือน)
ข้อมูลของต้นทุนทางอ้อม	
13.	กรณีที่ไม่ต้องจ้างผู้ดูแลผู้ป่วย แต่มีญาติดูแล ปกติญาติที่ดูแลถ้าไปทำงานจะได้ค่าตอบแทน ……บาท (ต่อเดือน) (ถ้าไม่มีให้ใส่ศูนย์)
14.	หลังฟอกเลือดแล้วผู้ป่วยกลับไปทำงานต่อ (คิดทั้งกรณีทำงานที่ทำงานหรืองานบ้าน) ในวันนั้นหรือไม่ ☐ 1. ไม่ ☐ 2. กลับไปทำงานต่อในวันนั้นได้

Appendix D

คำแนะนำในการกรอก Record form ของโครงการวิจัย "การวิเคราะห์ต้นทุนอรรถประโยชน์ของการใช้ยา Erythropoietin เพื่อรักษาภาวะโลหิตจางในผู้ป่วยที่ฟอกไต"

- กรอกข้อมูลจากแฟ้มประวัติ โดยใช้ข้อมูลจากแฟ้มประวัติของผู้ป่วยที่มาทำการฟอกไตระหว่างปีพ.ศ.2547 ถึงปัจจุบัน
- แฟ้มประวัติสามารถสืบค้นได้จาก
    1. หอผู้ป่วย ผะอบ 3, กว 1, กว 2, กว 3, กว 4
    2. Database ที่ศูนย์คอมพิวเตอร์ส่งมาให้
    3. File scan แฟ้มประวัติจากเวชระเบียน
- ข้อมูลใน Case record form ประกอบด้วย 3 ส่วน คือ

1. ข้อมูลทั่วไป จะมีคำถาม 13 ข้อ ซึ่งเป็นคำถามเพื่อให้ได้ข้อมูลที่เป็นลักษณะประชากร เช่น เพศ, โรคร่วม, สิทธิการรักษาพยาบาล (มีในแฟ้มประวัติปัจจุบัน ผู้ป่วยทุกคน)

เอกสารแนบหมายเลข 2

เลขที่. ...52075.

วันที่ส่งแบบบันทึก.....1 พ.ย. 52....วันที่รับแบบบันทึกคืน.....10 พ.ย. 52..... วันที่ส่งเพื่อปรับปรุง.....วันที่รับหลังปรับปรุง.....

ชื่อผู้บันทึก .....น้ำใจ ไมตรี.....วัน เดือน ปี ที่บันทึก .....5 พ.ย. 52

Case record form

การบันทึกข้อมูลทั่วไปของผู้ป่วยซึ่งเป็นข้อมูลจากการเปิดแฟ้มประวัติของผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมตั้งแต่ ปีพ.ศ. 2547 ถึง พ.ศ. 2552

ส่วนที่ 1 ข้อมูลทั่วไป (ใช้จากเวชระเบียนและแฟ้มประวัติที่หน่วยฟอกไต)

	Question	Code
1.1	เพศ ☑ 1. ชาย ☐ 2. หญิง	Sex.....
1.2	สถานภาพ ☐ 1. โสด ☑ 2. สมรส ☐ 3. หย่าร้าง ☐ 4. คู่สมรสเสียชีวิตแล้ว	Marital.....
1.3	สาเหตุที่ทำให้ผู้ป่วยต้องบำบัดทดแทนไต (End-Stage Renal Disease) ☐ 1. Hypertension ☑ 2. Diabetes nephopathy ☐ 3. Ischemic nephropathy ☐ 4. Renal artery stenosis ☐ 5. Glomerulonephritis ☐ 6. ADPKD ☐ 7. Unknown ☐ 8. อื่นๆ (โปรดระบุ)	CauRF.....
1.4	Underlying disease ที่ผู้ป่วยเป็นอยู่ในปัจจุบัน ☑ 1. Hypertension ☑ 2. Diabetes mellitus ☑ 3. Ischemic nephropathy ☐ 4. Renal artery stenosis ☐ 5. Myocardial infarction ☐ 6. อื่นๆ (โปรดระบุ)	Comorb.....
1.5	สิทธิการเบิกจ่ายของผู้ป่วย ☐ 1. ประกันสุขภาพถ้วนหน้า ☑ 2. ข้าราชการ/ รัฐวิสาหกิจ ☐ 3. ประกันสังคม ☐ 4. ผู้ป่วยทั่วไป (จ่ายเงินเอง) ☐ 5. อื่นๆ (โปรดระบุ)	Scheme.....
1.6	ปัจจุบันผู้ป่วย ☐ 1. เสียชีวิตแล้ว ☑ 2. ยังคงฟอกไตอยู่ที่ร.พ.ศิริราช (ข้ามไปข้อ 1.8) ☐ 3. ย้ายไปรักษาตัวที่อื่น ☐ 4. อื่นๆ(โปรดระบุ)	Pstatus.....

