

# Cost-Effectiveness Analysis of Thiazolidinediones in Uncontrolled Type 2 Diabetic Patients Receiving Sulfonylureas and Metformin in Thailand

Suphachai Chirakup, MS,<sup>1,2</sup> Nathorn Chaiyakunapruk, PharmD, PhD,<sup>1,3,4</sup> Usa Chaikledkeaw, PhD,<sup>5,6</sup> Petcharat Pongcharoensuk, PhD,<sup>5</sup> Boonsong Ongphiphadhanakul, MD,<sup>7</sup> Stephane Roze, MSc,<sup>8</sup> William J. Valentine, PhD,<sup>8</sup> Andrew J. Palmer, MD<sup>8</sup>

<sup>1</sup>Department of Pharmacy Practice, School of Pharmacy, Naresuan University, Phitsanulok, Thailand; <sup>2</sup>Faculty of Pharmacy, Payup University, Chiangmai, Thailand; <sup>3</sup>Ministry of Public Health, Bangkok, Thailand; <sup>4</sup>School of Population Health, The University of Queensland, Brisbane, Australia; <sup>5</sup>Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand; <sup>6</sup>Health Intervention and Technology Assessment Program, Ministry of Public Health, Bangkok, Thailand; <sup>7</sup>Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; <sup>8</sup>CORE-Center for Outcomes Research, Binningen/Basel, Switzerland

## ABSTRACT

**Objective:** The national essential drug committee in Thailand suggested that only one of thiazolidinediones be included in hospital formulary but little was known about their cost-effectiveness values. This study aims to determine an incremental cost-effectiveness ratio of pioglitazone 45 mg compared with rosiglitazone 8 mg in uncontrolled type 2 diabetic patients receiving sulfonylureas and metformin in Thailand.

**Methods:** A Markov diabetes model (Center for Outcome Research model) was used in this study. Baseline characteristics of patients were based on Thai diabetes registry project. Costs of diabetes were calculated mainly from Buddhachinaraj hospital. Nonspecific mortality rate and transition probabilities of death from renal replacement therapy were obtained from Thai sources. Clinical effectiveness of thiazolidinediones was retrieved from a meta-analysis. All analyses were based on the government hospital policymaker perspective. Both cost and outcomes were discounted with the rate of 3%. Base-case analyses were analyzed as incremental cost per quality-adjusted life year (QALY) gained. A series of sensitive analyses were performed.

**Results:** In base-case analysis, the pioglitazone group had a better clinical outcomes and higher lifetime costs. The incremental cost per QALY gained was 186,246 baht (US\$ 5389). The acceptability curves showed that the probability of pioglitazone being cost-effective was 29% at the willingness to pay of one time of Thai gross domestic product per capita (GDP per capita). The effect of pioglitazone on %HbA1c decrease was the most sensitive to the final outcomes.

**Conclusions:** Our findings showed that in type 2 diabetic patients who cannot control their blood glucose under the combination of sulfonylurea and metformin, the use of pioglitazone 45 mg fell in the cost-effective range recommended by World Health Organization (one to three times of GDP per capita) on average, compared to rosiglitazone 8 mg. Nevertheless, based on sensitivity analysis, its probability of being cost-effective was quite low. Hospital policymakers may consider our findings as part of information for the decision-making process.

**Keywords:** cost-effectiveness analysis, pioglitazone, rosiglitazone, thiazolidinediones.

## Introduction

Diabetes is a chronic disease associated with increases in morbidity, mortality, and health-care expenditures worldwide [1]. Prevalence of diabetes diseases in Thailand is also high. The estimated national prevalence of Diabetes in Thai adult (age over 35) in year 2000 was up to 9.6% or 2.4 million people [2]. The Diabetes Registry Project 2003 [3] reported that among 9419 diabetes patients in Thailand had blindness due to diabetes (1.5%), history of amputation (1.6%),

coronary diseases (8.5%) and cerebral vascular diseases (4.5%). In 2002, diabetes was one of the four leading chronic diseases that caused 29 million deaths worldwide [4]. The health-care expenditure on treatment of diabetes is high in many countries. In Japan, the health-care expenditures on diabetes are \$ 8 billions or 4% of total health-care expenditures of the government in 1996 [5] and up to \$ 98 billion in the USA in 1997 [6].

