

1-1-2016

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### Recommended Citation

Sakulsupsiri, Anut and Sakthong, Phantipa (2016) "Cost-utility analysis of lifestyle modification program for Thai patients with metabolic syndrome," *Chulalongkorn Medical Journal*: Vol. 60: Iss. 1, Article 2.

DOI: <https://doi.org/10.58837/CHULA.CMJ.60.1.2>

Available at: <https://digital.car.chula.ac.th/clmjournal/vol60/iss1/2>

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## Cost-utility analysis of lifestyle modification program for Thai patients with metabolic syndrome

Anut Sakulsupsiri\*

Phantipa Sakthong\*\*

**Sakulsupsiri A, Sakthong P. Cost-utility analysis of lifestyle modification program for Thai patients with metabolic syndrome. Chula Med J 2016 Jan – Feb;60(1): 13 - 30**

- Background** : *Several foreign trials indicated clinical benefits and cost-effectiveness of the lifestyle programs for patients with metabolic syndrome (MetS) but the economic benefit of such programs has not yet been evaluated in Thailand.*
- Objective** : *This study was aimed to assess the cost-effectiveness of the lifestyle modification program for Thai MetS patients compared with the usual care.*
- Design** : *Secondary data analysis with modelling design.*
- Setting** : *Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University*
- Methods** : *A cost-utility analysis was performed based on Praphasil and colleagues' study of 90 MetS patients randomly allocated to the lifestyle modification program and control groups. A Markov micro-simulation model with the Differences-in-Differences method was used to predict the lifetime costs from societal perspective and quality-adjusted life years (QALYs) from patients' metabolic parameters. The 3% discount rate per annum was employed to discount the costs and outcomes. Parameter uncertainties were identified using a sensitivity analysis.*

\* Master of Science in Pharmacy Program in Clinical Pharmacy, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University

\*\* Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University

- Results** : *The lifetime costs calculated from patients' metabolic parameters tended to decrease from week 0 to week 12 in both groups. The decrease in the costs of intervention group was more than that of control group. Hence, the program could save the lifetime costs 2,280 baht and gain 0.0098 QALYs, compared with the usual care. From the sensitivity analysis, probability of cost-effectiveness of the program was up to 99.6% as determined by the Thai willingness to pay threshold.*
- Conclusion** : *The lifestyle modification program for MetS patients implemented in the Thai settings provide lower lifetime cost and higher outcome or QALY.*
- Keywords** : *Cost-utility analysis, cost-effectiveness analysis, lifestyle modification program, metabolic syndrome, Thailand.*

Reprint request: Sakthong P. Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok 10330, Thailand.

E-mail: phantipa.s@pharm.chula.ac.th

Received for publication. June 15, 2015.

อาณัติ สกุลทรัพย์ศิริ, พรรณพิพา ศักดิ์ทอง. การวิเคราะห์ต้นทุนอรรถประโยชน์ของ  
โปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิตสำหรับผู้ป่วยกลุ่มอาการเมแทบอลิกชาวไทย.  
จุฬาลงกรณ์เวชสาร 2559 ม.ค. – ก.พ; 60(1): 13 – 30

- เหตุผลของการทำวิจัย** : หลายงานวิจัยในต่างประเทศพบว่าโปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิตสำหรับผู้ป่วยกลุ่มอาการเมแทบอลิกมีประโยชน์ทางคลินิกและมีความคุ้มค่าทางเศรษฐศาสตร์ แต่ยังไม่พบการประเมินความคุ้มค่าทางสาธารณสุขของโปรแกรมดังกล่าวในประเทศไทยมาก่อน
- วัตถุประสงค์** : การวิจัยครั้งนี้จึงมีวัตถุประสงค์เพื่อประเมินความคุ้มค่าของโปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิตสำหรับผู้ป่วยกลุ่มอาการเมแทบอลิกชาวไทยเปรียบเทียบกับ การรักษาตามปกติ
- รูปแบบการวิจัย** : การวิเคราะห์ข้อมูลทุติยภูมิร่วมกับการใช้แบบจำลอง
- สถานที่ทำการวิจัย** : ภาควิชาเภสัชกรรมปฏิบัติ คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
- วิธีการวิจัย** : การวิจัยครั้งนี้เป็นการวิเคราะห์ต้นทุนอรรถประโยชน์ โดยใช้เทคนิค Markov micro-simulation ร่วมกับ Differences-in-Differences method ในการคาดการณ์ต้นทุนในมุมมองของสังคมและปัญหาที่เกิดขึ้นจากองค์ประกอบทางเมแทบอลิกของผู้เข้าร่วมงานวิจัย 90 รายจากการศึกษาของ อรรถวน ประภาศิลป์และคณะ ในกลุ่มที่เข้าร่วมโปรแกรมและกลุ่มที่ได้รับการรักษาตามปกติ กำหนดอัตราลดร้อยละ 3 ต่อปีในการปรับลดต้นทุนและผลลัพธ์ อีกทั้งวิเคราะห์ความไวเพื่อให้เห็นถึงผลที่เกิดขึ้นจากความไม่แน่นอนของข้อมูลที่น่ามาวิเคราะห์ในแบบจำลอง
- ผลการวิจัย** : ต้นทุนตลอดชีพของทั้งสองกลุ่มที่คำนวณจากองค์ประกอบทางเมแทบอลิก ในสัปดาห์ที่ 12 มีแนวโน้มลดลงเมื่อเปรียบเทียบกับต้นทุนในสัปดาห์แรก ซึ่งกลุ่มทดลองมีต้นทุนลดลงมากกว่ากลุ่มควบคุม ดังนั้นโปรแกรมนี้สามารถประหยัดต้นทุนตลอดชีพได้ 2,280 บาท และเพิ่มปีสุขภาวะได้ 0.0098 ปี เมื่อเปรียบเทียบกับ การรักษาตามปกติ และจากการวิเคราะห์ความไวพบว่า โปรแกรมนี้มีโอกาสที่จะคุ้มค่าถึงร้อยละ 99.6 เมื่อพิจารณาจากเพดานความเต็มใจที่จะจ่ายของสังคมไทย
- สรุป** : โปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิตสำหรับผู้ป่วยกลุ่มอาการเมแทบอลิก มีความคุ้มค่า สามารถลดต้นทุนตลอดชีพและเพิ่มจำนวนปีสุขภาวะได้
- คำสำคัญ** : การวิเคราะห์ต้นทุนอรรถประโยชน์, การวิเคราะห์ต้นทุนประสิทธิผล, โปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิต, กลุ่มอาการเมแทบอลิก, ประเทศไทย.

