Economic evaluation of an integrated care on delaying chronic kidney disease progression in rural communities of Thailand

Background and Rationale

In Thailand, the prevalence of chronic kidney disease (CKD) is 17.5% of the population (Ingsathit et al., 2010). According to Thailand's National Health Security Office (2021), in each year, this public health agency spends approximately 10,000 million Baht in renal dialysis and 1,000 million Baht for the CKD treatment and other related expenses. Seven characteristics that are associated with CKD in Thailand context are older age, gender, diabetes, hypertension, hyperuricemia, history of kidney stones and the use of traditional herbal medicines (Ingsathit et al., 2010). Despite the fact that the CKD is mostly detected in populations from Bangkok, Northern and Northeastern regions, the awareness of the disease remains low in the general Thai population (Ingsathit et al., 2010). Evidence suggested that adverse outcomes of CKD (e.g., kidney failure, cardiovascular disease, and premature death) can be prevented or delayed by early referral and treatment (Levey et al., 2003; Eknoyan et al., 2004).

In previous research, the ESCORT-1 (Effectiveness of Integrated Care on Delaying Progression stage 3-4 Chronic Kidney Disease in Rural Communities of Thailand) studies measured the different impacts between a conventional treatment and integrated care on delaying in CKD progression, specifically on stage 3 or 4 CKD patients. Using a randomized controlled trial method, the CKD patients from different districts were randomly assigned into two conditions. The CKD patients from the control condition received the conventional treatment which included standard clinical care, medications, and educational programs during patients' hospital visits. Rather than only receiving the conventional treatment, the CKD patients from the intervention condition saw a multidisciplinary care team (MDCT) every three months. The MDCT was responsible for providing CKD information, such as medical care, optimal diets, and training to the patients. The results showed that the intervention had a potential to slow down the progression in the pre-dialysis CKD patients (Jiamjariyapon et al., 2017).

In 2021, the ESCORT-2 study was published. The differences between the ESCORT-1 and ESCORT-2 studies were that, in the ESCORT-2 study, researchers applied intervention to all CKD patients. It was an observational study with the aim to assess the real-world effectiveness of the intervention in a Thai rural primary care setting. The intervention was adjusted (see detail below) to be easier to understand and less stringent than the ESCORT-1 study. As a result, the researchers found that the new intervention was more effective, compared to the control group from the ESCORT-1 study (Thanachayanont et al., 2021). In the current study, our objective is to assess the economic value of the intervention, thus, a comparison group is necessary.

Srisubat et al. (2017) analyzed cost-effectiveness alongside the ESCORT-1 study. They found that the integrated care was not cost-effective, compared with the conventional care. However, there were some limitations that can be improved in this study. Firstly, the sample size of this study was considerably small. In the original ESCORT-1 study, they used 442 participants in total. However, in the study by Srisubat et al. (2017), only 120 patients' datum were used. In the present study, model-based health economic evaluation will be applied using evidence from various relevant sources including data from both ESCORT-1 and ESCORT-2 to increase the power of the estimation. Secondly, the time length of the ESCORT-1 study was only 2 years. According to Ku et al., (2018), 7.9, 5, 4.2, 0.8 were the numbers of median years that patients spend in stage 3a, 3b, 4, and 5 of CKD, respectively. Therefore, combining the ESCORT-1 and ESCORT-2 studies would provide us benefits since it gives us 5 years of the study in total. In addition, this model-based study allows us to estimate life-time cost and outcome of each policy choice. Thirdly, Srisubat et al. (2017) study did not provide much information about cost-utility of the program intervention. To be more specific, the study only reported the results in terms of incremental cost-per-ESRD patient averted.

Ultimately, the purpose of this paper is to evidence the impact of integrated care intervention on the Thai population. Economic evaluations of the intervention provide information to researchers and policymakers about which intervention is the most suitable in a particular context. This study proposes that the cost-utility analysis is applied with the outcome presented in terms of quality-adjusted life year (QALY) since it is more generalizable than other health economic analyses (e.g., cost-benefit analysis, cost-effectiveness analysis) (Angevine & Berven, 2014). This particular outcome would be beneficial when considering allocative efficiency by comparing the interventions related to kidney care against other public interventions (e.g., cancer screening) (Turner et al., 2021). The next question to be asked is whether the intervention is worth the investment by the public resources and if the intervention could be part of the Universal Healthcare Coverage (UHC)'s benefit package.

