

Treatment Costs for Patients with Chronic Kidney Disease Who Received Multidisciplinary Care in a District Hospital in Thailand

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Aim: To estimate direct medical treatment costs in patients with pre-dialysis chronic kidney disease (CKD) in a district hospital and to analyze the factors that affected the treatment costs.

Patients and Methods: Data were retrospectively retrieved from the hospital database in the period from January 2015 to December 2017. Patients who were diagnosed with CKD and had visited ambulatory care services at least two times during the index year (January to December 2015) were included. Patients' data were excluded if they had cancer, had received renal replacement therapy, or had been referred to receive treatment at other hospitals. Treatment costs based on the providers' perspectives in the first and second years after the index year were assessed. Descriptive statistics were used to analyze patients' characteristics, and multiple linear regression was used to analyze the factors in the cost model.

Results: Data of 212 patients with CKD stage G3a, G3b, or G4 who met inclusion and exclusion criteria were included for analysis. Average costs for treatment in year 1 and year 2 were not statistically different. Total cost was 5701.34 Thai Baht (THB) per year. The total cost for patients with CKD stage G4 was two times greater than for patients with CKD stage G3. Costs were increased for longer hospitalization, more frequent ambulatory visits, having diabetes mellitus or dyslipidemia as a comorbidity, and uncontrolled fasting blood glucose (FBG). A cost model with $R^2=0.906$ was provided. Significant predictors were length of stay, ambulatory visits, diabetes mellitus, dyslipidemia, serum creatinine, FBG, and body mass index.

Conclusion: Total annual treatment costs for the 2 years were not different. A more advanced stage of CKD, having diabetes mellitus or dyslipidemia as comorbidities, and uncontrolled FBG were significantly associated with increased costs for treatment in patients with pre-dialysis CKD.

Keywords: cost, chronic kidney disease, district hospital, multidisciplinary

Introduction

Chronic kidney disease (CKD) is a chronic disease that causes a public health burden worldwide. Global CKD prevalence is approximately 13.4%¹ while it has increased to 17.7% in Thailand.² Hypertension and diabetes mellitus are common comorbidities in CKD patients. Uncontrolled comorbidities precipitate CKD progression^{3,4} and lead to costly medical treatment,⁵⁻⁷ especially in dialysis patients.⁸⁻¹⁰

The multidisciplinary care (MDC) approach, compared with the usual care model, has shown benefits in terms of lower risk of all-cause mortality, lower rate of hospitalization, slower rate of glomerular filtration rate (GFR) decline, and less requirement for long-term dialysis.^{6,7,11,12} However, its benefit in cost savings

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is still controversial among different countries. The studies conducted in Taiwan indicated that the MDC approach has lower direct medical treatment costs for patients with advanced stages of CKD than the costs associated with usual care.^{6,11}

A study conducted in the USA showed that the MDC approach was more cost-effective for patients with CKD stage G3 to G4 compared with usual care.⁷ Conversely, studies conducted in Germany reported greater direct medical costs incurred with MDC than those with usual care.¹³

Based on the scoping review of 40 studies in 2019,¹⁴ there is inconsistency due to various MDC team compositions. In Thailand, the MDC approach has been utilized for a decade. Thai MDC teams are composed of 2 general practitioners, 2 chronic care nurses, 1 pharmacist, 1 physical therapist, and 1 nutritionist.¹⁵ Teams are aimed at reducing the incidence of CKD and end-stage renal disease, improving patients' quality of life, and increasing access to renal replacement therapy (RRT). From a previous randomized controlled trial in Thailand comparing integrated care with an MDC approach and usual care,¹⁶ the result shows that patients who received integrated care with MDC have better GFR over the 2 years of follow up. However, studies related to costs and outcomes of the MDC approach are still limited; therefore, this study aimed to estimate the direct medical treatment costs for patients with pre-dialysis CKD in Thailand.