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities induced by insulin resistance.<sup>(1, 2)</sup> The major features of MetS include central obesity, hypertriglyceridemia, hypertension, hyperglycemia, and low level of high-density lipoprotein (HDL). Thus, MetS increases the risk of type 2 diabetes (T2DM), cardiovascular disease (CVD),<sup>(1, 3)</sup> and economic burden.<sup>(4)</sup> The disparity of MetS prevalence around the world was reported by Cameron *et al.*<sup>(5)</sup> They suggested that the prevalence variations may stem from the differences in patients' genetic background, population age, gender structure, the level of physical activity, or nutritional status in various countries. An increase in the overweight, obesity, sedentary lifestyles, and rapid urbanization has been associated with the escalation of MetS incidence worldwide.<sup>(6, 7)</sup> MetS is therefore a crucial public health problem nowadays.<sup>(8)</sup>

Regarding MetS management, drug therapy can be used to adjust the metabolic components, e.g., blood pressure or glucose, but a bariatric surgery is indicated for some cases.<sup>(1)</sup> Additionally, a lifestyle intervention is applicable to promote healthy eating habits, suitable exercise, and weight reduction in patients. The lifestyle modification is usually a prime MetS management, as it improves the insulin sensitivity and simultaneously reduces all metabolic risk factors.<sup>(1, 9)</sup> In addition, many studies pointed out that lifestyle modification programs are not only clinically effective, but also cost-effective for MetS patients in primary care settings.<sup>(10 - 12)</sup>

In Thailand, the MetS prevalence for adults aged 35 years and over is 32.6% based on the ATP III criteria.<sup>(13)</sup> The tendency is dramatically increasing on account of sedentary lifestyles and unhealthy

consumption behaviors.<sup>(14-17)</sup> The government sector, i.e., the Ministry of Public Health, has been aware of the MetS threat and initiated the Diet and Physical Activity Clinic (DPAC), in collaboration with the Network of Fatless Belly Thais, to be established in public hospitals since 2006.<sup>(18)</sup> The objective of DPAC is to promote the healthy behaviors of Thai population in terms of healthy food, exercise, and emotion or behaviors.<sup>(19)</sup> Several Thai researchers have already assessed lifestyle programs available for MetS patients<sup>(20 - 24)</sup> and found they could improve patients' metabolic parameters and reduce CVD risks. However, the cost-utility issue remained unexplored in these studies. This study hence aimed to assess the cost-utility of lifestyle modification program, which was a lifestyle alteration program that partly adopted the DPAC procedures.

## Methods

This cost-utility analysis (CUA) based on the intervention study of Praphasil and her team regarding the self-management program (SMP) for Thai MetS patients.<sup>(22)</sup> The study was selected, as it provided complete clinical data, especially for CVD risks and total cholesterol levels. The original findings revealed favorable therapeutic outcomes, but no result on economic outcomes was reported. Details of the methodology are summarized below.

