Received: 2 November 2020 | Revised: 29 December 2020 | Accepted: 4 January 2021

DOI: 10.1111/nep.13849

ORIGINAL ARTICLE

NEPHROLOGY WILEY

Effectiveness of integrated care on delaying chronic kidney disease progression in rural communities of Thailand (ESCORT-2) trials

Teerawat Thanachayanont[1] | Methee Chanpitakkul[1] | Jukkapong Hengtrakulvenit[2] | Podjanee Watcharakanon[3] | Watcharapong Wisansak[4] | Teerapong Tancharoensukjit[5] | Phosri Kaewsringam[6] | Vinai Leesmidt[6] | Krit Pongpirul[7] | Salyaveth Lekagul[1] | Kriang Tungsanga[1,7] | On behalf of the ESCORT-2 Research Team

[1]Bhumirajanagarindra Kidney Institute, Bangkok, Thailand

[2]Khlong Lan Hospital, Kamphaeng Phet, Thailand

[3]Phran Kratai Hospital, Kamphaeng Phet, Thailand

[4]Saithong Wattana Hospital, Kamphaeng Phet, Thailand

[5]Lan Krabue Hospital, Kamphaeng Phet, Thailand

[6]Khlong Khlung Hospital, Kamphaeng Phet, Thailand

[7]Department of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand

Correspondence
Teerawat Thanachayanont, Bhumirajanagarindra Kidney Institute, 8/99 Phayathai Road, Khwaeng Thung Phaya Thai, Khet Ratchathewi, Bangkok 10400, Thailand.
Email: tthanachayanont@gmail.com

Funding information
Bhumirajanagarindra kidney institute hospital

Abstract

Aim: We conducted a prospective cohort study to evaluate the effectiveness of an integrated care model on delaying chronic kidney disease (CKD) progression in routine clinical practice in rural primary care setting.

Methods: After enrolment, patients with stages 3 to 4 CKD patients from five district hospitals in a northern province of Thailand (400 km from Bangkok) received integrated care comprising hospital multidisciplinary care and home visits by community care teams. Clinical characteristics and biochemical data were collected at baseline and every 3-month interval thereafter for 36 months. The primary outcome was the rate of estimated glomerular filtration rate (eGFR) decline.

Results: Nine hundred and fourteen stage −3 and − 4 CKD patients were enrolled. The mean age of our cohort was 62 years. Diabetic kidney disease (DKD) was the main cause of CKD (53%) whereas hypertension was the most common co-morbidity (92%). The mean rate of eGFR decline was −0.92 mL/min/1.73 m^2/year. The rate of eGFR decline among patients with DKD was about three times faster than patients without DKD. Patients with higher blood pressure, metabolic acidosis, proteinuria or anaemia had a faster rate of eGFR decline.

Conclusion: This integrated care model at the community level was effective in delaying CKD progression in routine clinical practice situation.

KEYWORDS
chronic kidney disease, community care networks, healthcare delivery, hypertension, integrated health care systems

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blockade; BMI, body mass index; CCN, community care network; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HMDT, hospital multidisciplinary team; IC, integrated care; NSAID, non-steroidal anti-inflammatory drug; SDHC, subdistrict health centre; VHV, village health volunteer

Chronic kidney disease (CKD) is a growing health problem worldwide. Management of CKD should consist of multidisciplinary care (MDC) approach and patient's self-care.[1] It has been consistently demonstrated that MDC approach yields better results,[2,3] especially among low- and middle-income countries where health-care resources are limited.[4] The public health-care structure in Thailand has been well-established for decades.[5,6] In each province, there is one provincial hospital taking care of 300 000 - 1 000 000 general population.

In each district, there is one 30- to 90-bed district hospital providing primary and simple secondary care to 20 000 to 60 000 population residing in that district. The personnel there comprise 3 to 6 general practitioners and nurses, 1 to 2 pharmacists, one physical therapist, and one nutritionist or none. In each district, there are 5 to 10 sub-district health centres (SDHC). Each consists of 2 to 3 community nurses and 1 to 2 public health officers taking care of 3000-6000 villagers. In addition, there are village health volunteers (VHV) who collaborate with health personnel at SDHC and district hospitals to oversee the general health of the villagers, each VHV is responsible for 15 to 20 households. All across the country, there are about 1 million VHV.[7] Sub-district health personnel and VHV had been proven to be effective tools for community health service and disease control.[8,9]

The prevalence of CKD stages 1 to 5 (non-dialysis) among Thai adults is about 17.5%.[10] Roughly, about 9 million Thais should have pre-dialysis CKD at any stage. With only 900 nephrologists available, most Thai CKD patients would be out of reach of nephrologists and be mostly taken care of by internists or general practitioners. In our previous study, 'Effectiveness of integrated care on delaying progression of stages 3 to 4 chronic kidney disease in rural communities of Thailand (ESCORT-1),' an integrated care (IC) model for management of pre-dialysis CKD at rural community level had been evaluated.[11] In that study, two district hospitals were randomly selected, one was assigned to the intervention group and the other to the control group. In the intervention group, the patients received integrated care from the hospital multidisciplinary team (HMDT) every 3 months interspersed with a home visit by village-based community care network (CCN) team. The HMDT consists of general practitioners, a CKD nurse manager, a nutritionist, a pharmacist and a physical therapist. The CCN team comprised community nurses working at SDHC and VHV. This IC model had been shown to be effective in delaying CKD progression.[11] However, that study was conducted in a research-setting condition. It is not known the model would remain effective were it implemented in usual clinical practice. This study was conducted to evaluate effectiveness of the IC model if it was modified to fit more with routine clinical care at the community level.

