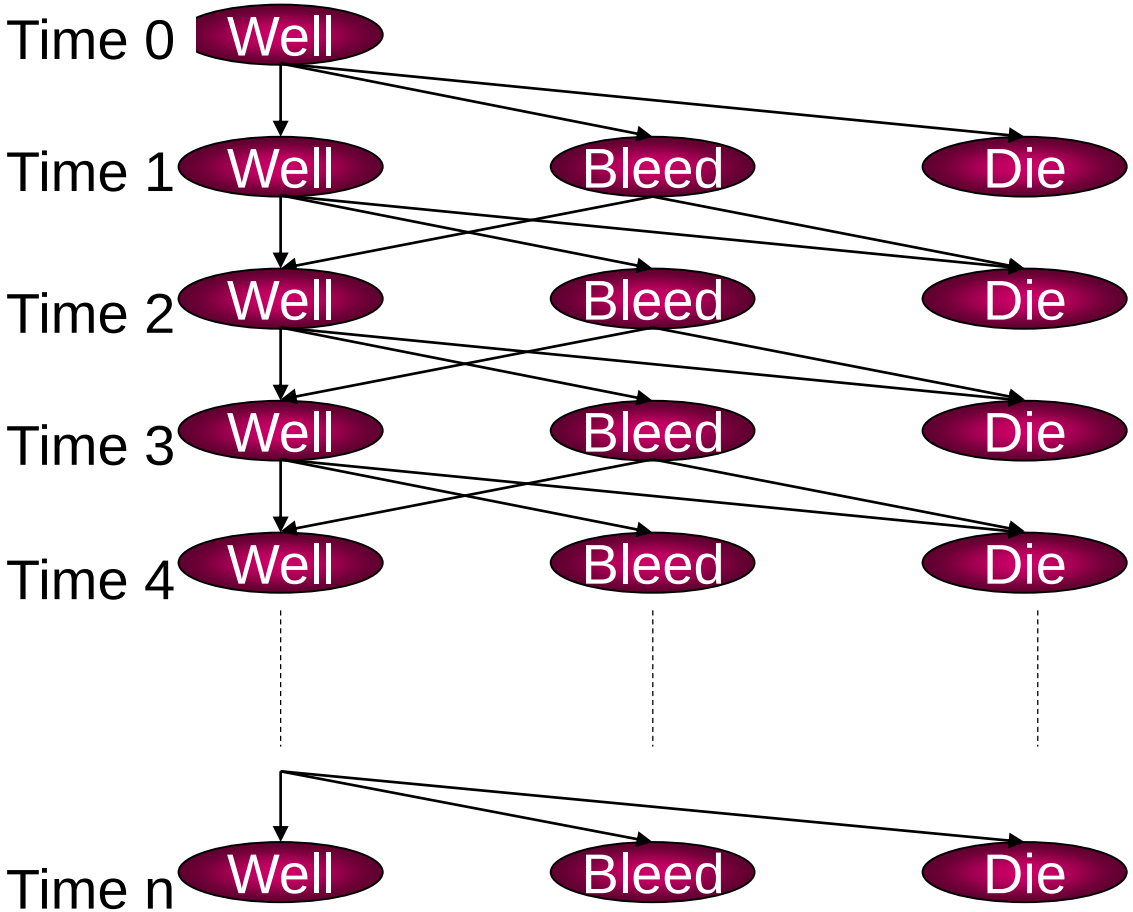
Mahidol University
Faculty of Medicine Ramathibodi Hospital
Department of Clinical Epidemiology and Biostatistics

Markov model

Recap : limitations of decision tree are:

1. Conclusion depends heavily on the assumptions, so sensitivity analysis is important
2. Force movement to occur in one direction from left to right
3. Hard to do the model with long cycle time



Hemophilia patient

The properties of Markov model

1. Patient is always in one of the health states at a time
2. Events are modeled as transitions from one state to another
3. Contribution of utility to overall prognosis depends on length of time spent in health states
4. During each cycle, the patient may make a transition from one state to another according to a set of transition probabilities which can be either constant over time or time dependent
5. Each patient will be followed until get into absorbing state and can not be move out from this state

Example 1: CUA

Question from MoPH (2014)

VALUE IN HEALTH REGIONAL ISSUES 3C (2014) 73–78

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Cost-Utility Analysis of Home-Based Care for Treatment of Thai Hemophilia A and B

Oraluck Pattanaprateep, PhD[1], Ampaiwan Chuansumrit, MD[2], Ronnachai Kongsakon, MD[3,]*

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A B S T R A C T

Objective: This study aimed to evaluate the cost-utility of the home-based care policy versus the no home-based care policy of factor VIII and factor IX concentrate in Thai patients with hemophilia A and B who had no inhibitor or less than 5 Bethesda units. **Methods:** A Markov model was used to evaluate the cost utility of the two policies. The first policy was "no home-based care" in which patients were treated with blood components only when admitted at the hospital but without home treatment. The second policy was "home-based care" in which factors were prescribed and infused for treatment of early bleeding episodes at home. Input parameters related to clinical and cost were obtained from primary data collection at the National Health Security Office, while patients' quality of life was surveyed from mailed questionnaires. Both costs and health outcomes were discounted at 3%. One-way analysis and probabilistic sensitivity analysis were performed to assess uncertainty surrounding model parameters. **Results:** Based on governmental perspective, the "home-based care" policy had cost saving in patients with moderate and severe hemophilia when compared with the "no home-based care" policy; in patients with mild hemophilia, the incremental cost-effectiveness ratio was 80,542 Thailand baht (THB) or US $2,684.73 (US $1 = 30 THB). **Conclusions:** At the ceiling threshold of one time of gross domestic product per capita (120,000 THB per quality-adjusted life-year gained), the "home-based care" policy was cost-effective when compared with the "no home-based care" policy.

Keywords: cost-utility, factor VIII concentrate, factor IX concentrate, hemophilia A, hemophilia B.

A Markov model : State Transition Diagram

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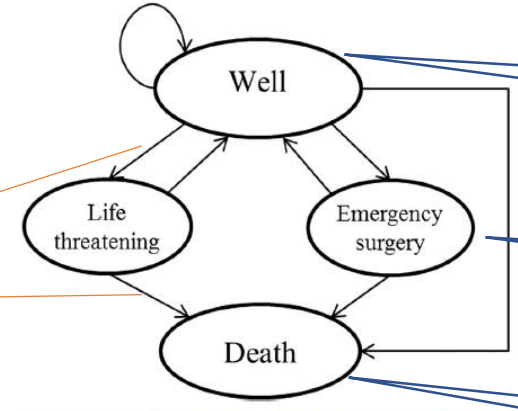

Fig. 1 – The health states included in the Markov model.

Transitional probability

Transient state

Temporary state

Absorbing state

Research methodology in economic evaluation

The steps in conducting economic evaluation are as follows:

a) Define the problem

b) Identify the alternative interventions

c) Identify and measure costs and outcomes

d) Value costs and outcomes

e) Interpret and present the results
   i. Structure a model
   ii. Identify and synthesize evidence
   iii. Deal with uncertainty

P = population/patient

I & C = intervention & comparator

O = outcomes & cost

1. Define the problem

Introduction

Hemophilia A and B are hereditary X-linked disorders caused by a deficiency of clotting factor VIII and IX in the blood [1,2]. The disease can be defined as mild, moderate, or severe depending on the degree of deficiency of the factor. Patients with hemophilia require lifelong replacement therapy to control bleeding episodes, with impact on their quality of life. Hemophilia, however, is not given the priority it deserves in economically less-developed countries because there is a high number of other serious health problems. The replacement therapy is mainly limited to locally prepared fresh frozen plasma, cryoprecipitate, and cryo-removed plasma, which are not virus-inactivated products. Patients risk contracting transfusion-transmitted diseases. The virus-inactivated factor concentrate is seldom used because of the high price. Impressively, the established home-based care for 85 patients with hemophilia at the International Hemophilia Training Center-Bangkok, with limited resources, has significantly decreased the risk of death and increased the survival time [3]. Home care treatment can be adopted even by parents with low literacy.

Factor VIII and factor IX concentrate have been listed in the National Drug List, an essential drug, since 2008 to support patients on home treatment under the Universal Coverage Scheme [4]. The mean per capita factor VIII use in Thailand in 2010, however, was 0.077 IU per year, compared with the global use at 1.433 IU per year [5]. In 2012, only 1171 or one fourth of estimated patients with hemophilia in Thailand were registered and able to access the medicines. No study, however, has been conducted in Thailand considering cost utility of home-based care treatment. This study was conducted to evaluate the cost utility of the home-based care policy versus the no home-based care policy of factor VIII and factor IX concentrate in Thai patients with hemophilia A and B who had no inhibitor or less than 5 Bethesda units (BU).

2. Identify the alternative interventions

Methods

Our study conducted a cost-utility analysis, an economic evaluation that estimates the cost per quality-adjusted life-year (QALY), and was designed to comply with Thai Health Technology Assessment Process Guidelines [6]. The Markov model was used to analyze the cost utility of the two treatment policies: providing

3. Identify and measure costs and outcomes

Resource Use

Lifetime cost of treatment in this study was considered as factor concentrate provided for early treatment of bleeding episodes at home for the home-based care policy and treatment cost at hospitals for emergency surgery and life-threatening operation. Treatment cost at hospital comprised the cost of factor concentrate and other medications used, such as blood components, medicines, and medical supplies, and cost for laboratory tests, room, doctor fee, and so forth. The calculation is as follows:

Direct medical cost = cost of factor concentrate provided at home per year +

[(rate of emergency surgery per year) × (length of stay per emergency surgery) × (cost of factor concentrate per day + cost of other medical use per day)] +

[(rate of life-threatening operation per year) × (length of stay per life-threatening operation) × (cost of factor concentrate per day + cost of other medical use per day)]

Cost of factor concentrate

Cost of factor concentrate used in the model was obtained from the Food and Drug Administration price quotation, which was 3424 and 6848 Thailand baht (THB) per vial, for 250 and 500 IU, respectively.