Patients and Methods

Study Design and Patients

This retrospective cohort study was conducted at a public district hospital in Kamphaengphet province, Thailand. MDC members of CKD clinic in this setting comprised of 1 general practitioner, 2 nurses, 1 pharmacist, 1 dietician, and 1 physical therapist. There was also a home visit team that provide health care at patients' homes for every 3 months. Home visit team members comprised of 2 nurses or public health officers and at least 3 village health volunteers. Patients included in the study were aged 18 years or above, had been diagnosed with CKD (ICD 10 N138, N184 and N185) according to eGFR calculated by CKD-EPI equation, regularly received treatment at the aforementioned hospital, and had visited ambulatory care services at least two times during the index year (January to December 2015). Serum creatinine or GFR data were required to confirmed CKD stage. Patients were excluded if they met at least one of the following criteria: 1) were diagnosed with having cancer, 2) received RRT

including chronic intermittent hemodialysis or peritoneal dialysis, 3) had been referred to other hospitals, or 4) were lost to follow up or death. CKD stages were classified by the recommendation of Kidney Disease Improving Global Outcomes (KDIGO).¹⁷ GFR was calculated using the CKD-EPI equation.¹⁸ The study protocol was in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Faculty of Pharmacy, Chiang Mai University (No. 010/2561). Since the hospital database was retrospectively retrieved in this study, written informed consent was not obtained from an individual patient. Code numbers were used in data collection to prevent individual identification and maintain patients' confidentiality.

Data Collection

Data were retrieved from the hospital database for 3 years starting from January 2015 to December 2017. The first year would be the index year. Patients who had visited the hospital in the index year and met the inclusion and exclusion criteria above would be included in this study. Demographic and clinical data of those included patients were collected in the first year; then costs would be collected for the next 2 years. Resource uses of these following items for both ambulatory care and in-patient care such as medications, parenteral nutrition, medical supplies, blood products, laboratory tests, and other medical services were collected. Unit costs of the items above were obtained from the standard unit cost list for medical and health services in Thailand.¹⁹

Cost Estimation

This study considered the health-care provider's perspective. Therefore, only direct medical costs were included. Direct medical costs comprised of cost in diagnosis, laboratory test, pharmacological and non-pharmacological treatment, and services for ambulatory care in outpatient clinics and emergency room, and hospitalization care. The cost estimation was analyzed by the multiplication of unit cost times the number of uses. Total cost was the summation of all cost items. Ambulatory cost was calculated for all patients, but hospitalization cost was calculated only for admitted patients. Costs were inflated using Thailand's consumer price index²⁰ and presented in the year 2019.

Statistical Analysis

Patients' characteristics and clinical data were reported as descriptive statistics. Annual costs of different years and patients' characteristics were analyzed using the

Independent *t*-test or the analysis of variance test as appropriate. Multiple linear regression analysis was used for forecasting cost models in CKD patient care. Stepwise method was used to plugged variables in the model. Statistical analyses were executed using SPSS 17.0 (SPSS, Chicago, IL, USA) and statistical significance was considered if $P < 0.05$.

Results

A total of 331 patients were eligible based on inclusion criteria. However, 116 patients were excluded due to the following reasons: 1) referral to other settings (53 patients), 2) having cancer (52 patients), 3) receiving RRT (11 patients), and 4) loss to follow up or death (3 patients). Therefore, 212 patients with CKD stage G3 to G4 were included in the analysis. The average age was 69.42 years and 35.40% were male. Hypertension (93.90%) was the most common comorbidity found in this group of patients. Diabetes mellitus was doubled in patients with CKD stage G4 compared with patients with CKD stage G3. Of the 41 total admissions, patients with stage G3a, G3b, and G4 were accounted for at 20 (48.78%), 12 (29.27%), and 9 (21.95%), respectively. Patients' characteristics are shown in [Table 1](#).

[Table 2](#) shows that the average total treatment costs in year 1 and year 2 were 5701.34 and 5697.24 THB per year, respectively. Total costs were divided into ambulatory and hospitalization costs. It was found that ambulatory costs were greater than hospitalization costs for both years. However, total costs in year 1 and year 2 were not statistically significantly different ($P > 0.05$).

Ambulatory costs for patients aged less than 65 years were higher than those of patients aged more than 65 years (4902.94 and 3995.19 THB per year, $P=0.018$). Ambulatory costs, hospitalization costs, and total costs for treatment were higher for patients who had been hospitalized, especially those who had lengths of stay for more than 8 days, as opposed to those who had not been hospitalized. Costs were also higher for patients who had visited ambulatory services more than eight times per year, had diabetes mellitus as a comorbidity, and/or uncontrolled fasting blood glucose (FBG) which is defined as FBG > 130 mg/dL. Treatment costs by patients' characteristics are shown in [Table 3](#) and [Supplementary Table 1](#).