SUMMARY AT A GLANCE

This report of a prospective cohort study shows the effectiveness of an integrated care model on delaying CKD progression in a Thai rural primary care setting.

1 | METHODS

1.1 | Study design and patient enrolment

The study was approved by the Ethics Committee of Institutional Review Board, Ministry of Public Health, Thailand, and was registered with www.clinicaltrials.in.th (TCTR20160614001). It was a prospective cohort study with a 3-year follow-up period. Five district hospitals of Kamphaeng Phet province, 400 km north of Bangkok, Thailand participated in this study. Inclusion criteria included patients who were (a) 18-70 years old, and (b) CKD stage 3 or 4 (with estimated glomerular filtration rate [eGFR] 30-59, or 15-29 mL/min/1.73 m^2, respectively). Exclusion criteria were (a) chronic kidney disease from secondary causes such as lupus nephritis, obstructive uropathy, autosomal dominant polycystic kidney disease, Alport's syndrome or renal cell carcinoma, (b) presence of microscopic haematuria or proteinuria more than 3.5 g per day, (c) body mass index (BMI) of less than 18 kg/m^2 or more than 40 kg/m^2, (d) pregnancy, (e) limb amputation or limb atrophy, (f) single kidney, (g) human immunodeficiency virus (HIV) infection, (h) malignancy and (i) connective tissue diseases (j) impaired communication ability.

1.2 | Study protocol

In order to make the integrated care model more compatible with routine clinical care, it was modified to be less stringent and less complicated than the previous study.[11]The IC model in this study comprised the HMDT approach during the patient's hospital visit every 3 months and home visits by CCN team every 6 months. HMDT provided systematically comprehensive medical care and multifaceted educational sessions including basic knowledge about CKD, its complications and management, renal replacement therapy, nutritional management, how to comply with prescribed medications, how to avoid nephrotoxic drugs or herbal medicine, and how to pursue proper exercise. Live demonstrations about how to prepare low salt and low protein diet were also provided. During a home visit, the blood pressure (BP) was recorded. Dietary assessment during a home visit by CCN team was made by using simple questionnaires. Patients were interviewed for recall of protein and salt intake and compliance to medications. They also received advice on exercise, lifestyle modification, avoidance of tobacco, herbs and nephrotoxic agents.

1.3 | Study data collection

A follow-up visit was scheduled every 3 months for 36 consecutive months. During each visit, demographic and laboratory parameters from the Hospital Information System were electronically collected. Additional clinical parameters were manually recorded on clinical record form (CRF). These included BP, body mass index and history of medication compliance. Use of non-steroidal anti-inflammatory drugs (NSAID) and herbal medicine was defined as using more than three times a week for at least four consecutive weeks. Serum creatinine

was standardized with Standard Reference Material 967a (SRM 967a, the National Institute for Standards and Technology, Gaithersburg, Maryland),[12] and CAP LN24 substance (College of American Pathologists, Northfield, Illinois),[13] The quality control system was also performed biweekly with RIQAS (Randox Laboratories, County Antrim, United Kingdom).

Serum creatinine was measured by enzymatic method[14] and eGFR was calculated by using CKD-EPI formula.[15] The fasting blood sugar, low-density lipoprotein, haemoglobin A1c (HbA1c), haematocrit, serum potassium, serum bicarbonate, serum albumin and presence of proteinuria (by urine dipstick) were measured at 3- to 6-month interval throughout the study period.

1.4 | Outcomes and definitions

The primary outcome was the rate of eGFR decline of each individual patient and the entire cohort to characterize the progression pattern of the cohort. The individual rate of eGFR decline was calculated with the simple linear regression method. The overall rate of eGFR decline of the study cohort was calculated with the linear mixed model.[16] Rapid progression of CKD was defined as a rate of eGFR decline more than 5 mL/min/1.73 m^2/year.[1] The secondary outcomes were associations between clinical characteristics and the rate of eGFR decline. Unadjusted and adjusted risks for rapid progression were analyzed with respect to clinical characteristics and biochemical parameters. Biochemical parameters of interest were office blood pressure level, HbA1c, serum bicarbonate and haematocrit. These were calculated on a time-average basis (values of each parameter were obtained from all hospital visits throughout the study period).

