CHAPTER V

CONCLUSION

Our base-case findings showed that using pioglitazone, compared to rosiglitazone, resulted in reduced incidence of long-term complications, improved life expectancy and quality adjusted life year (QALY) in type 2 diabetes 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 [14] while 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[8], [85]. 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 538,896 Baht per QALY gained or 2.6 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 World Health Organization (WHO) recommendation regarding the cost-effectiveness thresholds criteria[86], [87], 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 20, 6125 Baht per QALYs which was about 1.8 times of the Thai GDP per capita (110,000 Bath 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, ICER in our study showed that using pioglitazone was likely to be cost effective, compared with rosiglitazone.

We interpreted our incremental cost-effectiveness ratio using the GDP per capita based on the WHO criteria because we did not have the standard acceptable criteria of cost-effectiveness in Thailand. A cost-effectiveness threshold set in one country also cannot be used in other countries because of the differences heath economic systems. In additon, most of cost-effectiveness thresholds that were used in each country currently seemed to be arbitrary. For example, in US health economic studies, we could see that US$50,000/QALY has frequently been used to define the intervention as being cost-effective [88].This value was originally based on the dialysis standard of Medicare program for patient with chronic renal failure but were used to defined a cost-effectiveness threshold in different diseases [88]. The GDP per capita is a national value that relates to the government consumption, international trade, and final household expenditure [87] . In addition, results of the "WHO-CHOICE population" model [84] show that GDP per capita in each country is highly correlated with the unit cost of healthcare utilization in the country. For example, the GDP per capita of a country can be used to predict average cost of admission in that country. Experts from many countries including Thailand were confirmed that the results had face validity [84].

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 [22], [19]. Based on a dossier submission, reported in the article of Veenstra and colleagues [22], using pioglitazone resulted in cost-savings of US$6,057 in year 2000. However, the analysis was performed for comparing pioglitazone 30 mg and rosiglitazone 4 mg in combination with metformin or sulfonylurea [22], which was different from our study in which a maximal dose of pioglitazone 45 mg and rosiglitazone 8 mg was studied. Henrikson [19] determined a cost-effectiveness of thiazolidinedione using Swedish perspective. The study compared pioglitazone 30 mg vs. rosiglitazone 8 mg in combination with metformin and found that the incremental cost-effectiveness ratio was SEK$148,561/ life years gained [19]. Both studies were not interpreted cost-effectiveness by WHO criteria. The cost-effectiveness interpretation was not a problem in Veenstra et al. study because they stated that using pioglitazone was cost-saving [22]. Henrikson study stated that Sweden authorities were not set threshold values for cost-effectiveness in healthcare expenditure. Henrikson applied data from the Swedish Road Safety Office for the cost-effectiveness threshold to interpret his result. The value that could be interpreted as cost-effective in Henrikson study was not more than SEK$ 430,000 per life years gained [19]. 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 [89].

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 [90] 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[90]. In addition, missing value

is commonly seen in the hospital database [28] . However, after we found that 90% of in-patient 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.

In modeling studies, it is inevitable to derive data from various sources. Our study used data obtained from several sources including governmental sources, the endocrine society of Thailand, the Nephrology society of Thailand, and a publication of the Health systems research institute. It was important to note that the utility parameters used in the model were not based on studies in Thailand. However, we found that the results are not sensitive to the uncertainty around the utility values. When the utility scores of the patients with myocardial infarction event was changed from -0.129 to -0.258 (2 times), the incremental cost-effectiveness ratio was changed from the base-case analysis only 0.61%. Another example was the change of the amputation event utility scores. After the amputation event utility score was changed from – 0.109 to -0.218 (2 times), the increment cost-effectiveness ratio was change from the base-case analysis only 0.16%.

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 diabetes 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 [39]. 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. Firstly, our study determines the effect of maximum dose of pioglitazone combination and maximum dose of rosiglitazone combination only. Secondly, this study was performed using the hospital perspective. The incremental cost-effectiveness ratio may be lower if the societal perspective is considered. Thirdly, 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 [77] demonstrated that peritoneal dialysis and hemodialysis are considered not cost-effective, according to WHO threshold recommendation. This does not mean that the hospital policy makers 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.

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 (1 to 3 times of GDP-per capita), the acceptability curves demonstrated probability that the use of pioglitazone is cost-effective are between 29% and 64% at the 1 time and 3 times of GDP-per capita, respectively. Hospital policy makers have to weigh these cost-effective probabilities against other choices. However, 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