Objectives

In the present study, cost-utility analysis will be conducted using societal perspective to evaluate a value for money in terms of incremental cost-per-QALY of the integrated care delivered by the MDCT on delaying CKD progression compared to the conventional treatment in the Thai setting.

Literature Review

Chronic Kidney Disease (CKD)

Kidneys have an ability to filter toxic and waste from our blood. CKD is defined as a reduced filtration rate of the renal system. People who are 60 years old or older, have hypertension, diabetes, cardiovascular disease (CVD), or have a family history of the disease are more likely to have CKD (Stevens et al., 2006). Glomerular Filtration Rate (GFR) and albuminuria are estimated to determine the different stages of the disease. This study will focus on the estimated GFR as it was used in Jiamjariyapon et al. (2017) and Thanachayanont et al. (2021).

In a healthy young adult, the GFR is estimated to be 120-130 mL/min/1.73 m^2 or higher (Levey et al., 2003). Having lower GFR than 60 mL/min/1.73 m^2 for three or more months would indicate decreased kidney function (Levey et al., 2005; Levey et al., 2003; Levey et al., 2011; Levin et al., 2013). According to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (Levey et al., 2011; Levin et al., 2013), based on the GFR levels, the CKD can be classified into five stages:

Table 1. The five stages of CKD

Stage	GFR (mL/min/1.73 m^2)	Description
1	> 90	Normal or high
2	60 - 90	Mildly decreased
3a	45 - 59	Mildly to moderately decreased
3b	30 - 44	Moderately to severely decreased
4	15 - 29	Severely decreased
5	< 15	Kidney failure

(Levey et al., 2011; Levin et al., 2013)

As such, much research has studied interventions to prevent progression of the disease before it reaches the last stage. Many of them found multidisciplinary care and education as main components in impactful causes for delaying the disease progression on pre-dialysis patients (e.g., Strand & Parker, 2012; Lin et al., 2018; Saldarriaga et al., 2021; Jiamjariyapon et al., 2017; Thanachayanont et al., 2021, etc.).

Cost-Utility Analysis (CUA)

Cost-utility analysis is recommended when using it to inform decisions regarding allocative health resource allocation across health problems (Robinson, 1993). The most commonly used outcome measure in the CUA is the quality-adjusted life year (QALY) (Angevine & Berven, 2014). The QALY outcome is the number of person-years of health gained from implementing the intervention in the care program (Saldarriaga et al., 2021). It is a composite indicator combining quantity of life–a number of years that each patient could live, and the quality of life (or utility)- which is arbitrarily defined at a range from 0 (death) to 1 (perfect health) (Angevine & Berven, 2014). For example, if the intervention results in a patient living 5 years longer with a poor health or 0.2, the QALY would be 1. The target outcome of this paper is the incremental cost-per-QALY or the cost of an intervention divided by the QALY gained. It is important to note that the intervention costs can consist of a direct medical costs (e.g., medications, staffs' wages), direct non-medical costs (e.g., patient transportation); and indirect cost (e.g., wages missed because of the illness)

According to the Guidelines for Health Technology Assessment in Thailand (Second Edition) (2013), CUA is suggested to be the first determinant factor for economic evaluation since its outcome can be both qualitative (quality of life) and quantitative (life year). It enables us to compare one intervention to other different interventions (Chaikledkaew & Kittrongsiri, 2014). This is to be in line with the national methodological guidelines for conducting health economic evaluation in Thailand and be subjected for consideration by the National Health

Security Board who authorize Universal Healthcare Coverage (UHC)'s benefit package in Thailand.

