CHAPTER 4

ANALYSIS AND RESULTS

4.1 The Results of Markov Modeling

In order to evaluate Markov models by matrix algebra as a cohort simulation, a 100-patient cohort is assumed to begin the model at time 0 in the initial health state (microalbuminuria in our model). Simulations are run using the parameters described previously as shown in table 3.5. The results are:

Under the drug therapy, our models give a cohort of 44-year old NIDDM patients with microalbuminuria the life expectancy 19.39 years for one patient, i.e. survival to age 63 on average (table 4.1). The discounted lifetime costs of the drug treatment (including treatment of renal complications) is 91,061.20 baht per person (medium price) and 104,143.87 baht per person (wholesale price).

Under no drug therapy, the model predicts the life expectancy 14.30 years for one patient, thus survival to age 58 on average. The discounted lifetime cost is 148,481.85 baht per person.

In addition, the discounted lifetime costs for a cohort of 100 patients treated with an ACE-Inhibitor are 9,106,120 baht (medium price) consisting of drug cost = 3,586,191 and ESRD cost = 5,519,929, and 10,414,387 baht (wholesale price) consisting of drug cost = 4,894,458 and ESRD cost = 5,519,929 compared with 14,848,185 baht for the untreated group as shown in table 4.2. The savings from delaying development of ESRD are more than the costs of drug so there will be an estimated discounted savings of 5,742,065 baht (medium price) and 4,433,798 baht (wholesale price), equivalent to a discounted savings of 57,420.65 and 44,337.98 baht per patient, respectively, with 152

life years saved. Therefore, for cost-effectiveness, incremental cost-effectiveness ratio is –37,776.74 (medium price) and –29,169.72 (wholesale drug price) baht per life year saved. In conclusion, drug therapy results in cost savings of 37,776.74 baht (medium price) and 29,169.72 baht (wholesale drug price) accompanying every life year gained.

Table 4.1 Results of a 100-Patient Cohort Simulation

Alternatives	Costs (baht)		Life expectancy (year)	
	Discounted	Not discounted	Discounted	Not discounted
Drug[a]	9,106,120	23,895,287	906	1,939
No drug	14,848,185	38,685,688	754	1,430
Difference	5,742,065	14,790,401	152	509
ICER	-37,776.74	-29,057.76		

[a] medium price

Alternatives	Costs (baht)		Life expectancy (year)	
	Discounted	Not discounted	Discounted	Not discounted
Drug[b]	10,414,387	26,562,658	906	1,939
No drug	14,848,185	38,685,688	754	1,430
Difference	4,433,798	12,123,030	152	509
ICER	-29,169.72	-23,817.35		

[b] wholesale price

Note sign "negative" means cost savings, all costs in 1998 baht, discounted at 8% per annum

Table 4.2 Components of the Cost of Each Program for a 100-Patient Cohort

Program	Costs[a] (baht)
1. Drug program	
a. Medium price	
- Program cost	9,106,120
- Drug cost	3,586,191
- ESRD cost	5,519,929
b. Wholesale drug price	
- Program cost	10,414,387
- Drug cost	4,894,458
- ESRD cost	5,519,929
2. No drug program	
- Program cost	14,848,185
- Drug cost	-
- ESRD cost	14,848,185

[a] All costs in 1998 baht, discounted at 8% per annum

Moreover, it can be estimated the cost burden of diabetic nephropathy in Thailand by using our data (cost of no drug therapy). In 1992, Health Systems Research Institute estimated that there was approximately 900,000 diabetic population in Thailand.

In USA, about 20% to 30% of NIDDM develop diabetic nephropathy. For Thailand, there is no this data available and our figure may be less than USA's because Thai people with diabetes die from other causes such as heart disease before they develop diabetic nephropathy until progression to ESRD. Supposedly, 10-15% of those develop diabetic nephropathy in Thailand. Thus, discounted lifetime cost (25 years) of diabetic nephropathy for 10-15% of diabetic population is about 1.3-2 billion baht (direct medical costs).

4.2 Markov Probability Analysis

Running cohort simulation for many cycles builds up a profile of how many patients are in each cycle of the model over time, which indicates the changing probability of being in each state at a particular time. (Table 4.2, 4.3).