The main goal of treating diabetic patients is to prevent macro- and microvascular complications by controlling blood glucose level. The United Kingdom Prospective Diabetes Study (UKPDS) [7] indicated that controlling blood glucose level could delay the progress of microvascular complications in type 2 diabetes. Although nonpharmacologic treatment can

*Address correspondence to:* Nathorn Chaiyakunapruk, Department of Pharmacy Practice, School of Pharmacy, Naresuan University, Phitsanulok, Thailand, 65000. E-mail: [nui@u.washington.edu](mailto:nui@u.washington.edu)

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**Table 1** Clinical effectiveness of the treatment used in the analysis

Interventions	HbA1c (%)	HDL (mg/dL)	Tot Chol (mg/dL)	Ref.
Pioglitazone 45 mg (combination*) Mean (95% CI)	-1.56 (-1.16 to -1.96)	+4.55 (+3.61 to +5.48)	-0.09 (-0.13 to +0.13)	[17]
Rosiglitazone 8 mg (combination*) Mean (95% CI)	-1.26 (-1.48 to -1.04)	+2.71 (+2.01 to +3.42)	+21.3 (+17.7 to +24.9)	[17]

\*Combination means the use of thiazolidinediones combined with either sulfonylurea or metformin. HDL, high density lipoprotein; Ref., references; Tot Chol, total cholesterol.

improve the glycemic control, the UKPDS reported that not more than 8% of diabetes patients can control their blood glucose with nonpharmacologic therapy within 9 years. Oral hypoglycemic drug treatment should be used in the next step.

Thiazolidinedione is an oral antihyperglycemic agent that can reduce insulin resistance in peripheral tissues and decrease hepatic glucose production [8]. There are two drugs in this class currently available in the market: rosiglitazone and pioglitazone. In the large clinical trial of pioglitazone, the PROactive (the Prospective Pioglitazone Clinical Trial in Macrovascular Events) [9], the use of pioglitazone could significantly reduce a composite secondary end point of all-cause mortality, stroke, and myocardial infarction with the relative risk reduction of 16%. Therefore, adding thiazolidinedione may help delay the progression of macrovascular diseases including myocardial infarction and stroke which the combination of sulfonylurea and metformin cannot [7].

From the hospital policymaker perspective, both cost and effectiveness of the interventions should be considered when a decision to include an intervention into hospital formulary needs to be made. There are many cost-effectiveness studies in thiazolidinediones conducted in other countries, but not in Thailand [10–15]. Only two studies compared the cost-effectiveness between rosiglitazone and pioglitazone [12,15], but both studies did not base their effectiveness on meta-analysis. In addition, the results in one country cannot be applied to other countries because of the differences in health-care systems and resource utilization pattern. A cost-effectiveness study of thiazolidinediones has not been conducted in Thailand. In this study, we determined an incremental cost-effectiveness ratio of the maximal dose of pioglitazone compared with the maximal dose of rosiglitazone in patients who cannot control their blood sugar with sulfonylureas and metformin. We adapted the Center for Outcome Research (CORE) diabetes model by Thai data to use as an analytical instrument in this study.

## Methods

### CORE Diabetes Model

The CORE diabetes model is the analytical tool that was used in this study. The model consists of 15 sub-

models including angina, cataract, congestive heart failure, foot ulcer and amputation, hypoglycemia, ketoacidosis, lactic acidosis, macular edema, myocardial infarction, nephropathy, neuropathy, peripheral vascular disease, retinopathy, stroke, and nonspecific mortality. Each submodel is a Markov model using Monte Carlo simulation using probabilities derived from published sources. The model can predict the long-term costs and outcomes in diabetes patients based on many large clinical and epidemiological studies that are currently available [16]. The model analyses data by taking into account of baseline characteristics of a cohort, clinical effectiveness and costs of intervention, and transition probabilities of each diabetes complication progressions. The final outcomes are reported as life expectancy, quality-adjusted life expectancy, cumulative incidence of each diabetes complications, and total lifetime costs of the diabetes populations.

