# CHAPTER IV

# RESULTS

1. First order simulation

1.1. Base-case analysis

1.1.1. Clinical outcomes

The results from the survival curves showed that the survival rate in patients treated with pioglitazone was slightly higher than rosiglitazone (Figure 8). Patients in the pioglitazone group had longer life expectancy and quality-adjusted life expectancy compared to the rosiglitazone group (Table 24). Life expectancy and quality-adjusted life expectancy in the pioglitazone group was 0.30 and 0.21 years higher than those in the rosiglitazone group, respectively. At the end of the 40 years simulation, the survival rate of the pioglitazone group was 0.3% and rosiglitazone group was 0.1%.

Table 24 Summary of clinical outcomes in base-case analysis

| Results | Pioglitazone group Mean (SD) | Rosiglitazone group Mean (SD) |
|---|---|---|
| Life expectancy (years) | 9.71 (5.56) | 9.41 (5.46) |
| Quality-adjusted life expectancy (years) | 6.74 (3.99) | 6.53 (3.89) |

The number of years of complication free of patients in the pioglitazone group was higher than that in the rosiglitazone group (Table 25). Patients in the pioglitazone group lived with free of myocardial infarction more 0.62 years higher than those in the rosiglitazone group. This was the largest difference among all complications.

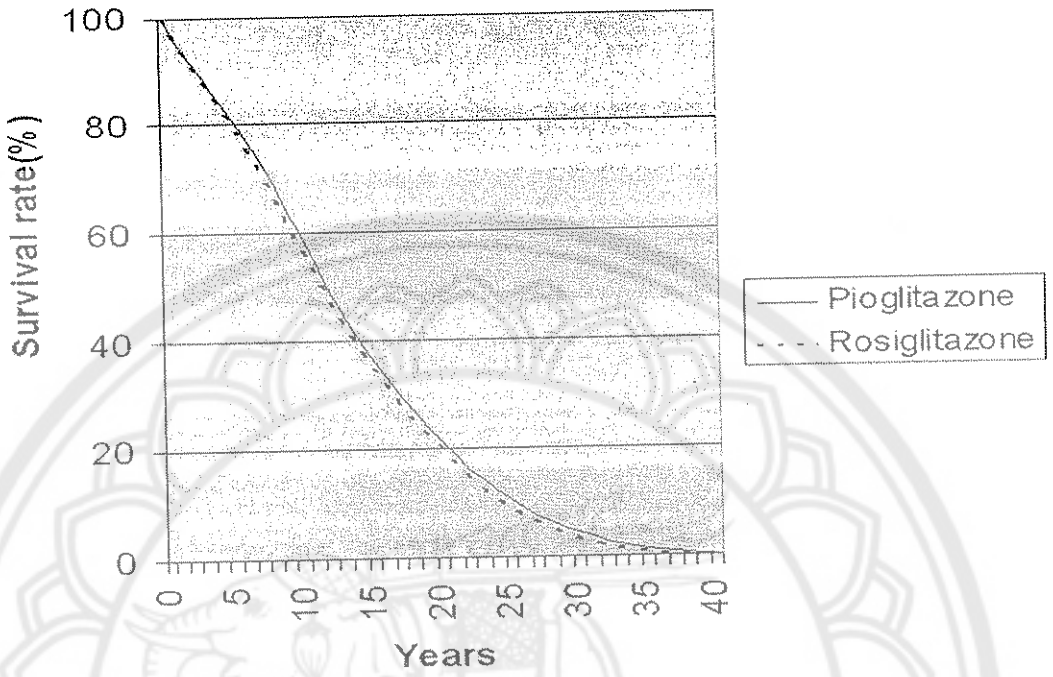


Figure 8 Survival rate

Table 25 Time alive and free of complication in base-case analysis

| Complication | Time alive and free of complication [in years] | |
|---|---|---|
| | Pioglitazone group | Rosiglitazone group |
| Any complications | 1.06 | 0.96 |
| Background Retinopathy | 7.82 | 7.45 |
| Proliferative Retinopathy | 11.25 | 10.70 |
| Microalbuminuria | 7.25 | 6.96 |
| Gross Proteinuria | 9.97 | 9.58 |
| End Stage Renal Disease | 12.30 | 11.85 |
| 1st Ulcer | 10.78 | 10.32 |
| Amputation | 12.19 | 11.73 |
| Neuropathy | 8.18 | 7.70 |
| Peripheral Vascular Disease | 11.56 | 11.07 |