4. Value costs and outcomes

Other direct medical costs and length of stay

All other medical costs and patients' length of stay (LOS) were obtained from data of registered patients under the NHSO (Tables 4–6). Resource use was considered by patient's age. A child was defined as an individual younger than 10 years, whereas an adult was defined as an individual 10 years or older.

Utility

Because of the lack of utility data on health-related quality of life of Thai individuals with hemophilia A and B, the study, with the Ethics Committee approval from Ramathibodi Hospital, surveyed the quality of life of 105 Thai patients by mailed questionnaires. The response rate was 54.28% or 57 cases. The questionnaire had three parts: first was patient's demographic characteristics.

Second and third parts were the visual analogue scale before and after attending home-based care, respectively. The visual analogue scale was scored between 0 and 1, where 0 meant dead and 1 meant perfect life. Utility was then calculated as QALY = quality of life × life-year saved (Table 7).

5.1. Structure a model

The health states included in the Markov model are shown in Fig. 1. The ovals represent the possible health states, and the arrows indicate the possible transition between those states. Life-threatening bleeding is defined as hemorrhage or bleeding leading to death, requiring prompt hospital intervention, whereas emergency surgery is a surgical procedure that risks bleeding; thus, prevention of bleeding in the operation room is requested.

With a 1-year cycle length, the model was structured with the following assumptions:

1. All individuals entered the model in the health state "well."
2. At the following cycle, individuals remained in the health state well or entered the health states "life threatening" or "emergency surgery" or "death."
3. In each cycle, individuals in the life-threatening state may also receive emergency surgery and individuals in the emergency surgery state may also be in the life-threatening state. After the treatment, individuals can pass to the well state or death at the end of the cycle.

The cycle will run until the individual reaches the age of 99 years or is dead. Our model was run for a hypothetical cohort of 5000 Thai patients with hemophilia A and B who had no inhibitor or less than 5 BU, with the severity proportion of severe: moderate:mild patients at 40:38:22 [8]. Patients' severity was considered by level of clotting factor activity. Patients with less than 1% were classified as having severe hemophilia, those with 1% to 5% and more than 5% to 40% had moderate and mild hemophilia, respectively. The model was run to simulate two scenarios. Scenario 1 was for "no home-based care" in which patients were treated with blood components only when admitted at the hospital but no home treatment. Scenario 2 was for "home-based care" in which factors were prescribed and infused by patients for treatment of early bleeding episodes at home.

Transition Probabilities

The 1-year transition probability matrix is shown in Table 1. Probability of death (Table 2) was estimated from a life table for Thai population by age group [9] adjusted by available evidence of mortality rate in people with hemophilia A or B but without HIV infection in the United Kingdom [10]. Data of annual probability of requiring emergency surgery and life-threatening operation (Table 3) were obtained from registered patients under the National Health Security Office (NHSO). The data were collected from electronic databases from 29 hospitals in 21 provinces in 2007 (n = 328) [11] and from drug reimbursement data between 2007 and 2012 submitted to the NHSO (n = 563) [8].

5.2. Identify and synthesize evidence

5.3. Deal with uncertainty

Sensitivity Analysis

One-way sensitivity analysis was performed for children with mild hemophilia, varying the discount rate (0%–6%), rate of hospitalization (95% confidence interval), LOS (95% confidence interval), and cost of factor concentrate (±10%). In addition, probabilistic sensitivity analysis was simulated by using the Monte-Carlo method. Using Microsoft Excel, the number was sampled 5000 times according to each parameter's distribution.

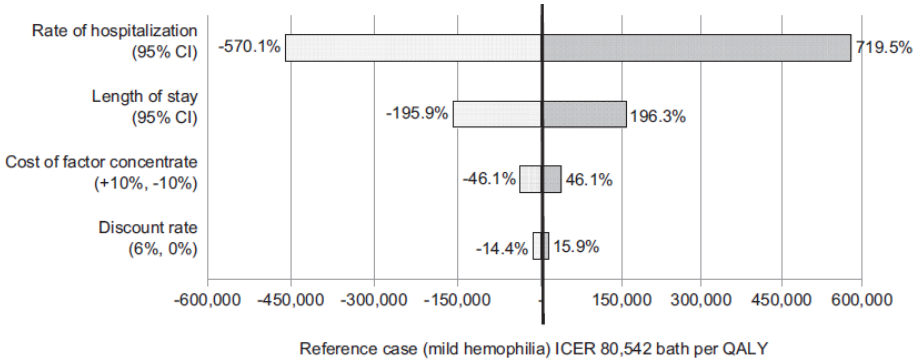

Fig. 2 – One-way sensitivity analysis. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

Table 8 – Lifetime cost of treatment, quality-adjusted life-year (QALY), and incremental cost-effectiveness ratios (ICERs) for patient with and without home-based care.

Severity	Policy	Lifetime cost of treatment (THB)	QALY	Cost per QALY	ICER
Mild	No home-based care	4,998,017	23.29	214,595	
	Home-based care	5,225,394	26.11	200,103	80,542
Moderate	No home-based care	13,659,490	16.47	829,504	
	Home-based care	11,198,618	22.44	499,157	Cost saving
Severe	No home-based care	25,908,099	12.21	2,122,085	
	Home-based care	20,189,367	20.61	979,557	Cost saving

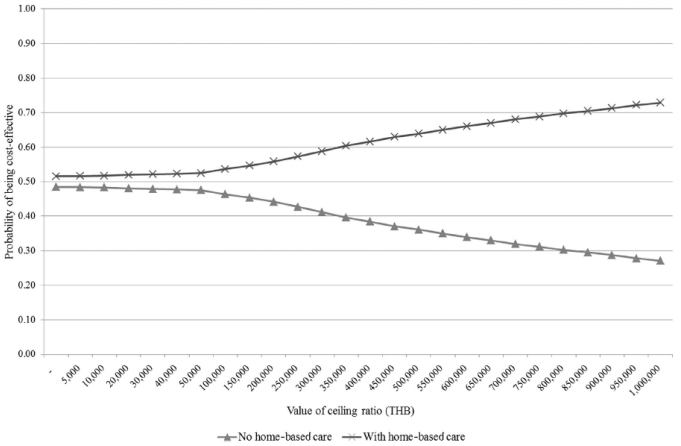

Fig. 3 – Probabilistic sensitivity analysis. THB, Thai Baht.

Example 2: from CEB

From **treatment effect** model → Research proposal for **EC approval** → To **cost-effectiveness** analysis

2017

Vejakama et al. BMC Nephrology (2017) 18:342
DOI 10.1186/s12882-017-0753-9

BMC Nephrology

RESEARCH ARTICLE Open Access

Treatment effects of renin-angiotensin aldosterone system blockade on kidney failure and mortality in chronic kidney disease patients

Phisitt Vejakama[1,2], Atiporn Ingsathit[1*], Gareth J. McKay[3], Alexander P. Maxwell[3], Mark McEvoy[4], John Attia[4] and Ammarin Thakkinstian[1]

Table 2. Estimation of average treatment effects and potential outcome mean of RAAS blockade on ESRD by diabetic groups

Model for diabetic patients	Treatments	RD	LL.	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	-0.0100	-0.0445	0.0246	-100.3	-447.6	247.0
	RAAS2 vs non-RAAS	-0.0712	-0.0878	-0.0547	-14.0	-17.3	-10.8
		Risk	LL	UL	RR	LL	UL
POM	Non-RAAS	0.1999	0.1917	0.2082	1		
	RAAS1	0.1899	0.0779	0.1905	0.950	0.778	1.123
	RAAS2	0.1287	0.1139	0.1435	0.644	0.567	0.721
Model for non-diabetic patients	Treatments	RD	LL.	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	-0.0205	0-.0863	0.0453	-48.7	-204.9	107.5
	RAAS2 vs non-RAAS	-0.0674	-0.1216	-0.0132	-14.8	-26. 8	-2.9
		Risk	LL	UL	RR	LL	UL
POM	Non-RAAS	0.1812	0.1745	0.1879	1		
	RAAS1	0.1607	0.0949	0.2265	0.887	0.523	1.250
	RAAS2	0.1139	0.0598	0.1679	0.628	0.3301	0.926

ATE, average treatment effect; LL, lower limit; POM, potential outcome mean; RAAS1, duration use of 0.25-1 year; RAAS2, duration us 1year; RD, risk difference; RR, rate ratio; UL, upper limit

คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
๒๗๐ ถนนพระราม ๖ แขวงทุ่งพญาไท เขตราชเทวี กทม. ๑๐๔๐๐
โทร. (๐๒) ๒๐๑-๑๐๐๐
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270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand
Tel. (662) 201-1000

Documentary Proof of Ethical Clearance
Committee on Human Rights Related to Research Involving Human Subjects
Faculty of Medicine Ramathibodi Hospital, Mahidol University

MURA2016/197

Title of Project (EC_590371)	Economic Evaluation of Renin-Angiotensin Aldosterone System Blockade on Progression of Chronic Kidney Disease: Derived from Thai Evaluation of Treatment Effectiveness Study
Protocol Number	ID 03-59-49
Principal Investigator	Dr. Oraluck Pattanaprateep
Official Address	Section for Clinical Epidemiology and Biostatistics Faculty of Medicine Ramathibodi Hospital Mahidol University

The aforementioned project has been reviewed and approved by the Committee on Huma Rights Related to Research Involving Human Subjects, based on the Declaration of Helsinki.