For example, after 15 cycles the model predicts that, in the absence of drug therapy, just 11% of the original cohort will remain in microalbuminuria while 32% and 5% will be in macroalbuminuria and ESRD, respectively, and 52% of the original cohort will have died. On the contrary, the model predicts that with drug therapy 56% of the patients will still be in microalbuminuria after 15 cycles, 16% and 2% will be in macroalbuminuria and ESRD, and 26% of the cohort will have died.

These data show that treatment with an ACE-Inhibitor can delay progression of renal disease in NIDDM patients. The postponement for requiring dialysis leads to money saving in hemodialysis costs and also prolongs life at the same time.

Table 4.3 Cohort Simulation for No Drug Therapy

State	Micro	Macro	ESRD	Death
Cycle				
0	1.00	0.00	0.00	0.00
1	0.86	0.12	0.00	0.02
2	0.74	0.22	0.01	0.03
3	0.64	0.29	0.01	0.06
4	0.55	0.34	0.02	0.09
5	0.48	0.37	0.03	0.12
6	0.41	0.39	0.04	0.16
7	0.35	0.40	0.04	0.20
8	0.31	0.41	0.05	0.24
9	0.26	0.40	0.05	0.28
10	0.23	0.39	0.05	0.33
11	0.20	0.38	0.05	0.37
12	0.17	0.37	0.05	0.41
13	0.15	0.35	0.05	0.45
14	0.13	0.33	0.05	0.49
15	0.11	0.32	0.05	0.52
16	0.09	0.30	0.05	0.56
17	0.08	0.28	0.04	0.60
18	0.07	0.26	0.04	0.63
19	0.06	0.24	0.04	0.66
20	0.05	0.23	0.04	0.69
21	0.04	0.21	0.03	0.71
22	0.04	0.19	0.03	0.74
23	0.03	0.18	0.03	0.76
24	0.03	0.17	0.03	0.78
25	0.02	0.15	0.03	0.80

Table 4.4 Cohort Simulation for Drug Therapy

State	Micro	Macro	ESRD	Death
Cycle				
0	1.00	0.00	0.00	0.00
1	0.96	0.03	0.00	0.01
2	0.93	0.05	0.00	0.02
3	0.89	0.07	0.00	0.03
4	0.86	0.09	0.01	0.05
5	0.82	0.11	0.01	0.06
6	0.79	0.12	0.01	0.08
7	0.76	0.13	0.01	0.10
8	0.73	0.14	0.01	0.12
9	0.71	0.14	0.02	0.14
10	0.68	0.15	0.02	0.16
11	0.65	0.15	0.02	0.18
12	0.63	0.16	0.02	0.20
13	0.60	0.16	0.02	0.22
14	0.58	0.16	0.02	0.24
15	0.56	0.16	0.02	0.26
16	0.54	0.16	0.02	0.28
17	0.52	0.16	0.02	0.30
18	0.50	0.16	0.02	0.33
19	0.48	0.15	0.02	0.35
20	0.46	0.15	0.02	0.37
21	0.44	0.15	0.02	0.39
22	0.43	0.15	0.02	0.41
23	0.41	0.14	0.02	0.43
24	0.39	0.14	0.02	0.44
25	0.38	0.14	0.02	0.46

4.3 Sensitivity Analysis

Sensitivity analyses are performed by varying key parameters to investigate the effect of uncertainties in the data on the results of the study. Thus, in this study, the sensitivities of the results to changes in the cost of the drug, the cost of treatment of ESRD (hemodialysis), the discount rate, and the effect of the drug are examined. These results are:

1. The cost of the drug:

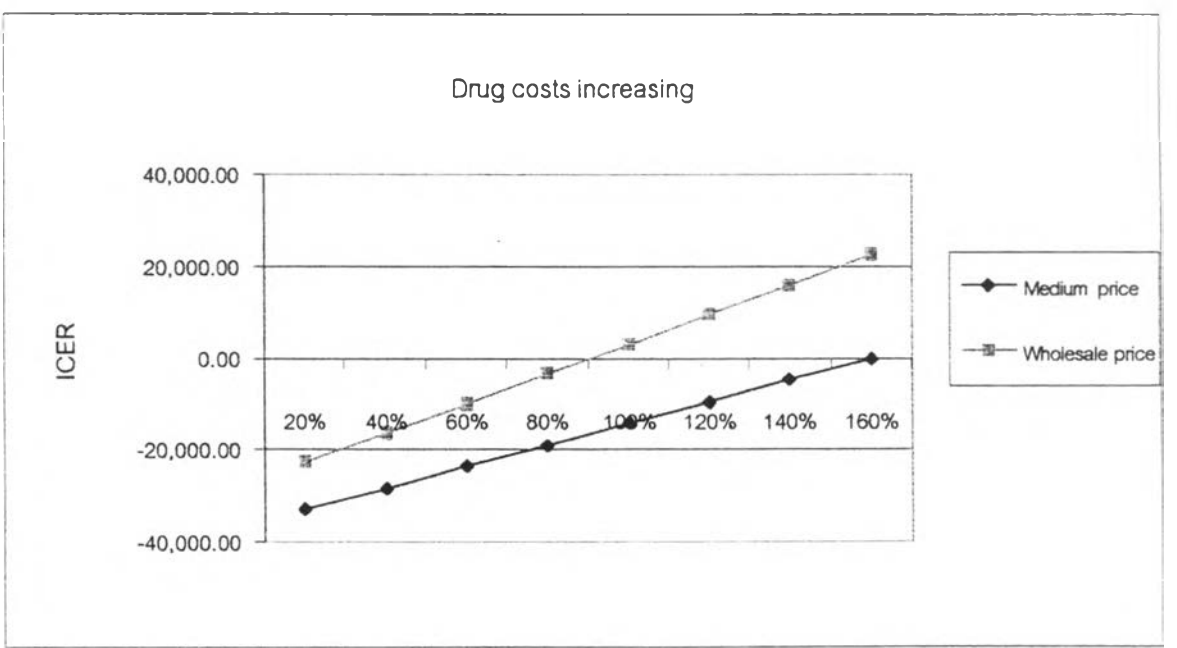
Due to exchange rate variation, the drug price could vary from time to time. In addition, the cost of the drug treatment may be increased in the future to account for costs associated with unanticipated long-term side effects. Thus, the effects of increasing the cost of the drug were examined from 20% until the break-even point.

Table 4.5 and figure 4.2 showed that an increase in drug costs would decrease cost-effectiveness of drug program. For example, when drug costs were increased from 20% to 160%, ICER increased from –33,058.07 baht to –27.37 baht (medium price) accounting for 99.93% from the baseline and from –22,729.65 baht to 22,350.88 baht (wholesale price) accounting for 176.62% from the baseline. Hence, the higher the costs of the drug are, the less cost-effectiveness of the drug program will be. The points of increasing in drug costs at which drug program would incur additional costs were approximately 160% (medium price) and 90% (wholesale price).

Table 4.5 The Effect of Increasing Drug Costs on ICER

Drug costs increasing	ICER (discounted)	
	Medium price	Wholesale price
20%	-33,058.07	-22,729.65
40%	-28,339.40	-16,289.57
60%	-23,620.73	-9,849.50
80%	-18,902.06	-3,409.42
100%	-14,183.39	3,030.65
120%	-9,464.72	9,470.73
140%	-4,746.04	15,910.80
160%	-27.37	22,350.88

Figure 4.1 The Effect of Increasing Drug Costs on ICER



2. The cost of treatment of ESRD:

The cost of treatment of ESRD is the major cost for this study. Hemodialysis cost is also subject to change. Now this cost is high but it is possible that the cost of hemodialysis will be reduced in the future if dialysis equipment is efficiently used. Due to subsidy program in the public hospital system, the real provider cost of hemodialysis may exceed the patient expenditure. Several government institutes do not take the staff wages, the facilities and management cost into consideration while setting up the fee for services. In addition, hemodialysis cost may be increased as a result of an increase in drug cost used in ESRD and dialysis processes. Therefore, the effects of ESRD cost are examined by varying it from 20% until the break-even point.

