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Economic Evaluation of an Integrated Care Program Compared to Conventional Care for Patients With Chronic Kidney Disease in Rural Communities of Thailand

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Introduction: An integrated care program for chronic kidney disease (CKD) in Thailand has shown its effectiveness in delaying the decline in kidney function, as evidenced by the Effectiveness of Integrated Care on Delaying Progression of Stages 3 to 4 CKD in Rural Communities of Thailand (ESCORT-1) randomized control trial and the ESCORT-2 prospective cohort study. Designed for sustainability within the primary healthcare system, the program optimizes the use of the existing workforce by fostering collaboration among local multidisciplinary care teams (MDCTs) and community care networks (CCNs).

Methods: A Markov model with a lifetime horizon was used to conduct a cost-utility analysis from a societal perspective. Individual participant level data from ESCORT studies, national registries, and relevant literature were used to estimate model parameters. A budget impact analysis from the payer's perspective was also assessed over a 5-year period.

Results: The integrated care program yielded a dominant result with 1.84 quality-adjusted life years (QALYs) gained with "less" lifetime cost, resulting in a negative incremental cost-effectiveness ratio (ICER). Probabilistic analysis showed that the intervention being cost-effective almost 100% of the time at the local willingness-to-pay threshold. The intervention maximized cost-effectiveness when delivered as early as possible, both in terms of age and stage. The budget impact analysis estimated that the introduction of the intervention could save about 7% of the Thai government's total health expenditure or 205 billion Thai-Baht ($5.9 billion) over 5 years with cost savings beginning from the third year onwards.

Conclusion: The integrated care program for CKD offers potential benefits and cost savings for patients, caregivers, and payers. Future efforts should focus on the screening and implementation processes across various regions and healthcare settings.

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CKD is a significant public health issue and a leading cause of death worldwide[1,2] with over 850 million patients globally in 2017 and numbers continuously rising.[3] Kidney replacement therapy (KRT) including kidney transplantation (KT), hemodialysis (HD), and peritoneal dialysis (PD) are life-saving treatments when patients with CKD progress to end-stage kidney failure (ESKF). Treatments, however, are costly and highly resource-consuming, with limited access in low-and middle-income countries.[4,5] In Thailand, CKD prevalence among adults runs as

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high as 17.5%.[6] The prevalence of patients with ESKF receiving KRT has risen from 100,970 patients in 2016 to 170,774 patients in 2020.[7] With limited access and capacity for KT,[8] the vast majority of patients in Thailand receive either HD or PD.[7]

Several strategies can mitigate the progression of CKD to ESKF by combining pharmacological and non-pharmacological management.[9] To effectively deliver these strategies, multidisciplinary care has demonstrated its efficacy in delaying CKD progression[10,11] as well as showing cost-effectiveness.[12,13] To date, most of the studies have been conducted in high-income countries with care teams including advanced practitioners, such as nephrologists and dieticians that may not be applicable in resource-limited settings.

An integrated care program for patients living with CKD was introduced and tested by a community-based cluster randomized controlled trial entitled the ESCORT-1 study[14,15] The program is delivered through existing resources in rural areas. It aims to promote sustainability and relevance within the primary healthcare system by collaborating with MDCT and CCN teams. Results of ESCORT-1 showed that the intervention could reduce the rate of estimated glomerular filtration rate (eGFR) declination over a 2-year follow-up period compared with conventional care.[15] The effectiveness of the program was also demonstrated in the ESCORT-2 study, a larger-scale, 3-year follow-up prospective cohort study that modified the program to be more compatible with routine clinical care.[16]

Despite its clinical benefits, national implementation of such an integrated care program requires robust evidence of its cost-effectiveness and long-term affordability. This study evaluated the cost-effectiveness of the integrated care program for stage 3 to 4 CKD, using data from the ESCORT studies compared with conventional care. It considered costs and outcomes over a lifetime horizon from a societal perspective and assesses the budget impact from the payer's perspective. The findings aimed to provide information needed for decisions on policy inclusion of the program in Thailand's universal coverage scheme benefits package. Results may also assist other low-and middle-income countries in developing similar evidence for integrated care programs.

METHODS

Study Design and Oversights

This study used a cost-utility analysis following Thailand's Health Technology Assessment guidelines.[17] We used patient-level data from ESCORT-1 (ClinicalTrials.gov number, NCT01978951),[15] a community-based cluster randomized controlled trial conducted between 2011 and 2013 comparing an integrated care program to conventional care, and ESCORT-2 (Clinicaltrials.in.th number, TCTR20160614001), the subsequent prospective cohort study conducted between 2016 and 2019,[16] to determine the effectiveness of the intervention in delaying CKD progression. Both studies were approved by the Institutional Review Board of the Ministry of Public Health of Thailand (approval number 45/2011 (ESCORT-1), 49/2015 (ESCORT-2)) and conducted in accordance with good clinical practice and the Declaration of Helsinki. The design of the present economic analysis was discussed by an expert panel and approved by the research committee of the Bhumirajanagarindra Kidney Institute. This study was reported following the Consolidated Health Economic Evaluation Reporting Standards 2022.[18]

Study Population and Settings

The ESCORT-1 and ESCORT-2 studies, targeting adults aged between 18 and 70 years with CKD stages 3a to 4, were conducted in rural areas of Kamphaeng Phet province, 400-km north of Bangkok, Thailand. This province consists of 12 districts, each with a population of 25,000 to 60,000,[19] where 70% population live in rural areas. Each district features 1 district hospital for primary healthcare and 8 to 15 subdistrict health centers, staffed by a public health officer, a community nurse, and a dental assistant. Additionally, each 10 to 15 households are supported by village health volunteers, lay villagers who volunteer to assist in public health activities at the village level.

