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Cost-utility analysis of lifestyle modification program forThai patients with metabolic syndrome

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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.*

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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.*

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เหตุผลของการทำวิจัย : *หลายงานวิจัยในต่างประเทศพบว่าโปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิตสำหรับผู้ป่วยกลุ่มอาการเมแทบอลิกมีประโยชน์ทางคลินิกและมีความคุ้มค่าทางเศรษฐศาสตร์ แต่ยังไม่พบการประเมินความคุ้มค่าทางสาธารณสุขของโปรแกรมดังกล่าวในประเทศไทยมาก่อน*

วัตถุประสงค์ : *การวิจัยครั้งนี้จึงมีวัตถุประสงค์เพื่อประเมินความคุ้มค่าของโปรแกรมปรับเปลี่ยนรูปแบบการดำเนินชีวิตสำหรับผู้ป่วยกลุ่มอาการเมแทบอลิกชาวไทยเปรียบเทียบกับการรักษาตามปกติ*

รูปแบบการวิจัย : *การวิเคราะห์ข้อมูลทุติยภูมิร่วมกับการใช้แบบจำลอง*

สถานที่ทำการวิจัย : *ภาควิชาเภสัชกรรมปฏิบัติ คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

วิธีการวิจัย : *การวิจัยครั้งนี้เป็นการวิเคราะห์ต้นทุนอรรถประโยชน์ โดยใช้เทคนิค Markov micro-simulation ร่วมกับ Differences-in-Differences method ในการคาดการณ์ต้นทุนในมุมมองของสังคมและปีสุขภาวะที่เกิดขึ้นจากองค์ประกอบทางเมแทบอลิกของผู้เข้าร่วมงานวิจัย 90 รายจากการศึกษาของ อรวรรณ ประภาศิลป์และคณะ ในกลุ่มที่เข้าร่วมโปรแกรมและกลุ่มที่ได้รับการรักษาตามปกติ กำหนดอัตราลดร้อยละ 3 ต่อปีในการปรับลดต้นทุนและผลลัพธ์ อีกทั้งวิเคราะห์ความไวเพื่อให้เห็นถึงผลที่เกิดขึ้นจากความไม่แน่นอนของข้อมูลที่นำมาวิเคราะห์ในแบบจำลอง*

ผลการวิจัย : *ต้นทุนตลอดชีพของทั้งสองกลุ่มที่คำนวณจากองค์ประกอบทางเมแทบอลิก ในสัปดาห์ที่ 12 มีแนวโน้มลดลงเมื่อเปรียบเทียบกับต้นทุนในสัปดาห์แรก ซึ่งกลุ่มทดลองมีต้นทุนลดลงมากกว่ากลุ่มควบคุม ดังนั้นโปรแกรมนี้สามารถประหยัดต้นทุนตลอดชีพได้ 2,280 บาท และเพิ่มปีสุขภาวะได้ 0.0098 ปี เมื่อเปรียบเทียบกับการรักษาตามปกติ 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.[1, 2] 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),[1, 3] and economic burden.[4] The disparity of MetS prevalence around the world was reported by Cameron *et al.*[5] 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.[6, 7] MetS is therefore a crucial public health problem nowadays.[8]

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.[1] 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.[1, 9] 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.[10 - 12]

In Thailand, the MetS prevalence for adults aged 35 years and over is 32.6% based on the ATP III criteria.[13] The tendency is dramatically increasing on account of sedentary lifestyles and unhealthy consumption behaviors.[14-17] 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.[18] The objective of DPAC is to promote the healthy behaviors of Thai population in terms of healthy food, exercise, and emotion or behaviors.[19] Several Thai researchers have already assessed lifestyle programs available for MetS patients[20 - 24] 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.[22] 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.[22] 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.[25] 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.[26] 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.[27, 28]

Table 1. Patients' characteristics and metabolic parameters.

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

[a] Presented as mean ± SE, otherwise specified

[A] ANCOVA; [C] Chi-square; [F] Fisher's Exact Test; [T] 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*.[10] 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.