1. กรณีที่ผู้ป่วยยังมีชีวิตอยู่ข้ามไปตอบข้อ 1.8 ได้เลย ถ้ากรณีที่เสียชีวิตแล้วต้องใช้ข้อมูลก่อนผู้ป่วยเสียชีวิต 1 ปี ในการเก็บข้อมูลด้านค่า Lab

2. กรณีที่ผู้ป่วยเสียชีวิตแล้วต้องกรอกข้อมูลสาเหตุการเสียชีวิต ว่าเสียชีวิตจากสาเหตุใด

- กรณีเสียชีวิตที่สัมพันธ์กับด้านหัวใจและหลอดเลือดให้เลือกด้านช่อง Cardiovascular
- กรณีที่เสียชีวิตด้วยสาเหตุที่ไม่สัมพันธ์กับด้านหัวใจและหลอดเลือดให้เลือกด้าน Non cardiovascular

เลขที่ ...52075.

	Question		Code
1.7	กรณีที่ผู้ป่วยเสียชีวิตแล้ว สาเหตุของการเสียชีวิตคือ		
	1. CARDIOVASCULAR	2. NONCARDIOVASCULAR	CVofD.....
	☐ 1. Myocardial/Cerebral infarction ☐ 2. Hemorrhage ☐ 3. Thrombosis ☐ 4. Arrhythmia ☐ 5. อื่นๆ (โปรดระบุ)	☐ 6. Sepsis ☐ 7. Pneumonia ☐ 8. อื่นๆ (โปรดระบุ)	CofD.....
1.8	ผู้ป่วยเคยมีการให้เลือดในช่วง 6 เดือน ที่ผ่านมา หรือ ช่วง 6 เดือน ก่อนเสียชีวิต หรือไม่ ☑ 1. ไม่มี ☐ 2. มี เมื่อ วัน/เดือน/ปี		Bldate __/__/____
1.9	จำนวนครั้งที่ทำ HD .....ครั้ง / สัปดาห์		HDTm.....
1.10	ผู้ป่วยเคยทำการรักษาดังนี้ (อดีต → ปัจจุบัน) ☑ 1. เริ่มที่ HD และทำ HD จนถึงปัจจุบัน ☐ 2. PD → HD (เคยทำ PD ล่าสุดเมื่อวัน/เดือน/ปี .....) ☐ 3. RT → HD (เคยทำ RT ล่าสุดเมื่อวัน/เดือน/ปี ..... ☐ 4. RT → PD → HD (เคยทำ RT ล่าสุดเมื่อวัน/เดือน/ปี .....PD ล่าสุดเมื่อวัน/เดือน/ปี .....)		HofD.....
1.11	ผู้ป่วยทำ HD มานานเพียงใด..... ปี.....เดือน ผู้ป่วยทำ HD ครั้งแรกเมื่อ วัน/เดือน/ปี พ.ศ. ...2542..... (ถ้าสามารถระบุวันเดือนปีที่เริ่มใช้ได้ กรุณาระบุ)		LOHD..... HDStD __/__/____
1.12	ผู้ป่วยมีการใช้ยา EPO หรือไม่ ☐ 1. ไม่มี ☐ 2. ใช้ น้อยกว่า 6 เดือน ☐ 3. ใช้ 6-12 เดือน ☑ 4. ใช้ มากกว่า 12 เดือน วัน/เดือน/ปีที่เริ่มใช้ EPO .....พ.ศ. 2544.....(ถ้าสามารถระบุวันเดือนปีที่เริ่มใช้ได้ กรุณาระบุ)		LOEPO..... EPOStD __/__/____
1.13	ผู้ป่วยเคยสูบบุหรี่หรือไม่ จำเคย ปัจจุบันยังสูบอยู่หรือไม่ ☑ 1. ไม่เคยสูบ ☐ 2. เคยสูบและเลิกแล้วมากกว่า 5 ปี ☐ 3. เคยสูบและเลิกแล้วน้อยกว่า 5 ปี ☐ 4. ยังสูบอยู่		Smok..... LOSm.....