Intervention and Comparator

The integrated care program was a collaboration between an MDCT at a district hospital and a CCN team at each subdistrict. The MDCT was a group of health care personnel available at each district hospital consisting of 1 to 2 general practitioners, a CKD nurse manager, 1 to 2 pharmacists, a nutritionist, and a physical therapist. Key education activities to be provided to patients by MDCT by live demonstration, included basic knowledges and treatment of CKD, optimal diets for patients living with CKD (appropriate protein intake, salt restriction, and diets for diabetes), adherence to prescribed medications, proper daily exercise, and the avoidance of over-the-counter painkillers, nephrotoxic and herbal medicines. Home visits were completed by the CCN teams, comprised of a community nurse from the subdistrict health center and village health volunteers from each village. During the home visit, the CNN team collected information on a 7-day diet recall, measured blood pressure, encouraged proper exercise and compliance with medications, and provided advice to patients in

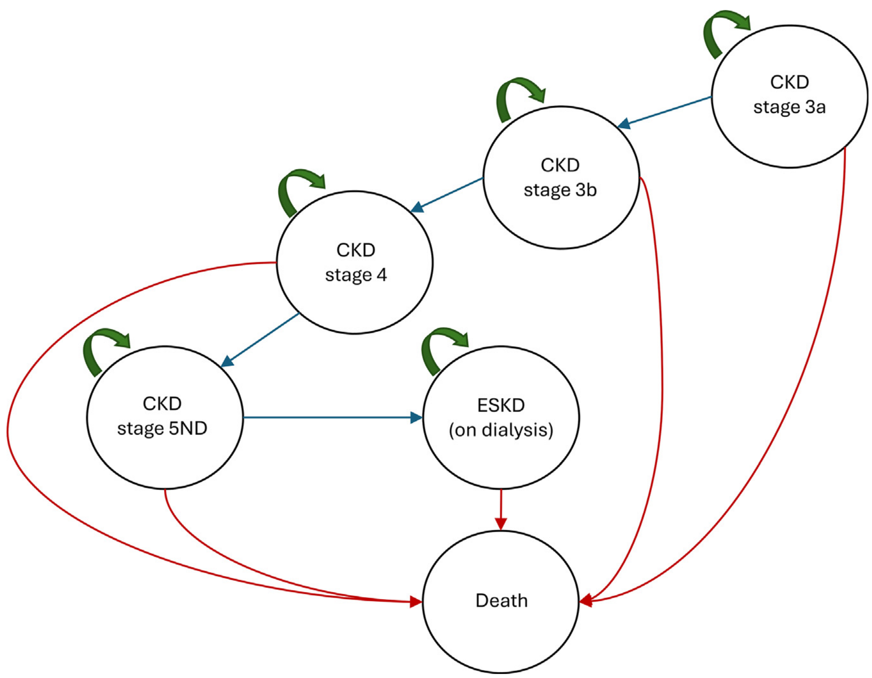

Figure 1. Schematic diagram of the Markov model: solid line ovals represent the different mutually exclusive health states a patient may experience including stages 3a, 3b, 4, and 5 of CKD (as defined by Kidney Disease: Improving Global Outcomes), dialysis, and death. Arrows indicate how patients can transition between the different health states (green: remaining in the same stage, blue: progress to the next stage, red: death).

avoiding the consumption of tobacco, herbal medicine, and other substances. Health personnel involved in both MDCT and CCN teams were trained on CKD care and treatments according to the 2002 National Kidney Foundation- Kidney Disease Outcomes Quality Initiative guidelines.[20] And the newer 2012 Kidney Disease: Improving Global Outcomes CKD guidelines[21] for the ESCORT-2 study. For ESCORT-1, participants in the control arm received conventional care at an outpatient clinic of the district hospital by general practitioners and chronic care nurses every 3 months. The comparison between integrated care program and conventional care is described in Supplementary Table S1. Patients in both groups received medications listed in the national list for essential medication (Supplementary Table S2). Details of the intervention were extensively described in Supplementary Tables S1 and S2 and previously published articles.[14-16]

Modeling Approach and Assumptions

A decision-analytic Markov model and Monte-Carlo simulation were applied to quantify and compare the lifetime costs and QALYs outcomes of the intervention and control groups from a societal perspective. The model structure is illustrated in Figure 1. Individuals may progress through each mutually exclusive health state: CKD stage 3a (eGFR 45–59 ml/min per 1.73 m^2), stage 3b (eGFR 30–44 ml/min per 1.73 m^2), stage 4 (eGFR 15–29 ml/min per 1.73 m^2), and stage 5: nondialysis (eGFR $<$ 15 ml/min per 1.73 m^2 without indication for KRT), dialysis (covering both HD and PD), and death. Stages of CKD were determined using the creatinine-based eGFR, calculated by the 2009 CKD-EPI creatinine equation.[22] Given that the transplantation rate in Thailand is under 1% of the total ESKF prevalence reported by the national registries in 2020,[7,8] KT was excluded from the model. It was assumed that there was no regression of health states or progression by $>$1 subsequent health state in each cycle, and events occurred only at the end of each cycle. The cycle length was 1 year. The Monte-Carlo simulations were performed over 99 cycles to calculate the ICER for the integrated care program relative to conventional care alone. Using a willingness-to-pay threshold of 160,000 THB ($\sim$4600 US dollars [USDs]) per QALY, as per the recommendation of the Thai Health Technology Assessment guidelines,[17] net monetary benefits (NMB) for the integrated care program and conventional care were calculated by multiplying the willingness-to-pay threshold by the total effectiveness in QALYs, and then subtracting total costs (Supplementary Appendix S1). QALY gains for the control and intervention groups were calculated by multiplying the total projected discounted life-years, as derived by the Monte-Carlo simulation, by the relevant health state utility weight. Future costs and QALY outcomes were both discounted at a rate of 3%

as recommended by the Thai Health Technology Assessment guidelines.[17] The Markov model was developed using Microsoft Excel 365 (Microsoft Corp, Redmond, WA, 2023).

CKD Progression and Dialysis Initiation

Predicted estimates of the transitional probabilities relating to CKD stage progression were derived from the individual participants' eGFR data from ESCORT-1 and ESCORT-2.[15,16] Linear mixed effect regression models were fitted using STATA Standard Edition version 18.0 (Stata Corp, 2023, College Station, TX) to model the CKD progression in the intervention and the control group using data from the ESCORT studies. To validate the model, the annual rate of eGFR decline was compared with the original ESCORT data[15,16] and other studies.[23,24] The details of the approach in modeling eGFR are outlined in the Supplementary Appendix S2.