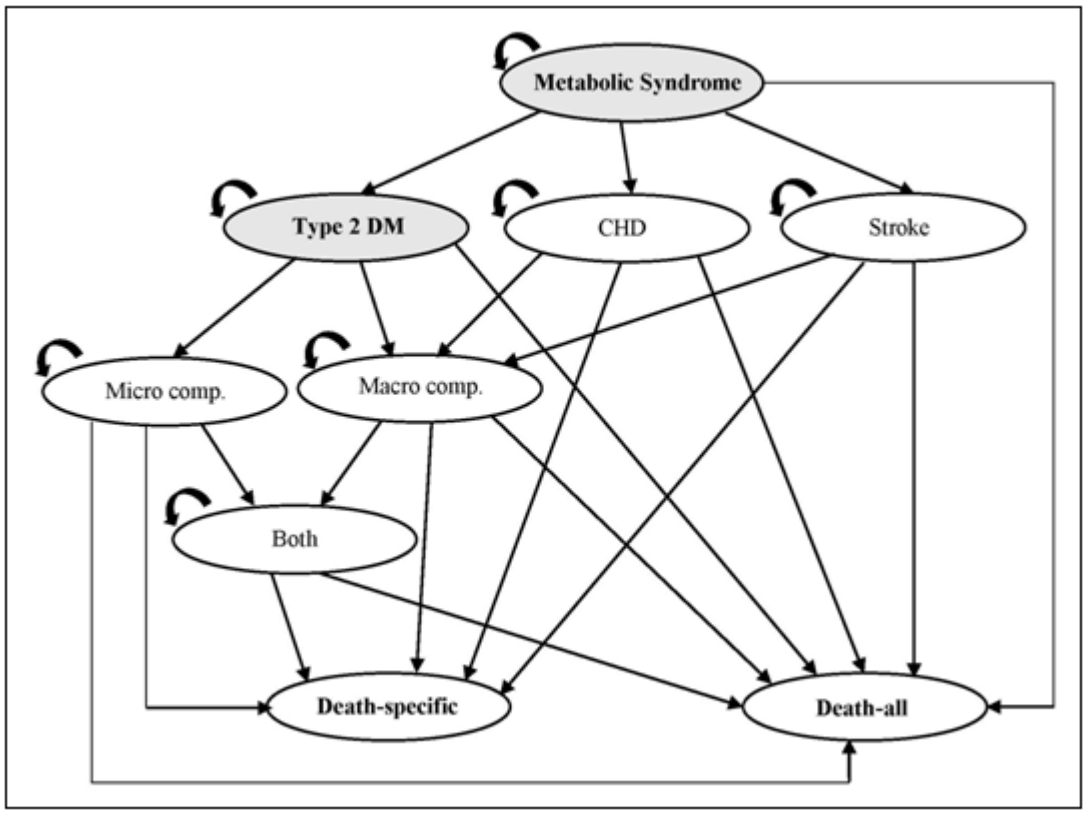

Figure 1. Markov model

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.[29] 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[22, 26, 30-40] 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.*[30] which was developed from Thai samples, while the CVD and macrovascular risks were computed by Khonputsa's equation.[33] 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.*[35]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.[30] The risks of death from diabetic complications were derived from the study of Pratipanawatr *et al.*[36] while the probability of death from all causes, CHD, and stroke were adopted from the Thai public health statistics.[26]

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.[41] 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.*[37] which was the first study carried out in Thailand. The costs of CHD and stroke were derived from the data of Anukoolsawat *et al.*[31] and Khiaocharoen *et al.*[32], 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.*[34] 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.*[38], Wannasiri *et al.*[40], and Sakthong *et al.*[39], 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.[27] 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[a]	Value (95% CI)[b]				
	Intervention group (n = 46)	**Within-group difference**	**Control group (n = 44)**	**Within-group difference**	**Differences-in-Differences**
Lifetime cost (baht)[c]					
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)	-2,280 (-5,640 to 1,220)
Week 12	556,200 (506,180 to 614,490)		553,000 (492,790 to 607,160)		
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)	0.0098 (-0.0011 to 0.0203)
Week 12	10.7762 (10.1301 to 11.4046)		9.8358 (9.2797 to 10.3708)		