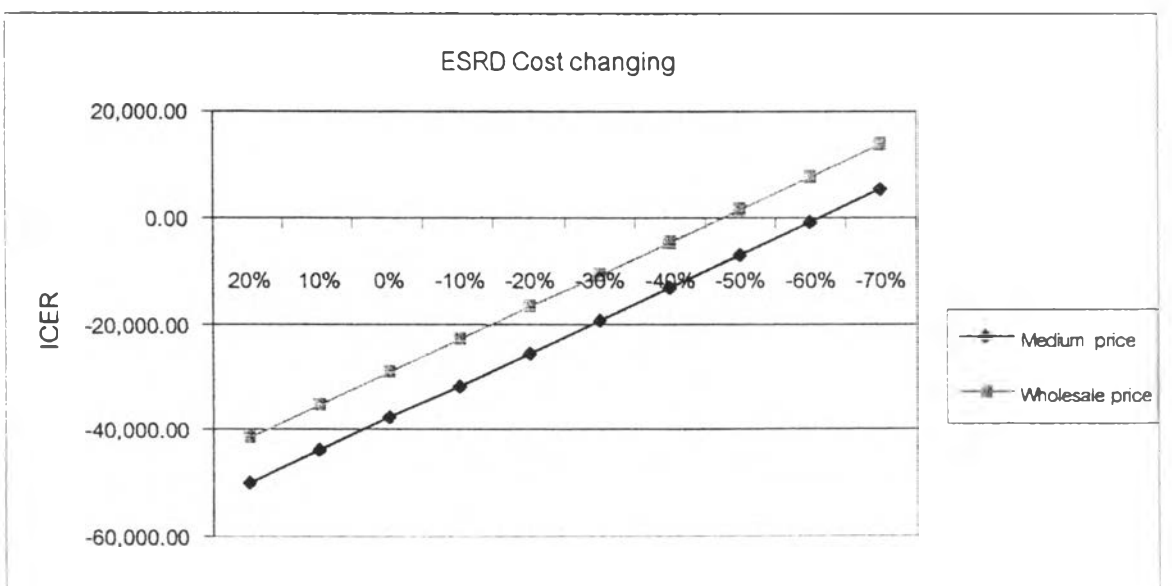
Table 4.6 and figure 4.2 showed that a decrease in hemodialysis cost would decrease the savings from drug treatment for delaying renal failure and deteriorate cost-effectiveness of drug program because the lifetime costs of no drug program would be reduced rather than the lifetime costs of drug program. But an increase in hemodialysis cost has the opposite effect. For example, when hemodialysis cost was varied from 20% to -70%, ICER changed from –50,050.78 baht to 5,182.32 baht and from –41,443.76 baht to 13,789.34 baht for medium price and wholesale drug price, respectively. Break-even points were at approximately –60% (medium price) and –48% (wholesale drug price). Therefore, when hemodialysis cost decreased by approximately 50%, drug treatment program would incur additional costs. The lower the ESRD cost is, the less cost-effectiveness of the drug program will be.

In addition, ESRD cost was more sensitive than drug costs because when 1% of hemodialysis cost and of drug costs were varied, ICERs were changed approximately 614 baht for ESRD cost, 236 baht for medium price and 322 baht for wholesale price, respectively.

Table 4.6 The Effect of Changing ESRD Cost on ICER

ESRD cost changing	ICER (discounted)	
	Medium price	Wholesale price
20%	-50,050.78	-41,443.76
10%	-43,913.76	-35,306.74
0%	-37,776.74	-29,169.72
-10%	-31,639.74	-23,032.72
-20%	-25,502.72	-16,895.70
-30%	-19,365.72	-10,758.70
-40%	-13,228.70	-4,621.68
-50%	-7,091.70	1,515.32
-60%	-954.68	7,652.34
-70%	5,182.32	13,789.34