Table 25 (Cont.)

| Complication | Time alive and free of complication [in years] | |
|---|---|---|
| | Pioglitazone group | Rosiglitazone group |
| Congestive Heart Failure | 11.24 | 10.78 |
| Angina | 11.76 | 11.31 |
| Myocardial Infarction | 11.83 | 11.21 |
| Stroke | 11.62 | 11.23 |
| Cataract | 6.82 | 6.40 |
| Macula Edema | 11.52 | 10.99 |
| Severe Vision Loss | 11.96 | 11.47 |

Most of cumulative incidences of diabetes complication were slightly different between the two groups (Table 26). Cumulative incidence of myocardial infarction was the most different between the pioglitazone group and rosiglitazone group. At the end of 40 years simulation, cumulative incidence of myocardial infarction in the pioglitazone group and the rosiglitazone group was 15.69% and 18.50 %, respectively. Stroke was the only complication that cumulative incidence slightly higher in the pioglitazone (0.64%). The possible reason was that patients in the pioglitazone group had a longer survival rate than the rosiglitazone group. Therefore, patients in the pioglitazone group had a longer life time and had more potential time to develop disease. (Figure 9)

Table 26 Cumulative incidence at the end of 40 years simulation

| Complication | Cumulative incidence from 40 years simulation (%) | |
|---|---|---|
| | Pioglitazone | Rosiglitazone |
| Congestive heart failure | 28.61 | 28.90 |
| Angina | 6.23 | 6.95 |
| Stroke | 12.88 | 12.24 |
| Myocardial infarction | 15.69 | 18.50 |

Table 26 (Cont.)

| Complication | Cumulative incidence from 40 years simulation (%) | |
|---|---|---|
| | Pioglitazone | Rosiglitazone |
| Background diabetes retinopathy | 13.49 | 14.18 |
| Peripherative diabetes retinopathy | 1.11 | 1.19 |
| Macular edema | 12.23 | 12.87 |
| Severe vision loss | 6.91 | 7.15 |
| Cataract | 6.71 | 6.89 |
| Microalbuminuria | 19.87 | 21.15 |
| Gross proteinuria | 9.12 | 9.85 |
| End stage of renal disease | 5.07 | 5.42 |
| Ulcer | 16.68 | 17.03 |
| Amputation | 6.64 | 6.70 |
| Neuropathy | 35.74 | 37.37 |