## Overview of intervention study

In the intervention study, there were two groups of MetS patients, i.e., the control and intervention groups. The control group received the usual care provided by the nurses or doctors as usual, whereas the intervention group obtained normal care

and self-management activities, as part of the self-management program (SMP). The SMP was set up in a community hospital and two health promoting hospitals in Kanchanaburi Province, Thailand. It was run by a nurse and her assistants. The program activities were created based on Creer's self-management theory and Bandura's self-efficacy theory.<sup>(22)</sup> A total of 46 and 44 patients were randomly allocated to the intervention and control groups, respectively. The characteristics and metabolic parameters of 90 patients are shown in Table 1. All patients were required to join in the following activities:

Week 0: The anthropometric data, e.g., waist circumference and height, and metabolic indicators were measured for all patients. They were also requested to complete a self-management questionnaire. The control group then received general advice or usual care, such as weight control and exercise, whereas the intervention participated in an educational session to get information about MetS, metabolic control, and self-management skills. After then, the patients in the intervention group were asked to attend a nutrition session and received the SMP manual.

Week 1: The intervention group joined in an exercise session.

Week 4: All patients were invited to fill out the self-management questionnaire.

Weeks 6 and 9: Each patient in the intervention group was telephoned by the researcher to check for their retention of healthy behaviors using the self-management skills and for any problems arisen.

Week 12: Anthropometric data, metabolic parameters, and the self-management questionnaire

were re-measured in both groups to identify any changes from the baseline (week 0).

### **Cost-utility analysis**

The cost-utility analysis (CUA) was presented by an incremental cost-utility ratio (ICUR), which is the cost differences between two study groups (self-management program vs. usual care) divided by the differences in QALYs. The CUA in this study was computed according to the societal perspective. A Markov micro-simulation model was utilized to predict the lifetime costs and QALYs for individual patients starting from week 0 or week 12 until death.

An inclusive introduction to Markov modelling has been described by Sonnenberg and Beck.<sup>(25)</sup> In brief, Markov model is suitable for predicting the progression of chronic diseases. The model can also extrapolate the long term costs and outcomes (e.g., QALYs) from the clinical trials. The interesting diseases are divided into different health states. These states should be clinically and economically important events in the disease process. The movement between these states are assigned by the transition probabilities over a discrete time period called Markov cycle. The costs spending in one cycle and utilities or quality of life in each state of the model are attached to the particular states. The model is run over a large number of cycles. The lifetime costs and QALYs are obtained by summing across those cycles. In this study, the termination ages for males and females were assumed being equal to the life expectancies of 72 and 79 years old based on the Thai statistics report.<sup>(26)</sup> A discount rate of 3% per annum was applied to the costs and QALYs as suggested by WHO and Thailand's Health Technology Assessment guidance.<sup>(27, 28)</sup>

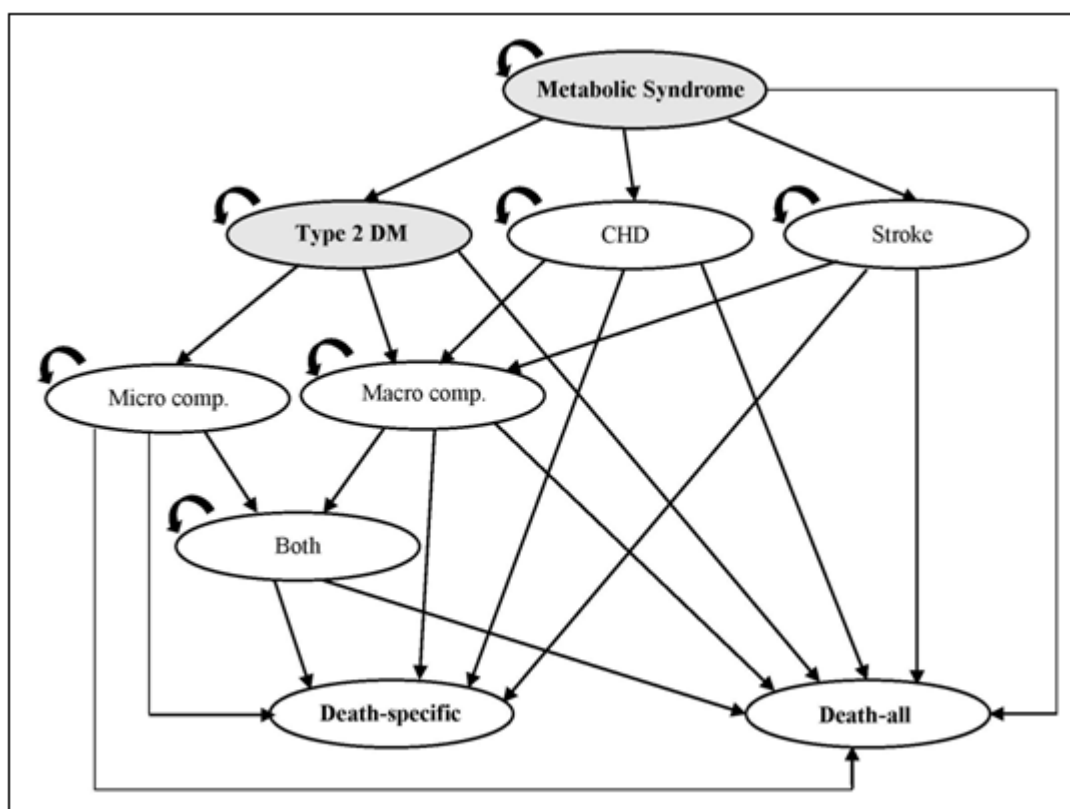
**Table 1.** Patients' characteristics and metabolic parameters.