[a]Result per participant

[b]Estimated by the bootstrapping method

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

[a] Rounded up to the nearest whole number

[b] Presented as the Differences-in-Differences value for the intervention and control groups between weeks 0 and 12

[c] Negative ICUR due to the lower lifetime cost and higher QALY of the intervention compared with the control group

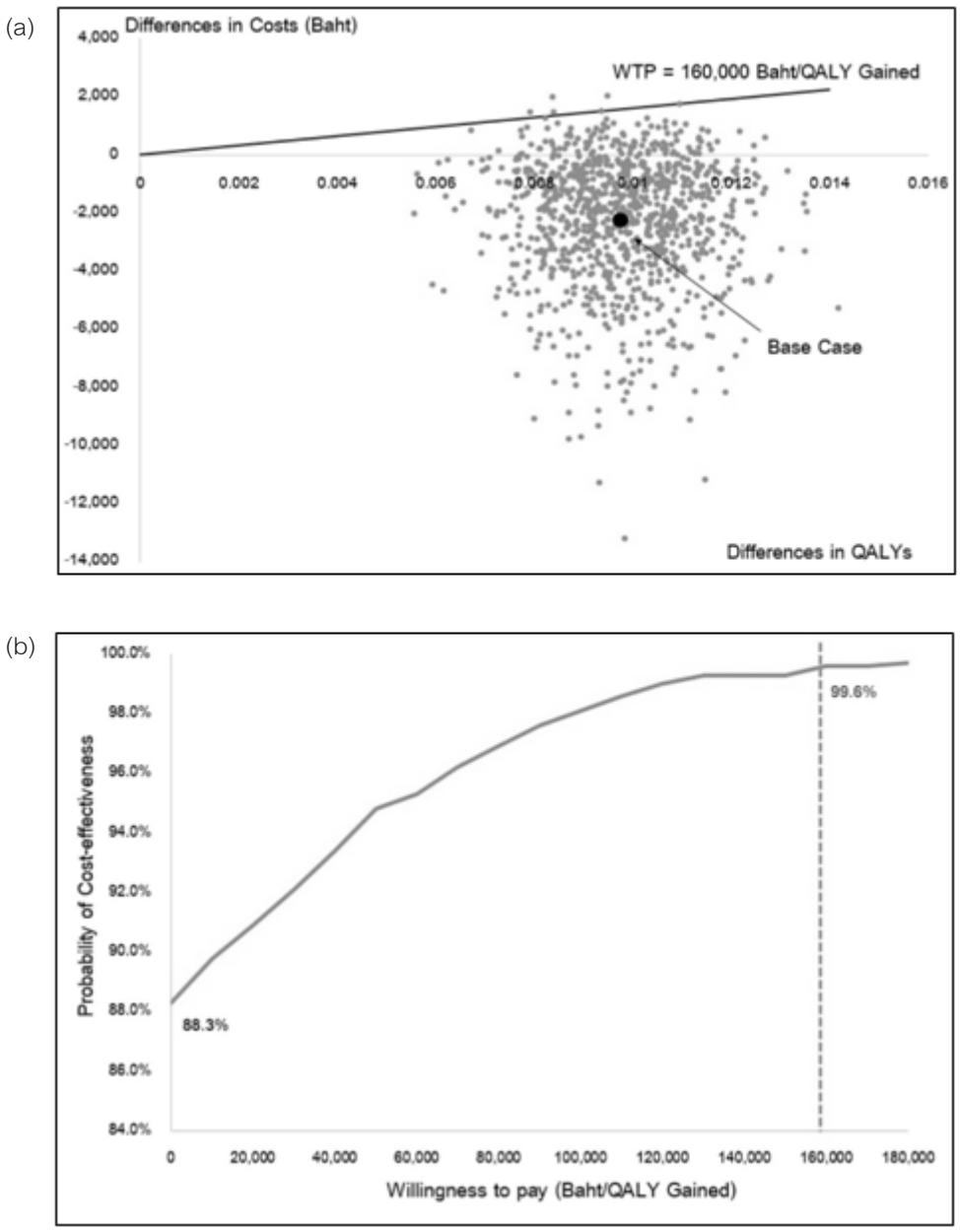

Figure 2. Probabilistic sensitivity results.
(a) cost-effectiveness plane of the self-management program compared with the usual care (the black dot denoting the base case value) and (b) acceptability curve of the self-management program for metabolic syndrome patients compared with the usual care.

