Markov Modeling

Part 8

Markov Models, Monte Carlo and Software Demonstration

Using Excel to build a Markov Model

- Create a sheet for transition probabilities
- Put transition probability names across columns
- Put probabilities for subsequent years in subsequent rows

Using Excel to build a Markov Model

- Create a sheet for health states
- Put names of health states across columns
- Populate “year 0” with desired starting populations
- Use transition probabilities to derive populations for each subsequent year

Using Excel to build a Markov Model

- Sum “occupancy” of each health state
- Apply discounting formula if desired
- Multiply time spent in each state by cost for that state and utility for that state

Using TreeAge

- Pros
  - Easy to build models
  - Good for model with many states
- Cons
  - Workings are a “black box” - difficult to understand the mechanics
  - More challenging to present to decision-makers

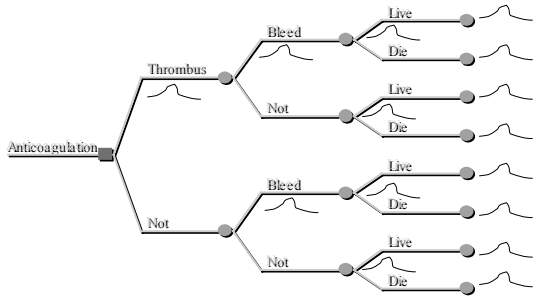
Monte Carlo simulation

- Primary use: evaluate uncertainty
- A numerical integration technique
  - (originally devised by Feynman during the Manhattan Project)
- Can be time-consuming, but
- Gives most reasonable estimate of overall uncertainty in the model

Limitations of deterministic sensitivity analysis

- No standard for permissible level of variation
- Analyst controls
  - which parameters varied
  - and over what range
- Complex interactions not captured by 1-, 2-, or 3-way sensitivity analysis
- Extreme case scenarios not realistic

MC simulation



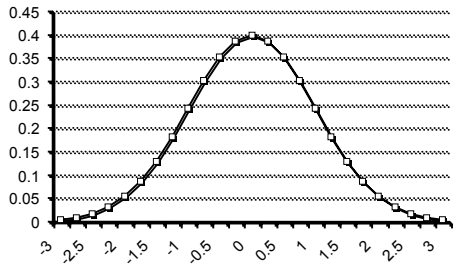
Probabilistic methods

- All costs, probabilities, and outcomes are associated with uncertainty simultaneously
- Certain values are “more likely”
- How do we calculate overall uncertainty in results?

Monte Carlo simulation

- Solve multiple integrals using numerical integration
- E.g.,
  - draw values randomly from all distributions
  - calculate expected values for tree
  - repeat until results converged

Probability density



Assigning distributions

- Probabilities and utilities
  - must be bounded by 0 and 1
  - use uniform, beta or logistic normal

Logistic normal

- Logistic normal easy to use
  - use formula of Doubilet et al
  - provide mean and upper or lower bound
  - formula provides mean and s.d. of normal distribution that when plugged into logistic function, EXP(y)/(1+EXP(y)), produces distribution with desired properties

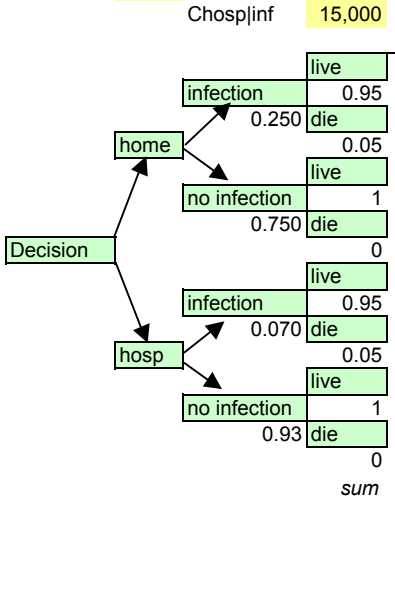
Assigning distributions

- Costs:
  - distribution should reflect uncertainty in the population mean, not the sample mean - so is often normal even though (sample) costs are often skewed
  - if range of possible population means is skewed, consider gamma function