### Interventions Compared

The interventions compared in this study are pioglitazone and rosiglitazone used in type 2 diabetic patients who cannot control their blood glucose under the combination of sulfonylurea and metformin. The dose regimen of pioglitazone was 45 mg orally taken once daily, while the dose regimen of rosiglitazone was 8 mg taken orally once daily. These two regimens were the full dose of each thiazolidinedione which are capable of achieving the best glycemic control level of each product. Clinical effectiveness of both regimens were derived from a meta-analytic study conducted by Chiquette and colleague (Table 1) [17].

### Cohort

Baseline characteristics of our hypothetical cohort were based on Thai Diabetes Registry Report (TDRP) [3]. This project is a multicenter registry of 9419 diabetic patients receiving medical care in diabetic clinics of 11 tertiary centers in Bangkok and major provinces. The registry data were collected from April to December 2003. Almost all patients (94.6%) were type 2 diabetic patients. Some characteristics that were not reported in TDRP were retrieved from other publication related with Thai population (Table 2).

### Costs and Perspective

The government policymaker perspective was taken in this study by considering only direct medical costs of

**Table 2** Base line characteristics of the Thai diabetic population

	Baseline characteristics		
	Mean	SD	Ref.
Start age	59.43 years	13.52 years	[3]
Duration of diabetes	10 years	7.61 years	[3]
Proportion of male	0.34		[3]
HbA1c	Mean: 7.75%	SD: 0.56%	Expert opinions
Systolic blood pressure	126.3 mmHg	0 mmHg	[2]
Total cholesterol	197.1 mg/dL	42.52 mg/dL	[3]
High density lipoprotein cholesterol (HDL)	53.9 mg/dL	15.31 mg/dL	[3]
Low density lipoprotein cholesterol (LDL)	114.5 mg/dL	35.76 mg/dL	[3]
Triglyceride	150.7 mg/dL	105.4 mg/dL	[3]
Body mass index	25.6 kg/m <sup>2</sup>	4.3 kg/m <sup>2</sup>	[3]
Proportion of myocardial infarction	0.42		[3], database*
Proportion of angina	0.43		[3], database*
Proportion of peripheral vascular disease	0.039		[3]
Proportion of stroke	0.044		[3]
Proportion of congestive heart failure	0.03		Database*
Proportion of atrial fibrillation	0.017		Database*
Alcohol consumption	35 oz/week		[32]
Proportion of smoker	0.141		[3]
Cigarettes/day	10.8		[33]
Proportion of left ventricular hypertrophy	0.13		[34]
Proportion of micro albuminuria	0.178		[3]
Proportion of gross proteinuria	0.178		[3]
Proportion of end state of renal disease	0.083		[3]
Proportion of background diabetic retinopathy	0.213		[3]
Proportion of proliferative diabetic retinopathy	0.094		[3]
Proportion of severe vision loss	0.015		[3]
Proportion of macular edema	0.022		[35]
Proportion of cataract	0.428		[3]
Proportion of uninfected ulcer	0.059		[3]
Proportion of healed ulcer	0.044		[36]
Proportion of history of amputation	0.016		[3]
Proportion of neuropathy	0.168		[36]

\*Buddhachinaraj hospital database.  
Ref., references.