The ESCORT-1 and ESCORT-2 studies did not contain information relating to the initiation of dialysis or case fatality of CKD. Results from an administrative health database report showed that patients concluding the previous year in CKD stage 5 had a 50% probability of initiating dialysis.[25] Of those who did not undergo dialysis, 37.5% will die,[26] and therefore 12.5% will continue to live with nondialysis CKD stage 5. When starting dialysis, we assumed that 50% of patients receive PD and 50% of patients receive HD, as HD and PD can be reimbursed under the Thailand universal coverage scheme as a first-line treatment.[27]

Survival Outcomes

In our primary analysis, we assumed baseline general mortality for patients with stage 3a to 4 CKD using data from the Thai Life Table 2014.[28] For CKD stage 5 nondialysis, we used an annual case fatality rate of 37.5% as previously described.[26] The survival rates of dialysis patients were derived from a previous study[29] using an age-adjusted Weibull survival model fitting data from national registry, the Thailand Renal Replacement Therapy registry,[7] consisting of 6272 patients records who underwent dialysis from 1997 to 2003. The summary of model parameters for CKD progression and survival are listed in Table 1.

Costs

The direct and indirect medical costs for predialysis CKD care in the intervention and control group were provided by the ESCORT-1 investigators.[15] Direct medical cost comprised of labor cost for personnel in both groups, cost of ambulatory care including medications, laboratory test, educational materials, and the cost of hospitalizations. Hospital overhead costs were obtained as the indirect medical cost. Nonmedical costs were collected directly from the ESCORT-1 participants by Srisubat *et al*.[30] who sampled 30% of participants for interview to gather the information. The direct nonmedical costs included transportation expenses for patients and up to 3 caregivers, along with additional expenditures on food. Indirect nonmedical costs were defined as losses incurred from time off or reduced working capacity owing to illness, affecting both patients and up to 3 caregivers. The dialysis (HD and PD) costs were sourced from the study by Teerawattananon *et al*.,[29] which assessed the expenses across different dialysis modalities in Thailand. This evaluation covered the costs of initiation, ongoing maintenance, treatment for complications, and the use of erythropoietin-stimulating agents.

Costs were calculated in Thai Baht (THB). Figures in USD were approximated for reader understanding (1 USD = 35 THB). As the costs for predialysis CKD care were measured in 2017 and the costs of dialysis were measured in 2014, all costs were inflation adjusted using the consumer price index in the relevant year reported by the Ministry of Commerce of Thailand[31] to the current consumer price index for the year 2024. The cost parameters are shown in Table 1.

Utility Outcomes

For each stage of pre-dialysis CKD, participant-level data were obtained from the ESCORT-2 study using the Thai Version of the EQ-5D-5L questionnaire. For patients receiving dialysis, we selected the same parameter as in the previous study[29] which was acquired from a scoping review and random-effects meta-analysis of 4 studies[32-35] with no adjustments for disutility when experiencing short-term complications.

Uncertainty Analyses

Scenario analysis determined how sensitive the ICER and NMBs of the intervention and control groups were to both the age when treatment was initiated and the CKD stage of the patient. We used the increased all-cause mortality in CKD stage 3a to 4 by applying adjusted hazard ratios (HRs) from an individual participant data meta-analysis.[36] Two HRs for each CKD stage were used to represent the highest (upper bound) and lowest (lower bound) mortality for the highest and lowest urine albumin-to-creatinine ratio (Supplementary Appendix S3). A 1-way deterministic sensitivity analysis was performed to understand the implications of individual parameter uncertainty including the effectiveness of the intervention for delaying CKD progression, probability of dialysis initiation in CKD stage 5 nondialysis, case fatality rate of CKD stage 5 nondialysis, and the ratio of HD to PD when starting KRT. Probabilistic sensitivity analysis

Table 1. Summary of model parameters

Parameters	Mean	SE	Parameter distribution	Data sources
Annual probability of progression from CKD stage 3a to stage 3b	0.0769	0.0020	Beta	15,16
Annual probability of progression from CKD stage 3b to stage 4	0.1429	0.0035	Beta	15,16
Annual probability of progression from CKD stage 4 to stage 5	0.2500	0.0053	Beta	15,16
Annual probability of initiating dialysis in CKD stage 5	0.5000	0.0023	Beta	25
Annual probability of dying when in CKD stage 5 without dialysis	0.3750	0.0354	Beta	26
Annual rate of having HD complications	0.27	0.52	Gamma	29
Annual rate of having PD complications	0.33	0.57	Gamma	29
Relative risk (RR) of CKD progression when in the intervention group relative to the control				
RR for progression from CKD stage 3a to stage 3b	1.00	0.0681	Normal	15
RR for progression from CKD stage 3b to stage 4	0.44	0.0218	Normal	15
RR for progression from CKD stage 4 to stage 5	0.33	0.0513	Normal	15
Constant value in baseline hazard	(−) 11.1771	0.2439	Log normal	29
Age coefficient in baseline hazard	0.0347	0.0021	Log normal	29
Ancillary parameter, in (g)	0.0722	0.0247	Log normal	29
Utility parameters				
Utility for CKD stage 3a	0.9169	0.0037	Beta	16[a]
Utility for CKD stage 3b	0.9145	0.0035	Beta	16[a]
Utility for CKD stage 4	0.9085	0.0050	Beta	16[a]
Utility for CKD stage 5 (nondialysis)	0.8660	0.0234	Beta	16[a]
Utility for ESKF receiving PD	0.6800	0.1000	Beta	29
Utility for ESKF receiving HD	0.7200	0.0800	Beta	29
Costs parameters (annualized cost)[b]				
Cost of CKD stage 3–5 (nondialysis) care with integrated care program (2017 THB)				
Direct medical cost: labor costs	THB 1 561.12 (USD 44.60)	1 561.12[c]	Gamma	30
Direct medical cost: costs of medical materials (medications, laboratory tests, and educational materials)	THB 4 604.51 (USD 131.56)	4 604.51[c]	Gamma	30
Indirect medical costs: (hospital overhead cost)	THB 1 233.13 (USD 35.23)	1 233.13[c]	Gamma	30
Direct nonmedical costs: additional food expenses and transportation (for patient and up to three care givers)	THB 1 046.83 (USD 29.91)	156.13	Gamma	30
Indirect nonmedical cost (a result of opportunity loss caused by illness for patients and caregiver)	THB 419.17 (USD 11.98)	145.33	Gamma	30
Direct medical cost: labor costs	THB 740.37 (USD 21.15)	740.37[c]	Gamma	30
Direct medical cost: costs of medical materials (medications, laboratory tests, and educational materials)	THB 4 167.83 (USD 119.08)	4 167.83[c]	Gamma	30
Indirect medical costs: (hospital overhead cost)	THB 981.64 (USD 28.05)	981.64[c]	Gamma	30
Direct nonmedical costs: additional food expenses and transportation (for patient and up to three care givers)	THB 564.83 (USD 16.14)	41.90	Gamma	30
Indirect nonmedical cost (a result of opportunity loss caused by illness for patients and caregiver)	THB 126.25 (USD 3.61)	40.86	Gamma	30
Set-up costs of PD	THB 47 000.00 (USD 1 342.86)	15 000.00	Gamma	29
Annual maintenance cost of PD (include erythropoietin)	THB 356 000.00 (USD 10 171.43)	7 000.00	Gamma	29
Annual direct nonhealth care costs per household with PD	THB 5 000.00 (USD 142.86)	1 000.00	Gamma	29
Annual indirect nonhealth care costs per household with PD	THB 3 000.00 (USD 85.71)	600.00	Gamma	29
Monthly cost of PD complications	THB 32 000.00 (USD 914.29)	24 000.00	Gamma	29
Set-up costs of HD	THB 21 000.00 (USD 600.00)	7 000.00	Gamma	29
Annual maintenance costs of HD (include erythropoietin)	THB 380 000.00 (USD 1 085.71)	132 000.00	Gamma	29
Annual direct nonhealth care costs per household with HD	THB 33 000.00 (USD 942.86)	8 000.00	Gamma	29
Annual indirect nonhealth care costs per household with HD	THB 41 000.00 (USD 1171.43)	8 000.00	Gamma	29
Monthly cost of HD complications	THB 15 000.00 (USD 428.57)	15 000.00	Gamma	29