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.[42] Thus, it was more accurate than a normal Markov model. Aside from that, all data entered into the model, except for the CVD risks[33],

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[33] 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[10-12] 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 [11] 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 contemplated owing to their variations.[43, 44] 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)[45] and the Finnish Diabetes Prevention Study[46], 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.[41] This cost concept differed from other studies,[10, 11] 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^2, 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^2 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.*[47] 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.

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References

1. Eckel RH. The metabolic syndrome. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. Harrison's Principle of Internal Medicine. Vol. 2. 18th ed. New York: McGraw-Hill, 2012: 1992-7
2. Wang M. Mechanisms and complications of metabolic syndrome. In: Wang M, ed. Metabolic Syndrome: Underlying Mechanisms and Drug Therapies. New Jersey: John Wiley & Sons, 2011: 179-97
3. Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 2005 Nov; 112(20):3066-72
4. Caro JJ, O'Brien JA, Hollenbeak CS, Spackman E, Ben Joseph R, Okamoto LJ, Paramore LC. Economic burden and risk of cardiovascular disease and diabetes in patients with different cardiometabolic risk profiles. Value in Health 2007;10(Suppl s1):S12-S20
5. Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence in worldwide populations. Endocrinol Metab Clin North Am 2004 Jun;33(2):351-75
6. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009 Oct;120(16):1640-5
7. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab 2008 Nov;93(11Suppl 1): s9-30
8. International Diabetes Federation. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. Belgium: IDF, 2006
9. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, et al. Diagnosis and management of the metabolic syndrome an American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005 Oct; 112(17):2735-52
10. Feldman I, Hellström L, Johansson P. Heterogeneity in cost-effectiveness of lifestyle counseling for metabolic syndrome risk groups-primary care patients in Sweden. Cost Eff Resour Alloc 2013;11(1):19
11. Saha S, Carlsson KS, Gerdtham U-G, Eriksson MK, Hagberg L, Eliasson M, Johansson P. Are lifestyle interventions in primary care cost-effective?–An analysis based on a Markov model, differences-in-differences approach and the Swedish Björknäs Study. PloS one 2013;8(11):e80672
12. Smith KJ, Hsu HE, Roberts MS, Kramer MK, Orchard TJ, Piatt GA, Seidel MC, Zgibor JC, Bryce CL. Cost-effectiveness analysis of efforts to reduce risk of type 2 diabetes and cardiovascular disease in southwestern