1.5 | Statistical analyses

Continuous variables were presented as means and SD, or medians and interquartile ranges when appropriate. Categorical variables were presented as percentages. An independent *t*-test was used for comparison of continuous variables, and a significant difference was defined as a *P*-value of less than .05. Rate of eGFR decline was calculated with linear regression and linear mixed model methods. The mean rates of eGFR decline in our study and the previous study cohorts were compared on the basis of the whole and propensity score matching cohorts. Propensity scores were calculated with multivariable logistic regression method. Age, gender, diabetes mellitus and proteinuria status were included as the covariates. Propensity scores were then used to match subjects from ESCORT-1 control group to subjects from ESCORT-2 in the ratio of 1:3 with the nearest neighbour within value of 0.25. Statistical analysis was made with SPSS software Version 23.[17]

2 | RESULTS

From August 1 to October 31, 2016; 1211 patients with CKD stages 3 to 4 aged 18 to 70 years old were screened for enrolment (Figure 1). Two hundred and ninety-seven patients were excluded due to presence of obstructive uropathy (33 cases), autosomal dominant polycystic kidney disease (1), microscopic haematuria or proteinuria more than 3.5 g per day (102), BMI of less than 18 kg/m^2 (43) or more than 40 kg/m^2 (1), single kidney (7), HIV infection (1), malignancy (7), connective tissue diseases (5), and impaired communication ability (29). Sixty-eight cases declined the study and 914 patients were enrolled (Figure 1). The mean age was 62 ± 6 years. About 67% of the cases were female. The majority of the study population (80%) had primary school education. Common comorbidities were hypertension (92%), diabetes (53%), hyperlipidaemia (68%), and hyperuricemia (20%). There were 23 cases (2.52%) who did not have any other systemic diseases to explain the cause of CKD (data not shown). The BMI of the study cohort was 24.5 ± 3.8 kg/m^2 and 60% of the cases had BMI equal to or more than 23.0 kg/m^2, the cut-off definition of overweight for Asian population.[18] Seventy-five percent of the study cohort had BP less than 140/90 mmHg. Prescription of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-receptor blockade (ARB) as antihypertensive drugs were found in 66%. However, the number had increased to 79% by the end of the first year and remained above 75% throughout the study period (data not shown).

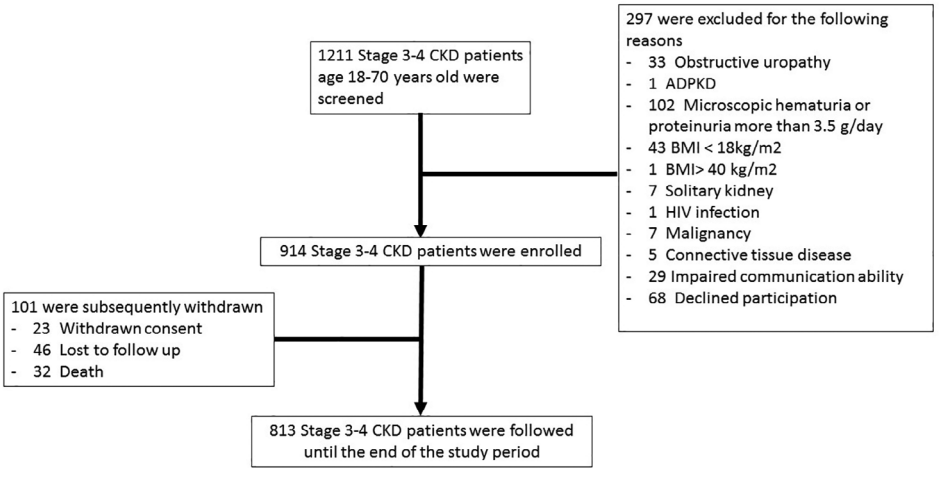

FIGURE 1 Study enrolment flow chart. ADPKD, autosomal dominant polycystic kidney disease; BMI, body mass index; CKD, chronic kidney disease; HIV, human immunodeficiency virus

TABLE 1 Baseline characteristics of participants

Parameters	
Age, years (mean ± SD)	62 ± 6
Female, cases (%)	609 (67%)
Co-morbidities	
Hypertension, cases (%)	838 (92%)
Diabetes, cases (%)	476 (53%)
Hyperlipidaemia, cases (%)	618 (68%)
Hyperuricemia, cases (%)	183 (20%)
Cardiovascular disease, cases (%)	32 (4%)
Cerebrovascular disease, cases (%)	9 (1%)
BMI, kg/m^2 (mean ± SD)	24.5 ± 3.8
Systolic BP, mmHg (mean ± SD)	129 ± 15
Diastolic BP, mmHg (mean ± SD)	74 ± 9
Number of patients with baseline BP <140/90 mmHg, cases (%)	682 (75%)
Number of patients who received ACEI/ARB prescription, cases (%)	603 (66%)
Stage of CKD	
Stage 3A, cases (%)	341 (37.3%)
Stage 3B, cases (%)	399 (43.7%)
Stage 4, cases (%)	174 (19%)

Note: Data were shown as mean (SD) for continuous variables and percentage for categorical variables.
Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease.