Figure 4.2 The Effect of Changing ESRD Cost on ICER



3. The discount rate:

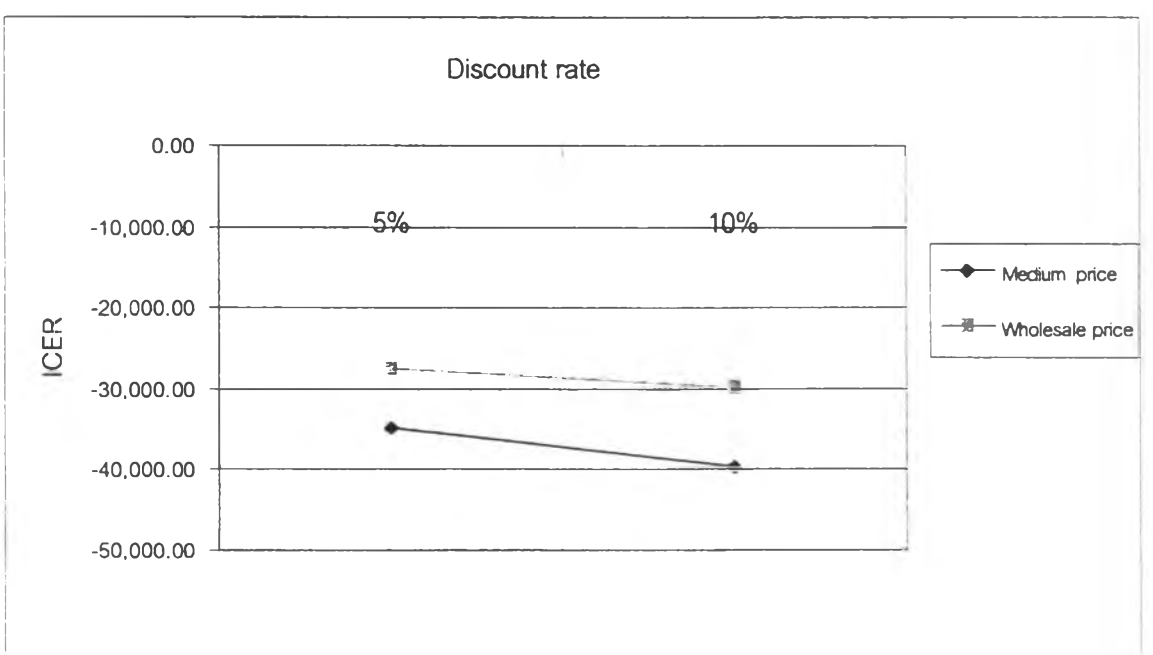
In this study, an 8% discount rate was used. However, because of the uncertainties of the discount rate, its effect was examined at 5% and 10%, respectively.

Table 4.7 and figure 4.3 indicated that the higher the discount rates are, the higher the cost savings per life year saved will be. For example, when a 10% discount rate was used rather than an 8% discount rate, the cost savings per life year saved increased while a 5% discount rate has the opposite effect.

Table 4.7 The Effect of Changing the Discount rate on ICER

Discount rate	ICER (discounted)	
	Medium price	Wholesale price
5%	-34,762.07	-27,624.16
10%	-39,658.89	-29,890.71

Figure 4.3 The Effect of Changing the Discount Rate on ICER



4. The effect of the drug:

Because the effect of the drug from clinical trials is under well-controlled conditions, in which effectiveness is overestimated, its effect under real situations should be examined. From Ravid's study, they found that cumulative incidence (CI) from microalbuminuria to macroalbuminuria for drug group is 18% (efficacy rate), so if the effectiveness of the drug is considered, CI of microalbuminuria to macroalbuminuria should be increased. Thus, the effects of the drug are examined by increasing CI to 28%, 38%, 48% and 58%, respectively.

Table4.7 and figure 4.4 showed the higher the cumulative incidence the steeper the curve of ICER line. At the CI of 48%, there was a big change; ICER highly increased. Because when the CI of the drug was higher, meaning the effect of the drug would be decreased, the incremental effectiveness (the net change in life expectancy) between two programs was reduced. In addition, the lifetime cost of drug program would be also increased since the patients must pay more for treating ESRD as a result of the reducing of the effect of the drug for delaying progression of DN.

Assuming drug administration results in risk reduction of progression from microalbuminuria to macroalbuminuria lower than 12% (60%-48%), it will be less cost-effective. Therefore, the factors affecting the effectiveness of the drug should be concerned.

Table 4.8 The Effect of Decreasing Drug Effect on ICER

Cumulative Incidence (Micro to Macro)	ICER (discounted)	
	Medium price	Wholesale price
18%	-37,776.64	-29,169.72
28%	-29,990.81	-20,335.08
38%	-18,013.55	-6,553.23
48%	-4,608.64	19,967.66
58%	75,794.96	104,384.56

Figure 4.4 The Effect of Decreasing Drug Effect on ICER