Signature of Chairman Committee on Human Rights Related to Research Involving Human Subjects	Prof. Pat Mahachoklertwattana, M.D.
Date of Approval	March 18, 2016
Duration of Study	2 Months

2018

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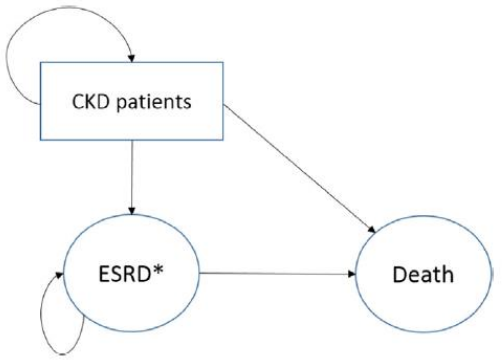
Cost-Effectiveness Analysis of Renin-Angiotensin Aldosterone System Blockade in Progression of Chronic Kidney Disease

Oraluck Pattanaprateep, PhD[1], Atiporn Ingsathit, MD, PhD[1,*], Mark McEvoy, PhD[2], John Attia, MD, PhD[2,3], Ammarin Thakkinstian, PhD[1]
[1]Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [2]Centre for Clinical Epidemiology and Biostatistics, Faculty of Health and Medicine, School of Medicine and Public Health, University of Newcastle, Callaghan, New South Wales, Australia; [3]Hunter Medical Research Institute, New Lambton Heights, New South Wales, Australia



Economic Evaluation of Renin-Angiotensin Aldosterone System Blockade on Progression of Chronic Kidney Disease: derived from Thai evaluation of treatment effectiveness study

Population: diabetic and non-diabetic group

Intervention: using RAAS vs. non-RAAS

Table 2. Estimation of average treatment effects and potential outcome mean of RAAS blockade on ESRD by diabetic groups

Model for diabetic patients	Treatments	RD	LL.	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	-0.0100	-0.0445	0.0246	-100.3	-447.6	247.0
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ATE, average treatment effect; LL, lower limit; POM, potential outcome mean; RAAS1, duration use of 0.25-1 year; RAAS2, duration use of > 1year; RD, risk difference; RR, rate ratio; UL, upper limit

1. nonDM, RAAS

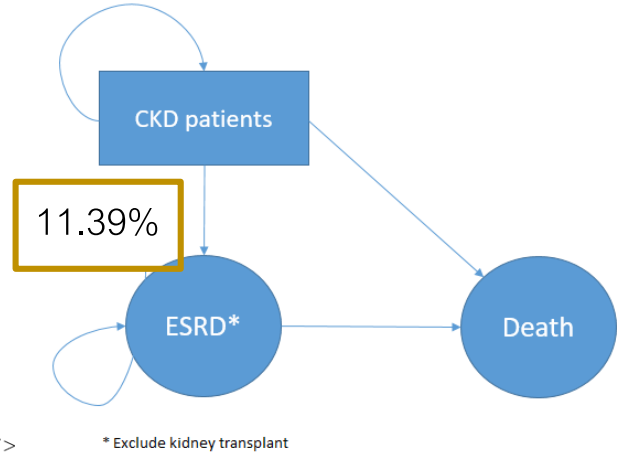


Table 3 Estimation of average treatment effects and potential outcome mean of RAAS treatment on death before ESRD by diabetic groups

Model for diabetic patients	Factors	RD	LL	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	0.030	−0.012	0.072	32.9	−12.6	78.5
	RAAS2 vs non-RAAS	−0.052	−0.069	−0.035	−19.1	−25.5	−12.9
		Risk	LL	UL	RR	LL	UL
POM	Non-RAAS	0.196	0.187	0.204			
	RAAS1	0.227	0.186	0.268	1.155	0.939	1.369
	RAAS2	0.144	0.129	0.159	0.773	0.652	0.815
Model for non-diabetic patients	Factors	RD	LL	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	−0.009	−0.066	0.048	−113.6	−848.7	621.5
	RAAS2 vs non-RAAS	−0.064	−0.099	−0.029	−15.6	−24.2	−71
		Risk	LL	UL	RR	LL	
POM	Non-RAAS	0.223	0.215	0.229			
	RAAS1	0.224	0.157	0.270	0.960	0.705	
	RAAS2	0.159	0.124	0.193	0.713	0.557	

ATE Average treatment effect, *LL* Lower limit, *POM* Potential outcome mean, *RAAS1* Duration use of 0.25–1 year, *RAAS2* Duration use of >1 year, *RD* *RR* Rate ratio, *UL* Upper limit

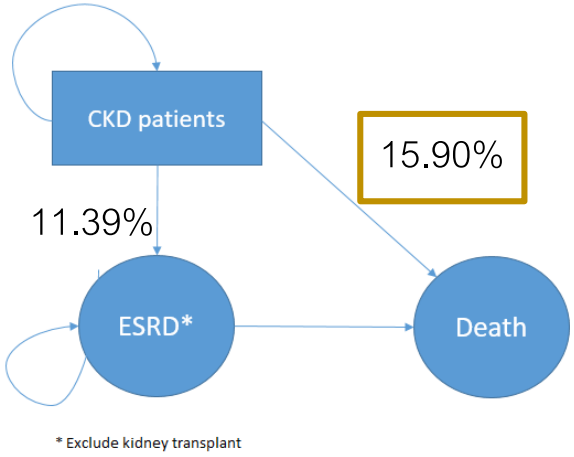
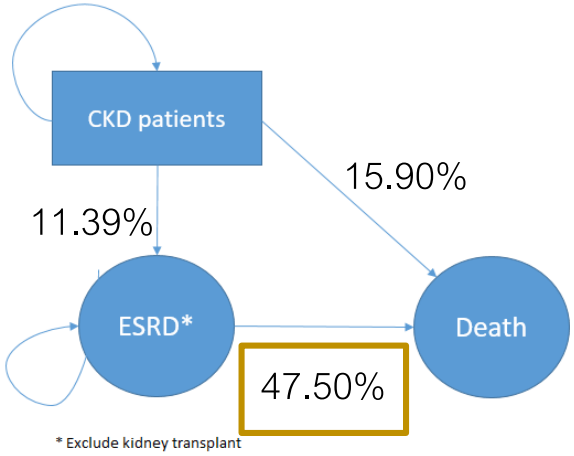
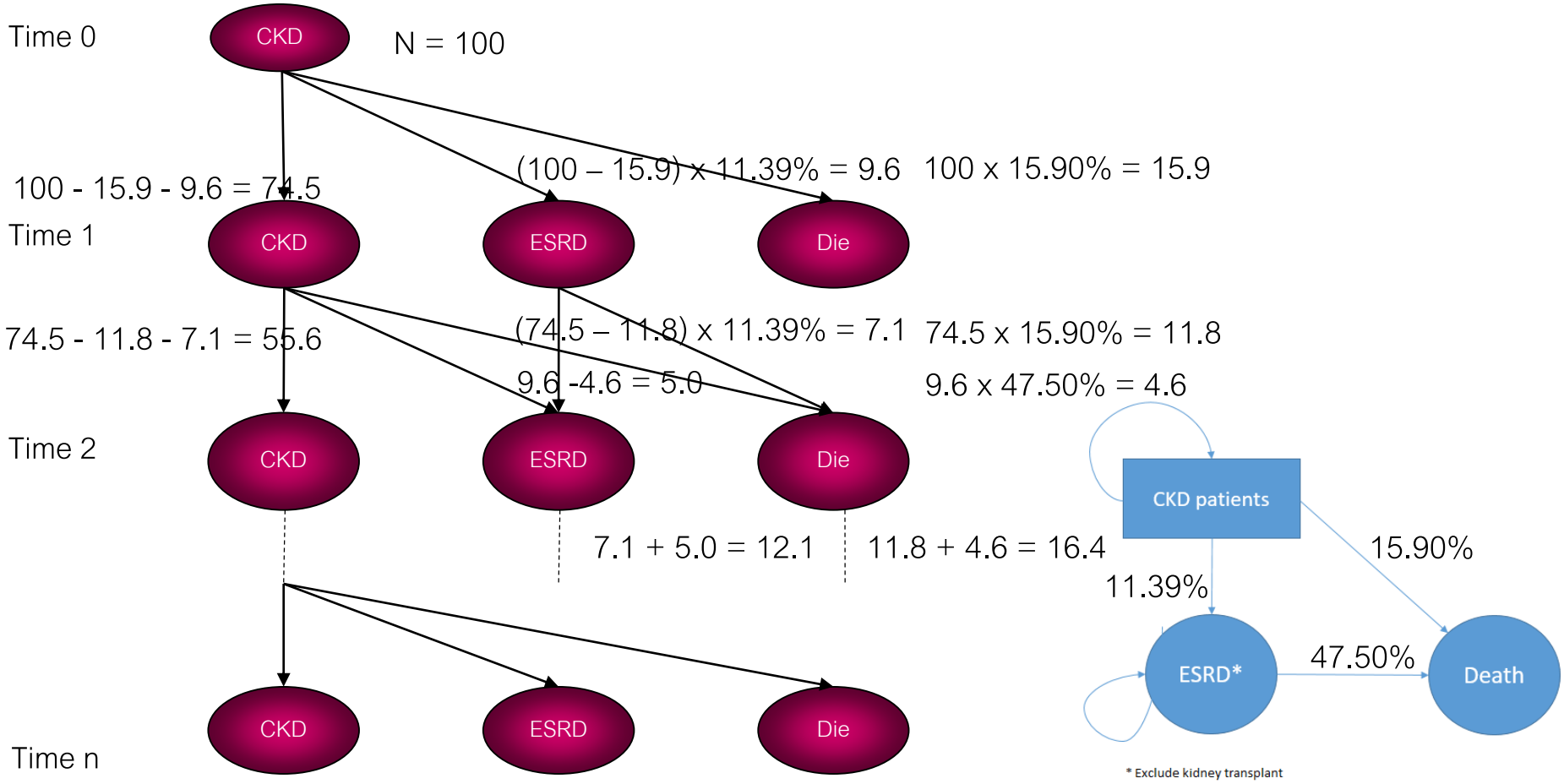