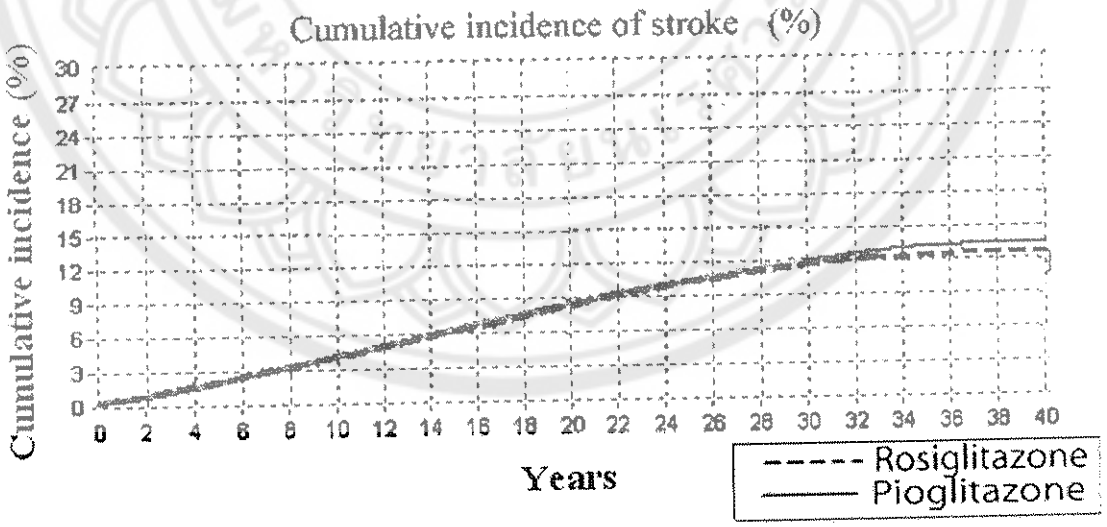


Figure 9 Cumulative incidence of stroke

1.1.2. Cost and cost effectiveness

The total costs in the pioglitazone group were higher than the total costs in the rosiglitazone group. The incremental cost effectiveness ratio showed that we had to pay 148,649 Baht for one life year gained or pay 206,125 Baht for an additional quality adjusted life year earned (Table 27).

Table 27 Summary of cost and incremental cost effectiveness analysis in base-case results

| Results | Pioglitazone group | Rosiglitazone group |
|---|---|---|
| Average total lifetime cost (Baht) (SD) | 502,326 (552,765) | 457,671 (512,383) |
| Average life expectancy (years) | 9.71 (5.56) | 9.41 (5.46) |
| Average QALE (years) | 6.74 (3.99) | 6.53 (3.89) |
| Incremental cost per life expectancy (Baht per life year gained) | 148,649 | |
| Incremental cost per QALE (Baht per QALE) | 206,125 | |

QALE= quality adjusted life expectancy

1.2. Sensitivity analyses

Sensitivity analyses showed that the most influential variable was the effect of %HbA1c change. When varying the effect of %HbA1c change (Figure 10), the incremental cost per quality adjusted life year gained varied from 109,215 to 538,896 Baht/ 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(Table 28).

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 value when using varying discounting rates fell between 109,115 and 243,941 Baht cost per quality adjusted life year gained. The incremental cost effectiveness ratio was slightly changed when we varied the effects of pioglitazone on lipid profiles (Figure 10). The effects of pioglitazone on 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 20 years and 30 years.

Table 28 Sensitivity analysis on the incremental costs effectiveness ratio

| Setting | Incremental cost-effectiveness ratio (Bath) | |
|---|---|---|
| | Based on LE | Based on QALE |
| Variation of discount rates | | |
| 0% discounted costs and clinical effects | 113,215 | 165,050 |
| 3% discounted costs and clinical effects (base-case) | 148,649 | 206,125 |
| 6% discounted costs and 0% discounted clinical effects | 76,966 | 109,115 |
| 5% discounted costs and clinical effects | 177,208 | 243,941 |
| Effect of pioglitazone on %HbA1c* | | |
| Reduce HbA1c -1.16% from baseline | 311,559 | 538,896 |
| Reduce HbA1c -1.56% from baseline (base-case) | 148,649 | 206,125 |
| Reduce HbA1c -1.96% from baseline | 91,342 | 109,251 |
| Effect of pioglitazone on HDL* | | |
| Increase HDL 3.61 mg/dL from baseline | 132,785 | 173,880 |
| Increase HDL 4.55 mg/dL from baseline (base-case) | 148,649 | 206,125 |
| Increase HDL 5.48 mg/dL from baseline | 148,745 | 194,157 |

Table 28 (Cont.)