3. ข้อมูลผลตรวจทางห้องปฏิบัติการ แบ่งเป็น

1) ผลการตรวจทางห้องปฏิบัติการ <u>**ในช่วงเวลา 1 ปี ที่ผ่านมา**</u> ***(กรณีที่ผู้ป่วยเสียชีวิตแล้วใช้ข้อมูลก่อนเสียชีวิต 1 ปี)*** <u>**แต่ละเดือน**</u> **ดังตัวอย่างข้างล่าง** *เช่น บันทึกเมื่อ 10/52 ก็ต้องย้อนกลับไปดู* ***ข้อมูลในย้อนหลัง*** *ไปคือ 9/52, 8/52, ...11/51* ผู้ป่วยมีค่าผล Lab อย่างไรบ้าง (กรณีมีค่า lab นั้นๆ หลายครั้งใน 1 เดือน กรุณากรอกทุกค่าซึ่งมีกำหนดในตารางที่กำหนดให้) โดยค่า Lab หากไม่มี

มีเก็บในแฟ้มประวัติ ให้สืบค้นจากโปรแกรม E-Cailr รายละเอียดค่า Lab และข้อมูลที่ต้องเก็บประกอบด้วย

1. Hb (g/dl) และ หรือ Hct (%) หากมีการตรวจทั้ง Hb และ Hct กรุณากรอกข้อมูลทั้ง 2 ค่า กรณีที่มีข้อมูลมากกว่า 1 ค่า ใน 1 เดือน กรุณากรอกข้อมูลที่มีทุกค่า
2. ค่า KTV, Albumin (g/dl), Creatinine (Cr), BUN, GFR (ml/min), Ferritin (ng/ml) , TSAT
3. ประวัติการใช้ยาฉีด EPO ใช้ยี่ห้อใด, ขนาดยาที่ใช้ต่อครั้ง, จำนวนครั้งที่ฉีดต่อสัปดาห์ และวิธีการฉีดเป็น iv, sc, other
4. ยา HTN ที่ผป.ต้องใช้ก่อนฟอก
5. ความดันโลหิตของผู้ป่วยก่อนและหลังฟอกเสร็จ เช่น 80/120 / 90/130

ส่วนที่ 2 ผลการตรวจทางห้องปฏิบัติการ ในช่วงเวลา 1 ปี ที่ผ่านมา *(กรณีที่ผู้ป่วยเสียชีวิตแล้วใช้ข้อมูลก่อนเสียชีวิต 1 ปี)* แต่ละเดือนผู้ป่วยมีค่าผล Lab มีการใช้ยาฉีด EPO อย่างไร (กรณีมีค่า lab นั้นๆ หลายครั้งใน 1 เดือน กรุณากรอกทุกค่าที่มีผลในแฟ้มประวัติ โดยกรอกข้อมูลจาก เดือนที่เริ่มบันทึก (ปัจจุบัน) → เดือนที่ผ่านๆ มา (อดีต)