Incremental Cost-Effectiveness Ratio (ICER)

Ultimately, to compare which treatment program is more worth the cost, incremental cost-effectiveness ratio (ICER) is utilized to compare which treatment program is more worthy of the cost. The formula for computation is as followed:

$$\text{ICER} = \frac{(Cost\ A - Cost\ B)}{(Effect\ A - Effect\ B)}$$

For instance, if treatment A costs $3,000 and treatment B costs $2,000. The treatment A leads to additional 10.0 QALYs, while the treatment B leads to additional 9.5 QALYs. The ICER would be ($3,000 - $2,000)/ (10.0 QALYs - 9.5 QALYs) = $2,000/QALY. This implies that the healthcare payer has to pay $2,000 more for the treatment A to obtain an additional QALY gained. Decision-makers may or may not opt for the treatment A, depending on their willingness to pay. If their willingness to pay exceeds the ICER, then the treatment A might be an optimal option. The current Thai government's willingness to pay per QALY is 160,000 Baht (Isaranuwatchai et al., 2020).

CUA on CKD Interventions in Other Countries

There is not much evidence of CUA on CKD interventions in other countries. Saldarriaga et al. (2021) conducted a CUA study in Lima, Peru, to evaluate the Renal Health Program (RHP). This program was aimed to delay progression to dialysis and death in CKD patients (Bravo-Zuniga et al., 2020). The researchers found that the intervention program was more effective than the conventional care with the RHP resulting in 0.04 additional QALYs per person. The ICER was $21,660 USD per QALY gained. The RHP was favored by the cost and QALYs in 996 out of 1000 evaluation scenarios (Saldarriaga et al., 2021).

Similarly, in the US, a research team measured economic values between usual care and multidisciplinary care (MDC) in stages 3 and 4 CKD patients. The researchers found that MDC was considerably more expensive in younger patients (age 45-64 years old) and led to greater improvement in health. The CUA of the MDC was 0.23 QALYs per person over usual care (Lin et al., 2018).

Conceptual Framework

Based on the objectives of this study, a conceptual framework is presented in Figure 1 below. Focusing on cost-utility analysis, we compare the intervention to the conventional care. We measure both the cost and outcome of each in units of Thai Baht and QALY, respectively.

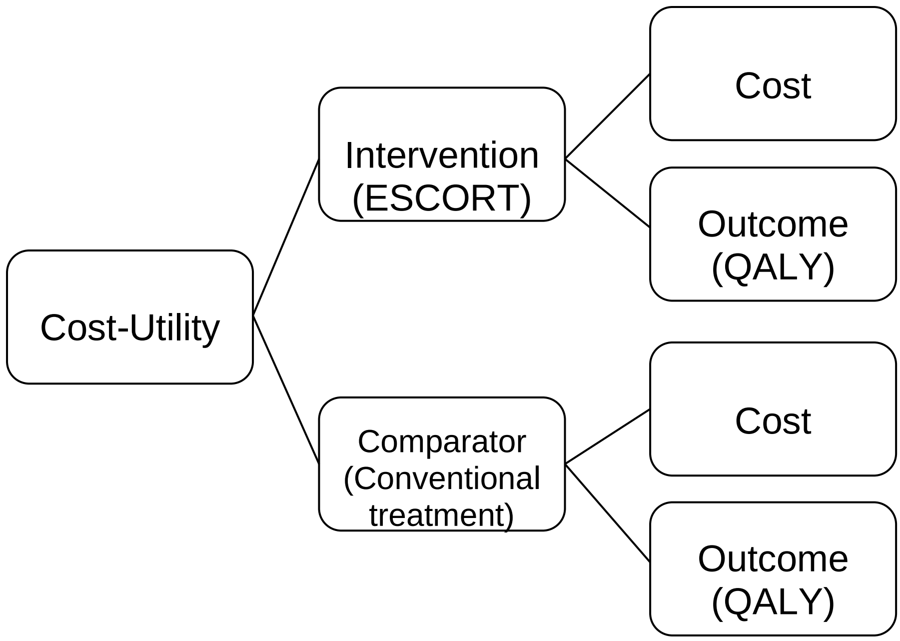


Figure 1. Conceptual framework for cost-utility analysis evaluation of CKD intervention.

Methodology

Intervention

The MDCT

The MDCT in the ESCORT-1 study consisted of two general practitioners, two chronic care nurses, a pharmacist, a nutritionist, a physical therapist and village-based community care network (CCN) teams. Each of the CCN team consisted of one subdistrict healthcare officer, 3-5 village health volunteers, and selected family members of the patients (Jiamjariyapon et al., 2017).