Table 4 Estimation of average treatment effects and potential outcome mean of RAAS treatment on death after ESRD by diabetic groups

Model for diabetic patients	Treatments	RD	LL	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	0.062	−0.037	0.161	16.1	−9.5	41.7
	RAAS2 vs non-RAAS	−0.059	−.0129	0.0112	−16.9	−36.9	3.18
		Risk	LL	UL	RR	LL	UL
POM	Non-RAAS	0.681	0.659	0.704	1		
	RAAS1	0.743	0.647	0.839	1.091	0.945	1.236
	RAAS2	0.622	0.555	0.689	0.913	0.810	1.016
Model for non-diabetic patients	Treatments	RD	LL	UL	NNT	LL	UL
ATE	RAAS1 vs non-RAAS	0.124	−0.059	0.306	8.1	−3.8	19.9
	RAAS2 vs non-RAAS	−0.121	−0.333	0.092	−8.3	−22.9	6.3
		Risk	LL	UL	RR	LL	UL
POM	Non-RAAS	0.596	0.576	0.617	1		
	RAAS1	0.719	0.539	0.901	1.209	0.909	
	RAAS2	0.475	0.264	0.687	0.798	0.435	

ATE Average treatment effect, *LL* Lower limit, *POM* Potential outcome mean, *RAAS1* Duration use of 0.25–1 year, *RAAS2* Duration use of >1 year, *RD* Ri
RR Rate ratio, *UL* Upper limit

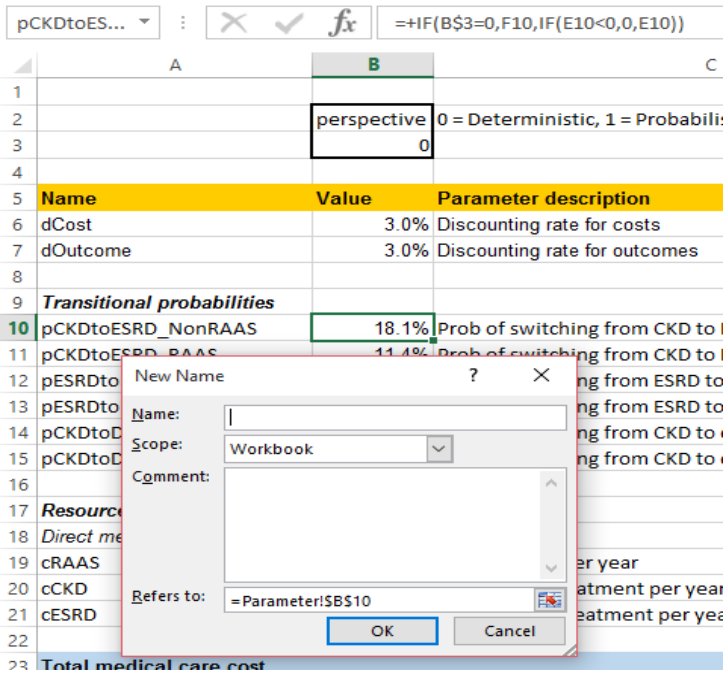


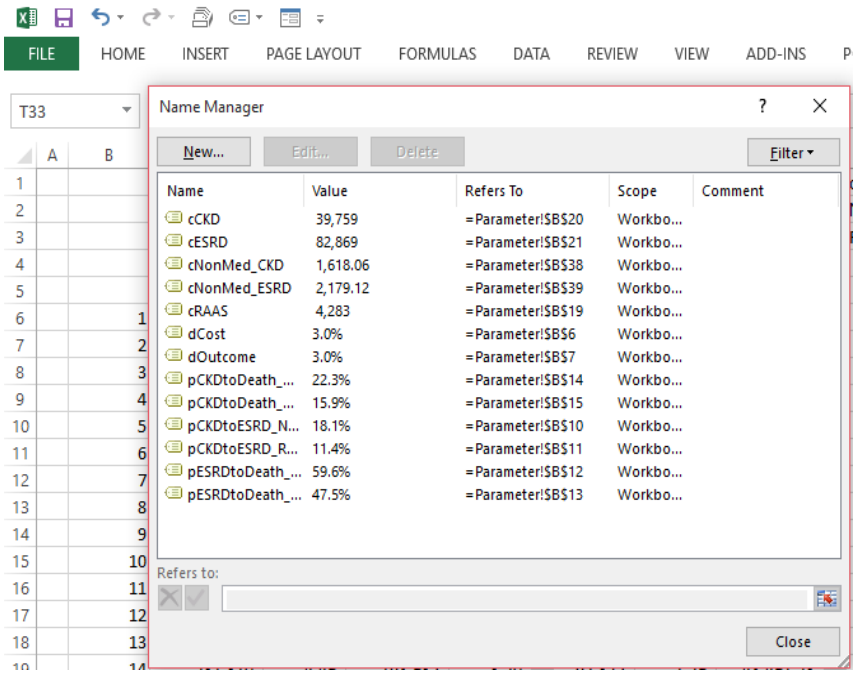

Time 0
CKD
N = 100
100 - 15.9 - 9.6 = 74.5
(100 – 15.9) x 11.39% = 9.6
100 x 15.90% = 15.9
Time 1
CKD
ESRD
Die
74.5 - 11.8 - 7.1 = 55.6
(74.5 – 11.8) x 11.39% = 7.1
74.5 x 15.90% = 11.8
9.6 -4.6 = 5.0
9.6 x 47.50% = 4.6
Time 2
CKD
ESRD
Die
7.1 + 5.0 = 12.1
11.8 + 4.6 = 16.4
Time n
CKD
ESRD
Die
CKD patients
15.90%
11.39%
ESRD*
47.50%
Death
* Exclude kidney transplant

Exercise: develop Markov model in MS Excel®

- define name for variables
- use formula to calculate
- Monte Carlo analysis by Macro

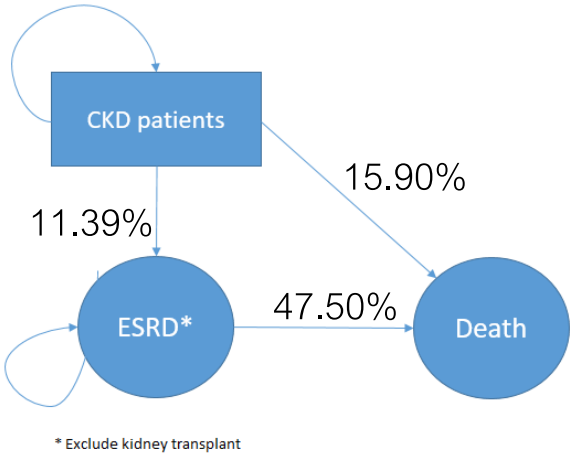
Define variables name



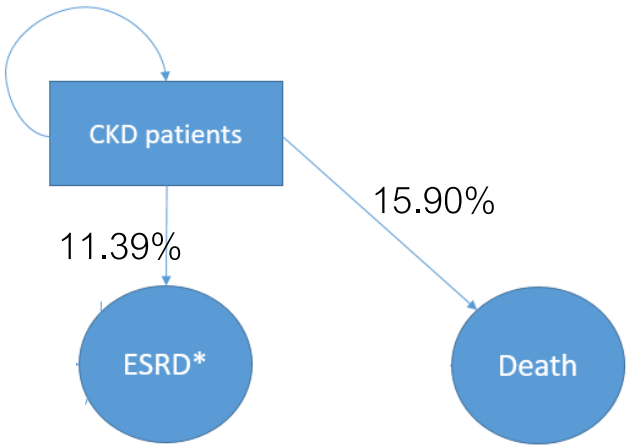


Markov_RAAS_1.1.xlsm

1. nonDM, RAAS



Name	Value	Parameter description	Mean
dCost	3.0%	Discounting rate for costs	
dOutcome	3.0%	Discounting rate for outcomes	
Transitional probabilities			
pCKDtoESRD_NonRAAS	18.1%	Prob of switching from CKD to ESRD in non RAAS group	0.1812
pCKDtoESRD_RAAS	11.4%	Prob of switching from CKD to ESRD in RAAS group	0.1139
pESRDtoDeath_NonRAAS	59.6%	Prob of switching from ESRD to death in non RAAS group	0.596
pESRDtoDeath_RAAS	47.5%	Prob of switching from ESRD to death in RAAS group	0.475
pCKDtoDeath_NonRAAS	22.3%	Prob of switching from CKD to death in non RAAS group	0.223
pCKDtoDeath_RAAS	15.9%	Prob of switching from CKD to death in RAAS group	0.159
Resource cost parameters			
Direct medical care costs			
cRAAS	4,283	Cost of RAAS per year	4,283
cCKD	39,759	Cost of CKD treatment per year	39,759
cESRD	82,869	Cost of ESRD treatment per year	82,869
Total medical care cost			
cMed			
Direct non-medical care costs i.e. travel cost			
	206.24	Cost per visit/admit	206.24
cDirNonMed_CKD	4.13	No. of visit/admit per year for CKD	4.13
cDirNonMed_ESRD	5.56	No. of visit/admit per year for ESRD	5.56
Indirect costs i.e. income loss			
	185.87	Income loss when visit/admit	185.87
cIndNonMed_CKD	4.13	Days of visit/admit per year for CKD	4.13
cIndNonMed_ESRD	5.56	Days of visit/admit per year for ESRD	5.56
Total cost			
cNonMed_CKD	1,618.06		
cNonMed_ESRD	2,179.12		



