Cost-Effectiveness and Decision Modeling in R
Basic Markov Model Exercise

The DARTH workgroup

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- Jalal H, Pechlivanoglou P, Krijkamp E, Alarid-Escudero F, Enns E, Hunink MG. An Overview of R in Health Decision Sciences. Med Decis Making. 2017; 37(3): 735-746. https://journals.sagepub.com/doi/abs/10.1177/0272989X16686559

- Krijkamp EM, Alarid-Escudero F, Enns EA, Jalal HJ, Hunink MGM, Pechlivanoglou P. Microsimulation modeling for health decision sciences using R: A tutorial. Med Decis Making. 2018;38(3):400–22. https://journals.sagepub.com/doi/abs/10.1177/0272989X18754513

- Krijkamp EM, Alarid-Escudero F, Enns E, Pechlivanoglou P, Hunink MM, Jalal H. A Multidimensional Array Representation of State-Transition Model Dynamics. BioRxiv 670612 2019.https://www.biorxiv.org/content/10.1101/670612v1

Exercise I: The Sick-Sicker model – A Markov model

A hypothetical disease affects individuals with an average age of 25 years and results in increased mortality, increased treatment costs and reduced quality of life. The disease has two levels; affected individuals initially become sick but can subsequently progress and become sicker. Two alternative strategies exist for this hypothetical disease: a no-treatment and a treatment strategy. Under the treatment strategy, individuals who become sick or progress and become sicker receive treatment and continue doing so until they recover or die. The cost of the treatment is additional to the cost of being sick or sicker for one year. The treatment improves quality of life for those individuals who are sick but has no effect on the quality of life of those who are sicker. You are asked to evaluate the cost-effectiveness of the treatment.

To model this disease, we will rely on a state-transition cohort model, called the Sick-Sicker model, first described by Enns et al. The Sick-Sicker model consists of four health states: healthy (H), two disease states sick (S1) and sicker (S2) and dead (D) (Figure 1). All individuals start in the healthy state. Over time, healthy individuals may develop the disease and can progress to S1. Individuals in S1 can recover (return to state H), progress further to S2 or die. Individuals in S2 cannot recover (i.e. cannot transition to either S1 or H). Individuals in H are assumed to have a fixed mortality rate and individuals in S1 and S2 have an increased mortality rate compared to healthy individuals. These rates are used to calculate the probabilities to die when in S1 and S2.
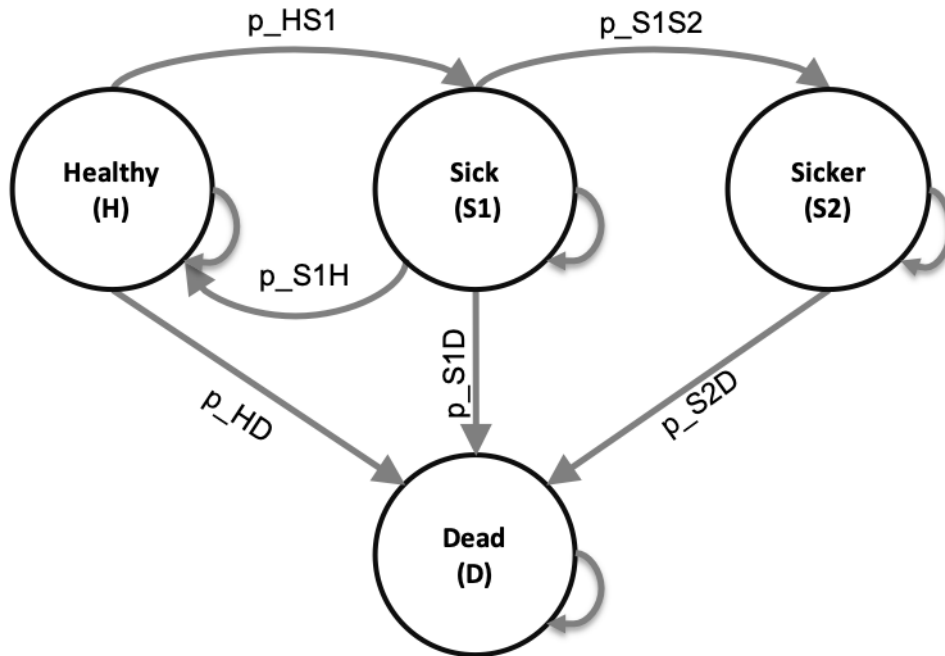