The MDCT in the ESCORT-2 study is made up of general practitioners, a CKD nurse manager, a nutritionist, a pharmacist, a physical therapist, and the CCN team – community nurses (Thanachayanont et al., 2021).

The Integrated CKD Care Program

Besides having usual routine clinical care at the hospital as the patients from the control group, the CKD patients in the intervention group meet with the MDCT. In the ESCORT-1 study, the MDCT facilitated medical care and education to the patients. The patients would meet the team every three months for two years. In addition to the ESCORT-1 elements, the ESCORT-2 study's integrated care program was adjusted to be more suitable for routine clinical care at the community level. In this study, the patients would see the MDCT every three months for three years. Further details are available in the published papers (Jiamjariyapon et al., 2017; Thanachayanont et al., 2021).

Setting

Both ESCORT-1 and ESCORT-2 studies were conducted in districts of Kamphaeng Phet province, Thailand. Two and five districts were selected in the ESCORT-1 and ESCORT-2 studies, respectively. Although these are purposive samples, the samples from the ESCORT-1 and ESCORT-2 studies should be representative for a majority of the general population living in Thailand.

Target Population

The study will utilize the data from the previous studies, ESCORT-1 and ESCORT-2, by Jiamjariyapon et al. (2017) and Thanachayanont et al. (2021), respectively. In the ESCORT-1 study, four hundred and forty-two patients with following characteristics participated throughout the study:

1. With CKD stages 3 to 4
2. Aged between 18 - 70
3. Had diabetes and/or hypertension
4. Had none of the following conditions:
    a. unstable/advanced cardiovascular diseases
    b. obstructive uropathy
    c. HIV infection
    d. pregnancy
    e. body mass index (BMI) less than 18 or more than 40 kg/m^2
    f. untreated malignancy
    g. urine protein-creatinine ratio exceeded 3.5 g/g creatinine or active urinary sediments

In the end, there were 208 patients in the conventional treatment (control) group and 234 patients in the intervention group (Jiamjariyapon et al., 2017).

In the ESCORT-2, eight hundred and thirteen patients completed the study. These participants were:

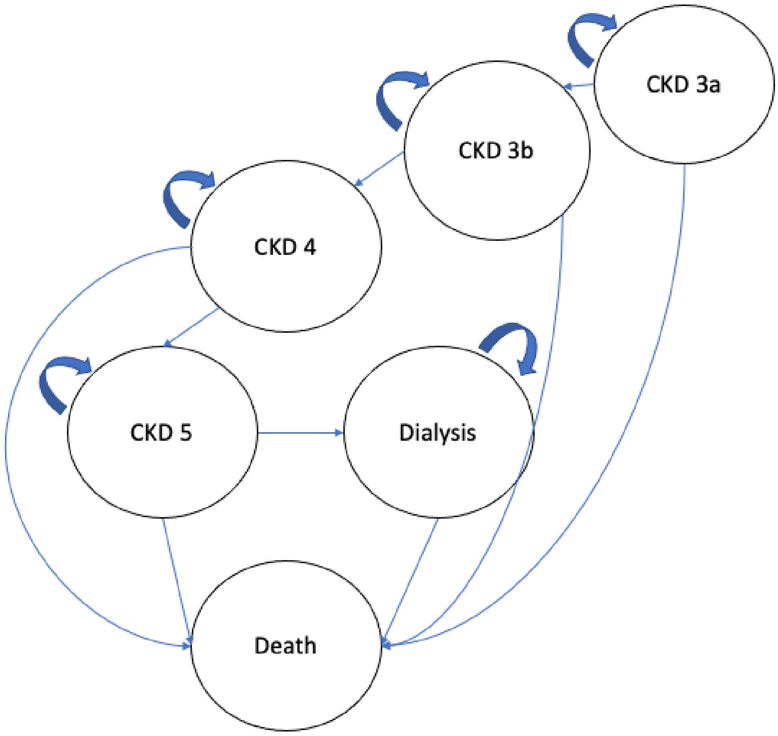
1. With CKD stages 3 to 4
2. Aged between 18 - 70
3. Had none of the following conditions:
    a. obstructive uropathy
    b. autosomal dominant polycystic kidney disease
    c. microscopic haematuria or proteinuria more than 3.5 g per day
    d. BMI less than 18 or more than 40 kg/m^2
    e. single kidney
    f. HIV infection
    g. malignancy
    h. connective tissue diseases
    i. impaired communication ability

Note that all patients were in the intervention condition in this study (Thanachayanont et al., 2021)

Modelling Approach

The new Markov model of CDK progression is introduced. In this model, stages 3a, 3b, and 4 of CKD are possible to progress to the next stage – 3b, 4, and 5, respectively. In stage 5, patients may or may not have access to dialysis, however. There are also possibilities that the CKD patients would stay on the same stage the entire time of the study or progress to death. Each arrow has different transition probability rates.