* Exclude kidney transplant

E	F	G	H	I	J	K	L	M	N
								Accum death	Check
DtoDeath	ESRDtoDeath	CKD	ESRD	Death	Cost	Life Years			
		1.00			45,660	1.0		-	1.00000
15.90%	47.50%	0.75	0.10	0.16	41,343	0.8		0.16	1.00000
15.90%	47.50%	0.56	0.12	0.16	34,146	0.6		0.32	1.00000
15.90%	47.50%	0.41	0.12	0.15	26,863	0.5		0.47	1.00000
15.90%	47.50%	0.31	0.10	0.12	20,536	0.4		0.59	1.00000
15.90%	47.50%	0.23	0.08	0.10	15,419	0.3		0.69	1.00000

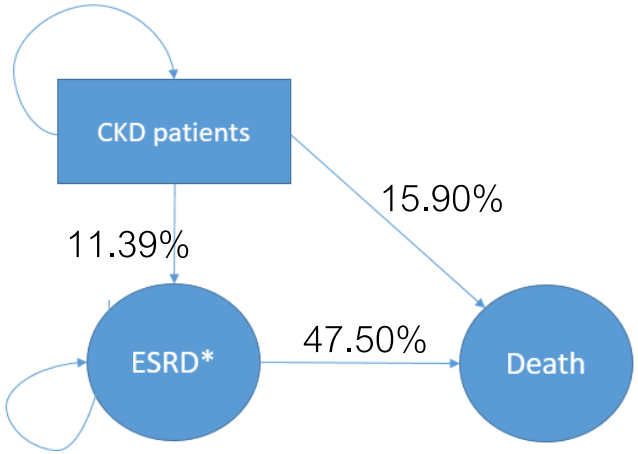
Cycle 0

=+pCKDtoESRD_RAAS | =+pCKDtoDeath_RAAS

=+(G6*E7) | =+G6*(1-E7)*D7 | =G6-H7-I7

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1														
2													Accum death	Check
3	Age	Cycle	days	CKDtoESRD	CKDtoDeath	ESRDtoDeath	CKD	ESRD	Death	Cost	Life Years			
4		(year)												
5														
6	40	0	-				1.00			45,660	1.0		-	1.00000
7	41	1	365	11.39%	15.90%	47.50%	0.75	0.10	0.16	41,343	0.8		0.16	1.00000
8	42	2	730	11.39%	15.90%	47.50%	0.56	0.12	0.16	34,146	0.6		0.32	1.00000
9	43	3	1,095	11.39%	15.90%	47.50%	0.41	0.12	0.15	26,863	0.5		0.47	1.00000
10	44	4	1,460	11.39%	15.90%	47.50%	0.31	0.10	0.12	20,536	0.4		0.59	1.00000
11	45	5	1,825	11.39%	15.90%	47.50%	0.23	0.08	0.10	15,419	0.3		0.69	1.00000

Cycle 1



Cycle 2…..

=+(G7*E8)+(H7*F8)

=(G7*(1-E8)*D8)+(H7*(1-F8))

=G7-(G7*(1-E8)*D8)-(G7*E8)

=+pESRDtoDeath_RAAS

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1														
2													Accum death	Check
3	Age	Cycle	days	CKDtoESRD	CKDtoDeath	ESRDtoDeath	CKD	ESRD	Death	Cost	Life Years			
4		(year)												
5														
6	40	0	-				1.00			45,660	1.0		-	1.00000
7	41	1	365	11.39%	15.90%	47.50%	0.75	0.10	0.16	41,343	0.8		0.16	1.00000
8	42	2	730	11.39%	15.90%	47.50%	0.56	0.12	0.16	34,146	0.6		0.32	1.00000
9	43	3	1,095	11.39%	15.90%	47.50%	0.41	0.12	0.15	26,863	0.5		0.47	1.00000
10	44	4	1,460	11.39%	15.90%	47.50%	0.31	0.10	0.12	20,536	0.4		0.59	1.00000
11	45	5	1,825	11.39%	15.90%	47.50%	0.23	0.08	0.10	15,419	0.3		0.69	1.00000

Cost and Life years

=((G6*(cRAAS+cCKD+cNonMed_CKD))+(H6*(cRAAS+cESRD+cNonMed_ESRD)))/(1+dCost)^B6

=(G6+H6)/(1+dOutcome)^B6

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1														
2													Accum death	Check
3	Age	Cycle	days	CKDtoESRD	CKDtoDeath	ESRDtoDeath	CKD	ESRD	Death	Cost	Life Years			
4		(year)												
5														
6	40	0	-				1.00			45,660	1.0		-	1.00000
7	41	1	365	11.39%	15.90%	47.50%	0.75	0.10	0.16	41,343	0.8		0.16	1.00000
8	42	2	730	11.39%	15.90%	47.50%	0.56	0.12	0.16	34,146	0.6		0.32	1.00000
9	43	3	1,095	11.39%	15.90%	47.50%	0.41	0.12	0.15	26,863	0.5		0.47	1.00000
10	44	4	1,460	11.39%	15.90%	47.50%	0.31	0.10	0.12	20,536	0.4		0.59	1.00000
11	45	5	1,825	11.39%	15.90%	47.50%	0.23	0.08	0.10	15,419	0.3		0.69	1.00000

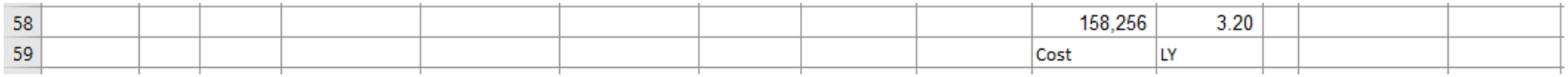
=SUM(J6:J56) =SUM(K6:K56)

58										226,420	4.30			
59										Cost	LY			

CE and ICER

RAAS : CE = 226,420/4.30 = 52,622.52 Baht/LY

nonRAAS : CE = 158,256/3.20 = 53,678.16 Baht/LY



CEA RAAS vs. non-RAAS use (incremental cost per life year saved)

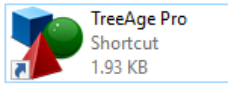
Deterministic	
Incremental cost	68,165
Incremental LYs saved	1.10
ICER per LY saved	62,032

226,420-158,256 = 68,165 Baht

4.30 – 3.20 = 1.10 LY

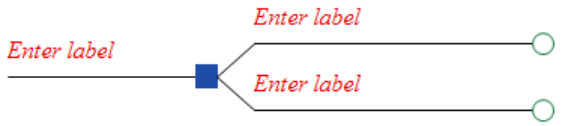
68,165/1.10 = 62,032 Baht/LY

Exercise: develop Markov model by TreeAge Pro®

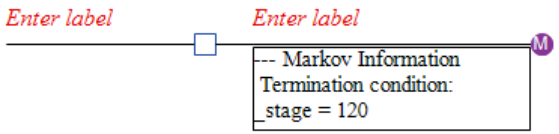
- install program 

- create new decision tree (Ctrl + N)
- run sensitivity analysis

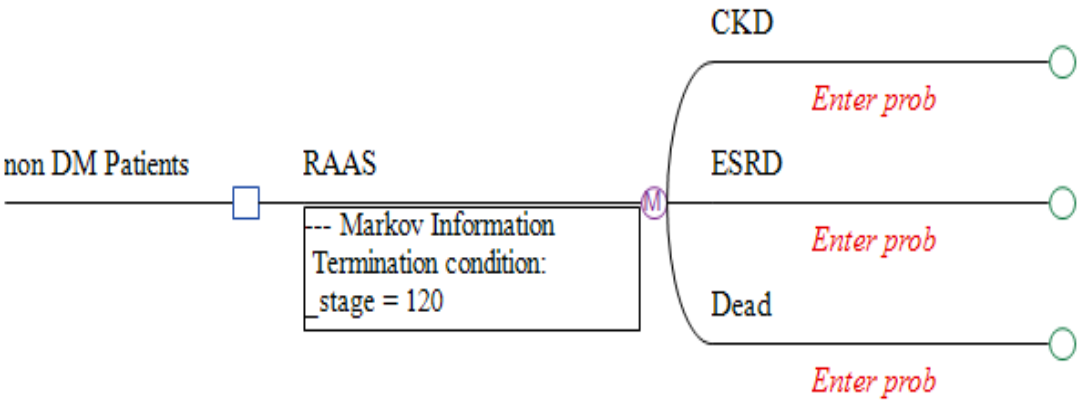
1. Add branch by double click on node



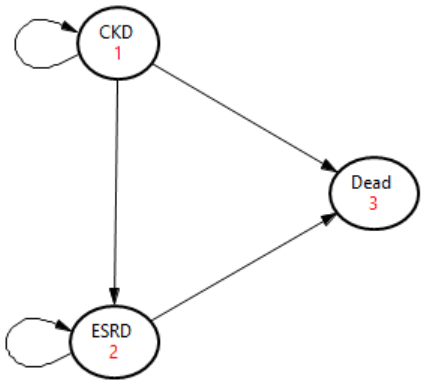
2. Add Markov node by drag and drop from Palette