Although 15 variables of patients' characteristics and clinical data obtained from the hospital database were plugged into the cost model, 6 variables demonstrated significant predictors at P -value <0.05. Those were age,

length of stay, ambulatory visits, body mass index, diabetes mellitus, and FBG ([Table 4](#) and [Supplementary Table 2](#)).

Discussion

The study estimated the direct medical costs for standard treatment with the MDC approach in patients with CKD stage G3 to G4 who received treatment at a district hospital. In Thailand, patients with an advanced CKD stage or who need RRT are referred to receive treatment with nephrologists at tertiary hospitals; hence, only CKD stages G3 and G4 patients receive treatment at district hospitals.

The average age of our sample population was 69.42 years, which was older than those in other studies.^{6,11,16} We found that all samples remained in the same CKD stage and received the same standard treatment over the 2 years. This led to no statistically significant difference in the estimated treatment costs.

More severe stages of CKD resulted in higher treatment costs. Although treatment costs for patients with CKD stage G3a and G3b were not different, it was doubled in patients with CKD stage G4 due to a higher hospitalization rate (16.26%, 17.91%, and 40.92% for patients with stage G3a, G3b, and G4, respectively). This finding was concordant with previous studies that estimated direct medical costs for treatment with the MDC approach.^{7,13}

The cost model showed that ambulatory visits, hospitalization, diabetes mellitus, dyslipidemia, serum creatinine, FBG, and body mass index are the main cost drivers. The more frequent ambulatory visits, the longer the hospitalization, having diabetes mellitus or dyslipidemia as a comorbidity, having higher serum creatinine or FBG, and greater body mass index independently increase treatment costs.

One-third of these CKD patients had diabetes mellitus and treatment costs were doubled compared to those with no diabetes mellitus. This might be due to a longer duration of hospitalization (1.20 vs 0.46 days) and more frequent ambulatory visits (6.81 vs 6.22 visits). Unexpectedly, patients with both CKD and diabetes mellitus who achieved the hemoglobin A1c (HbA1c) target had no significant difference in treatment costs compared with those who did not achieve the HbA1c target. This might be attributable to a small sample size ([Table 1](#)) and criteria. Due to FBG monitoring being more convenient and less expensive than HbA1c monitoring, it can be measured