Decision Tree

Pinf|home	0.250	Chome	12,000	U|home	0.9
Pinf|hosp	0.070	Chosp	15,000	U|hosp	0.8
Plive|inf	0.950	Cwtpnurse	1,000	discLE	1
Plive|noinf	1.000	Cfam|inf	0		
		Chosp|inf	15,000		

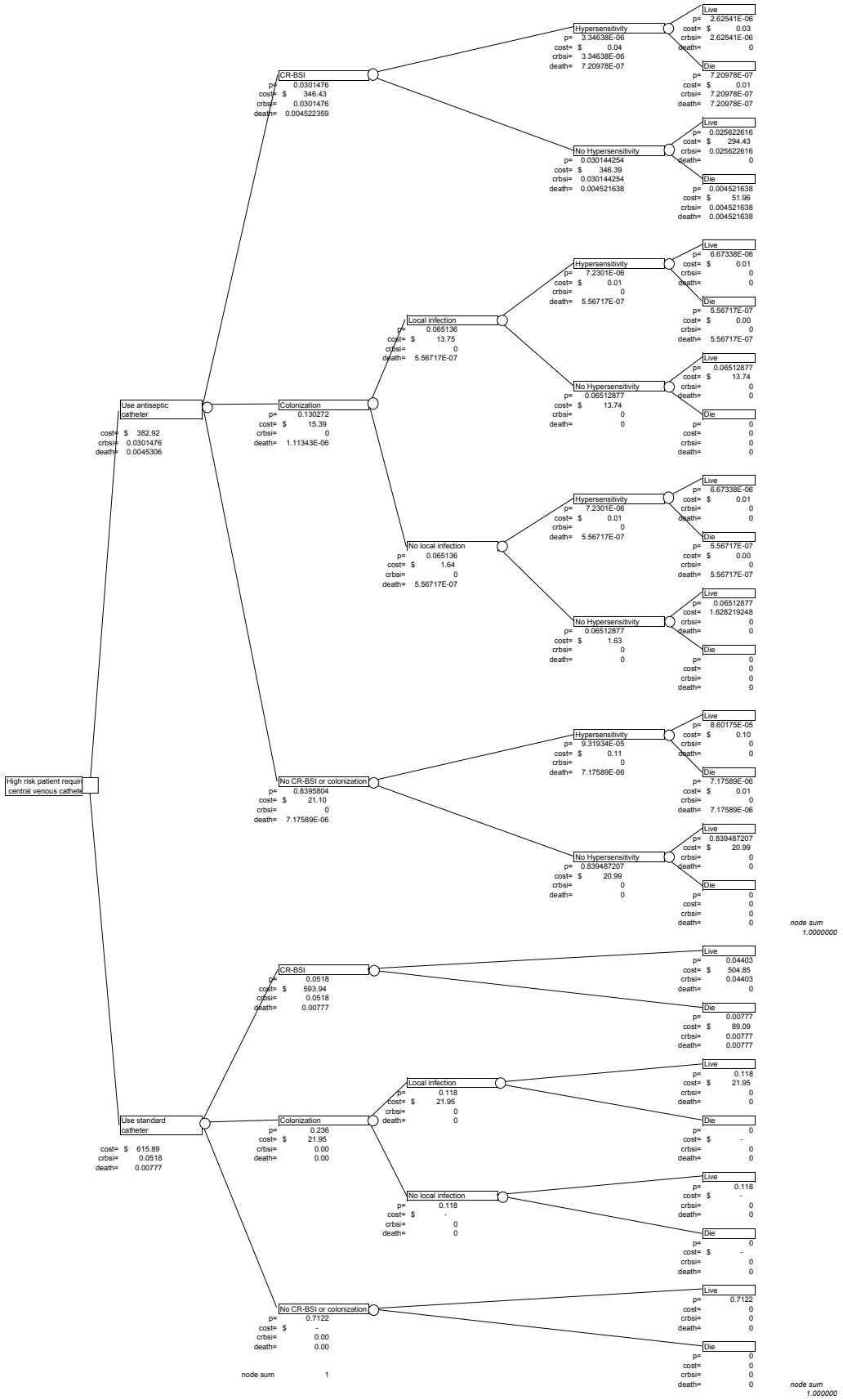
	Differences			
	Hosp	Fam	Soc	Societal
Total cost	**$ (300)**	**$ 1,000**	$ 700	ICER
Total Qaly			0.092	**$ 7,646**