Characteristic	Intervention group <sup>a</sup> (n = 46)	Control group <sup>a</sup> (n = 44)	p-value
Age (year)	54.98 ± 1.16	56.82 ± 0.92	0.221 <sup>T</sup>
Male; n (%)	2 (4.35)	7 (15.91)	0.087 <sup>F</sup>
Diabetes; n (%)	20 (43.48)	32 (72.73)	0.005 <sup>C*</sup>
Hypertension; n (%)	33 (71.74)	36 (81.82)	0.258 <sup>C</sup>
Body mass index (kg/m <sup>2</sup> )			
Week 0	28.74 ± 0.77	26.67 ± 0.65	0.044 <sup>T*</sup>
Week 12	27.90 ± 0.70	26.66 ± 0.61	0.016 <sup>A*</sup>
Waist circumference (cm)			
Week 0	97.16 ± 1.51	93.71 ± 1.18	0.078 <sup>T</sup>
Week 12	93.65 ± 1.42	93.97 ± 1.26	0.001 <sup>A*</sup>
Fasting blood glucose (mg/dL)			
Week 0	119.33 ± 6.29	131.95 ± 6.20	0.157 <sup>T</sup>
Week 12	114.41 ± 6.63	132.05 ± 7.49	0.304 <sup>A</sup>
Total cholesterol (mg/dL)			
Week 0	231.26 ± 7.83	203.41 ± 6.54	0.008 <sup>T*</sup>
Week 12	229.50 ± 8.29	211.39 ± 7.01	0.899 <sup>A</sup>
High-density lipoprotein (mg/dL)			
Week 0	52.00 ± 1.79	47.50 ± 1.67	0.069 <sup>T</sup>
Week 12	57.20 ± 1.55	49.11 ± 1.31	0.001 <sup>A*</sup>
Low-density lipoprotein (mg/dL)			
Week 0	147.49 ± 7.08	126.18 ± 4.27	0.012 <sup>T*</sup>
Week 12	144.63 ± 7.30	129.69 ± 6.88	0.650 <sup>A</sup>
Triglyceride (mg/dL)			
Week 0	159.09 ± 8.54	168.27 ± 10.74	0.503 <sup>T</sup>
Week 12	132.85 ± 8.38	160.41 ± 13.13	0.097 <sup>A</sup>
Systolic blood pressure (mmHg)			
Week 0	135.00 ± 1.15	134.32 ± 1.32	0.697 <sup>T</sup>
Week 12	123.26 ± 2.90	133.18 ± 1.71	0.002 <sup>A*</sup>
Diastolic blood pressure (mmHg)			
Week 0	83.26 ± 1.08	85.23 ± 1.15	0.215 <sup>T</sup>
Week 12	79.13 ± 1.28	85.91 ± 0.99	0.001 <sup>A*</sup>


<sup>a</sup> Presented as mean ± SE, otherwise specified<sup>A</sup> ANCOVA; <sup>C</sup> Chi-square; <sup>F</sup> Fisher's Exact Test; <sup>T</sup> Independent t-test; \* Statistically significant with  $p < 0.05$

The Markov model was the backbone of the study as shown in Figure 1. The model was adapted from Feldman *et al.*<sup>(10)</sup> and checked for the face validity by four endocrinologists and one cardiologist. It comprised the Metabolic Syndrome state plus six complication states and two types of deaths. The entire Markov model was analyzed using Microsoft Excel 2013 (Microsoft Corp., Bangkok, Thailand). All states were presented by the ovals and mutually exclusive with collective, exhaustive nature. The cycle length of changing from one state to another was

determined in one year. The assumption of this model was that the metabolic parameters at week 12 would be extended to one year and then returned to the baseline (week 0) values before receiving the SMP intervention or usual care again in the following years. In Figure 1, the arrows signified the possible transition of the health states. The transition probabilities in the model were calculated from the metabolic parameters of individual participants or relevant incidences found in Thailand.



**Figure 1.** Markov model

Type 2 DM = type 2 diabetes mellitus without complications; Micro comp. = microvascular complications; Macro comp. = macrovascular complications; CHD = coronary heart disease; Stroke = ischemic or hemorrhagic stroke; Both = both microvascular and macrovascular complications; Death-specific = death caused by the specific disease; Death-all = death from all causes;  = probability of staying at the same state; arrow (→) connecting two different states to indicate the state transition.



From Metabolic Syndrome at the outset, it may progress to Type 2 DM, CHD, or Stroke (ischemic or hemorrhagic types). If patients with coronary heart disease (CHD) or stroke experienced diabetes mellitus, their health states would be considered as *Macro comp.* (type 2 DM with macrovascular complications). Since in this study there were MetS patients with or without type 2 DM, the model was run from two starting points, i.e., Metabolic Syndrome and Type 2 DM states. All states, except Metabolic Syndrome and Type 2 DM, could end up with specific death (Death-specific) caused by a particular health state or any types of death (Death-all).