each competing treatment. The direct medical costs include cost of medications, cost of laboratory monitoring, and cost of managing diabetes-related complications incurred either inpatient or outpatient services. The estimated costs of diabetes-related complications in Thailand were derived from different sources. Most of diabetic complication costs were calculated from Buddhachinaraj hospital's database (Phitsanulok, Thailand). A total of 12,902 type 2 diabetic patients were identified by ICD-10 (International Classification of Disease version 10) diagnosis or the use of medications specific for diabetes between June 2001 and July 2005. Other complication costs that could be not calculated from the hospital database were derived from Thai published literature, expert opinions, and DRGs (Diagnosis-Related Groups) guidebook (Table 3). Based on the average cost derived from the Drug and Medical Supply information center [18], the daily cost of pioglitazone and rosiglitazone was 107.87 baht (US\$3.12) and 86.08 baht (US\$2.49), respectively. All costs were adjusted to 2004 value. To present the results in US\$, we used the currency exchange rate of April 23, 2007, 34.56 baht/US\$1 [19]

refer to Bank of Thailand website ([http://www.bot.or.th/bothomepage/index/index\\_e.asp](http://www.bot.or.th/bothomepage/index/index_e.asp)).

**Transition Probabilities**

Most of diabetic complication transition probabilities were based on the CORE model default [16] except probability value of nonspecific mortality and death related to hemodialysis and peritoneal dialysis. Nonspecific mortality probability values in the model were replaced by age-specific mortality data in Thai population [20]. Probabilities values of death related to hemodialysis and peritoneal dialysis were derived from Thai renal registry project 2003 [21].

**Time Horizon**

Time horizon of the simulation was 40 years. We used 40 years to confirm that the simulation would cover the average life time of our cohort.

**Discounting**

Costs and clinical outcomes were discounted at 3% annually in base-case analysis, according to

**Table 3** Thai diabetes-related costs used in the CORE diabetes model

Description of event or state	Cost per event or state (baht)	References
Annual cost of screening for microalbuminuria	150	Expert opinion*
Annual cost of screening for gross proteinuria	10	Expert opinion*
Annual cost of eye screening	118	[37]
Myocardial infarction, year of event	67,653	Database†
Myocardial infarction, each subsequent year	27,447	Database†
Angina, year of event	67,192	Database†
Angina, each subsequent year	32,323	Database†
Congestive hear failure, year of event	60,801	Database†
Congestive hear failure, each subsequent year	24,779	Database†
Stroke, year of event	63,984	Database†
Stroke, each subsequent year	31,996	Database†
Cost of hemodialysis (HD), year of event	352,665	[31,38]
Annual costs HD, each subsequent year	331,165	[31,38]
Cost of peritoneal dialysis (PD), year of event	408,083	[31]
Annual costs of PD, each subsequent year	361,416	[31]
Cost of renal transplant (RT), year of event	333,228	[39]
Annual costs RT each subsequent year	91,329	[39]
Major hypoglycaemic event	12,472	Database†
Ketoacidosis event	42,375	Database†
Lactic acid event	40,510	Database†
Cost of eye laser treatment	1,756	[37]
Cost of cataract operation	11,403	[40]
Neuropathy, year of event	21,515	Database†
Neuropathy, each subsequent year	24,034	Database†
Amputation (event-based)	76,688	Database†
Amputation Prosthesis (event-based)	2,900	Expert opinion*
Gangrene treatment (monthly-based)	62,245	Database†
Standard uninfected ulcer (monthly-based)	8,371	Database†

\*Albuminuria screening costs got from an expert opinion who had worked as the head of Chemical clinic laboratory department, Buddhachinaraj hospital. Amputation prosthesis cost was cost of artificial limb that got from the opinions of two experts who had worked at the artificial limb center at Buddhachinaraj hospital.

†Data were average costs calculated from diabetic patients in Buddhachinaraj hospital database between June 2001 and July 2005.  
CORE, Center for Outcome Research.

World Health Organization (WHO) guide of cost-effectiveness analysis [22].

### Data Analysis

In the model simulation, each of 1000 nonidentical patients with different baseline characteristics was run for 1000 times. The mean incremental costs versus mean incremental effectiveness of 1000 simulations of each 1000 patients were used to generate a scatter plot. Mean of the mean incremental costs versus mean incremental effectiveness of 1000 patients was reported as the incremental cost-effectiveness ratio.