				Poutcome	Chosp	Cfam	Csoc	WtC hosp	WtC fam	WtC soc	Util	LE	QALY	Wtd Qaly
			live	0.2375	27,000	1,000	28,000	6412.5	237.5	6650	0.9	1	0.9	0.21375
		infection	0.95											
		0.250	die	0.0125	27,000	1,000	28,000	337.5	12.5	350	0	0	0	0
	home		0.05											
			live	0.75	12,000	1,000	13,000	9000	750	9750	0.9	1	0.9	0.675
		no infection	1											
		0.750	die	0	12,000	1,000	13,000	0	0	0	0	0	0	0
Decision			0											
			live	0.0665	30,000	0	30,000	1995	0	1995	0.8	1	0.8	0.0532
		infection	0.95											
		0.070	die	0.0035	30,000	0	30,000	105	0	105	0	0	0	0
	hosp		0.05											
			live	0.93	15,000	0	15,000	13950	0	13950	0.8	1	0.8	0.744
		no infection	1											
		0.93	die	0	15,000	0	15,000	0	0	0	0	0	0	0
			0											
			sum			***SUMS***	*Home*	*$ 15,750*	*$ 1,000*	*$ 16,750*				*0.88875*
							Hosp	*$ 16,050*	*$ -*	*$ 16,050*				*0.7972*
							Diff	*$ (300)*	*$ 1,000*	*$ 700*				*0.09155*

Societal perspective	
Cost/QALY	$ 18,847
Cost/QALY	$ 20,133
ICER	**$ 7,646**

Catheter Decision Tree

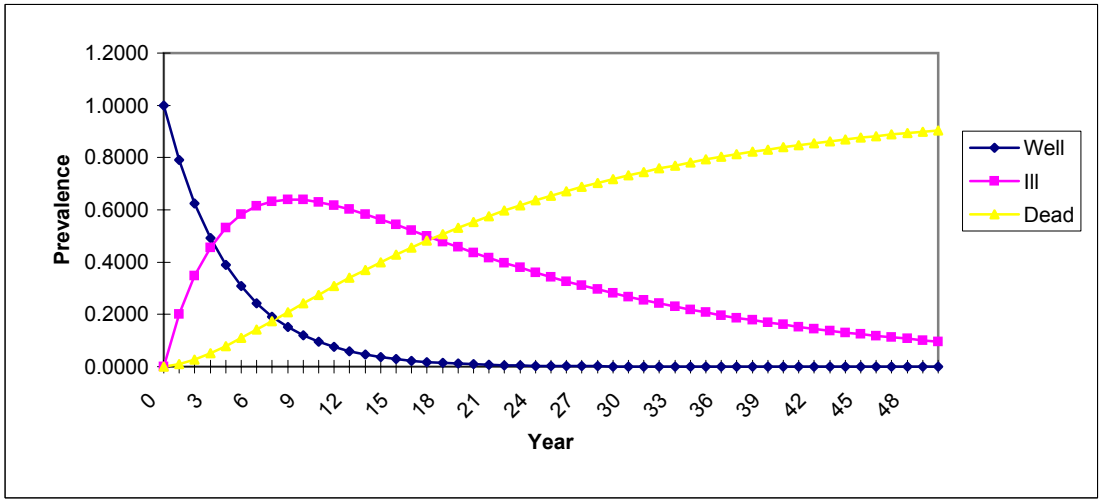


Example of a 3-state Markov Model

Change data in yellow cells.