Since some patients' baseline parameters, namely the body mass index, total cholesterol, and low-density lipoprotein, were significantly different between the two groups, the Differences-in-Differences (DD) method was adopted to find the intervention effects from the unequal baseline data of the two groups. The DD method follows the assumption of common trends that states the trends of outcomes would be the same in both groups in case of the intervention absence and the deviation from these common trends is affected by the intervention given.<sup>(29)</sup> In this study, the outcomes were costs and QALYs. As for the control and intervention groups, the metabolic components of each patient in weeks 0 and 12 were calculated for their costs and QALYs. Then the costs and QALYs in week 12 were subtracted from those in week 0 of each group. After then, the subtraction products from both groups were further subtracted to yield between-group differences or DD results that were utilized for all cost-utility analysis.

To analyze the cost-utility of the SMP, the best available incidences, costs, and utility weights from various Thai literatures<sup>(22, 26, 30-40)</sup> were entered into the Markov model. The data were described below:

**Transition probabilities:** A probability of each participant for developing T2DM was calculated from their metabolic components by using the risk equation of Akeplakorn *et al.*<sup>(30)</sup> which was developed from Thai samples, while the CVD and macrovascular risks were computed by Khonputsu's equation.<sup>(33)</sup> This equation was recalibrated from the Framingham's equation by using the Thai epidemiologic data. A probability for developing microvascular complications was derived from the study of Potisat *et al.*<sup>(35)</sup> which included the risks of retinopathy and nephropathy. The patients with CVD or stroke would transit to the *Macro comp.* state with the risks calculated from Akeplakorn's equation.<sup>(30)</sup> The risks of death from diabetic complications were derived from the study of Pratipanawat *et al.*<sup>(36)</sup> while the probability of death from all causes, CHD, and stroke were adopted from the Thai public health statistics.<sup>(26)</sup>

**Cost data:** The costs of SMP and usual care were computed from the activities reported in the literature and interviews with the SMP organizer. The costs included staff wages, travelling expenses, telephone bill, productivity losses, program manuals, and medical devices. Since the SMP program was assumed to occur every year until the patients die, the costs of the program and the usual care were calculated based on a yearly basis. The program costs were divided into two periods of time. The first year cost was involved in the investment of devices, such as scale, sphygmomanometer, and pedometers; the devices were supposed to be used for at least

five years.<sup>(41)</sup> The second to fifth year costs excluded the device expenditures but embraced other costs. As for the sixth year, the costs of the program and usual care would restart with the same costs as the first year and so on. All diabetic costs were gathered from the study of Riewpaiboon *et al.*<sup>(37)</sup> which was the first study carried out in Thailand. The costs of CHD and stroke were derived from the data of Anukoolsawat *et al.*<sup>(31)</sup> and Khiaocharoen *et al.*<sup>(32)</sup>, respectively. All costs were accounted from societal perspective in 2013 Thai baht.

**Utility data:** The utility data on all health states were gathered from the EuroQoL (EQ-5D-3L) instrument with the Thai preference weights. The utility of participants with MetS and T2DM was from the result of Kimman *et al.*<sup>(34)</sup> The data of Kimman's study were derived from a large cohort study in Thailand. The utility of CHD, stroke, T2DM and its complications was from the study of Saiguay *et al.*<sup>(38)</sup>, Wannasiri *et al.*<sup>(40)</sup>, and Sakthong *et al.*<sup>(39)</sup>, respectively. These utility results were collected from the patients with specific disease in Thailand.

In this study, the cost-utility analysis was performed with two aspects: base case and sensitivity analyses. The former was to report an ICUR calculated from the means of costs, utilities, and transition probabilities, whereas the latter illustrated the effects of parameter uncertainties. To estimate the 95% confidence interval (CI) of the base case data, a non-parametric bootstrapping with 1,000 samples was generated by Microsoft Excel 2013. The sensitivity analysis was categorized into two types: deterministic and probabilistic. The deterministic sensitivity analysis was accomplished by varying the situations, i.e., MetS with or without diabetes, time horizon (life expectancies until 120 years), and discount rates (0%

vs. 6%), to examine the uncertainties of the results. Similarly, the probabilistic sensitivity analysis was conducted by the Monte Carlo simulation of 1,000 iterations. To interpret the cost-utility result, ICUR was compared with the willingness to pay (WTP) threshold for Thailand, which was 160,000 baht/QALY gained.<sup>(27)</sup> If the ICUR was lower than this value, the SMP program would be regarded as cost-effective.

## Results

### Study parameters

The data input for the Markov model indicated three interesting health states, i.e., Type 2 DM, CHD, and Stroke. The yearly probabilities of developing type 2 diabetes decreased from weeks 0 to 12 by 2.69% (0.19463 vs. 0.18940) in the intervention group and 3.81% (0.18217 vs. 0.17523) in the control. For the yearly risks of CHD and stroke, the tendency was rather opposite. The reduction in the yearly risks of CHD was 12.96% and 1.52% found in the intervention and control groups. In case of developing stroke, the risks reduced by 18.33% and 9.09% in the two groups.