TABLE 2 Baseline laboratory parameters

Parameters	Mean ± SD
Serum creatinine, mg/dL	1.61 ± 0.45
eGFR, mL/min/1.73 m^2	40.43 ± 10.6
Fasting blood sugar, mg/dL	118.5 ± 48.8
Haemoglobin A1c, %	7.2 ± 1.8
Haematocrit, volume %	36.0 ± 5.3
Serum low-density liproprotein, mg/dL	101.5 ± 30.5
Serum sodium, mmol/L	139.8 ± 5.9
Serum potassium, mmol/L	4.30 ± 0.58
Serum bicarbonate, mmol/L	23.0 ± 3.3
Serum albumin, g/dL	4.22 ± 0.39

Note: Data were shown as mean (SD) for continuous variables.
Abbreviation: eGFR, estimated glomerular filtration rate.

There were 341 (37.3%), 399 (43.7%) and 174 (19%) cases in CKD stages 3A, 3B and 4, respectively (Table 1). Due to the precedent exclusion of cases with heavy proteinuria, the majority of our study population (80%) had negative proteinuria by urine dipstick test. There were 8% and 12% of cases who had +1 and + 2 proteinuria, respectively (data not shown). At baseline, the serum creatinine and eGFR of all study population were 1.61 ± 0.45 mg/dL and 40.4 ± 10.6 mL/min/1.73 m^2, respectively (Table 2). Among diabetic patients, the average haemoglobin A1c was 7.2 ± 1.8% and 50.3% of the cases had HbA1c more than 7%. The average haematocrit at baseline was 36 ± 5%. Other biochemical parameters were shown in Table 2.

The individual rate of eGFR decline calculated with linear regression method had a mean of - −0.92 (95% CI −1.2 to −0.64) mL/min/1.73 m^2/year, median – 0.78, and interquartile range 3.42. mL/min/1.73 m^2/year. The overall rate of eGFR decline calculated with the linear mixed model method in our study cohort during the 36-month follow-up was −1.06 (95% CI −1.27 to −0.85) mL/min/1.73 m^2/year. On the entire cohort comparison basis, the rates of eGFR decline calculated with both methods in our study were significantly less than that of the control group of the ESCORT-1 study; the linear regression method: −0.92 vs −2.27 mL/min/1.73 m^2/ year (mean difference 1.4, 95% CI 0.62-2.18, P = .001; the linear mixed model method: −1.06 vs −2.11 mL/min/1.73 m^2/year (mean difference 0.93, 95% CI 0.3-1.56, P = .004) (Table 3). Hypothetical lines representing the rates of eGFR decline calculated with the linear mixed model method from our study cohort and the control group of the previous study were drawn for visual comparison (Figure 2). For propensity score matching cohort, the rates of eGFR decline in our study were also significantly less than that of the control group of the previous study; the linear regression method; −1.14 vs −2.47 mL/min/1.73 m^2/year (mean difference 1.32, 95% CI 0.54-2.11, P = .001; the linear mixed model method; −1.24 vs −2.26 mL/min/1.73 m^2/year (mean difference 0.87, 95% CI 0.12-1.61, P = .022) (Table 3). About 10% of the study cohort had a rate of eGFR decline greater than −5 mL/min/1.73m^2/year, so-called rapid progression.[1]

Patients who had CKD from diabetes had a faster decline of eGFR than patients without diabetes; −1.46 vs −0.36 mL/min/1.73 m^2/year (mean difference 1.09, 95% CI 0.56-1.63, P < .001). Patients with proteinuria (at any degree of positivity by urine dipstick) had faster rate of decline of eGFR than patients without proteinuria (−2.08 vs −0.61 mL/min/1.73 m^2/year, respectively, mean difference 1.46, 95% CI 0.80-2.12, P < .001) (Table 4). Patients with time-average BP less than 140/90 mmHg had a slower rate of eGFR decline than those with time-average BP equal to or more than 140/90 mmHg (−0.73 vs −1.96 mL/min/1.73 m^2/year, mean difference 1.23 [95% CI 0.52-1.94] P < 0.001). Moreover, patients with time-average BP less than 130/80 mmHg had even a slower rate of eGFR decline than those with time-average BP at or higher than this level (−0.54 vs −1.33 mL/min/1.73 m^2/year, mean difference 0.79, and (95% CI 0.25-1.33, P = .004). A level of the haematocrit of less than 33% was also associated with faster eGFR decline. In this study cohort, prescription of angiotensin-converting enzyme inhibitors or angiotensin receptor blockades, time-average serum bicarbonate equal to or more than 22 mmol/L, and the presence of HbA1C levels lower than 7% were not significantly associated with a slower rate of eGFR decline.