prob. Well->Ill	0.20
prob. Well->Dead	0.01
prob. Ill->Dead	0.05

	Well	Ill	Dead
SUM	**3.8**	**17.2**	**29.0**



3-state Markov Model

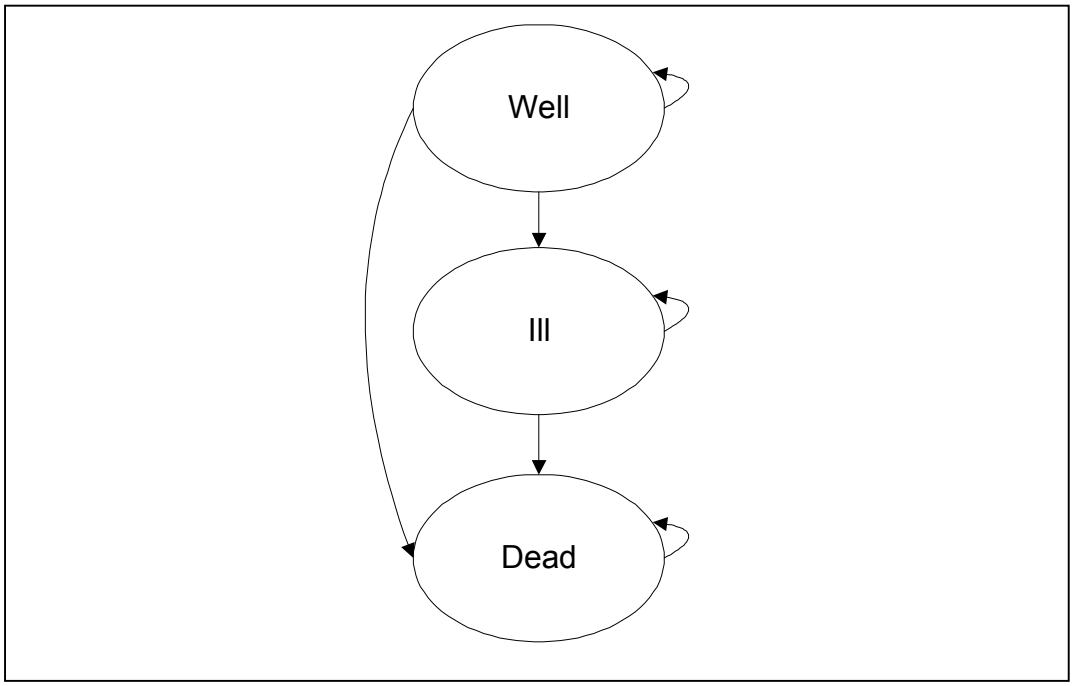
Input: Transition probabilities

Year	pW->W	pW->I	pW->D	*sum*	pI->W	pI->I	pI->D	*sum*
1	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
2	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
3	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
4	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
5	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
6	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
7	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
8	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
9	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
10	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
11	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
12	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
13	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
14	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
15	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
16	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
17	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
18	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
19	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
20	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
21	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
22	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
23	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
24	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
25	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
26	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
27	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
28	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
29	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
30	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
31	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
32	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
33	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
34	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
35	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
36	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
37	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
38	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
39	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
40	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
41	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
42	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
43	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
44	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
45	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
46	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
47	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
48	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
49	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*
50	0.7900	0.2000	0.0100	*1.0000*	0.0000	0.9500	0.0500	*1.0000*

Output: Probablities of being in each state.