CKD, chronic kidney disease; ESKF, end-stage kidney failure; HD, hemodialysis; PD, peritoneal dialysis; THB, Thai Baht; USD, US dollars.
[a]Parameters were obtained from unpublished participant-level data in ESCORT-2 study by personal communication with the investigator, Methee Chanpitakkul.
[b]All costs were presented in THB according to the year of data collection and were adjusted for the current consumer price index (CPI) in the year 2024 (CPI 2024 = 107.22, 2017 = 97.93, 2014 = 82.00). Currency conversion to USD is provided to facilitate the reader's understanding (1 USD = 35 THB).
[c]Standard errors were not available from the reference source, so they are assumed equal to their respective mean value.

was conducted by second-order Monte-Carlo simulation at 1000 iterations. Cost-effectiveness acceptability curves were constructed by plotting the cost-effectiveness and willingness-to-pay using a threshold range of 0 to 200,000 THB per QALY.

Budget Impact Analysis

As recommended by Thailand's Health Technology Assessment guidelines,[17] financial impact and affordability of the intervention over 5 years were investigated from the payer's perspective, excluding nonmedical

Table 2. Results of deterministic cost utility analysis of providing integrative CKD care program compared to conventional care, using the societal perspective of the base case scenario with 42-year-old patients starting treatment at CKD stage 3a

Result	Conventional care	Integrated care
Total lifetime costs	THB 1,703,632 (USD 48,675)	THB 1,293,295 (USD 36,951)
Total life-yr	15.11	17.09
Total lifetime QALYs	13.25	15.23
Incremental costs[a]	(−) THB 410,337	
Incremental QALYs[a]	1.84	
Cost per QALY gained (ICER)[a]	Dominant (cost-saving) (−) THB 207,645	
Net monetary benefit (THB)	THB 416,252 (USD 32,651)	THB 1,142,772 (USD 11,893)

ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; THB, Thai Baht; USD, US dollars.
[a]Incremental measures represent measures relating to the use of the integrated care program relative to conventional care.

costs. The analysis followed identical assumptions to the cost-utility analysis previously conducted with half-cycle correction. The target population was the total Thai population (66,025,615 people reported by the Ministry of Interior at the end of 2023).[19] Prevalence of CKD was determined from the latest national survey report[6] and the national dialysis registry.[7] It was assumed that half of the number of patients diagnosed with stage 3 CKD were stage 3a and the other half stage 3b. The annual incidence rate was assumed to be 7800 patients based on the latest report from the Ministry of Public Health.[37]

RESULTS

Baseline Characteristics of Modeled Population

The mean age of participants was 62.4 ± 7.9 and 62.3 ± 6.4 years in ESCORT-1's control and intervention groups, respectively. The mean age of ESCORT-2's participants was 62.0 ± 6.0 years. Approximately 50% of the participants had diabetes and 90% had hypertension. Mean eGFRs were 41.8 ± 10.6, 41.2 ± 10.3, and 40.43 ± 10.6 ml/min per 1.73 m^2 in ESCORT-1's control group, intervention group, and ESCORT-2, respectively. The detailed baseline characteristics and time-averaged parameters during treatment of the study population can be found in Supplementary Tables S3 and S4, respectively.

Deterministic Cost-utility Base-case Analysis

The results of a cost-utility analysis using a societal perspective of the base case scenario when all patients enter the model with CKD stage 3a at the age of 42 years are shown in Table 2. Implementing the integrated care program yielded a dominant result with 1.84 QALYs gained with "less" total lifetime costs, resulting in a negative ICER of (−)207,645 THB/QALY gained. The findings indicated that using the integrated care program is a more cost-effective treatment compared with conventional care. Figure 2a illustrates total life years that patients receiving integrated care live longer than their counterparts. The duration spent in the dialysis stage is also shorter for the integrated care group, leading to reduced dialysis costs, which represents the majority of the expenses compared with the cost of predialysis CKD care, as shown in Figure 2b.