Figure 1: Schematic representation of the Sick-Sicker model

Table I: Input parameters

Parameter	R name	Value
Time horizon	n_t	30 years
Cycle length		1 year
Names of health states	v_n	H, S1, S2, D
Annual discount rate (costs/QALYs)	d_r	3%
Annual transition probabilities		
- Disease onset (H to S1)	p_HS1	0.15
- Recovery (S1 to H)	p_S1H	0.5

Parameter	R name	Value
- Disease progression (S1 to S2) in the time-homogeneous model	p_S1S2	0.105
Annual mortality		
- All-cause mortality (H to D)	p_HD	0.005
- Hazard ratio of death in S1 vs H	hr_S1	3
- Hazard ratio of death in S2 vs H	hr_S2	10
Annual costs		
- Healthy individuals	c_H	$2,000
- Sick individuals in S1	c_S1	$4,000
- Sick individuals in S2	c_S2	$15,000
- Dead individuals	c_D	$0
- Additional costs of sick individuals treated in S1 or S2	c_trt	$12,000
Utility weights		
- Healthy individuals	u_H	1.00
- Sick individuals in S1	u_S1	0.75
- Sick individuals in S2	u_S2	0.50
- Dead individuals	u_D	0.00
Intervention effect		
- Utility for treated individuals in S1	u_trt	0.95

*Note: To calculate the probability of dying from S1 and S2, use the hazard ratios provided. To do so, first convert the probability of dying from healthy, p_HD, to a rate; then multiply this rate by the appropriate hazard ratio; finally, convert this rate back to a probability. Recall that you can convert between rates and probabilities using the following formulas: $r = -loga(1-p)$ and $p = 1 - e^{(-rt)}$

Table II: Input parameters for probabilistic analysis

Parameter	Distribution	Distribution values
Number of simulation	n_sim	1000
Annual transition probabilities		
- Disease onset (H to S1)	Beta	$\alpha = 30,\ \beta = 170$
- Recovery (S1 to H)	Beta	$\alpha = 60,\ \beta = 60$
- Disease progression (S1 to S2) in the time-homogeneous model	Beta	$\alpha = 84,\ \beta = 716$
Annual mortality		
- All-cause mortality (H to D)	Beta	$\alpha = 10,\ \beta = 1990$
- Hazard ratio of death in S1 vs H	Lognormal	$\mu = log(3),\ \sigma = 0.01$
- Hazard ratio of death in S2 vs H	Lognormal	$\mu = log(10),\ \sigma = 0.02$
Annual costs		
- Healthy individuals	Gamma	shape = 100.0, scale = 20.0
- Sick individuals in S1	Gamma	shape = 177.8, scale = 22.5
- Sick individuals in S2	Gamma	shape = 225.0, scale = 66.7
- Additional costs of sick individuals treated in S1 or S2	Gamma	shape = 73.5, scale = 163.3
Utility weights		
- Healthy individuals	Tr. Normal	$\mu = 1.00,\ \sigma = 0.01,\ b = 1$
- Sick individuals in S1	Tr. Normal	$\mu = 0.75,\ \sigma = 0.02,\ b = 1$
- Sick individuals in S2	Tr. Normal	$\mu = 0.50,\ \sigma = 0.03,\ b = 1$
Intervention effect		
- Utility for treated individuals in S1	Tr. Normal	$\mu = 0.95,\ \sigma = 0.02,\ b = 1$

Tasks

1. Load the PSA dataset title "psa_sick_sicker.csv".

2. Use the PSA dataset to compute EVPI for the overall model.

3. Compute EVPPI for each parameter in the model, and plot your results.

4. Compute EVSI for cost of treatment `c.trt` [hint n0 = shape parameter of the gamma distribution].