### Sensitivity Analysis

The sensitivity analyses were done by varying some variables including effects of pioglitazone on %HbA1c decreasing, effects of pioglitazone on lipid profiles, time horizon that used to run the simulation, drug treatment costs of the pioglitazone group, and the discounting rate. In the HbA1c sensitivity analysis, we use %HbA1c change from baseline in pioglitazone group between -1.16 and -1.96 (upper bound and lower bound of the confident interval of %HbA1c changing in pioglitazone treatment report in the Chiquette's Meta-analysis [17]). Effects of pioglitazone on lipid profiles were also varied by using upper bound and lower bound of 95% confidence interval from the Meta-analysis. Drug treatment cost of the pioglitazone

group was varying by +25% of the pioglitazone treatment cost in base-case. For the sensitivity analysis of discounting rate, we use the recommendation from WHO [22] including 0% discount costs and clinical effects, 0% discount clinical effects and 6% discount costs, and 6% discount cost and clinical effects. Finally, we vary time horizon from 10 years to 30 years.

## Results

### Base-Case Analysis

The results from the base-case analysis showed that patients in the pioglitazone group had slightly lower cumulative incidence of diabetes complications than those in the rosiglitazone group. The incidence of proliferative diabetic retinopathy, end stage renal disease, amputation ulcer, and myocardial infarction in the pioglitazone group compared to the rosiglitazone group was 1.11% versus 1.19%, 5.07% versus 5.42%, 6.64% versus 6.70%, and 15.90% versus 18.50%, respectively. In addition, patients in the pioglitazone group had longer life expectancy and quality-adjusted life expectancy compared to the rosiglitazone group. Life expectancy and quality-adjusted life expectancy in the pioglitazone group was 0.16 and 0.14 years higher than those in the rosiglitazone group, respectively. At the end of the 40 years

**Table 4** Summary of cost and incremental cost-effectiveness analysis in base-case results

	Pioglitazone group	Rosiglitazone group
Average total lifetime cost (baht) (SD)	491,457 (16,202)	465,839 (16,136)
Average life expectancy (years)	9.62 (0.171)	9.47 (0.177)
Average quality adjusted life year (years)	6.69 (0.124)	6.55 (0.123)
Incremental cost per life expectancy (baht per life year gained)	161,777	
Incremental cost per quality adjusted life expectancy (baht per quality adjusted life year gained)	186,246	

simulation, the survival rate of the pioglitazone group was 0.3% and rosiglitazone group was 0.1%.

The total costs in the pioglitazone group were higher than the total costs in the rosiglitazone group. An incremental cost-effectiveness ratio showed that we had to pay 161,777 Baht (US\$ 4681) for one life year gained or pay 186,246 Baht (US\$ 5389) for an additional quality-adjusted life year (QALY) earned (Table 4).

The incremental cost-effectiveness scatter plot of 1000 sample generated from mean incremental costs versus mean incremental effectiveness of 1000 simulation of each 1000 patients (Fig. 1) showed that majority of the cost-effectiveness ratio fell in the upper right quadrant. This indicates that most simulations showed that the pioglitazone treatment is both higher costs and more effective than the rosiglitazone treatment.

When we used the scatter plot to generate an acceptability curve (Fig. 2), the acceptability curve show how likely it will be that the pioglitazone treatment is cost-effective for any particular willingness to pay value. With a willingness to pay value of 110,000 and 33,000 Baht per QALY gained, there is a 29% and

64% probability that the pioglitazone treatment will be cost-effective compared to the rosiglitazone treatment, respectively.