Scenario Analysis

Figure 3 shows the ICERs and NMBs for starting CKD treatment at stages 3a, 3b, or 4 across various ages. The ICER rises with age, but integrated care is consistently more cost-effective than standard care. Treatment

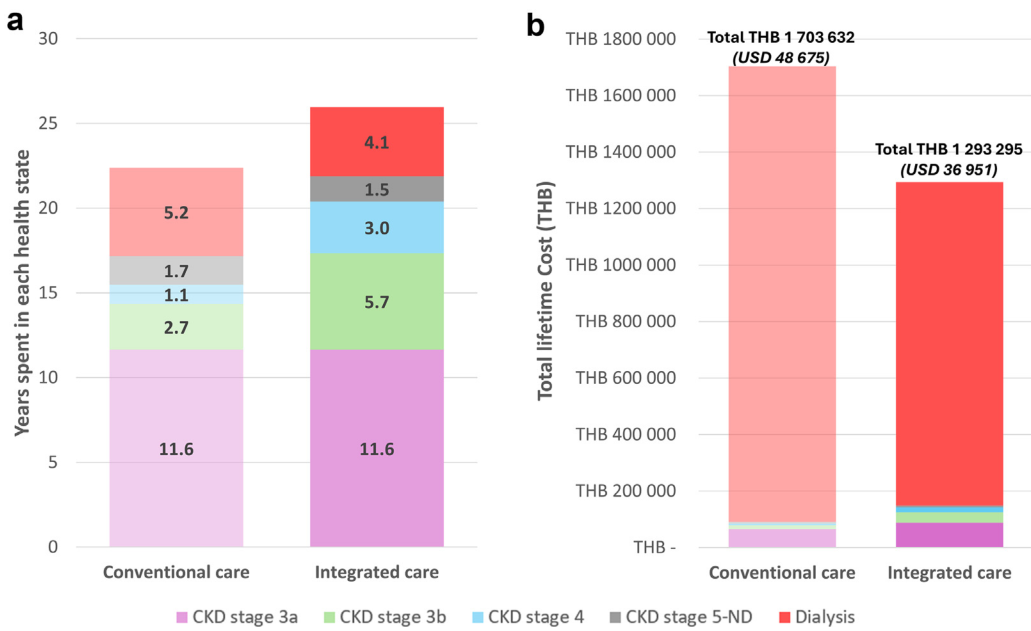

Figure 2. The total years spent in each health state (a) and total discounted costs spent during the time spent in each health state (b) for a single individual, predicted by the model through simulation.

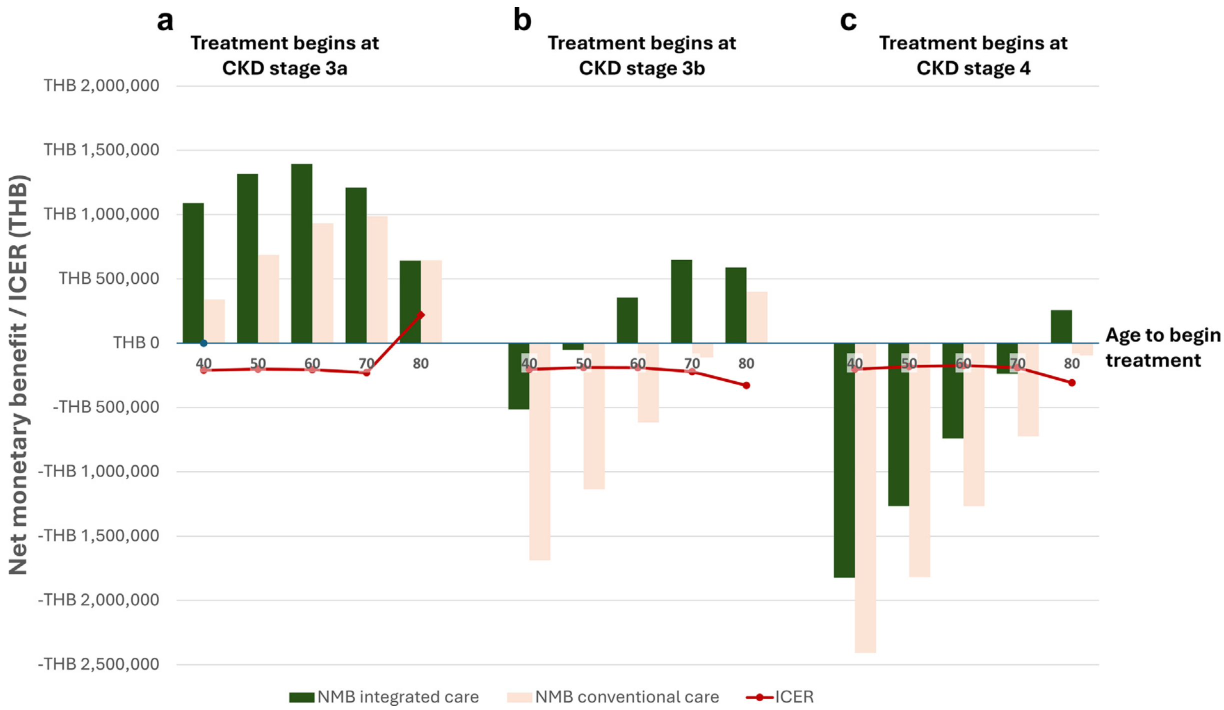

Figure 3. Scenario analysis when treatment begins in (a) CKD stage 3a, (b) stage 3b, and (c) stage 4; Left axis/Bar chart = Net monetary benefit, Right axis/Line = Incremental cost-effectiveness ratio.

initiation at stage 3a is generally more cost-effective than at stage 3b, except for 80-year-old patients at stage 3a, in whom NMBs are similar.

Uncertainty Analysis

The deterministic sensitivity analysis revealed the 5 most influential parameters to be the cost of medical materials to provide the integrated care program, annual maintenance cost for HD, ancillary parameters, and the constant of the Weibull survival model for patients on dialysis, and the cost of medical materials to provide conventional care. The results are shown as a tornado diagram in Supplementary Figure S1A and S1B in brief, the intervention is still cost saving when applying both upper and lower 95% confidence intervals of each parameters.