Pennsylvania, 2005-2007. Prev Chronic Dis 2010 Sep;7(5):A109

13. Aekplakorn W, Chongsuvivatwong V, Tatsanavivat P, Suriyawongpaisal P. Prevalence of metabolic syndrome defined by the International Diabetes Federation and National Cholesterol Education Program criteria among Thai adults. Asia Pac J Public Health 2011 Sep;23(5):792-800
14. Aekplakorn W, Hogan MC, Chongsuvivatwong V, Tatsanavivat P, Chariyalertsak S, Boonthum A, Tiptaradol S, Lim SS. Trends in obesity and associations with education and urban or rural residence in Thailand. Obesity (Silver Spring) 2007 Dec;15(12):3113-21
15. Kongsomboon K, Loetthiraphan S. Metabolic syndrome and related factors of Thai people on routine health check-up in Her Royal Highness Princess MahaChakriSirindhorn Medical Center. Songklanagarind Medical Journal 2010 May - Jun;28(3):145-53
16. Puttaruk P, Kongkhum S, Siripurkpong P. Prevalence and risk factors of metabolic syndrome among Thammasat university personnels. Songklanagarind Med J 2012 May - Jun;30(3):123-34
17. Santibhavank P. Prevalence of metabolic syndrome in NakhonSawan population. J Med AssocThai 2007 Jun;90(6):1109-15
18. Network of Fatless Belly Thais. Introduction to Network of Fatless Belly Thais [online]. The Royal College of Physicians of Thailand. 2011 [cited 2014 JUN 10]. Available from: http://www.raipoong.com/content/detail.php?slug=news_about&page_size=full_width&header=no
19. 7th Regional Health Promotion Center. DPAC clinic manual [online]. Department of Health. 2010 [cited 2014 JUN 6]. Available from:http://kcenter.anamai.moph.go.th/groupcontents.php?DEPT_ID=&group_id=165&base_gpid=66&SUBORG_ID=0
20. Jopa R, Suntayakorn C, Prachanban P, Wanitchakorn N. Effects of self-management program on controlling metabolic syndrome among middle age people. JNurs Health Sci 2010 May - Aug;4(2):36-44
21. Ponghan P, Suntayakorn C, Prachanban P, Wannapira W. Effects of health promotion program on metabolic syndrome preventive behaviors among health volunteers. J Nurs Health Sci 2011 Sep - Dec;5(3):54-64
22. Praphasil O, Wattana C, Tharavanij T. Effects of promoting self-efficacy in a self-management program on self-management behaviors, obesity, cardiovascular disease risk, and regression of metabolic syndrome among persons with metabolic syndrome. Nurs J 2013 Jan - Mar;40(1):34-48
23. Suksiri P. Metabolic syndrome reduction program for the SomdejPhranangchaosirikit hospital personnel. Chonburi: Naval Medical Department, 2010
24. Suwankruhasn N, Pothiban L, Panuthai S, Boonchuang P. Effects of a self-management support program for Thai people diagnosed with metabolic syndrome. Pac Rim Int JNursRes 2013 Oct - Dec;17(4):371-83
25. Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide.

Med Decis Making 1993 Oct - Dec;13(4): 322-38

26. Bureau of Policy and Strategy, Ministry of Public Health. Public health statistics. Bangkok: War Veterans Organization Press, 2012
27. Chaikledkaew U, Teerawattananon Y. Thai national health technology assessment guidelines 2013. Nonthaburi: Wacharin PP, 2014
28. Tan Torres Edejer T,Baltussen R, Adam T, Hutubessy R, Acharya A, Evans DB, Murray CJL. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: World Health Organization, 2003
29. Parallel worlds: Fixed effects, differences-in-differences, and panel data. In: Angrist JD, Pischke JS, eds. Mostly Harmless Econometrics: An Empiricist's Companion. New Jessey: Princeton University Press, 2009: 227-43
30. Aekplakorn W, Bunnag P, Woodward M, Sritara P, Cheepudomwit S, Yamwong S, Yipintsoi T, Rajatanavin R. A risk score for predicting incident diabetes in the Thai population. Diabetes Care 2006 Aug;29(8):1872-7
31. Anukoolsawat P, Sritara P, Teerawattananon Y. Costs of lifetime treatment of acute coronary syndrome at Ramathibodi Hospital. Thai Heart J 2006 Oct;19(4):132-43
32. Khiaocharoen O, Pannarunothai S, Riewpaiboon W, Ingsrisawang L, Teerawattananon Y. Economic evaluation of rehabilitation services for inpatients with stroke in Thailand: a prospective cohort study. Value in Health Regional Issues 2012;1(1):29-35
33. Khonputsa P, Veerman J, Bertram M, Yamwong S, Vathesatogkit P, Lim S, Vos T. Recalibration of the Framingham equations in the Thai population [onlinet]. Stanford Asia Health Policy Program Working Paper No. 22. 2011 [cited 2013 OCT 22]. Available from: http://dx.doi.org/10.2139/ssrn.1837702
34. Kimman M, Vathesatogkit P, Woodward M, Tai E-S, Thumboo J, Yamwong S, Ratanachaiwong W, Wee HL, Sritara P. Validity of the Thai EQ-5D in an occupational population in Thailand. Qual Life Res 2013 Aug;22(6): 1499-506
35. Potisat S, Krairittichai U, Jongsareejit A, Sattaputh C, Arunratanachote W. A 4-year prospective study on long-term complications of type 2 diabetic patients: the Thai DMS diabetes complications (DD. Comp.) project. J Med Assoc Thai 2013 Jun;96(6):637-43
36. Pratipanawatr T, Rawdaree P, Chetthakul T, Bunnag P, Ngarmukos C, Benjasuratwong Y, Leelawatana R, Kosachunhanun N, Plengvidhya N, Deerochanawong C, et al. Thailand Diabetic Registry cohort: predicting death in Thai diabetic patients and causes of death. J Med Assoc Thai 2010 Mar;93Suppl 3:S12-20
37. Riewpaiboon A, Chatterjee S, Riewpaiboon W, Piyauthakit P. Disability and cost for diabetic patients at a public district hospital in Thailand. Int J Pharm Pract2011 Apr;19(2): 84-93
38. Saiguay W, Sakthong P. The psychometric testing of the Thai version of the Health Utilities Index in patients with ischemic heart disease.