Table 1 Patients' Characteristics

Characteristics	CKD G3a (n=123)	CKD G3b (n=67)	CKD G4 (n=22)	All (n=212)	P-value
Male sex (n)	50 (40.70)	17 (25.40)	8 (36.40)	75 (35.40)	0.110
Age (years)	68.11 ± 10.05	72.00 ± 9.70	68.82 ± 10.52	69.42 ± 10.10	0.038*
<65	44 (35.80)	15 (22.40)	8 (36.40)	67 (31.60)	
≥65	79 (64.20)	52 (77.60)	14 (63.60)	145 (68.40)	
Hypertension (n)	117 (95.10)	64 (95.50)	18 (81.80)	199 (93.90)	0.045*
Diabetes mellitus (n)	37 (30.10)	23 (34.30)	14 (63.60)	74 (34.90)	0.009*
Dyslipidemia (n)	61 (49.60)	31 (46.30)	13 (59.10)	105 (49.50)	0.584
MI/CHF (n)	1 (0.80)	3 (4.50)	2 (9.10)	6 (2.80)	0.060
Length of stay (day)	1.19 ± 0.45	1.19 ± 0.44	1.50 ± 0.67	1.29 ± 0.68	0.001*
0	103 (83.74)	55 (82.09)	13 (59.08)	171 (80.70)	
1–7	17 (13.82)	11 (16.42)	7 (31.82)	35 (16.50)	
≥8	3 (2.44)	1 (1.49)	2 (9.10)	6 (2.80)	
Ambulatory visit (visit)	6.55 ± 2.74	6.22 ± 2.21	6.32 ± 1.96	6.42 ± 2.50	0.674
1–4	15 (12.20)	11 (16.40)	3 (13.60)	29 (13.70)	
5–7	82 (66.70)	44 (65.70)	13 (59.10)	139 (65.60)	
≥8	26 (21.10)	12 (17.90)	6 (27.30)	44 (20.80)	
BMI (kg/m ²)	23.94 ± 3.85	23.77 ± 4.92	23.93 ± 3.55	23.89 ± 4.17	0.962
SBP (mmHg)	140.38 ± 14.42	140.54 ± 13.67	141.59 ± 15.51	140.55 ± 14.24	0.935
FBG (mg/dL)	103.41 ± 28.63	109.10 ± 41.98	121.11 ± 25.60	107.04 ± 33.47	0.060
HbA1c (%), n=74	6.46 ± 0.84	7.10 ± 1.70	6.80 ± 1.30	6.72 ± 1.26	0.151
<7%	29 (78.40)	13 (56.50)	7 (50.00)	49 (66.20)	
≥7%	8 (21.60)	10 (43.50)	7 (50.00)	25 (33.80)	
TG (mg/dL)	159.82 ± 83.65	165.69 ± 119.90	180.34 ± 79.79	163.81 ± 96.00	0.643
LDL (mg/dL)	114.80 ± 31.31	110.48 ± 39.13	120.89 ± 39.76	114.07 ± 34.82	0.449
HDL (mg/dL)	45.82 ± 11.76	43.80 ± 8.68	42.18 ± 10.58	44.80 ± 10.78	0.227
BUN (mg/dL)	16.65 ± 4.97	22.28 ± 12.54	29.12 ± 7.77	19.72 ± 9.29	<0.001*
Scr (mg/dL)	1.20 ± 0.17	1.45 ± 0.21	2.29 ± 0.56	1.39 ± 0.41	<0.001*
eGFR (mL/min/1.73m ²)	53.11 ± 3.41	39.43 ± 4.02	25.08 ± 6.33	45.88 ± 10.23	<0.001*

Note: *P-value <0.05.

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; CHF, chronic heart failure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; MI, myocardial infarction; SBP, systolic blood pressure; Scr, serum creatinine; TG, triglyceride; CKD G3a, chronic kidney disease stage G 3a (GFR 45–59 mL/min/1.73 m²); CKD stage 3b, chronic kidney disease stage G 3b (GFR 30–44 mL/min/1.73 m²); CKD G4, chronic kidney disease stage G 4 (GFR 15–29 mL/min/1.73 m²).

more frequently in district hospitals. We found that treatment costs for patients with uncontrolled FBG were substantially higher than for those who met the recommended FBG target of <130 mg/dL.²¹

About half of the patients had dyslipidemia as a comorbidity. Patients with dyslipidemia had slightly higher treatment costs than those without dyslipidemia. The difference in treatment costs was mainly from drug costs instead of laboratory monitoring, frequency of ambulatory visits, length of hospitalization, or CKD stage.

Again, drug costs were the major component that affected the treatment costs for patients with serum creatinine ≥2 mg/dL compared with those with serum creatinine less than 2

mg/dL. All patients with serum creatinine ≥2 mg/dL, 92.31% were categorized into CKD stage G4.

Ambulatory costs for patients aged less than 65 years were higher than those of patients aged more than 65 years. This finding was in line with results of the study conducted in Italy by Turchetti and colleagues.²² They reported that CKD patients aged more than 74 years had lower direct medical cost compared to those who aged less than 74 years due to lower costs of diagnostic exams, laboratory tests and hospital cares.²²

A previous cost-effectiveness study of MDC in CKD patients in Thailand reported direct medical costs of 6265.86 THB per year²² (presented in the year 2019),

Table 2 Treatment Cost by Chronic Kidney Disease Stages (per Year)