Unadjusted odds ratio analysis revealed that presence of proteinuria, time-average BP higher than 140/90 mmHg, time-average serum bicarbonate less than 22 mmol/L, time-average haematocrit below 33% and time-average serum albumin less than 4 g/dL were about 2 to 3 times more likely to have rapid progression of CKD. Moreover,

TABLE 3 Comparison of rates of eGFR decline

	Entire cohort			Propensity score matching cohort[a]	
	Linear regression method	Linear mixed model method		Linear regression method	Linear mixed model method
ESCORT-2 (N = 914)	−0.92	−1.06	ESCORT-2 (N = 432)	−1.14	−1.24
ESCORT-1 control group (N = 201)	−2.27	−2.11	ESCORT-1 control group (N = 144)	−2.47	−2.26
Mean difference (95% CI)	1.4 (0.62-2.18)	0.93 (0.3-1.56)	Mean difference (95% CI)	1.32 (0.54-2.11)	0.87 (0.12-1.61)
P-value	.001	.004	*P*-value	.001	.022

Note: Data of the present study (ESCORT-2) were compared with the control group of the previous study (ESCORT-1) for the entire cohort and propensity score matching cohort. Both linear regression and linear mixed model methods were used for comparison.
Abbreviation: CI, confidence interval.
[a]Propensity score matching with age, gender, diabetes mellitus and proteinuria status.

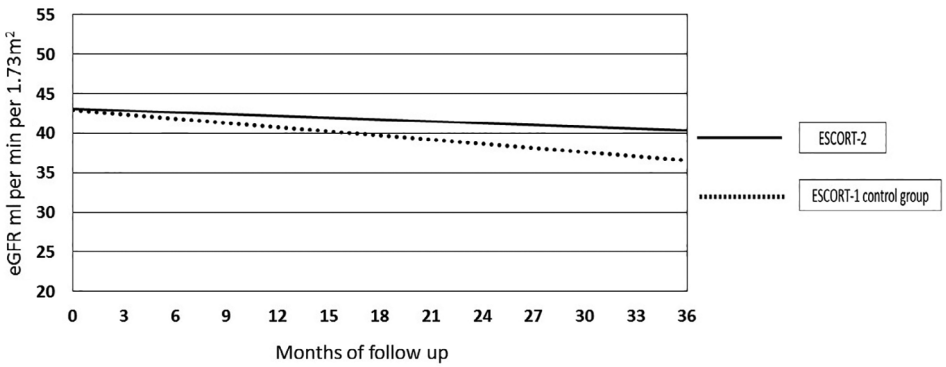

FIGURE 2 Comparison of extrapolation lines represent eGFR decline rate calculated with the linear mixed model between ESCORT2 and ESCORT1 control group. eGFR, estimated glomerular filtration rate; ESCORT, Effectiveness of Integrated Care on Delaying Progression of stage 3-4 Chronic Kidney Disease in Rural Communities of Thailand

TABLE 4 Association between Clinical parameters and rates of eGFR declined

Clinical parameters	Reference group	Number	Rate of eGFR decline (mL/min/1.73 m^2/year) mean	Difference (95% CI)	*P* value
DKD	DKD	476	−1.46	1.09 (0.56 to 1.63)	<.001
	Non-DKD	418	−0.36		
Proteinuria	Negative	708	−0.61	1.46 (0.80 to 2.12)	<.001
	Positive	163	−2.08		
ACEI or ARB	Not received	298	−1.11	−0.30 (−0.81 to 0.33)	.41
	Received	593	−0.87		
BP control	Average BP <130/80 mmHg	437	−0.54	0.79 (0.25 to 1.33)	.004
	Average BP ≥130/80 mmHg	456	−1.33		
	Average BP <140/90 mmHg	740	−0.73	1.2 (0.52 to 1.94)	<.001
	Average BP ≥140/90 mmHg	153	−1.96		
HbA1c	HbA1c <7%	155	−1.53	−0.88 (−0.75 to 0.57)	.79
	HbA1c ≥7%	315	−1.44		
Metabolic acidosis treatment	Average serum bicarbonate ≥22 mmol/L	694	−0.89	0.27 (−0.38 to 0.92)	.41
	Average serum bicarbonate <22 mmol/L	199	−1.16		
Anaemia management	Time average haematocrit ≥33%	666	−0.71	1.04 (0.44 to -1.65)	.001
	Time average haematocrit <33%	226	−1.75		

Note: Presence of diabetic kidney disease, proteinuria and receiving angiotensin-converting enzyme inhibitor or angiotensin receptor blockade were identified from the baseline characteristics. The average values of blood pressure, glycaemic control as indicated by HbA1c level, and treatment of metabolic acidosis, as indicated by serum bicarbonate concentration, were obtained from all hospital visits throughout the study period. Data were analyzed with independent *t*-test.
Abbreviations: DKD, diabetic kidney disease; ACEI, angiotensin-converting enzyme inhibitor; ARB angiotensin receptor blockers; BP, blood pressure; HbA1c; haemoglobin A1c.

in an adjusted model for age and baseline eGFR, these findings remained statistically significant (Table 5).