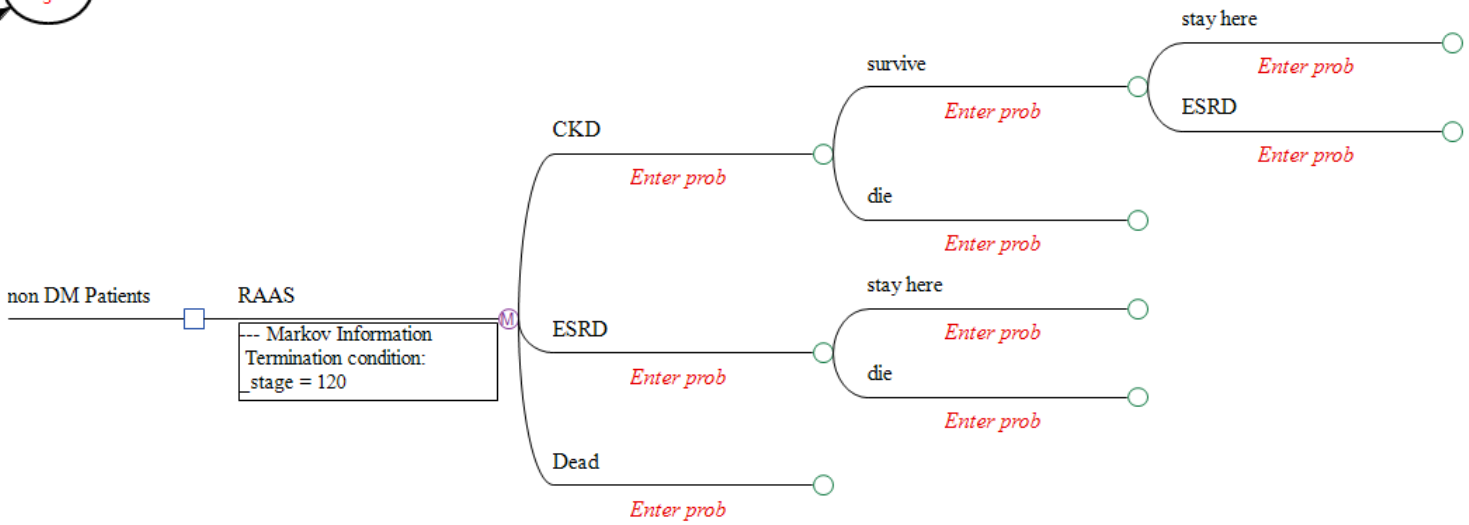


3. Define name and insert node for Markov

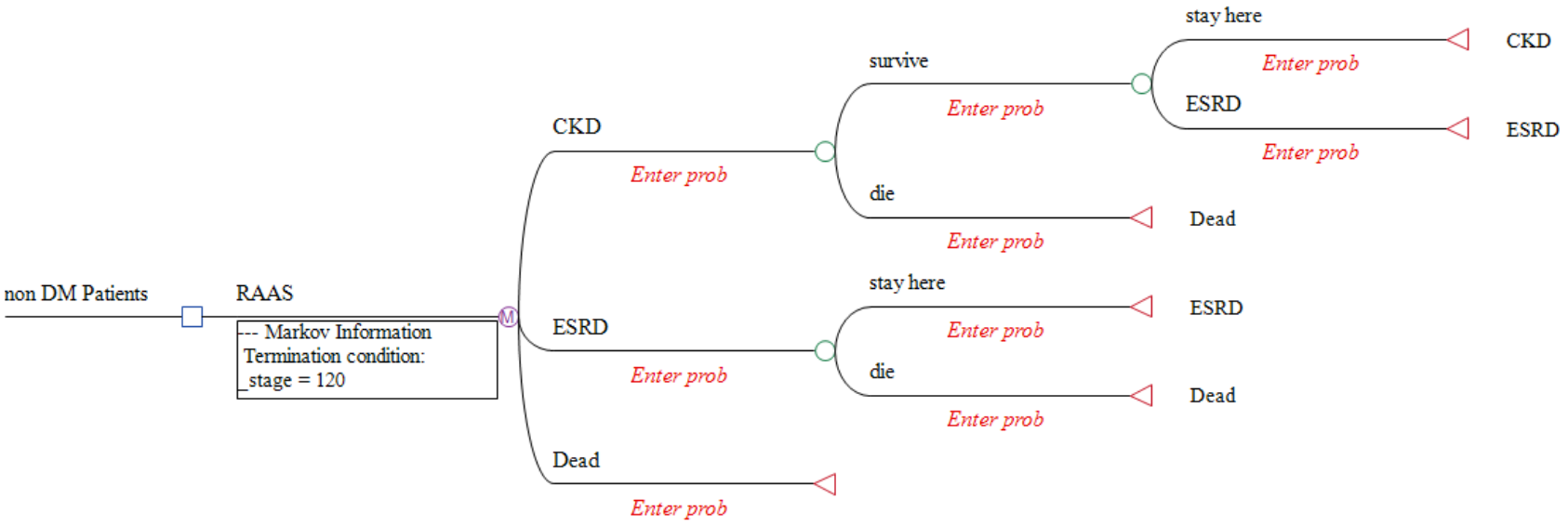


4. Complete chance nodes as shown in State Transition Diagram

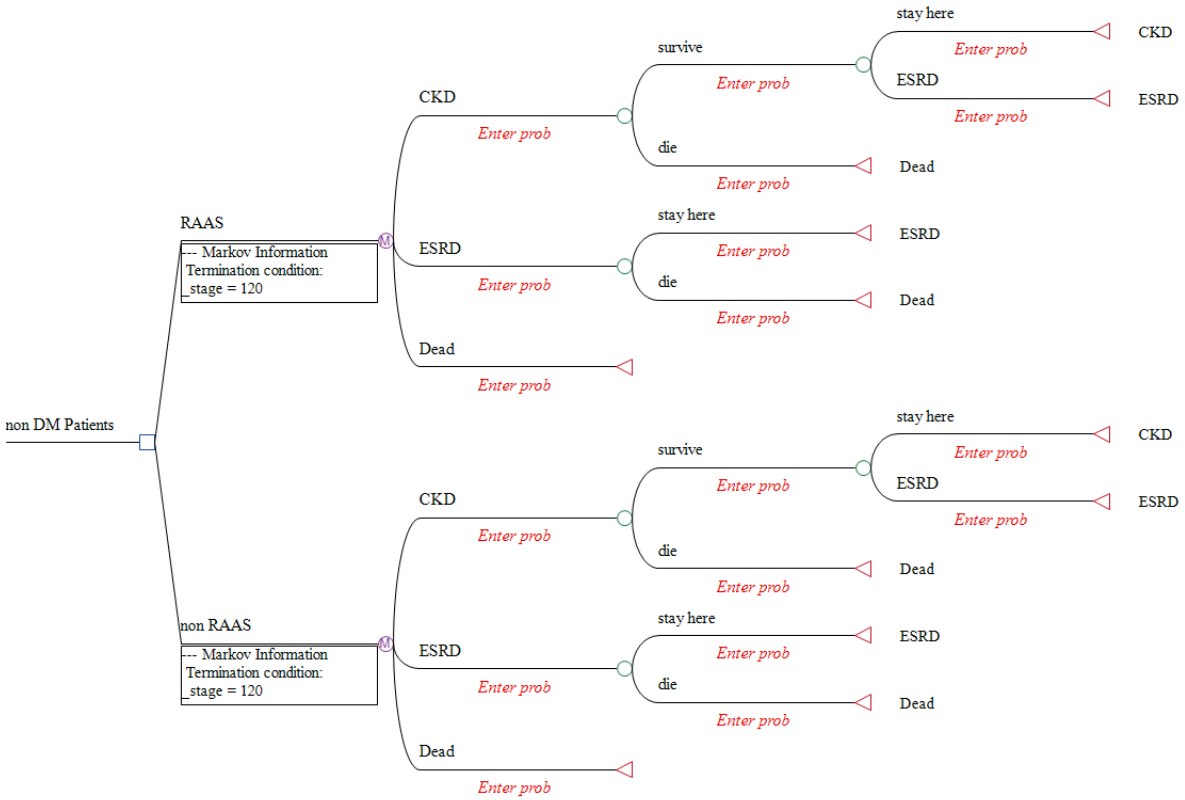




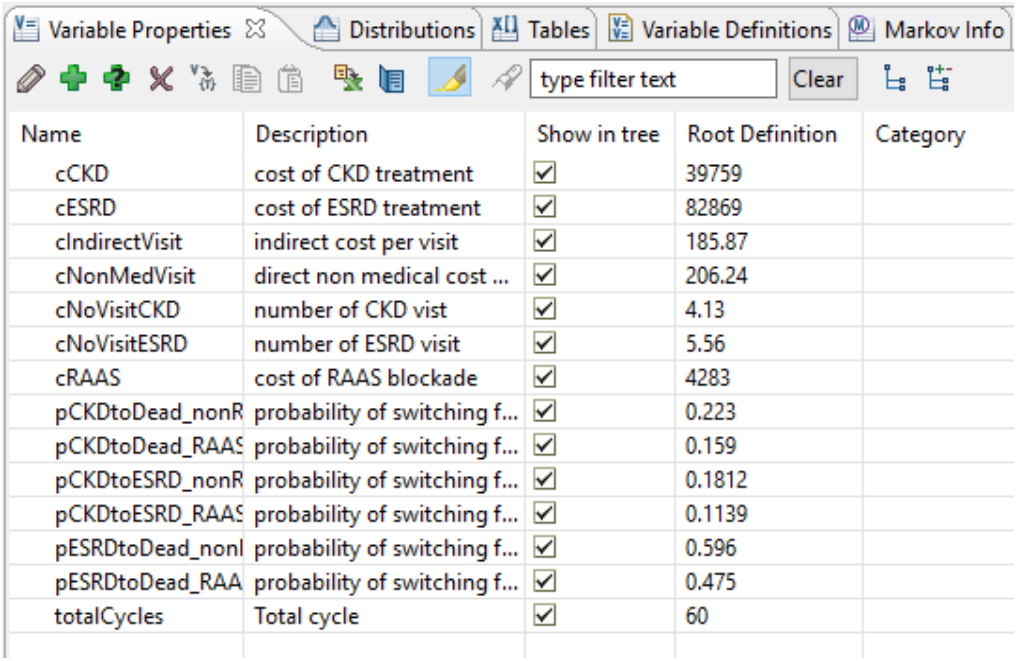
5. Assign terminal nodes for each branch