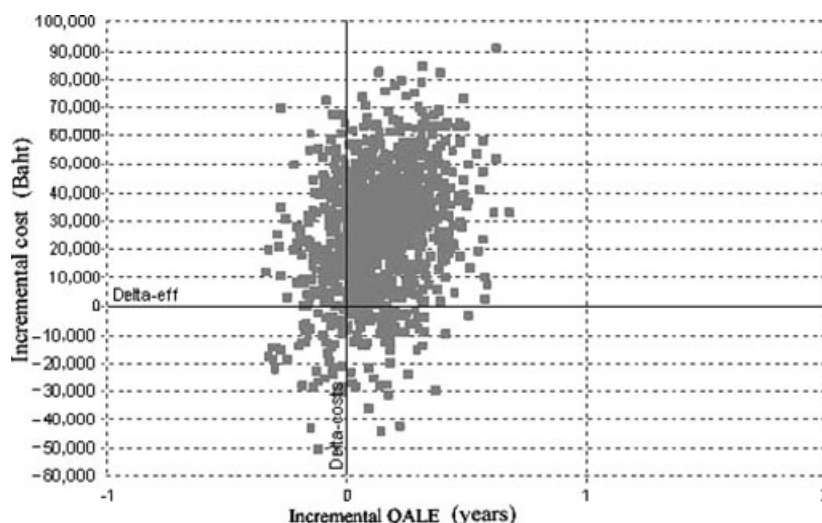
**Sensitivity Analyses**

Sensitivity analyses showed that the most influential variable was the effect of %HbA1c change. When varying the effect of %HbA1c change (Fig. 3), the incremental cost per QALY gained varied from 79,586 to 951,204 baht (US\$ 2302–US\$ 27,523)/QALY. When %HbA1c change from pioglitazone using was -1.16% (lower bound of the confidence interval of %HbA1c change from pioglitazone used in the base-case analysis) and %HbA1c change from rosiglitazone using was -1.26% as in the base-case analysis, the pioglitazone group remained dominant to rosiglitazone.

Varying other variables for the sensitivity analysis also affected the final outcome but the effects were less than the effect of %HbA1c change. The cost-effectiveness values, when using varying discount rates, fell between 130,224 and 262,681 Baht (US\$ 7600)/QALY. Varying the pioglitazone drug costs by + 25% showed the incremental cost per QALY fell between 64,329 (US\$ 1861) and 308,163 Baht (US\$ 8916)/QALY. The incremental cost-effectiveness ratio was slightly changed when we varied the effects of pioglitazone on lipid profiles (Fig. 3). The effects of pioglitazone on low density lipoprotein (LDL) and triglyceride did not affect the cost-effectiveness values. Varying time horizontal showed that using thiazolidinediones for 40 years was more cost-effective than 10 years and 20 years.

**Discussion**

Our base-case findings showed that using pioglitazone, compared to rosiglitazone, resulted in reduced incidence of long-term complications, improved life



**Figure 1** The incremental cost per quality adjusted life expectancy scatter plot. QALE, quality adjusted life expectancy.



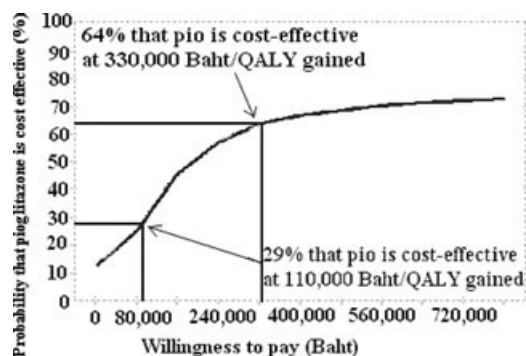


Figure 2 Acceptability curve. QALY, quality-adjusted life year.

expectancy and QALY in type 2 diabetic patients who have previously failed on treatment with sulfonylurea or metformin. These clinical benefits of pioglitazone over rosiglitazone are mostly derived from the better lipid profile and glycemic control [17] although the higher cost in the pioglitazone group is mostly due to the medication cost.

