Decision Modeling for Public Health
Markov Model Variants Exercise

The DARTH workgroup

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Please cite our publications when using this code:

- 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. Med Decis Making. 2020 Online first. https://doi.org/10.1177/0272989X19893973

Exercise I: Variations on the Sick-Sicker Markov Model

Previously, you built a Markov of the Sick-Sicker model where transition probabilities were assumed to be constant over time. In this exercise, you will expand on that model to incorporate dependence on time since model start and on state residence.

Time since model start

Healthy individuals are no longer assumed to have a fixed mortality rate. Their mortality rate depends on their age. The Human Mortality Database (HMD) (www.mortality.org) provides these age specific mortality rates (Mx1x1). You can load this data in R using different packages, for example the HMDHFplus, demography or data.table package. Registration (free) on the HMD website is required in order to use the data. For this exercise, we provide you with this mortality rate for the US in the file `HMD_USA_Mx_2015.csv`.

Remember: individuals in S1 and S2 still have an increased mortality relative to healthy individuals, as described in the original exercise. The same hazard ratios are used to calculate the probabilities of dying from S1 and S2 in this exercise.

State residence

It has been recently discovered that the risk of progression from Sick to Sicker increases the longer a person has been sick. This increase follows a Weibull growth curve, calculated as

$$p_{S1S2(t)} = \lambda_\gamma t^{(\gamma-1)}$$

where t is the t-th cycle (year) that a person has been in the Sick state. $\lambda = 0.08$ and $\gamma = 1.1$ are the scale and shape parameters of the Weibull function, respectively.

We will now expand the model to include age and state residence dependency by adding age varying probabilities for death and tunnel states for S1, as shown in Figure 2.
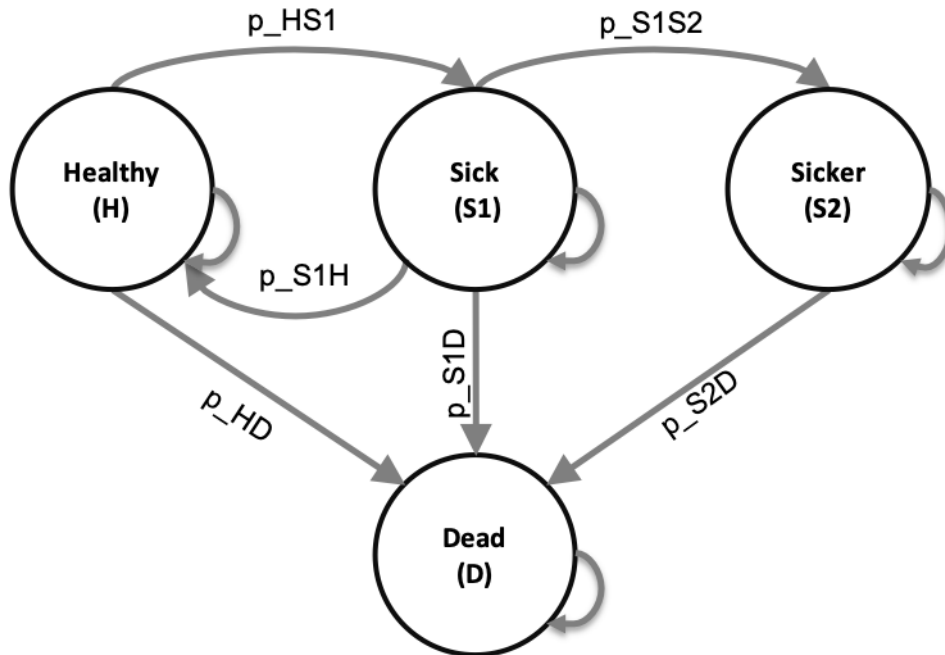

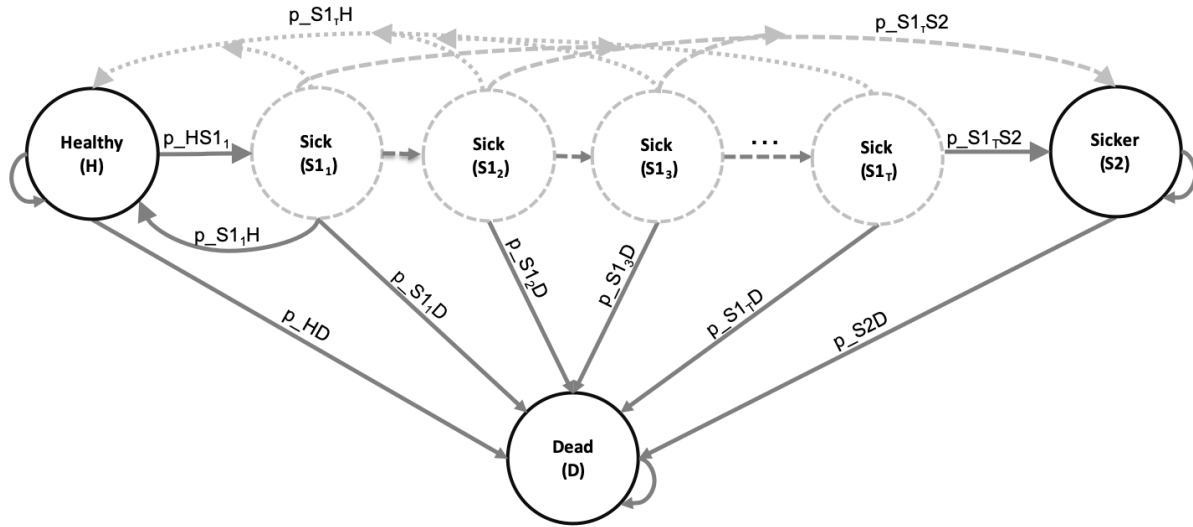Figure 1: Schematic representation of the Sick-Sicker model

Figure 2: Schematic representation of the Sick-Sicker model with tunnels states for S1

Tasks

Using the template `markov_sick-sicker_variants_template.Rmd`, please do the following:

1. Incorporate the tunnel states in the Markov trace and initialize it with everyone being healthy at model start.

2. Create a 3D transition probability array to account for tunnels and age dependency.

3. Fill in the 3D transition probability array accounting for the tunnel states for S1 and the age dependence of transitioning to death

4. Costs and utilities for all tunnel states are the same. Therefre, aggregate the Markov trace back to a healthy sick-sicker-dead trace and estimate total costs and QALYs for both strategies.

5. Estimate incremental costs and QALYs and the ICER.

6. Plot the survival curve for the cohort under no treatment.

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_c d_e`	3%
Annual transition probabilities		
- Disease onset (H to S1), conditional on surviving	`p_HS1`	0.15
- Recovery (S1 to H), conditional on survival	`p_S1H`	0.5
- Disease progression (S1 to S2), conditional on surviving	`p_S1S2`	Weibull function
Annual mortality		
- All-cause mortality (H to D)	`p_HD`	Age-dependent
- Hazard ratio of death in S1 vs H	`hr_S1`	3
- Hazard ratio of death in S2 vs H	`hr_S2`	10

Parameter	R name	Value
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: $r = -log(1 - p)$ and $p = 1 - e^{(-rt)}$