Throughout the present study, the percentages of cases who achieved treatment targets for correction of anaemia, optimum control of blood pressure and metabolic acidosis were 75%, 78% and 83%, respectively, whereas those of the control group of the previous study were 84%, 55% and 88%, respectively (Figure 3).

3 | DISCUSSION

In the previous ESCORT-1 study, the IC model has been proven to be effective in delaying pre-dialysis CKD progression in a primary health-care setting of Thailand.[11] The pattern of IC in this study was simplified to match with the current context of clinical care in the rural area. Although the rate of eGFR decline of this study was remarkably low. It was slightly greater than the intervention group but significantly less than the control group of the ESCORT-1 study.[11] Indeed, it was comparable to or far better than those reported elsewhere which were under the care of nephrologists and multidisciplinary teams at tertiary care hospitals.[2,3]

In this study, it was found that DKD, presence of proteinuria, sub-optimal BP control and presence of anaemia were associated with faster rates of eGFR decline (Table 4). Interestingly, patients with the time-average BP lower than 130/80 mmHg had a rate of eGFR decline better than those who have time-average BP lower than 140/80 mmHg. The result of this study is in contrast to the AASK, REIN-2 and SPRINT studies which demonstrated no beneficial effect of BP of <130/80 mmHg on the rate of CKD progression.[20,21,22] However, the beneficial effect of intensive BP control at 120-125/75-80 mmHg on delay CKD progression was previously demonstrated in the MDRD study.[19] Therefore, target BP level for CKD patient is still debatable and further studies are needed to clarify this issue. Expectedly, achieving optimal HbA1c level (<7%) was not associated with a slower rate of eGFR decline. This finding was in accord with previous observations which showed no benefit of strict glycaemic control in delaying CKD progression in a setting of late-stage CKD. [23,24]

Although the associations between the presence of higher BP, lower haematocrit, lower serum bicarbonate or lower serum albumin with rapid CKD progression identified in this study has been previously observed, [25-27] our data were derived from the time-average values which should be better representative of these parameters than the single values. These findings reaffirm the general concept that close monitoring of the above-mentioned parameters are of prime importance for caring of patients with CKD, even at the primary health-care setting where resources are limited. It is noteworthy that the treatment goal of each parameter could be achieved in only 75% of cases, had higher percentage of the treatment goal could be

TABLE 5 Factors associated with rapid progression on unadjusted analysis and adjusted analyses

Factors	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Time-average HbA1c > 7%	0.94 (0.52-1.69)	0.96 (0.52-1.75)
Receiving ACEI/ARB	0.69 (0.44-1.07)	0.66 (0.42-1.03)
Presence of proteinuria	2.91 (1.83-4.63)*	2.82 (1.76-4.52)*
Time-average BP > 140/90	2.70 (1.83-4.38)*	2.74 (1.68-4.48)*
Time-average serum bicarbonate less than 22 mmol/L	1.72 (1.07-2.76)*	1.86 (1.13-3.07)*
Time-average haematocrit less than 33%	1.85 (1.17-2.92)*	1.95 (1.21-3.16)*
Time-average serum albumin less than 4 g/dL	1.95 (1.20-3.17)*	2.10 (1.28-3.45)*

Note: Adjusted model with age and baseline eGFR.
Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB angiotensin receptor blockers; BP, blood pressure; HbA1c; haemoglobin A1c.
*Significant $P < .05$.

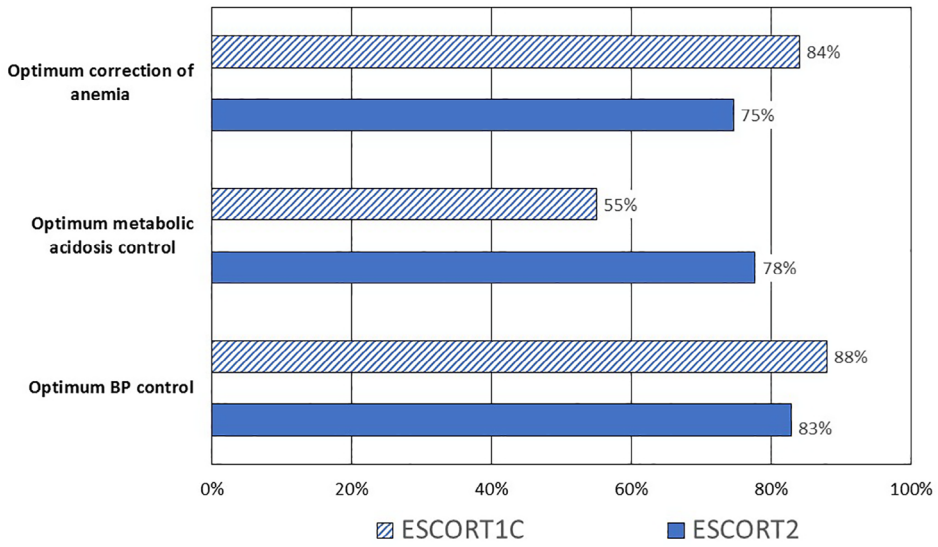

FIGURE 3 Target achievement of important parameters: Optimum treatment of anaemia (haematocrit > 33%), optimum treatment of metabolic acidosis (serum bicarbonate >22 mmol/L) and optimum control of BP (<140/90 mmHg). Data were shown as percentage. BP, blood pressure; ESCORT, Effectiveness of Integrated Care on Delaying Progression of stage 3-4 Chronic Kidney Disease in Rural Communities of Thailand, ESCORT1 study control group; ESCORT2, our study

reached, the control of CKD progression could have been more successful.