### Base case

The base case results are delineated in Table 2. The lifetime costs of the intervention group decreased from weeks 0 to 12 approximately by -3,630 baht (95% CI: -6,200 to -1,640), whereas in the control was -1,360 baht (95% CI: -4,280 to 930). When taking the change in costs into account, it rendered the between-group difference (or Differences-in-Differences, DD) of -2,280 baht (95% CI: -5,640 to 1,220). Regarding QALYs, the DD value was 0.0098 (95% CI: -0.0011 to 0.0203). The negative resultant ICUR was interpreted as cost-effective from the societal perspective.

Table 2. Base case results for the cost-utility analysis.

Result <sup>a</sup>	Value (95% CI) <sup>b</sup>			
	Intervention group (n = 46)	Within-group difference	Control group (n = 44)	Within-group difference Differences
Lifetime cost (baht) <sup>c</sup>				
Week 0	559,830 (505,730 to 612,060)	-3,630 (-6,200 to -1,640)	554,350 (493,520 to 615,970)	-1,360 (-4,280 to 930)
Week 12	556,200 (506,180 to 614,490)		553,000 (492,790 to 607,160)	-2,280 (-5,640 to 1,220)
Quality-adjusted life year (QALY)				
Week 0	10.7642 (10.0991 to 11.4673)	0.0120 (0.0047 to 0.0195)	9.8335 (9.2429 to 10.4460)	0.0022 (-0.0040 to 0.0105)
Week 12	10.7762 (10.1301 to 11.4046)		9.8358 (9.2797 to 10.3708)	0.0098 (-0.0011 to 0.0203)

<sup>a</sup>Result per participant  
<sup>b</sup>Estimated by the bootstrapping method  
<sup>c</sup>Rounded up to the nearest whole number

### Deterministic sensitivity analysis

Regarding the deterministic sensitivity results in Table 3, the SMP was also cost-effective when patients' ages were extended from the termination age (72 for males and 79 for females) to 120 years. From the provider's point of views, the lifetime costs (530 baht) were slightly reduced with the same QALYs gained as the societal perspective, thus suggesting the SMP was cost-effective from both perspectives. Considering a subgroup analysis, the SMP for diabetic patients ( $n = 20$ ) was construed as cost-effective, but the program for those without diabetes ( $n = 26$ ) needed to pay 848,440 baht per QALY gained. Additionally, the annual undiscounted (0%) or 6% discount rate provided a cost-effective program. However, with the 6% rate the program providers were able to save less money and gain less QALYs.

### Probabilistic sensitivity analysis

The results of probabilistic sensitivity analysis were reported by the cost-effectiveness plane and the acceptability curve as illustrated in Figure 2. From the Monte Carlo simulation, the plane with 1,000 ICURs implied that the SMP could increase the QALYs from 0.0056 to 0.0142 and impact on the lifetime costs ranging from -13,200 to 2,020 baht (data not included in Figure 2a). Almost all gray dots (or ICURs), except four of them, gathered around the base case value and below the willingness to pay (WTP) line. This signified the SMP program was cost-effective whether being negative or positive cost impacts. In Figure 2b, the WTP was varied from 0 to 180,000 baht/QALY gained. As determined by the Thai WTP threshold (160,000 baht/QALY gained), the SMP was cost-effective up to 99.6%. If the society was not willing to pay for the program (0 baht/QALY gained), the probability of cost-effectiveness would still be 88.3%.