Year	Well	Ill	Dead	*sum*
0	1.0000	0.0000	0.0000	*1.0000*
1	0.7900	0.2000	0.0100	*1.0000*
2	0.6241	0.3480	0.0279	*1.0000*
3	0.4930	0.4554	0.0515	*1.0000*
4	0.3895	0.5313	0.0792	*1.0000*
5	0.3077	0.5826	0.1097	*1.0000*
6	0.2431	0.6150	0.1419	*1.0000*
7	0.1920	0.6329	0.1751	*1.0000*
8	0.1517	0.6396	0.2087	*1.0000*
9	0.1199	0.6380	0.2422	*1.0000*
10	0.0947	0.6301	0.2752	*1.0000*
11	0.0748	0.6175	0.3077	*1.0000*
12	0.0591	0.6016	0.3393	*1.0000*
13	0.0467	0.5833	0.3700	*1.0000*
14	0.0369	0.5635	0.3996	*1.0000*
15	0.0291	0.5427	0.4282	*1.0000*
16	0.0230	0.5214	0.4556	*1.0000*
17	0.0182	0.4999	0.4819	*1.0000*
18	0.0144	0.4786	0.5071	*1.0000*
19	0.0113	0.4575	0.5311	*1.0000*
20	0.0090	0.4369	0.5541	*1.0000*
21	0.0071	0.4168	0.5761	*1.0000*
22	0.0056	0.3974	0.5970	*1.0000*
23	0.0044	0.3787	0.6169	*1.0000*
24	0.0035	0.3606	0.6359	*1.0000*
25	0.0028	0.3433	0.6540	*1.0000*
26	0.0022	0.3267	0.6711	*1.0000*
27	0.0017	0.3108	0.6875	*1.0000*
28	0.0014	0.2956	0.7031	*1.0000*
29	0.0011	0.2811	0.7178	*1.0000*
30	0.0008	0.2672	0.7319	*1.0000*
31	0.0007	0.2540	0.7453	*1.0000*
32	0.0005	0.2415	0.7580	*1.0000*
33	0.0004	0.2295	0.7701	*1.0000*
34	0.0003	0.2181	0.7816	*1.0000*
35	0.0003	0.2073	0.7925	*1.0000*
36	0.0002	0.1970	0.8028	*1.0000*
37	0.0002	0.1872	0.8127	*1.0000*
38	0.0001	0.1778	0.8220	*1.0000*
39	0.0001	0.1690	0.8309	*1.0000*
40	0.0001	0.1605	0.8394	*1.0000*
41	0.0001	0.1525	0.8474	*1.0000*
42	0.0001	0.1449	0.8550	*1.0000*
43	0.0000	0.1377	0.8623	*1.0000*
44	0.0000	0.1308	0.8692	*1.0000*
45	0.0000	0.1243	0.8757	*1.0000*
46	0.0000	0.1181	0.8819	*1.0000*
47	0.0000	0.1122	0.8878	*1.0000*
48	0.0000	0.1066	0.8934	*1.0000*
49	0.0000	0.1012	0.8988	*1.0000*
50	0.0000	0.0962	0.9038	*1.0000*
SUM	**3.8**	**17.2**	**29.0**	*50.00*

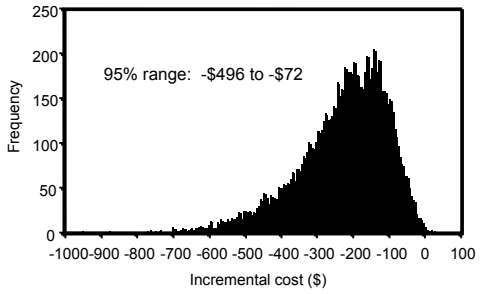
Model Diagram

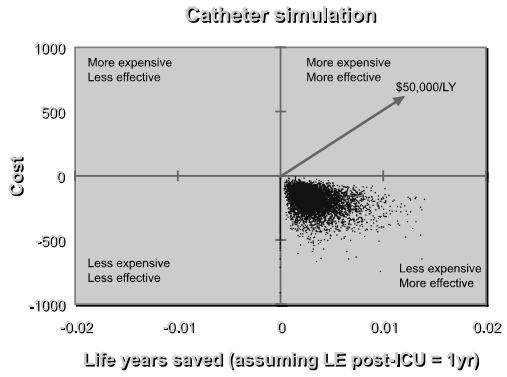


Evaluating results

- Once simulation is complete, look at distribution of *expected* results
- Determine 95% central range of results, or percentiles within quadrants on CE plane

Incremental cost





Levels of uncertainty

- 1st order
  - sampling distribution
  - track outcomes of individual patients
  - no distributions used
- 2nd order
  - population distribution
  - track expected values for tree (population)
  - employ distributions

Software

- TreeAge
- AtRisk simulation package in conjunction with Excel spreadsheet