Cost	CKD Stage G3a (n=123)			CKD Stage G3b (n=67)			CKD Stage G4 (n=22)			All (n=212)		
	Mean ± SD	Diff	P-value	Mean ± SD	Diff	P-value	Mean ± SD	Diff	P-value	Mean ± SD	Diff	P-value
Ambulatory Cost												
Year 1 THB (USD)	3843.01 ± 1697.63 (117.13 ± 51.74)	12.42 (0.38)	0.929	4407.83 ± 3238.75 (134.34 ± 98.71)	156.58 (4.78)	0.235	6353.90 ± 3551.12 (193.66 ± 108.23)	-98.89 (-3.02)	0.851	4282.08 ± 2601.43 (130.51 ± 79.29)	46.43 (1.41)	0.658
Year 2 THB (USD)	3855.43 ± 1642.64 (117.51 ± 50.06)			4564.41 ± 2926.20 (139.12 ± 89.18)			6255.00 ± 2901.36 (190.64 ± 88.43)			4328.51 ± 2368.84 (131.92 ± 8.19)		
Hospitalization Costs (All Cases)												
Year 1 THB (USD)	1070.58 ± 3353.69 (32.63 ± 102.21)	-260.30 (-7.93)	0.411	1066.23 ± 2974.42 (32.50 ± 90.66)	1144.28 (34.87)	0.106	4443.83 ± 6956.42 (135.44 ± 212.02)	-2516.42 (76.7)	0.126	1419.26 ± 3892.43 (43.26 ± 118.63)	-50.52 (-1.54)	0.880
Year 2 THB (USD)	810.28 ± 2169.13 (24.70 ± 66.11)			2210.51 ± 6503.92 (67.37 ± 198.23)			1927.41 ± 3242.37 (58.74 ± 98.82)			1368.74 ± 4175.85 (41.72 ± 127.27)		
Hospitalization Cost (only Admitted Patients)												
Year 1 THB (USD)	(n=20) 6584.08 ± 5831.56 (200.67 ± 177.74)	-1838.15 (-56.02)	0.209	(n=12) 5953.11 ± 4620.21 (181.44 ± 140.82)	6388.92 (144.28)	0.074	(n=9) 10,862.70 ± 6970.38 (331.08 ± 212.44)	-4805.13 (-146.46)	0.109	(n=41) 7338.62 ± 5949.43 (223.67 ± 181.33)	-84.32 (-2.57)	0.954
Year 2 THB (USD)	(n=21) 4745.93 ± 3014.80 (144.65 ± 91.88)			(n=12) 12,342.03 ± 10,834.89 (376.16 ± 330.23)			2758.04 (184.62 ± 84.06)			(n=40) 7254.30 ± 7110.02 (221.10 ± 216.70)		
Total Cost												
Year 1 THB (USD)	4913.59 ± 4266.90 (149.76 ± 130.05)	-247.88 (-7.56)	0.529	5474.06 ± 5230.63 (166.84 ± 159.42)	1300.86 (39.65)	0.068	10,797.73 ± 8950.33 (329.10 ± 272.79)	-2615.31 (-79.72)	0.187	5701.34 ± 5490.35 (173.77 ± 167.34)	-4.10 (-0.13)	0.991
Year 2 THB (USD)	4665.71 ± 3027.52 (142.20 ± 92.27)			6774.92 ± 7976.68 (206.49 ± 243.12)			8182.41 ± 5235.81 (249.38 ± 159.58)			5697.24 ± 5437.23 (173.64 ± 165.72)		

Notes: 1 THB = 0.03048 USD (exchange rate from Bank of Thailand on March 30, 2020). Diff, difference which calculated by cost in year 1 minus cost in year 2; P, p-value; CKD stage 3a, GFR 45–59 mL/min/1.73 m²; CKD stage 3b, GFR 30–44 mL/min/1.73 m²; CKD stage 4, GFR 15–29 mL/min/1.73 m².

Abbreviations: SD, standard deviation; CKD, chronic kidney disease.

Table 3 Treatment Costs by Patients' Characteristics (THB per Year)