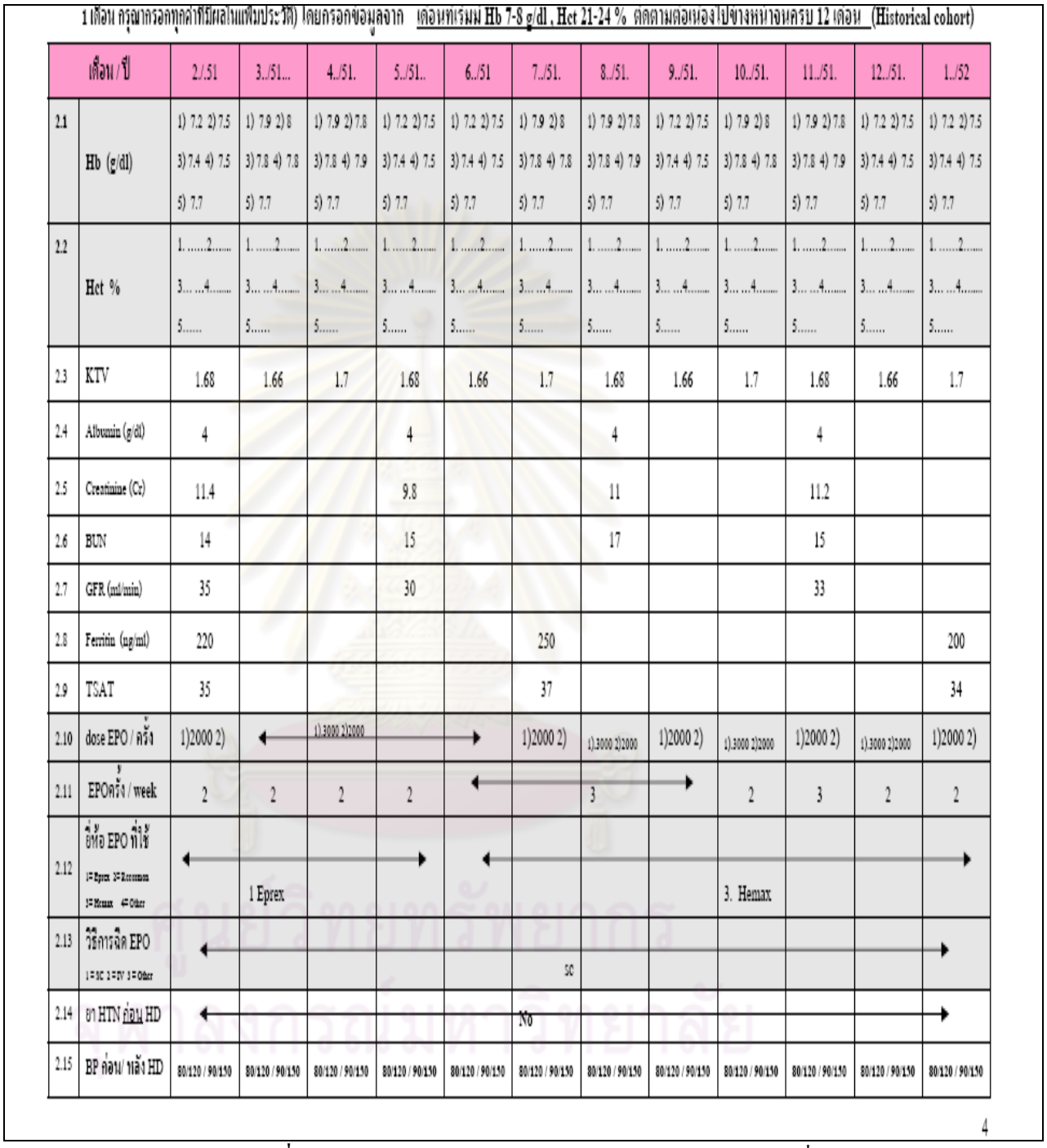
	เดือน / ปี	10./.52	9../52..	8./52	7./52	6./52	5./52	4./52	3./52	2./52	1./52	12./51	11./51
2.1	Hb (g/dl)	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.9 2) 8 3) 7.8 4) 7.8 5) 7.7	1) 7.9 2) 7.8 3) 7.8 4) 7.9 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.9 2) 8 3) 7.8 4) 7.8 5) 7.7	1) 7.9 2) 7.8 3) 7.8 4) 7.9 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.9 2) 8 3) 7.8 4) 7.8 5) 7.7	1) 7.9 2) 7.8 3) 7.8 4) 7.9 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7
2.2	Hct %	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....	1. ....2.... 3.... 4.... 5.....
2.3	KTV	1.68	1.66	1.7	1.68	1.66	1.7	1.68	1.66	1.7	1.68	1.66	1.7
2.4	Albumin (g/dl)	4			4			4			4		
2.5	Creatinine (Cr)	11.4			9.8			11			11.2		
2.6	BUN	14			15			17			15		
2.7	GFR (ml/min)	35			30						33		
2.8	Ferritin (ng/ml)	220					250						200
2.9	TSAT	35					37						34
2.10	dose EPO / ครั้ง	1)2000 2)	←	1).3000 2)2000	→		1)2000 2)	1).3000 2)2000	1)2000 2)	1).3000 2)2000	1)2000 2)	1).3000 2)2000	1)2000 2)
2.11	EPOครั้ง / week	2	2	2	2	←		3	→	2	3	2	2
2.12	ยี่ห้อ EPO ที่ใช้ 1= Eprex 2= Recormon 3= Hemax 4= Other	←	1 Eprex		→	←				3. Hemax			→
2.13	วิธีการฉีด EPO 1=SC 2=IV 3= Other	←					SC						→
2.14	ยา HTN ก่อน HD	←					No						→
2.15	BP ก่อน/ หลัง HD	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150