Although there have been several studies which could demonstrate beneficial effect of integrated care approach and enhancement of self-management on delaying CKD progression or short-term clinical outcomes.[28,29] Our study as well as the previous publication[11] are quite unique that regular home visit by community nurses and village health volunteers was included in the programme. There have been a few integrated care models which utilized community-based approach for CKD care.[4,30] This direct home-based approach might have been one of the main key success factors of this study. It may have had an influence on patients' lifestyle modification, adherence to medication, and more effective control of BP, leading to more effective control of CKD progression.[30] Had this IC model been generalized to a larger scale, it is likely that patients with CKD at an early stage would get benefit from the programme. Health and economic losses due to an overwhelming number of patients with the end-stage renal disease would be minimized.

There are certain limitations to this study. First, it is not a randomized control study. It was designed for a proof-of-concept of the previous ESCORT-1 study to evaluate if the IC model as such would remain effective in real-world health-care practice at the community level. Second, there was some discrepancy in the manner and details of group education among different HMDT and CCN teams. Although the main theme of the protocol was unchanged, certain part was slightly modified to fit with the context of health service pattern of each community. Third, due to a large number of patient load with respect to the number and time allowable of the health personnel of each community hospital or each sub-district health office, individual case education and counselling were quite limited and group education had to be utilized instead. This might have had some impact on the final outcome of the study.

In conclusion, the IC model provided by HMDT at the community hospitals and by CCN teams during home visits, was effective in delaying CKD progression in stages 3 to 4 CKD patients residing in the rural area.

A LIST OF OTHER ESCORT-2 STUDY PARTICIPANTS

Bhumirajanagarindra Kidney Institute: Teerayuth Jiamjariyapon, MD, Somrat Lertmaharit, MPH; **Faculty of Medicine Siriraj Hospital, Bangkok:** Duangjit Kanistanon, MD, PhD, Patimaporn Wongprompitak, PhD; **Kamphaengphet Provincial Health Office:** Petchrurk Tansawad, MD, Morakot Samaphant, RN, MEd, Sawitree Apairat, RN; **Khlong Khlung Hospital, Kamphaengphet:** Suchanya Promnim, RN, Suchada Niyomchon, PharmD, Pannipa Sripan, BSc, Panupong Paiboon, BSc, Laksamee Jumrassri, BSc, Noppadon Tiammon, BSc; **Khlong Lan Hospital, Kamphaengphet:** Kanokwan Prommachat, RN, MNS, Wasuthorn, PharmD, Kwanruen Lamputa, BSc, Surangkana Ramsiri, BSc, Rattana Loblom, BSc, Phasin Raksasit, BEd; **Lan Krabue Hospital, Kamphaengphet:** Patraporn Meesiri, RN, Kamonwan Wichitphongsa, PharmD, Amonrat Ketsawad, BSc, Phannaray Klinrung, BSc, Sararat Homkanjan, BSc, Kanchit Suriyo, BSc; **Phran Kratai Hospital, Kamphaengphet:** Yawoluk Bunyanant, RN, Thidaswan Ittiwitayawat, PharmD, MSc, Thipgasorn Jalernsuphasin, BSc, Waridtha Sornthip. BSc, Sukanya Phowee, BSc, Somsak Daha, BSc; **Saithong Wattana Hospital, Kamphaengphet:** Napaporn Boonyuen, RN, MSc, Phatcharada Dueandao, PharmD, Ampaipon Rueangsrichan, BSc, Jarkarin Ganta, BSc, Sucheera Sennoy, BSc, Duangnate Thajuang, BSc, Med.