Figure 2. The proposed Markov model for CKD from stage 3 to death.



Cost Assessment

For the direct medical care costs, the cost data obtained from ESCORT-1 study will be used with adjustment for inflation rate. Direct non-medical care costs, i.e. traveling costs, will be calculated using health service utilization data from ESCORT-1 study and the applicable unit cost of traveling from HITAP's costing menu. Indirect cost, i.g. the cost of absenteeism from using health services, will be calculated based on health service utilization data from ESCORT-1 study plus average daily income of the Thai population from the National Statistical Office.

Healthcare costs are estimated in Thai Baht, adjusting inflation rate to 2023 value. Adjusting costs from the past to the current year is adjusted by the consumer price index (consumer price index, CPI) to determine the monetary value in the year analyzed (2023) As shown in the formula:

$$\text{Value at the current year} = \frac{CPI_{2023}}{CPI_t} \times Cost_t$$

Health Consequences

QALY can be calculated based on a formula as follows: QALY = year of life × utility. Year of life will be derived from the Markov model. Utility weight will be derived from the ESCORT-2 study in which all samples were interviewed using a standard utility measure namely EQ-5D. All samples were interviewed at the baseline and annually for three years. The local score of EQ5D will be based on local study to reflect the Thai population's value on different relevant health states (Pattanaphesaj, J et al 2018).

Discounting

This is because the time frame for the analysis is longer than one year. Therefore, the values of costs and results achieved at different periods will be adjusted to present values. Future costs and health outcomes will be discounted at a rate of 3% per annum considering the guidelines for health technology assessment in Thailand using the following formula.

Value at the present year = $\frac{Future\ value}{(1 + discounting\ rate)^t}$,where t is the passing year

Analysis

The model will report standard cost-effectiveness outcomes: costs, dialysis free life-year, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratio (ICER). Based on the Thai guideline (Chaikledkaew & Kittrongsiri, 2014), the ICER threshold of 160,000 Bath per QALY will be used.

$$ICER = \frac{(total\ costs\ of\ MDCT - total\ costs\ of\ the\ conventional\ treatment)}{(QALY\ gained\ from\ MDCT - QALY\ gained\ from\ the\ conventional\ treatment)}$$

A deterministic sensitivity analysis (DSA) will also be conducted to understand which parameters have the largest impact on the model results. The most influential parameters will be displayed in the form of a tornado diagram and ranked in order of their influence. In addition, a probabilistic sensitivity analysis (PSA) will be conducted using a second order Monte Carlo simulation to assess the probability of MDCT being cost-effective compared to standard care at a given willingness-to-pay (WTP) threshold. The probability distributions for each parameter in the PSA will be defined as follows: 1) beta-distribution will be assigned where parameter values range from zero to one, such as transition probabilities and utility parameters; 2) gamma-distribution will be specified when parameter values are above zero and positively skewed, such as for cost variables; and 3) a log-normal distribution will be used for odds ratios or relative risks derived from meta-analysis. The PSA will simulate for 1,000 iterations to yield a range of plausible values for costs, QALYs, and ICERs. The results will be depicted in graphs where the probability of MDCT being cost-effective against standard care are plotted. If deemed of interest, two-way sensitivity analyses could be conducted for parameters of interest where variables are expected to be correlated. Similarly, a cost-effectiveness acceptability curve (CEAC), where the WTP is varied over a range of values, could be produced and depicted in graphical format, if deemed of relevance for this analysis.

Study Parameters

Table 2 below displays study parameters that will be used in the Markov model. Each parameter was retrieved from ESCORT-1, ESCORT-2, and Grover et al. (2019).