A more conservative analysis omitting the intervention's effect on the progression from CKD stage 4 to 5 still demonstrated dominance with an ICER of −265,900 THB per QALY (Figure 4 and Supplementary Table S5). A 1-way sensitivity analysis examined varying the effect on progressing from CKD stage 3b to 4 without the effect on CKD stage 4 to 5. Results showed that integrated care effectiveness could drop to 7% (with the highest relative risk of progression up to 0.92) and still outperform conventional care (Supplementary Figure S2)

Adjusting for the higher mortality rates linked to CKD stages 3 to 4 by incorporating stage-specific HRs alongside baseline mortality, integrated care remained more cost-effective than conventional care across the lower-bound and upper-bound HR variations (Figure 4). Further analysis altering the annual mortality probability, probability of dialysis initiation in CKD stage 5 nondialysis, and ratio of HD to PD when patients entered dialysis still showed integrated care's superiority (Supplementary Tables S6, S7, and S8, respectively).

A probabilistic sensitivity analysis, using 1000 Monte-Carlo simulations, depicted on a cost-effectiveness plane (Figure 5), revealed integrated care yielding higher QALYs at lower costs than conventional care, dominating ∼100% of the time <160,000 THB threshold. The average ICER stood at −196,844 THB per QALY (95% confidence interval: −202,504 to −192,463). The integrated care average NMB was 1,179,191 THB (33,691 USD), compared with conventional care NMB results of 474,781 THB (13,565 USD). Cost-acceptability curves indicated a >99.9% chance of integrated care being more cost effective than conventional care for thresholds up to 66,000 THB (1886 USD) per QALY, reaching 100% for thresholds ∼68,000 THB (1943 USD) per QALY or higher (Supplementary Figure S3).

Budget Impact Analysis

Considering Thailand's current CKD prevalence and an annual incidence of 7800 patients, the introduction of this intervention would lead to initial budget deficits in the first 2 years. However, from the third year onwards, significant cost savings are projected to offset initial losses, with an estimated total savings of

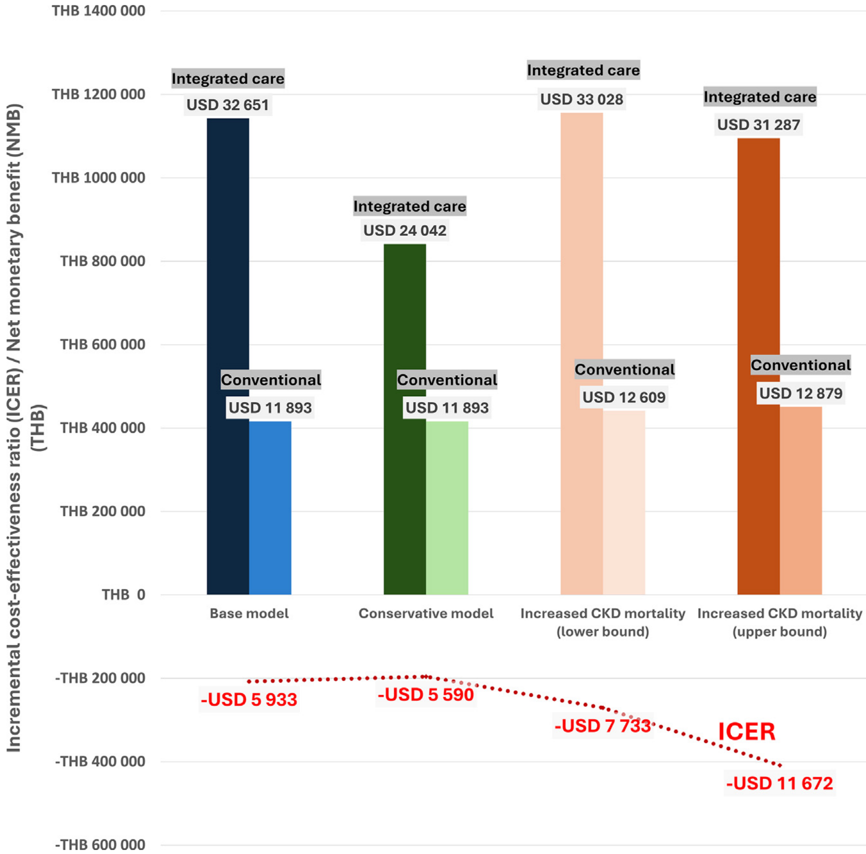

Figure 4. Sensitivity analysis for the conservative model (omitting the intervention's effect on CKD stage 4 onwards and applying increased CKD mortality on top of the baseline mortality).

∼205 billion THB (5.9 billion USD) over 5 years (Figure 6). These savings are anticipated to persist even when adjusting for specific HRs for each CKD stage alongside baseline mortality, excluding the impact of integrated care on the progression from CKD stage 4 to 5, and modifying the HD and PD ratio (Supplementary Table S9).

DISCUSSION

This cost-utility analysis from a societal perspective has demonstrated that the integrated care program for patients with stages 3 to 4 CKD could increase patient QALYs while saving costs compared with conventional care. Despite potential uncertainties, all scenario and

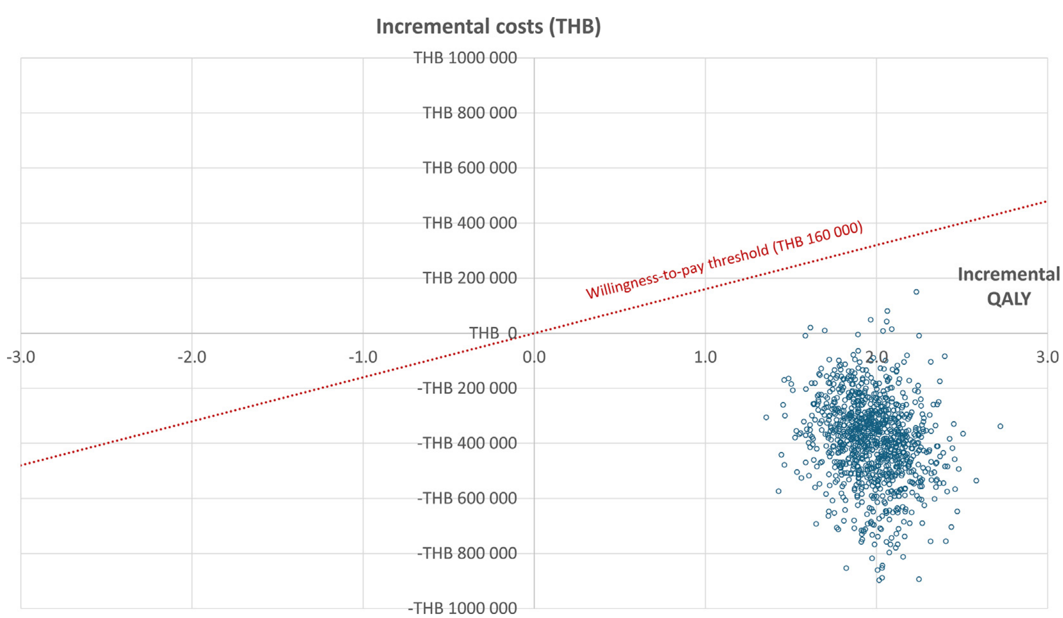

Figure 5. Results of the probabilistic sensitivity analysis simulation in a cost-effectiveness plane.