6. Add “non RAAS” Markov node, then copy and paste Markov tree

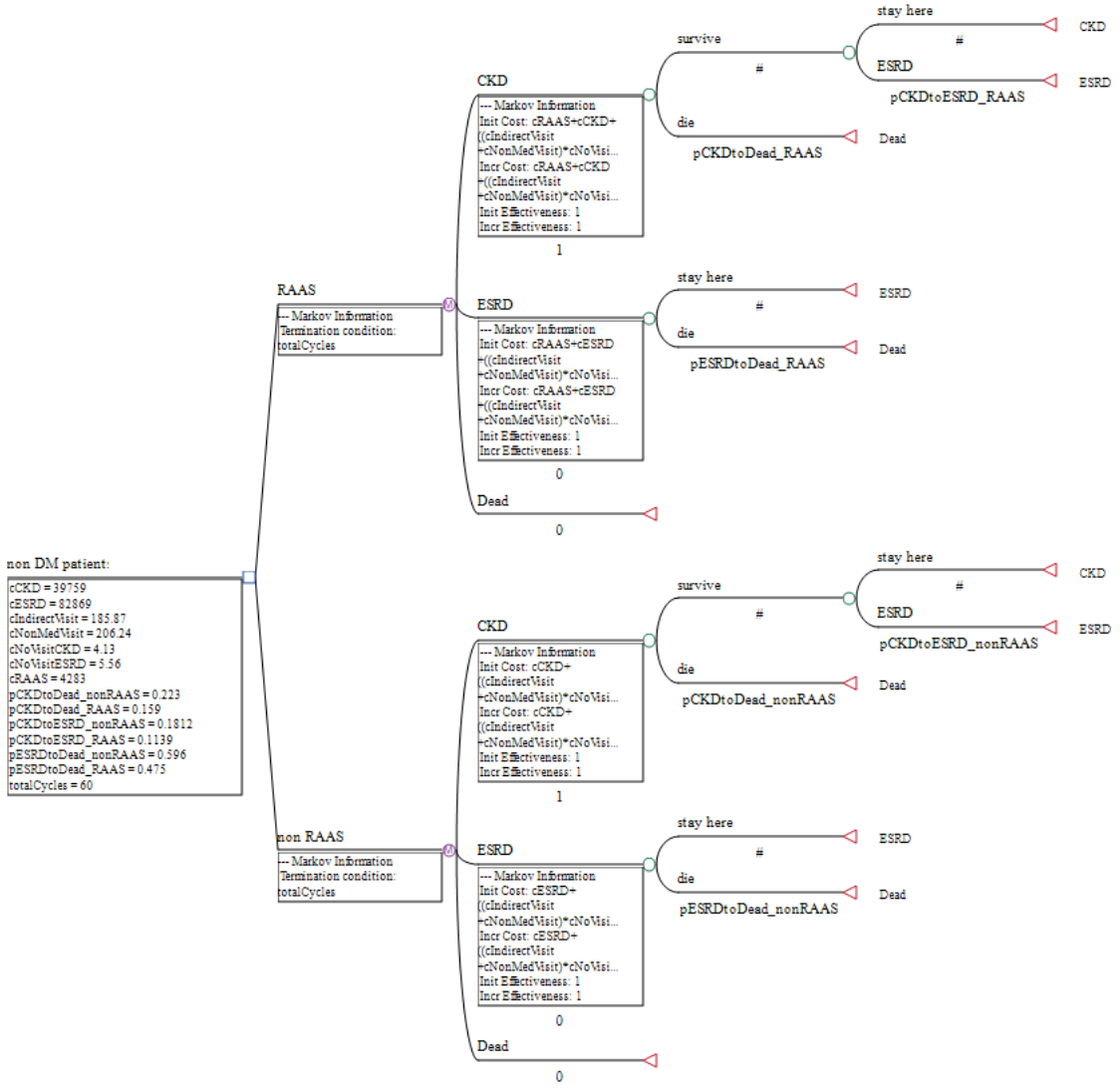


7. Add variables and their properties



Name	Description	Show in tree	Root Definition	Category
cCKD	cost of CKD treatment	☑	39759	
cESRD	cost of ESRD treatment	☑	82869	
cIndirectVisit	indirect cost per visit	☑	185.87	
cNonMedVisit	direct non medical cost ...	☑	206.24	
cNoVisitCKD	number of CKD vist	☑	4.13	
cNoVisitESRD	number of ESRD visit	☑	5.56	
cRAAS	cost of RAAS blockade	☑	4283	
pCKDtoDead_nonR	probability of switching f...	☑	0.223	
pCKDtoDead_RAAS	probability of switching f...	☑	0.159	
pCKDtoESRD_nonR	probability of switching f...	☑	0.1812	
pCKDtoESRD_RAAS	probability of switching f...	☑	0.1139	
pESRDtoDead_nonI	probability of switching f...	☑	0.596	
pESRDtoDead_RAA	probability of switching f...	☑	0.475	
totalCycles	Total cycle	☑	60	

8. Add variables and their properties



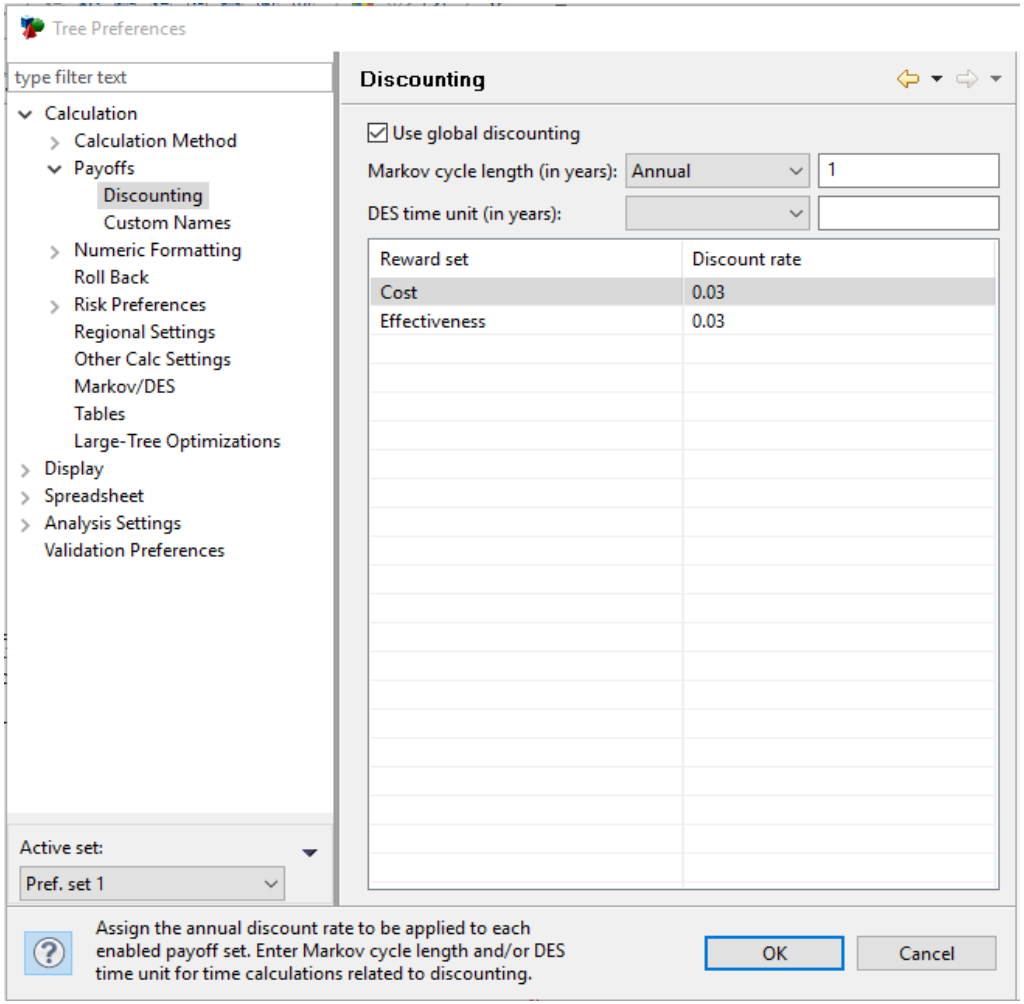
Variable Properties | Distributions | Tables | Variable Definitions | Markov Info

Name	Value
Calculate temp state initial probs	false
Initial probability	1
Rewards (Active Sets)	
Init Cost (Discounted)	cRAAS+cCKD+((cIndirectVisit+cNonMedVisit)*cNoVisitCKD)
Incr Cost (Discounted)	cRAAS+cCKD+((cIndirectVisit+cNonMedVisit)*cNoVisitCKD)
Final Cost (Discounted)	0
Init Effectiveness (Discounted	1
Incr Effectiveness (Discountec	1
Final Effectiveness (Discounte	0
Rewards (Inactive Sets)	
Tunnel max	0
Tunnel state	false

Markov Info

Name	Value
Calculate temp state initial probs	false
Initial probability	0
Rewards (Active Sets)	
Init Cost (Discounted)	cRAAS+cESRD+((cIndirectVisit+cNonMedVisit)*cNoVisitESRD)
Incr Cost (Discounted)	cRAAS+cESRD+((cIndirectVisit+cNonMedVisit)*cNoVisitESRD)
Final Cost (Discounted)	0
Init Effectiveness (Discounted	1
Incr Effectiveness (Discountec	1
Final Effectiveness (Discounte	0
Rewards (Inactive Sets)	
Tunnel max	0
Tunnel state	false