| Setting | Incremental cost-effectiveness ratio (Bath) | |
|---|---|---|
| | Based on LE | Based on QALE |
| Effect of pioglitazone on Total cholesterol(T-chol)* | | |
| Decrease T-chol -5 mg/dL from baseline | 156,424 | 211,433 |
| Decrease T-chol -1 mg/dL from baseline(base-case) | 148,649 | 206,125 |
| Increase T-chol 5 mg/dL from baseline | 136,171 | 182,040 |
| Time horizontal | | |
| 20 years time horizontal | 214,311 | 272,775 |
| 30 years time horizontal | 228,221 | 273,792 |
| 40 years time horizontal (base-case) | 148,649 | 206,125 |

*Effects of rosiglitazone are constant as base-case analysis. At the base-case analysis, rosiglitazone decrease HbA1c -1.26%, increase HDL 2.71 mg/dL, increase T-chol 21.3 mg/dL.

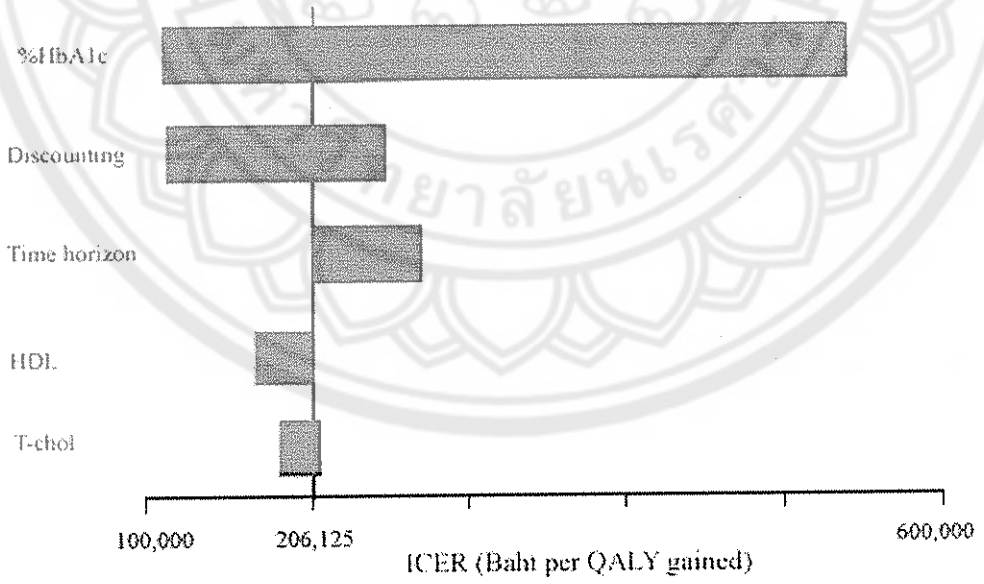


Figure 10 Sensitivity analyses in tornado diagram

2. Second order simulation

In the second order simulation, the incremental cost-effectiveness scatter plot of 1,000 sample generated from mean incremental costs versus mean incremental effectiveness of 1,000 simulation of each 1,000 patients (Figure 11) 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 higher effectives than the rosiglitazone treatment.