3

2) ผลการตรวจทางห้องปฏิบัติการ Historical cohort

ในช่วงเวลา 5 ปี ที่ผ่านมา (ตั้งแต่มกราคม พ.ศ. 2547-ปัจจุบัน) กรอกข้อมูลเหมือนตารางก่อนหน้า แต่ใช้ค่าเริ่มแรก ณ วันเวลาที่ผู้ป่วย มีระดับ Hb 7-8 g/dl หรือ Hct 21-24 % เช่น เริ่มที่เดือนก.พ. พ.ศ. 2551 ให้กรอกเป็น 2/51 ที่หัวคอลัมน์ดังตัวอย่างข้างล่าง แล้วไล่ไปเดือน 3/51, 4/51 …ถึง 1/52

(ติดตามต่อเนื่องไปจนครบ 1 ปี) ว่ามีค่า Lab, ใช้ยา EPO อย่างไร (Historical cohort) **กรณีที่มีจุดเริ่มต้นที่ 7-8 มากกว่า 1 ครั้ง** ให้เลือกที่เวลาซึ่งมีการใช้ EPO ถ้าไม่มีการใช้ EPO เลย ให้เลือกที่เป็นครั้งล่าสุด



1 เดือน กรุณากรอกทุกค่าที่มีผลในแฟ้มประวัติ) โดยกรอกข้อมูลจาก เดือนที่เริ่มมี Hb 7-8 g/dl , Hct 21-24 % ติดตามต่อเนื่องไปข้างหน้าจนครบ 12 เดือน (Historical cohort)

	เดือน / ปี	2../.51	3../51...	4../51.	5../51..	6../51	7../51.	8../51.	9../51.	10../51.	11../51.	12../51.	1../52
2.1	Hb (g/dl)	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.9 2) 8 3) 7.8 4) 7.8 5) 7.7	1) 7.9 2) 7.8 3) 7.8 4) 7.9 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.9 2) 8 3) 7.8 4) 7.8 5) 7.7	1) 7.9 2) 7.8 3) 7.8 4) 7.9 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.9 2) 8 3) 7.8 4) 7.8 5) 7.7	1) 7.9 2) 7.8 3) 7.8 4) 7.9 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7	1) 7.2 2) 7.5 3) 7.4 4) 7.5 5) 7.7
2.2	Hct %	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....	1. ....2..... 3.... ..4..... 5.....
2.3	KTV	1.68	1.66	1.7	1.68	1.66	1.7	1.68	1.66	1.7	1.68	1.66	1.7
2.4	Albumin (g/dl)	4			4			4			4		
2.5	Creatinine (Cr)	11.4			9.8			11			11.2		
2.6	BUN	14			15			17			15		
2.7	GFR (ml/min)	35			30						33		
2.8	Ferritin (ug/ml)	220					250						200
2.9	TSAT	35					37						34
2.10	dose EPO / ครั้ง	1)2000 2)	← 1).3000 2)2000 →				1)2000 2)	1).3000 2)2000	1)2000 2)	1).3000 2)2000	1)2000 2)	1).3000 2)2000	1)2000 2)
2.11	EPOครั้ง / week	2	2	2	2	←		3 →		2	3	2	2
2.12	ยี่ห้อ EPO ที่ใช้ 1=Eprex 2=Recormon 3=Hemax 4=Other	←	1 Eprex →			←				3. Hemax →			
2.13	วิธีการฉีด EPO 1=IC 2=IV 3=Other	←					5C →						
2.14	ยา HTN ก่อน HD	←					No →						
2.15	BP ก่อน/ หลัง HD	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150	80/120 / 90/150

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4. **ข้อมูล Event ที่เกิดกับผู้ป่วยในช่วงเวลา 2547-ปัจจุบัน** ว่าเคยเกิดเหตุการณ์ที่ทำให้ผู้ป่วยต้องเข้ามารักษาตัวในร.พ. หรือเข้าพบแพทย์ เป็นพิเศษเพื่อรักษาเหตุการณ์ดังกล่าวไม่ว่าเป็นในแง่ของผลข้างเคียงจากการใช้ยา หรือกรณีเกิด complication อะไรบ้าง ที่สัมพันธ์กับภาวะโรคที่เป็นอยู่หรือการใช้ยา (หาจาก database) เมื่อทราบช่วงว่ามีข้อมูลเมื่อใดจะรู้ AN ผู้ป่วยแล้วใช้เลข AN ดังกล่าวไปเปิดหาข้อมูลรายละเอียด