In addition, the sensitivity analysis results demonstrated that the effects of pioglitazone on %HbA1c changes from base line were the most sensitive to the final outcomes. This is not surprising as glycemic level is a strong predictor of developing microvascular and macrovascular complications [7,23]. In a scenario when the effects of glycemic control of pioglitazone were inferior to rosiglitazone (%HbA1c change of -1.16% vs. -1.26%), the incremental cost per QALY gained was 951,204 baht (US\$ 27,523) per QALY gained or five times higher than the incremental cost per QALY gained in the base-case analysis. The glycemic control results were affected directly with our interventions. Although life style modification was also a potential effect on glycemic control in a clinical practice, it did not affect to the results of our analysis. We assumed that the life style modification in both the pioglitazone group and the rosiglitazone group were not different. Therefore, our final incremental

effectiveness was reflected from the difference of effectiveness between both thiazolidinediones only.

Based on the WHO recommendation regarding the cost-effectiveness thresholds criteria [24-26], an intervention with an incremental cost-effectiveness ratio less than one or falling between one to three times of gross domestic product per capita (GDP per capita) would be deemed very cost-effective and potentially cost-effective, respectively. On the other hand, an intervention with a cost-effectiveness ratio beyond the three times of GDP per capita would be interpreted as not cost-effective. Based on the results of this study, the incremental cost per QALY gained in our base-case analysis was 186,246 baht (US\$ 5389) per QALYs which was about 1.7 times of the Thai GDP per capita (110,000 baht per year) in 2005 fiscal year. The results fell between one to three times GDP per capita. When we applied the criteria based on WHO recommendation, the incremental cost-effectiveness ratio in our study showed that using pioglitazone was likely to be cost-effective, compared with rosiglitazone.

When taken into account the join probability of values of the incremental cost and effectiveness simultaneously, the cost-effectiveness acceptability curve graphically presents the probability of being cost-effective as a function of the maximal willingness to pay value. The cost-effectiveness acceptability curves in our study illustrated that the probability per QALY gained was only 29% at 110,000 baht per QALY gained and 64% at 330,000 baht per QALY gained (a value of one and three times of GDP per capita, respectively). This way of presenting findings is easy to understand and provides more meaningful interpretation, compared to the base-case analysis.

Our cost-effectiveness results were different from the findings in previous cost-effectiveness studies [12,15]. Based on a dossier submission, reported in the article of Veenstra and colleagues [15], using pioglitazone resulted in cost-savings of US\$ 6057 in year 2000. Nevertheless, the analysis was performed for comparing pioglitazone 30 mg and rosiglitazone 4 mg

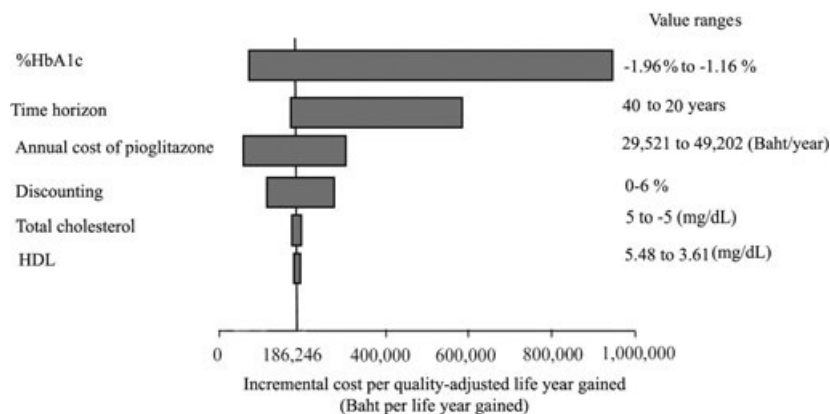


Figure 3 Tornado diagram of the sensitivity analyses.\* \*Effect of pioglitazone on %HbA1c, total cholesterol (T-Chol), and HDL were varied in the sensitivity analysis, when effect of rosiglitazone on each parameters were set as constant as the base case analysis. HDL, high density lipoprotein.