Characteristics	Ambulatory Cost (n=212)			Hospitalization Cost (n=41)			Total Cost (n=212)		
	Mean ± SD	Difference	P-value	Mean ± SD	Difference	P-value	Mean ± SD	Difference	P-value
Age (years)									
<65	4902.94 ± 3405.33	-907.75	0.018*	9545.47 ± 8838.39	-2918.74	0.181	6327.64 ± 7220.89	-915.70	0.260
≥65	3995.19 ± 2083.03			6626.73 ± 4648.88			5411.94 ± 4472.62		
Length of Stay (days)									
0	4002.04 ± 1940.27	Reference	-	-	-	-	4002.04 ± 1940.27	Reference	-
1-7	4547.37 ± 4586.44	545.32	0.428	3903.96 ± 1550.77	2465.14	0.182	9979.88 ± 5068.61	5977.84	<0.001*
≥8	10,715.47 ± 7697.89	6713.43	<0.001*	6369.09 ± 5265.09			29,173.01 ± 9021.07	25,170.97	<0.001*
Ambulatory Visit									
1-4	2527.25 ± 1483.11	Reference	-	3903.95 ± 3101.54	Reference	-	3065.73 ± 2233.43	Reference	-
5-7	4176.08 ± 2013.18	1648.83	0.003*	6369.09 ± 5265.09	2465.14	0.447	5046.68 ± 3807.18	1980.95	0.142
≥8	5773.50 ± 3792.00	3246.25	<0.001*	9125.26 ± 6710.31	5221.31	0.114	9506.57 ± 8789.96	6440.84	<0.001*
CKD Stage									
G3a	3843.01 ± 1697.63	Reference	-	6584.08 ± 5831.56	Reference	-	4913.59 ± 4266.90	Reference	-
G3b	4407.83 ± 3238.75	564.82	0.299	5953.11 ± 4620.21	-630.97	0.767	5474.06 ± 5230.63	560.47	0.076
G4	6353.90 ± 3551.43	2510.89	<0.001*	10,862.70 ± 6970.38	4278.62	0.073	10,797.73 ± 8950.33	5884.14	<0.001*
Diabetes Mellitus									
No	3352.95 ± 1390.18	2661.82	<0.001*	5598.83 ± 3794.46	3754.28	0.042*	4245.52 ± 3133.92	4170.73	<0.001*
Yes	6014.77 ± 3355.36			9353.10 ± 7340.05			8416.24 ± 7564.27		
Dyslipidemia									
No	3759.87 ± 1924.76	1054.36	0.003*	7121.05 ± 6438.63	594.69	0.762	5490.22 ± 5624.31	426.26	0.573
Yes	4814.23 ± 3063.93			7715.74 ± 5182.83			5916.48 ± 5368.77		
Hypertension									
No	3276.24 ± 2057.61	1071.54	0.151	4585.05 ± 4015.54	2970.95	0.412	4334.33 ± 3578.07	1456.31	0.355
Yes	4347.78 ± 2623.82			7556.00 ± 6060.59			5790.64 ± 5587.17		
SBP (mmHg)									
<140	4603.53 ± 3108.22	-577.52	0.068	7771.54 ± 6105.70	-682.68	0.728	5843.66 ± 5857.02	-321.81	0.703
≥140	4026.00 ± 2091.91			7088.86 ± 5964.83			5587.96 ± 5202.42		
DBP (mmHg)									
<90	4300.28 ± 2678.46	-35.81	0.953	7309.20 ± 6139.52	1635.26	0.609	5677.93 ± 5539.30	375.43	0.772
≥90	4264.48 ± 1701.44			8944.45 ± 4375.18			6053.37 ± 5237.80		
LDL (mg/dL)									
<100	4433.17 ± 2307.64	-368.19	0.507	5661.73 ± 3591.88	2750.09	0.151	5551.54 ± 3740.60	242.42	0.756
≥100	4188.65 ± 2772.00			8411.82 ± 6917.72			5793.96 ± 6347.66		

Table 4 Cost Model of Chronic Kidney Disease Treatment

	Unstandardized Coefficients		t	Sig.	95% Confidence Interval for B	
	B	SE			Lower Bound	Upper Bound
Constant	-5072.638	924.560	-5.487	<0.001	-6895.557	-3249.720
Length of stay	2191.776	65.023	33.708	<0.001	2063.573	2319.980
Ambulatory visit	456.560	50.936	8.963	<0.001	356.131	556.989
Diabetes mellitus	1290.311	303.550	4.251	<0.001	691.813	1888.808
Dyslipidemia	719.157	245.677	2.927	0.004	234.765	1203.550
Serum creatinine	1672.233	290.772	5.751	<0.001	1098.930	2245.536
Fasting blood glucose	9.982	4.259	2.344	0.020	1.584	18.380
Body mass index	86.737	28.777	3.014	0.003	29.998	143.476

Notes: Adjusted $R^2 = 0.906$; probability of F-test <0.001

Abbreviations: SE, standard error; Sig., significance.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no conflicts of interest in this work.

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