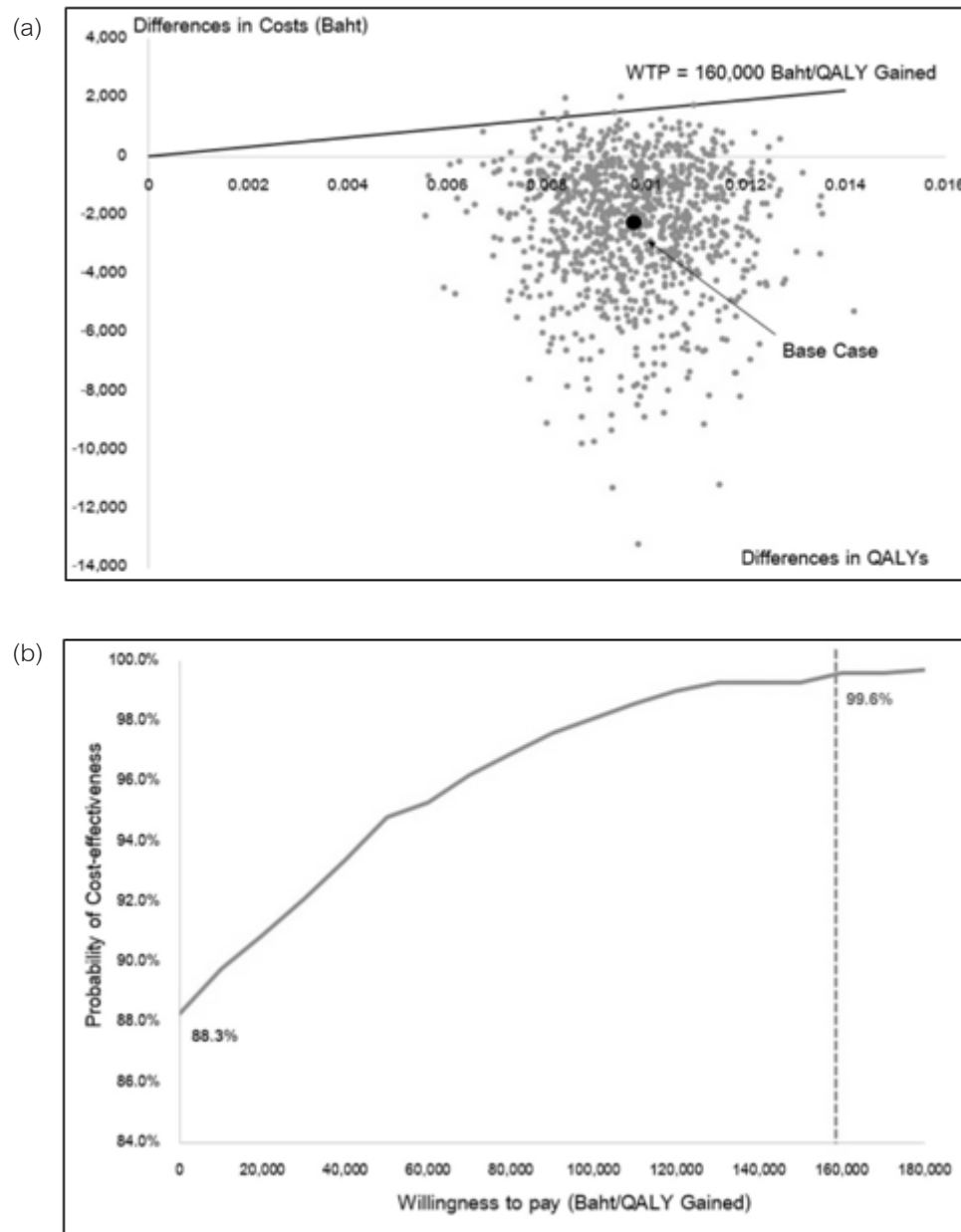
**Table 3.** Deterministic sensitivity results.

Data	Lifetime Cost (baht) <sup>a,b</sup>	QALY <sup>b</sup>	ICUR <sup>a</sup> (baht/QALY gained)
Societal perspective			
Base case for all patients (from Table 2)	-2,280	0.0098	Dominant <sup>c</sup>
Patients with extended termination age of 120 years	-3,250	0.0156	Dominant <sup>c</sup>
Patients with diabetes ( $n = 20$ vs. $n = 32$ )	-1,600	0.0070	Dominant <sup>c</sup>
Patients without diabetes ( $n = 26$ vs. $n = 12$ )	1,220	0.0014	848,440
Discount rate per annum			
0%	-3,430	0.0149	Dominant <sup>c</sup>
6%	-1,590	0.0067	Dominant <sup>c</sup>
Provider perspective	-530	0.0098	Dominant <sup>c</sup>

<sup>a</sup> Rounded up to the nearest whole number

<sup>b</sup> Presented as the Differences-in-Differences value for the intervention and control groups between weeks 0 and 12

<sup>c</sup> Negative ICUR due to the lower lifetime cost and higher QALY of the intervention compared with the control group



**Figure 2.** Probabilistic sensitivity results.

(a) cost-effectiveness plane of the self-management program compared with the usual care (the black dot denoting the base case value) and (b) acceptability curve of the self-management program for metabolic syndrome patients compared with the usual care.

## Discussion

This was the first CUA of the self-management program (SMP) for metabolic syndrome patients in Thailand. The study was unique in that it made use of a micro-simulation technique that took account of all

factors, such as total cholesterol, body mass index (BMI), and systolic blood pressure, that affected the studied outcomes.<sup>(42)</sup> Thus, it was more accurate than a normal Markov model. Aside from that, all data entered into the model, except for the CVD risks<sup>(33)</sup>,

were obtained from various studies in Thai samples. This mirrored the authentic findings in the Thai population. Although the CVD risk equation was derived from the Framingham's, Khonputsa and her team<sup>(33)</sup> previously recalibrated the equation using the Thai epidemiologic data.