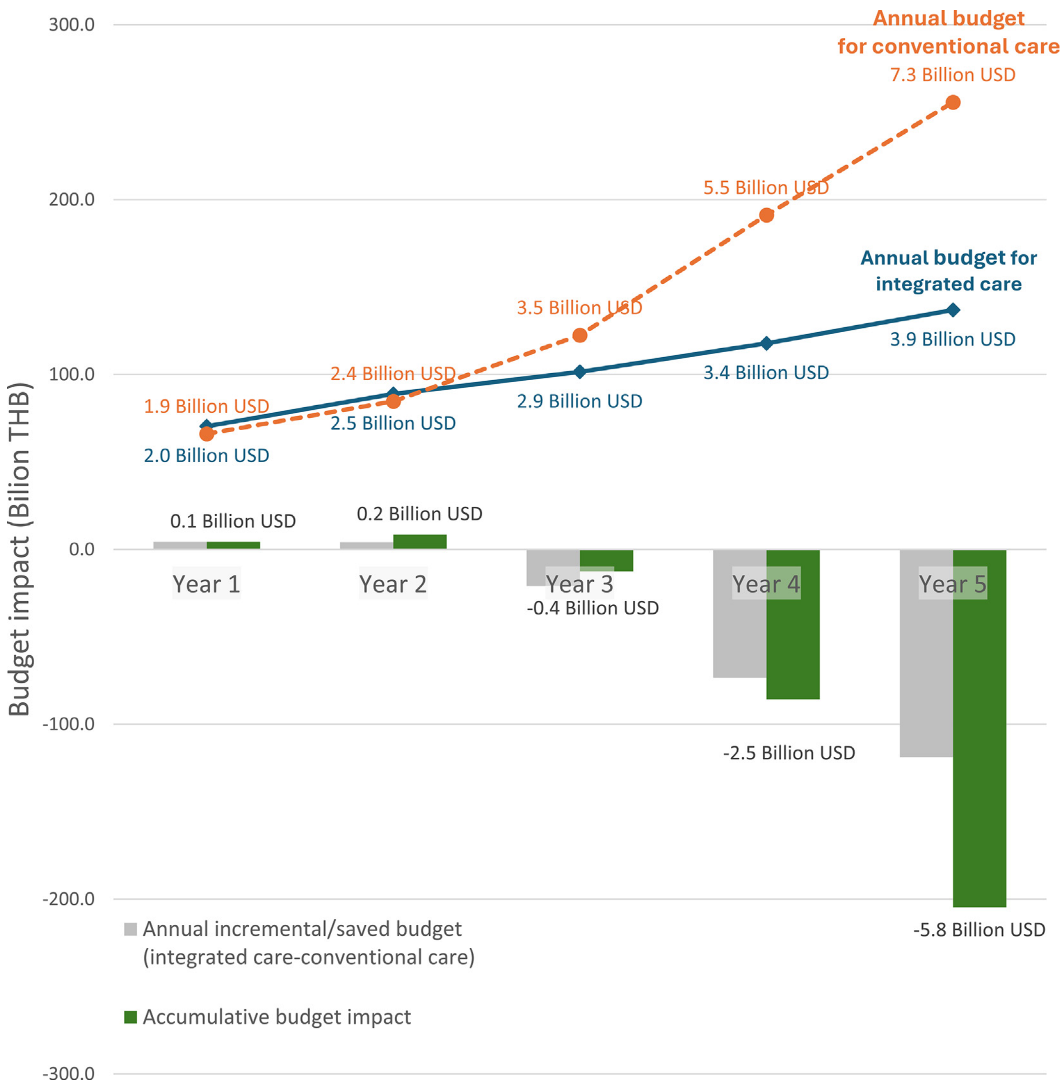

Figure 6. Budget impact analysis.

sensitivity analyses were consistent with this result. For the payer and health system, implementing the integrated care program could save significant budgetary funds from the third year onwards.

The increased life years gained, coupled with less time required for dialysis in the integrated care group, can be attributed to the intervention's effect of delaying the decline of kidney function. Individuals in this group may eventually die from other causes, including cancers, according to local general mortality data, before or shortly after the initiation of dialysis. As the cost offsets are primarily driven by patients' delayed progression to dialysis, the delayed time to dialysis initiation implies a delay in the costly maintenance of KRT, producing an overall monetary gain.

Patients with CKD usually progress to end-stage kidney disease in which KRT is needed to sustain their lives and well-being. KRT maintenance is usually a protracted course and very costly as compared to treatment of other chronic illnesses. It is commonly observed that financial constraints are the main barrier to achieve KRT maintenance in developing countries.[5,38,39] Delaying CKD progression by early recognition and effective treatment are commonly identified as an effective means to alleviate kidney disease burden.[40,41] Few countries, mainly developing countries, have shown that implementing integrated care at earlier stages of CKD could help delay the disease progression.[42]

The result of this study contrasts with the previous cost-effectiveness analysis by Srisubat *et al.*[30] because of a larger sample size, longer time horizon, consideration of QALY and costs when patients in the analytical models enter the dialysis stage and employing a decision-analytic Markov model rather than a decision tree.