Table 2. Study parameters

Parameter	Transition Probability	Source
CKD 3a to CKD 3a		ESCORT1 and ESCORT2
CKD 3a to CKD 3b		ESCORT1 and ESCORT2
CKD 3a to death		Thai Burden of Disease study
CKD 3b to CKD 3b		ESCORT1 and ESCORT2
CKD 3b to CKD 4		ESCORT1 and ESCORT2
CKD 3b to death		Thai Burden of Disease study
CKD 4 to CKD 4		ESCORT1 and ESCORT2
CKD 4 to CKD 5		ESCORT1 and ESCORT2
CKD 4 to death		Thai Burden of Disease study
CKD 5 to CKD 5		ESCORT1 and ESCORT2
CKD 5 to dialysis		Literature
CKD 5 to death		Thai Burden of Disease study
Dialysis to death		Literature

Expected Outcomes

The results of this study can be used to inform kidney treatment policy including clinical practice guidelines for chronic kidney disease treatment. The study results will also be published in an international journal in order to demonstrate the value for money of MDCT in an upper middle-income country which may be relevant to other countries with limited capacity and evidence.

Study Timeframe

Task	2023

	April	May	Jun	Jul	Aug	Sep
Planning of research - Literature search						
Building a model						
Ethics review - Study protocol - Ethics committee review and approval						
Data analysis						
Research dissemination - Manuscript writing - Appraisal of results - Final revisions - Conference, presentation						

Budget

รายการ	รายละเอียด	งบประมาณที่ใช้ (บาท)
1. หมวดเงินเดือน ค่าจ้าง ค่าตอบแทน		**108,000**
1.1 หัวหน้าโครงการ		
1.1.1 หัวหน้าโครงการ (นักวิจัยหลัก)	-	-
1.2 ค่าตอบแทนผู้ร่วมวิจัย		
1.2.1 ผู้ร่วมวิจัย	30,000 บาท * FTE 0.6 * 6 เดือน	108,000
2. หมวดค่าบริหารจัดการ		**15,000**
2.1 ค่าโทรศัพท์	500 บาท * 6 เดือน	3,000
2.2 ค่าอินเทอร์เน็ต	500 บาท * 6 เดือน	3,000
2.3 ค่ารับส่งเอกสาร ติดต่อประสานงาน ค่าไปรษณีย์	500 บาท * 6 เดือน	3,000
2.4 ค่าถ่ายเอกสาร	500 บาท * 6 เดือน	3,000
2.5 ค่าวัสดุสำนักงาน	500 บาท * 6 เดือน	3,000
3. หมวดค่าดำเนินงานของโครงการ		**205,500**
3.1 ค่าจัดประชุมผู้เชี่ยวชาญ/ผู้มีส่วนได้ส่วนเสีย - ค่าตอบแทนผู้เข้าร่วมประชุม - ค่าอาหาร ค่าอาหารว่างและเครื่องดื่ม	 900 บาท * 2 ครั้ง = 18,000 บาท 350 บาท * 2 ครั้ง = 7,000 บาท	25,000
3.2 ค่าจัดประชุมทีมวิจัย - ค่าอาหาร ค่าอาหารว่างและเครื่องดื่ม	 350 บาท * 5 คน * 6 ครั้ง	10,500

3.3 ค่าธรรมเนียมการขออนุมัติจริยธรรมการวิจัยในมนุษย์	10,000 บาท * 1 ครั้ง	10,000
3.4 ค่าพิสูจน์อักษร จัดทำรายงานฉบับสมบูรณ์ หรือสื่อประชาสัมพันธ์	25,000 บาท * 1 ครั้ง	25,000
3.5 ค่าตีพิมพ์วารสารระดับนานาชาติ	90,000 บาท * 1 ครั้ง	90,000
3.6 ค่าจ้างตรวจสอบความถูกต้องของข้อมูล จัดการข้อมูล วิเคราะห์ข้อมูล	45,000 บาท * 1 ครั้ง	45,000
ค่าธรรมเนียมอุดหนุนหน่วยงานต้นสังกัด		32,850
รวมงบประมาณทั้งสิ้น		**361,350**

Research Team

Name		Position	Affiliation	Contact	Responsibility		FTE
					Role	Proportion	
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