The findings confirmed the SMP was cost-effective. The program demonstrated that it has lower lifetime cost and higher QALY. The base case results were comparable to other studies in the US or Sweden<sup>(10-12)</sup> that reported the lifestyle modification programs are cost-effective in comparison with the thresholds of US\$ 20,000 or € 20,000/QALY gained. Nevertheless, the sensitivity analysis disclosed the cost-ineffectiveness in the non-diabetic group. These results differed from the study of Saha and his colleagues<sup>(11)</sup> that found the ICER of this patient group, including the base case, was cost-effective. The self-management program was supposed to benefit all MetS patients with or without diabetes, but as pointed out above it was untrue in case of the non-diabetic subgroup. The possible explanations were as follows: Firstly, the Swedish study applied the three-year Björknäs intervention with more sessions and longer periods of active activities, but this CUA was performed based on only one study, which provided only three sessions within three months, and the proportion of diabetic patients at baseline was significantly different due to the effect of random error. Secondly, the diabetic equation used in this model was not sensitive enough to identify any changes in patients' metabolic parameters because the body mass index and waist circumference in the equation are in range, instead of actual values. Finally, relevant costs and data for the Markov model were

considerably different from the Scandinavian context.

However, in the non-diabetic subgroup the SMP could still help reduce 5,770 baht. This meant promoting the SMP among non-diabetic patients was also worthwhile, as it would decrease the future costs of the disease management.

The findings from the acceptability curve seemed to be promising, i.e., 88.3% of cost-effectiveness if without willingness to pay and 99.6% if paid with the threshold of 160,000 baht/QALY gained. This demonstrated the program capacity to modify patients' metabolic risk factors, thus leading to a reduction in the MetS complications and future costs. However, details of any lifestyle alteration programs need to be contemplated owing to their variations.<sup>(43, 44)</sup> For example, the DPAC program, which is the government policy, offered more sessions with longer intervention period, the program costs would be augmented. The probability of cost-effectiveness might be less than this SMP result.

Owing to the impermanent effects of all lifestyle modification programs, the retention time, or the duration of the program effects, is usually assumed. Few studies, e.g., the Diabetes Prevention Program (DPP)<sup>(45)</sup> and the Finnish Diabetes Prevention Study<sup>(46)</sup>, concluded that the effects of lifestyle interventions can retain more than one year. The SMP in this study provided only three intervention sessions in three months, whereas the DPP had 16 sessions in the core curriculum and the Finnish one provided 20 sessions. Therefore, in this study only one-year retention was assumed rather than longer periods like the two studies. Furthermore, the SMP was assumed to have a yearly activity and patients were self-motivated or self-managed to maintain their healthy

behaviors throughout the year. The program costs of the present study were thus separated into the first year and subsequent year costs (years 2 to 5) according to the 5-year service guidance.<sup>(41)</sup> This cost concept differed from other studies,<sup>(10, 11)</sup> as they treated the program costs as a one-time investment and assumed the program effects could sustain for 1-10 years or a lifelong period.

### **Limitations of the study**

In any intervention studies, the baseline characteristics should be equal so that the impacts of the SMP can be directly assessed, but it was not the case for this study. The Differences-in Differences method was therefore exploited to adjust the variations. As with most lifestyle intervention studies, this SMP study was not initially planned for an economic evaluation. Therefore, the program costs, as well as cost-of-illness and utility data, were not directly measured in the first place. Furthermore, the equation used to predict diabetic risks allowed only the body mass index (BMI) and waist circumference (WC) in ranges, i.e., BMI < 23, 23 – 27.5, or > 27.5 kg/m<sup>2</sup>, or WC > 90 cm for males or > 80 cm for females, to be substituted with corresponding coefficients. This made it not sensitive enough to detect any changes in diabetic risks from weeks 0 to 12, such as BMI = 24 or 27 kg/m<sup>2</sup> yielding the same risk scores. Ideally, the actual values should be put in the equation instead. In the Markov model, the risk of cancers was not included although Brown *et al.*<sup>(47)</sup> found lifestyle interventions can prevent some cancers in addition to MetS complications. The benefits of the SMP might be slightly underestimated given the findings of the study.

### **Conclusion**

This study could reveal the positive impacts of the lifestyle modification program for patients with metabolic syndrome on raised quality-adjusted life years (QALYs) and saving the future costs. The program can help minimize the complications and economic burden of the patients. Further studies are still required to evaluate the clinical benefits of the interesting programs in a large group of patients with metabolic syndrome or other chronic diseases. The metabolic parameters or clinical outcomes of these studies could be directly used to conduct the economic evaluation. If feasible, a large-scale assessment should be carried out in the Diet and Physical Activity Clinics (DPAC) across the country with more participants, several sessions, and longer intervention periods in order to reflect the actual benefits of the lifestyle modification program as a whole. Finally, a more sensitive diabetic equation, which may be developed in the future, should be employed to conduct the CUA.

### **Acknowledgements**

This study was funded by the National Research Council of Thailand (fiscal year 2015). We authors would like to acknowledge the assistance of the experts (i.e., Dr. Thiti Snabboon, Sunant Benjareanwong, Poj Tannirandorn, Prin Vathesatogkit, and Panudda Srichomkwan) for their useful recommendations and model validation. In addition, we would like to thank Miss Orawan Praphasil and other researchers for providing the necessary data for this study, and also health economists for their valuable suggestions.



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