Results from the scenario analysis also support utilizing the integrated care program at earlier stages of CKD including stages 3a or 3b, because the model demonstrated better cost-effectiveness at these CKD stages. One group that did not show cost effectiveness were elderly patients (age > 80 years) with early stage of CKD as this group of patients might likely die from other causes or might not be eligible for initiation of dialysis, due to multiple comorbidities or limited performance status, further reducing the overall costs of dialysis during a patient's lifetime.

Early implementation of the integrated care program in patients with CKD demonstrated potential cost savings of ∼205 billion THB (5.9 billion USD) over 5 years, or ∼41 billion THB (1.2 billion USD) annually. This annual monetary savings is roughly equivalent to about 7% of the Thai government's total health expenditure (2021) of 587 billion THB (16 billion USD).[43]

The integrated care program, investigated in the ESCORT study, was designed to promote applicability and sustainability in resource-limited settings by using the pre-existing local workforce to deliver the program.[14-16] In contrast to the previous studies conducted in resource-sufficient areas,[11,44] which used specialized practitioners such as nephrologists and dieticians, the MDCT in our program was run by primary health care provider including general practitioners, CKD nurse manager, pharmacists, and nutritionists, which are available in most district hospitals in Thailand.

Another key success factor of the integrated care program is the strong community health-care system in the rural area of Thailand, which has been developed over several decades[45,46] that features the presence of subdistrict health centers and village health volunteers. This model bridges the gap between patients and healthcare providers, fostering stronger patient engagement and compliance, potentially leading to more effective CKD progression control.[47] Village health volunteers, who are ordinary villagers volunteering in primary healthcare for their peers, initially worked without compensation. Now, they receive a monthly stipend and additional welfare benefits from the government, recognizing and sustaining their vital contribution to community healthcare.

This study has limitations. First, the effectiveness parameters of the intervention primarily relied on the ESCORT-1 study results. Given potential uncertainties, a 1-way sensitivity analysis was conducted to examine a range of values for the relative risk of progression from CKD stage 3a to 3b. The analysis found that the intervention remained cost effective, even with the estimated effect being less than half. The intervention remained dominant in the conservative model when omitting the effectiveness of the intervention from CKD stage 4 onwards. Secondly, the model did not include KT as an alternative health state. Despite this limitation, ESCORT studies are the most relevant data to be used in this setting. The model specifically did not consider KT due to its limited availability in Thailand, where KT rates are slowly increasing but still represent <1% compared with the prevalence of ESKF receiving dialysis in 2020,[7] with a small fraction of potentially eligible patients on the transplant waiting list.[8] Thirdly, novel medications such as sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1receptor agonists were not included in both the clinical effectiveness and cost parameters. Both ESCORT studies were conducted before sodium-glucose cotransporter-2 inhibitors became the standard of care. Despite their efficacy, their high costs make them financially challenging, though some studies suggest they could be cost saving in the long term.[48] Further analyses on budget impact of these new regimens are still warranted to ensure sustainability of the overall health system. Fourthly, the intervention was designed and tested for rural areas, and future research would need to test whether it will offer similar benefits at similar costs when offered in urban settings.

Further challenges lie in the practical implementation of the program across different countries, each with its distinct context and culture. Because patients with early CKD are mostly asymptomatic, active screening measures are essential for identifying patients who are at risk for early intervention.

In conclusion, the integrated care program presents promising benefits and cost-saving solutions for patients with CKD, caregivers, payers, and society. Further steps should explore the screening and implementation process in different areas and health system structures, as well as the development of a quality assurance system for the program.

DISCLOSURES

All the authors declared no competing interests.

Declaration of Generative AI in Scientific Writing

During the preparation of this work the authors used ChatGPT 4.0 in order to assist with drafting and refining the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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DATA AVAILABILITY STATEMENT

A Microsoft Excel Macro containing Markov model for the cost-utility analysis is publicly accessible at https://github.com/jeerathp/ESCORT_EE. Summary statistics from the ESCORT-1 and ESCORT-2 studies are published online (ESCORT-1; https://doi.org/10.1186/s12882-016-0414-4; ESCORT-2; https://doi.org/10.1111/nep.13849) and included in Supplementary Table S3. Access to the participant-level data from ESCORT-1 and ESCORT-2 is granted to researchers with approved proposals by the Bhumirajanagarindra Kidney Institute and respective principal investigators (Dr. Jiamjariyapon for ESCORT-1; Thanachayanont for ESCORT-2). Patient-level EuroQoL-5D-5L data, acquired through personal communication with Chanpitakkul and currently under publication process, are available upon justified request. Data from the Thailand Renal Replacement Therapy (TRT) registry, sourced from The Nephrology Society of Thailand, have summary statistics on their website (https://www.nephrothai.org/annual-report-thailand-renal-replacement-therapy-2007-2019-th/). For more information, contact the corresponding author at Jeerath.p@chula.ac.th.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 checklist.

Appendix S1. Calculation of cost-effectiveness parameters.

Appendix S2. Modeling eGFR and CKD progression.

Appendix S3. Adjusted hazard ratios for all-cause mortality in CKD stage 3a-4 for sensitivity analysis.

Figure S1A. Tornado diagram showing percentage change of ICER when applying upper and lower bound 95% CI.

Figure S1B. Tornado diagram showing ICER when applying upper and lower bound 95% CI.

Figure S2. One-way sensitivity analysis: ranges of values of the relative risk of progression from CKD stage 3b to 4 (when omitting relative risk of progression from CKD stage 4 to 5).

Figure S3. The cost-acceptability curves under a threshold range of 0 to 200,000 Thai baht per QALY gain.

Table S1. Intervention of the ESCORT study.

Table S2. Treatment target for patients in both groups in the ESCORT study.

Table S3. Summary of the baseline characteristics of the study population.

Table S4. Time-averaged parameters during the ESCORT-1 and ESCORT-2 study period.

Table S5. Deterministic sensitivity analysis based on omitting effectiveness on CKD stage 4 and applying CKD mortality add-on to general mortality.

Table S6. One-way deterministic sensitivity analysis altering the annual mortality probability in CKD stage 5 non-dialysis.

Table S7. One-way deterministic sensitivity analysis altering the annual probability of dialysis in CKD stage 5 non-dialysis.

Table S8. One-way deterministic sensitivity analysis altering HD:PD ratio.

Table S9. Sensitivity analysis for budget impact.

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