ORCID

Teerawat Thanachayanont https://orcid.org/0000-0003-4801-1094

REFERENCES

1. Kidney Disease Improving Global Outcomes [KDIGO]. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):1-150.
2. Peeters MJ, Van Zuilen AD, Van Den Brand JJG, et al. Nurse practitioner care improves renal outcome in patients with CKD. *J Am Soc Nephrol*. 2014;25:390-398.
3. Chen PM, Lai TS, Chen PY, et al. Multidisciplinary care program for advanced chronic kidney disease: reduces renal replacement and medical costs. *Am J Med*. 2015;128:68-76.
4. Stanifer JW, Von Isenburg M, Chertow GM, Anand S. Chronic kidney disease care models in low- and middle-income countries: a systematic review. *BMJ Glob Health*. 2018;3(2):1-8.
5. Nitayarumphong S. Evolution of primary health care in Thailand: what policies worked? *Health Policy Plan*. 1990;5(3):246-154.
6. Kitreeawutiwong N, Jordan S, Hughes D. Facility type and primary care performance in sub-district health promotion hospitals in northern Thailand. *PLoS One*. 2017;12(3):1-14.
7. Primary Health Care Division, Ministry of Public Health, Thailand.Village Health Volunteers Database. Available from: http://thaiphc.net [Accessed 26th May 2020].
8. Therawiwat M, Fungladda W, Kaewkungwal J, Imamee N, Steckler A. Community-based approach for prevention and control of dengue hemorrhagic fever in Kanchanaburi Province. *Thailand Southeast Asian J Trop Med Public Health*. 2005;36(6):1439-1449.
9. Sanguanprasit B, Leerapan P, Taechaboonsermsak P, Chongsuwat R. Village health volunteers as peer supports for glycemic control among type 2 diabetes patients in Thailand. *J Public Health Develop*. 2016;14(2):49-60.
10. Ingsathit A, Thakkinstian A, Chaiprasert A. Prevalence and risk factors of chronic kidney disease in the Thai adult population: Thai SEEK study. *Nephrol Dial Transplant*. 2010;25:1567-1575.
11. Jiamjariyapon T, Ingsathit A, Pongpirul K, et al. Effectiveness of integrated care on delaying progression of stage 3-4 chronic kidney disease in rural communities of Thailand (ESCORT study): a cluster randomized controlled trial. *BMC Nephrol*. 2017;18:83.
12. Dodder NG, Tai SS, Sniegoski LT, Zhang NF, Welch MJ. Certification of creatinine in a human serum reference material by GC-MS and LC-MS. *Clin Chem*. 2007;53(9):1694-1699.
13. Recommendation for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem*. 2006;52(1):5-18.
14. Moss GA, Bondar RJL, Buzzelli DM. Kinetic enzymatic method for determining serum creatinine. *Clin Chem*. 1975;21(10):1422-1426.
15. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-612.
16. Rifkin DE, Shlipak MG, Katz R, et al. Rapid kidney function declines and mortality risk in older adults. *Arch Intern Med*. 2008;168(20):2212-2218.

17. IBM Corp. *IBM SPSS Statistics for Windows, Version 23*. IBM Corp: Armonk, NY; 2015.
18. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363:157-163.
19. Wright JI Jr, Williamson JD, Whelton PK, et al. Ambrosius WT; SPRINT Research Group: a randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103-2116.
20. Klahr S, Levey AS, Beck GJ, et al. Modification of diet in renal disease study group: the effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. *N Engl J Med*. 1994;330:877-884.
21. Wright JT Jr, Bakris G, Greene T, et al. Rostand SG African American study of kidney disease and hypertension study group effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA*. 2002;288:2421-2431.
22. Ruggenenti P, Perna A, Loriga G, et al. REIN-2 study group. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicenter, randomized controlled trial. *Lancet*. 2005;365:939-946.
23. MacIsaac RJ, Jerums G, Ekinci EI. Effects of glycaemic management on diabetic kidney disease. *World J Diabetes*. 2017;15:172-186.
24. Duckworth W, Abraira C, Moritz T, et al. Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med*. 2009;360:129-139.
25. Vigil A, Condes E, Camacho R, et al. Predictors of a rapid decline of renal function in patients with chronic kidney disease referred to a nephrology outpatient clinic: a longitudinal study. *Advances in Nephrology*. 2015;3:1-8.
26. Go AS, Yang J, Tan TC, et al. Contemporary rates and predictors of fast progression of chronic kidney disease in adults with and without diabetes mellitus. *BMC Nephrol*. 2018;19:146.
27. Tsai CW, Ting IW, Yeh HC, Kuo CC. Longitudinal change in estimated GFR among CKD patients: a 10-year follow-up study of an integrated kidney disease care program in Taiwan. *PLoS One*. 2017;12:e0173843.
28. Nicoll R, Robertson L, Gemmell E, Sharma P, Black C, Marks A. Models of care for chronic kidney disease: a systematic review. *Nephrol Ther*. 2018;23:389-396.
29. Yang CW, Harris DCH, Luyckx A, et al. Global case studies for chronic kidney disease/end-stage kidney disease care. *Kidney Int*. 2020;10:e24-e448.
30. Jafar HT, Allen JC, Jehan I, et al. Health education and general practitioner training in hypertension management: long-term effects on kidney function. *Clin J Am Soc Nephrol*. 2016;11:1044-1053.

How to cite this article: Thanachayanont T, Chanpitakkul M, Hengtrakulvenit J, et al. Effectiveness of integrated care on delaying chronic kidney disease progression in rural communities of Thailand (ESCORT-2) trials. *Nephrology*. 2021;26:333–340. https://doi.org/10.1111/nep.13849