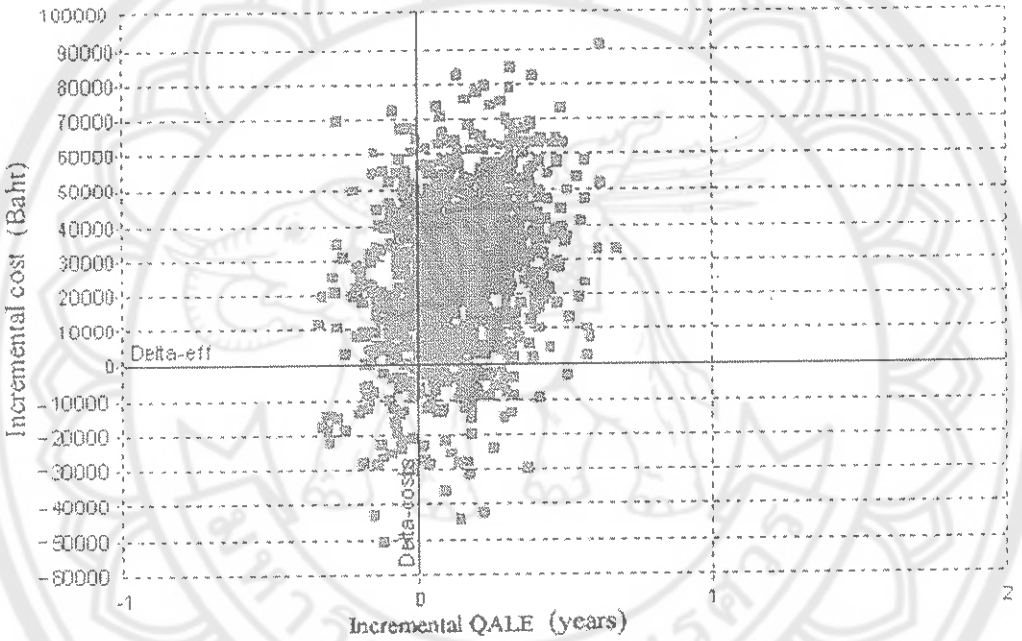


Figure 11 The incremental cost per quality adjusted life expectancy scatter plot

When we used the scatter plot to generate an acceptability curve (Figure 12), the acceptability curve show how likely it will be that the pioglitazone treatment is cost-effective for any particular willingness to pay. With a willingness to pay 110, 000 and 33,000 Baht per quality adjusted life year gained, there is a 29% and 64% probability that the pioglitazone treatment will be cost-effective compared to the rosiglitazone treatment, respectively.

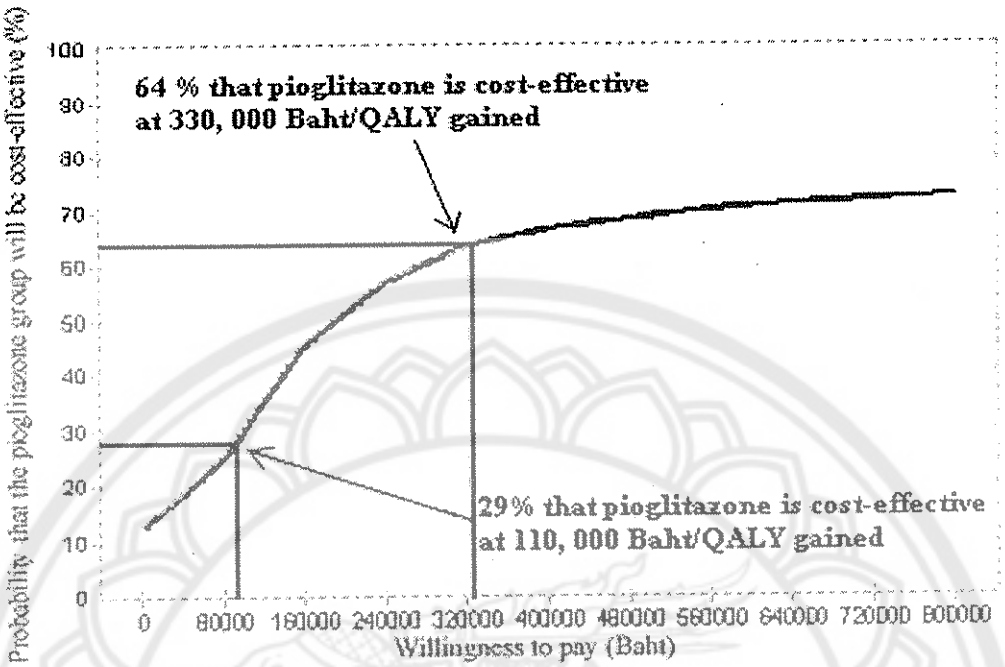


Figure 12 Acceptability curve