in combination with metformin or sulfonylurea [15], which was different from our study in which a maximal dose of pioglitazone 45 mg and rosiglitazone 8 mg was studied. Henrikson [12] determined a cost-effectiveness of thiazolidinedione using Swedish perspective. The study compared pioglitazone 30 mg versus rosiglitazone 8 mg in combination with metformin and found that the incremental cost-effectiveness ratio was SEK\$ 148,561/life years gained [12]. Both studies were not interpreted cost-effectiveness by WHO criteria. The cost-effectiveness interpretation was not a problem in Veenstra et al. study because they stated that using pioglitazone was cost-saving [15]. Henrikson study stated that Sweden authorities were not set threshold values for cost-effectiveness in health-care expenditure. Henrikson applied data from the Swedish Road Safety Office for the cost-effectiveness threshold to interpret his result. The value that could be interpreted as cost-effective in Henrikson study was not more than SEK\$ 430,000 per life years gained [12]. It was important to note the model used in both studies was based on the diabetes model, developed by the Institute for Medical Informatics and Biostatistics (IMIB), which was the original model version of CORE diabetes model [27].

One limitation of our study was that we calculated diabetes complication costs mainly from a hospital. As this hospital is a teaching, tertiary care, government hospital, the cost estimates may be different in other hospitals. Kunaratanapruk and colleagues [28] reported that the charge was different between the government hospital in Bangkok and the government hospital in other provinces in 1995. Total charges of the accident treatment in out-patient visit in the government hospital in Bangkok were two times higher than that in the government hospital in outside of Bangkok [28]. In addition, missing value is commonly seen in the hospital database [29]. Nevertheless, after we found that 90% of inpatient room charge was missing, we could replace the room charge by calculating average room charges in each year of the hospital and multiplied it with the length of stay of each patient to replace the missing data. Coding error was another problem that can occur in the database. This problem is also commonly found in the database of other countries [6]. Given that almost 10,000 observations were included in our analysis, the effect of wrong coding was unlikely to be large.

We believe that our results are valid for Thai population because of several reasons. First, the transition probabilities of diabetes complication progression that used in the model were based on two large, longitudinal cohort studies, The Framingham cohort and UKPDS studies. These studies had a follow-up period more than 10 years. They were landmark studies which the relationship of glycemic control, lipid profiles, and other factors and the risk of developing dia-

betes complications were derived from. Second, the CORE diabetes model is one of a few models that have been validated in several clinical studies using different population including for Asians [30]. Last, many of Thai specific data were used to input in our analysis including baseline characteristic of diabetes patients, age-specific mortality, renal replacement therapy specific mortality, diabetes complication costs and associated medical costs.

Several crucial issues need to be considered, when decision-makers interpreted our findings. First, our study determines the effect of maximum dose of pioglitazone combination and maximum dose of rosiglitazone combination only. Second, this study was performed using the hospital perspective. The incremental cost-effectiveness ratio may be lower if the societal perspective is considered. Third, we have to consider many factors when we decide to choose a treatment for our organization including the ethical, and health equity issue. For example, a study of cost-utility analysis of renal replacement therapy in Thailand by Teerawattananon [31] demonstrated that peritoneal dialysis and hemodialysis are considered not cost-effective, according to WHO threshold recommendation. This does not mean that the hospital policymakers should discard the renal replacement therapy in their organization for budget saving. On the other hand, government has decided to allow peritoneal dialysis and hemodialysis to be used in a certain situation despite the findings of non-cost-effective.

## Conclusion

To our knowledge, this study is the first to evaluate the cost-effectiveness of pioglitazone, compared to rosiglitazone, in terms of long-term health outcomes and economic consequences in the context of Thai health-care system. Although the base-case analysis found that the use of pioglitazone fell in the cost-effective range recommended by WHO cost-effective as threshold criteria (one to three times of GDP per capita), the acceptability curves demonstrated probability that the use of pioglitazone was cost-effective were between 29% and 64% at the one time and three times of GDP per capita, respectively. Nevertheless, if we considered using pioglitazone in diabetic patients with higher risk of cardiovascular diseases, the incremental cost-effectiveness ratio comparing pioglitazone and rosiglitazone may be lowered.

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