จากแฟ้มประวัติที่เป็น file จากเวชระเบียนและเปิด E-Cailr เพื่อกรอกข้อมูลด้านค่า Lab ณ ช่วงเวลานั้น ย้อนหลังไป 1 ปี ถ้ามีค่า Lab อื่นที่ควรสนใจให้จดเพิ่มเติมได้ แต่ค่าที่สำคัญคือค่า Hb, การใช้ยา EPO

เลขที่. ...52075.

ส่วนที่ 3 ข้อมูล Event และยาที่ผู้ป่วยต้องใช้ ระบุชื่อยา, วิธีใช้ยา, ระยะเวลาที่ใช้ เช่น ยาลดความดันที่ต้องหาเพิ่มขึ้นจากปกติ, ยาฆ่าเชื้อ ในช่วงปี 2547-2552 นี้ ที่ไม่ใช่ครณีอุบัติเหตุ และคาดว่ามีความสัมพันธ์กับภาวะโรคไตที่เป็นอยู่ *Event ใช้รหัส CV1=MI, CV2= stroke, CV3=HF, CV4= revascularization (percutaneous transluminal coronary angioplasty, or coronary-artery bypass grafting), CV5=other CV SE (ระบุรายละเอียด), NCV1=infection, NCV2=headache, NCV3=dizziness, NCV4=GT disorders, NCV5=other NCV SE (ระบุรายละเอียด)*

	ครั้งที่	1		2		3		4		5		6	
3.	Event เกี่ยวกับ วัคป ที่เกิด	CV5:Artherosclerosis. ☐ EPO ☑ อื่น ๆ ...19 ต.ค. 2549..... ☐ 1. OPD ☑ 2. IPD		..... ☐ EPO ☐ อื่น ๆ ..... ☐ 1. OPD ☐ 2. IPD		..... ☐ EPO ☐ อื่น ๆ ..... ☐ 1. OPD ☐ 2. IPD		..... ☐ EPO ☐ อื่น ๆ ..... ☐ 1. OPD ☐ 2. IPD		..... ☐ EPO ☐ อื่น ๆ ..... ☐ 1. OPD ☐ 2. IPD		..... ☐ EPO ☐ อื่น ๆ ..... ☐ 1. OPD ☐ 2. IPD	
	ยาที่ใช้รักษา วิธี ระยะเวลา	...Plavix 1x1OD ตลอดไป	Peritrate 1x2 pc ตลอดไป	....	....	....	....	....	....	....	....	....	....
	ยาที่ใช้รักษา วิธี ระยะเวลา	....	....	....	....	....	....	....	....	....	....	....	....
	ยาที่ใช้รักษา วิธี ระยะเวลา	....	....	....	....	....	....	....	....	....	....	....	....
	Hb / Hct ย้อนหลัง 6 เดือน	1. .12...2...13..3...12.5... 4 12.5 .5...13...6...12.... 7. .13...8...12.4..9...12. 10) 11..11).11.5 12)11.2.		1. .....2.....3..... 4.....5.....6..... 7. .....8.....9..... 10.....11.....12.....		1. .....2.....3..... 4.....5.....6..... 7. .....8.....9..... 10.....11.....12.....		1. .....2.....3..... 4.....5.....6..... 7. .....8.....9..... 10.....11.....12.....		1. .....2.....3..... 4.....5.....6..... 7. .....8.....9..... 10.....11.....12.....		1. .....2.....3..... 4.....5.....6..... 7. .....8.....9..... 10.....11.....12.....	

VITAE

The authors, Miss Tanita Thaweethamcharoen, was born on July 16th 1978 in Bangkok, Thailand. She obtained the Bachelor of Pharmacy from the Faculty of Pharmacy, Chulalongkorn University in 2001 and the Master degree from the Faculty of Pharmacy, Naresuan University in 2005. She enrolled in this Doctoral in Social and Administrative Pharmacy (International Program), Chulalongkorn University in 2007 and working as a pharmacist at Siriraj Hospital.