9. Select Calculation method and Discounting in Payoffs



10. Run analysis by select decision node : Analysis → Rankings

Cost-Effectiveness Rankings

Category	Strategy	Cost	Incr Cost	Eff	Incr eff	Incr C/E (ICER)	NMB	C/E
Excluding dominated								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	226,427.92	68,167.26	4.30	1.10	62,034.01	-226,427.92	52,624.27
All								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	226,427.92	68,167.26	4.30	1.10	62,034.01	-226,427.92	52,624.27
All referencing common baseline								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	226,427.92	68,167.26	4.30	1.10	62,034.01	-226,427.92	52,624.27
All by Increasing effectiveness								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	226,427.92		4.30			-226,427.92	52,624.27

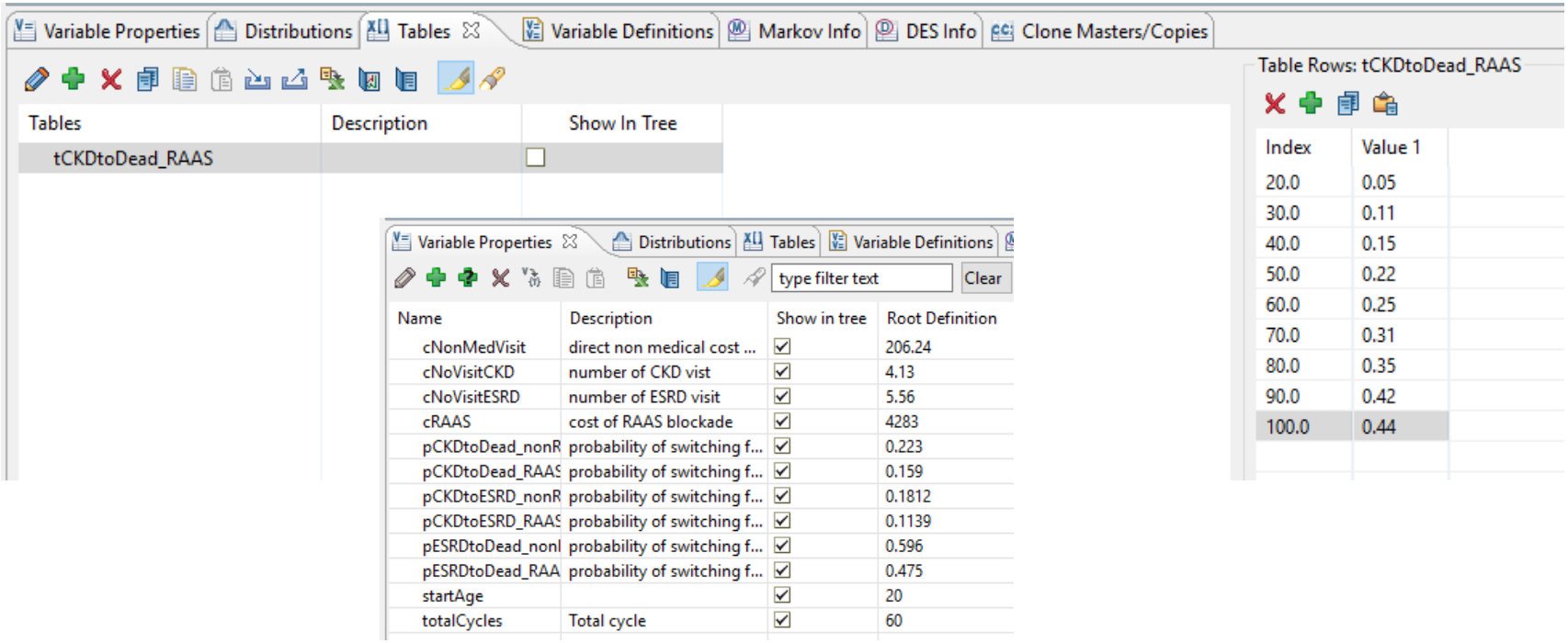
11. At Markov node: run Markov cohort to view the details of analysis at each stage

RAAS_nonDM.trex | *Markov Cohort (Basic) - RAAS_nonDM.trex - D~1_Epide~TreeAge~RACE607~RAAS_nonDM.trex

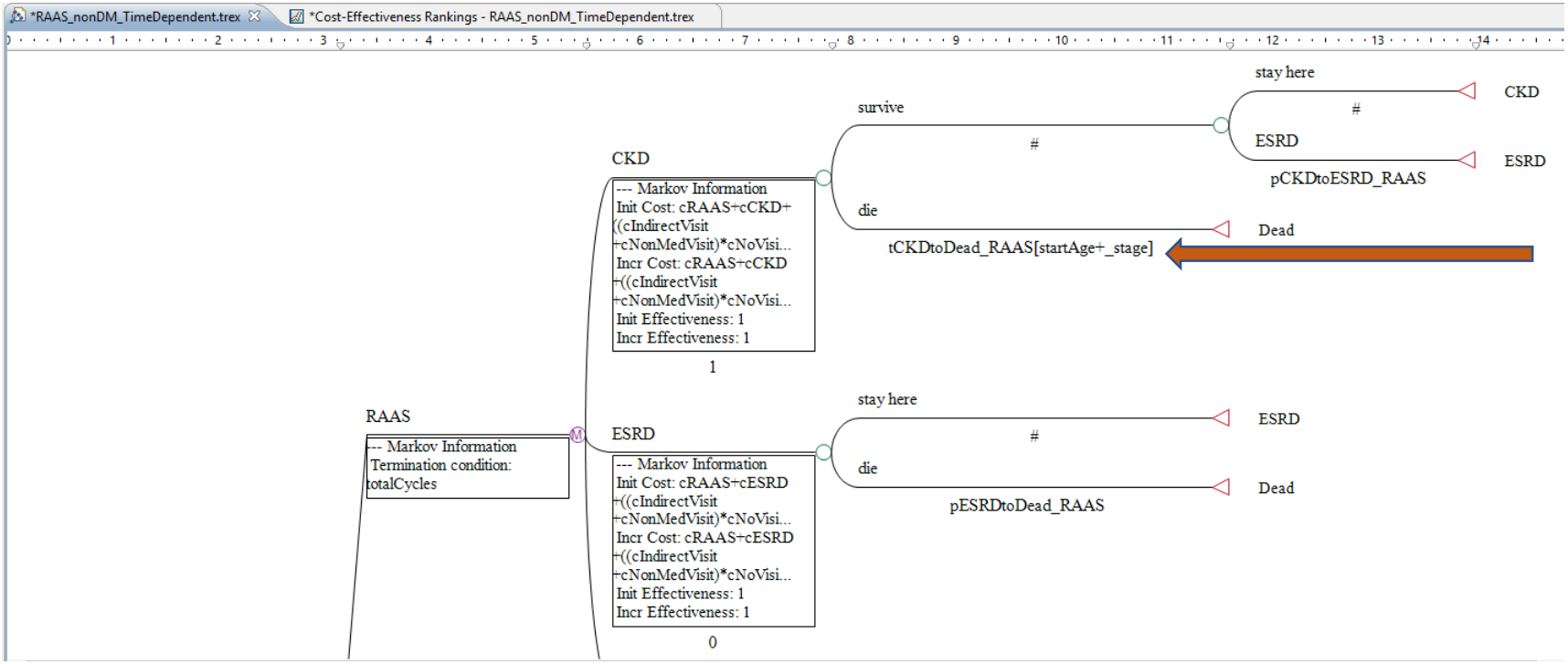
Markov Cohort (Basic)

Stage	State	Cohort %	Cost State Cohort Disc	Cost Transition Cohort Disc	Stage Cost	Cum Cost	Effectiveness State Cohort Disc	Effectiveness Transition Cohort Disc	Stage Effectiveness	Cum Effectiveness
⊟ 0	Summary		45661.4143	0	45661.4143	45661.4143	1	0	1	1
0	CKD	1.000	45661.4143	0			1	0		
0	ESRD	0.000	0	0			0	0		
0	Dead	0.000	0	0			0	0		
⊟ 1	Summary		41344.1389	0	41344.1389	87005.5532	0.8165	0	0.8165	1.8165
1	CKD	0.745	33036.25934	0			0.7235	0		
1	ESRD	0.096	8307.87957	0			0.093	0		
1	Dead	0.159	0	0			0	0		
⊟ 2	Summary		34147.28802	0	34147.28802	121152.84122	0.63815	0	0.63815	2.45465
2	CKD	0.555	23901.89721	0			0.52346	0		
2	ESRD	0.122	10245.39081	0			0.11469	0		
2	Dead	0.323	0	0			0	0		
⊟ 3	Summary		26864.14397	0	26864.14397	148016.98519	0.48587	0	0.48587	2.94052
3	CKD	0.414	17293.14098	0			0.37873	0		
3	ESRD	0.117	9571.00299	0			0.10714	0		
3	Dead	0.469	0	0			0	0		

Markov modeling techniques : Time-dependence



Markov modeling techniques : Time-dependence



Markov modeling techniques : Time-dependence

RAAS_nonDM_TimeDependent.trex | *Cost-Effectiveness Rankings - RAAS_nonDM_TimeDependent.trex - D~1_Epide~TreeAge~RACE607~RAAS_nonDM_Time

Cost-Effectiveness Rankings

Category	Strategy	Cost	Incr Cost	Eff	Incr eff	Incr C/E (ICER)	NMB	C/E
Excluding dominated								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	320,169.06	161,908.41	6.02	2.81	57,586.19	-320,169.06	53,224.52
All								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	320,169.06	161,908.41	6.02	2.81	57,586.19	-320,169.06	53,224.52
All referencing common baseline								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	320,169.06	161,908.41	6.02	2.81	57,586.19	-320,169.06	53,224.52
All by Increasing effectiveness								
undominated	non RAAS	158,260.65		3.20			-158,260.65	49,396.89
undominated	RAAS	320,169.06		6.02			-320,169.06	53,224.52