Qual Life Res2013 Sep;22(7):1753-9

39. Sakthong P, Charoenvisuthiwongs R, Shabunthom R. A comparison of EQ-5D index scores using the UK, US, and Japan preference weights in a Thai sample with type 2 diabetes. Health Qual Life Outcomes 2008; 6:71

40. Wannasiri Y, Kapol N. The health utility of stroke patients at Ratchaburi hospital. Region 4-5 Med J 2010 Apr - Jun;29(2):95-103

41. Public Accounting Standards and Policies Division. Accounting principles and policies for government departments no. 2 [online]. Office of Public Accounting Standards. 2003 [cited 2013 OCT 22]. Available from: http://finance.ipst.ac.th/assets/downloads/04.%E0%B8%AB%E0%B8%A5%E0%B8%B1%E0%B8%81%E0%B8%81%E0%B8%B2%E0%B8%A3%E0%B9%81%E0%B8%A5%E0%B8%B0%E0%B8%99%E0%B9%82%E0%B8%A2%E0%B8%9A%E0%B8%B2%E0%B8%A2%E0%B8%9A%E0%B8%B1%E0%B8%8D%E0%B8%8A%E0%B8%B5%E0%B8%AA%E0%B8%B3%E0%B8%AB%E0%B8%A3%E0%B8%B1%E0%B8%9A%E0%B8%AB%E0%B8%99%E0%B9%88%E0%B8%A7%E0%B8%A2%E0%B8%87%E0%B8%B2%E0%B8%99%E0%B8%A0%E0%B8%B2%E0%B8%84%E0%B8%A3%E0%B8%B1%E0%B8%90%20%E0%B8%89%E0%B8%9A%E0%B8%B1%E0%B8%9A%E0%B8%97%E0%B8%B5%E0%B9%88%202.pdf

42. Roberts M, Russell LB, Paltiel AD, Chambers M, McEwan P, Krahn M. Conceptualizing a model: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–2. Med Decis Making 2012 Sep;32(5): 678-89

43. Dunkley A, Charles K, Gray L, Camosso Stefinovic J, Davies M, Khunti K. Effectiveness of interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: systematic review and mixed treatment comparison meta analysis. Diabetes Obes Metab 2012 Jul;14(7):616-25

44. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. BMC Med 2012;10:138

45. Knowler WC, Fowler SE, Hamman RF, Christophi CA, Hoffman HJ, Brenneman AT, Brown-Friday JO, Goldberg R, Venditti E, Nathan DM. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009 Nov; 374(9702):1677-86

46. Lindström J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemiö K, Hämäläinen H, Härkönen P, Keinänen-Kiukaanniemi S, Laakso M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet 2006 Nov; 368(9548):1673-9

47. Brown CH, Baidas SM, Hajdenberg JJ, Kayaleh OR, Pennock GK, Shah NC, Tseng JE. Lifestyle interventions in the prevention and treatment of cancer. Am J Lifestyle Med 2009;3(5):337-34