Microsimulation Modeling in R

Exercises – Microsimulation models

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: A Microsimulation model – The Sick-Sicker model

In this exercise, we will model a hypothetical disease using an individual-based state-transition model, or what we often call a microsimulation model, called the "Sick-Sicker" model. This model has four health states (Figure 1): Healthy (H); two disease states, Sick (S1) and Sicker (S2); and Dead (D).

Advantages of using a microsimulation implementation is the ability to incorporate variation in the baseline characteristics for every individual and to keep track of state-residence. To illustrate this, we assume that individual mortality rates depend on baseline characteristics as well as time spend in the sick health state.

After you have successfully implemented the Sick-Sicker model, you can expand the model to include the possibility of treatment and evaluate whether it is cost-effective given a willingness to pay of $20,000. This hypothetical treatment improves the quality of life for those in the Sick (S1) state but not for those in the Sicker (S2) state. However, it is not possible to distinguish between individuals in the Sick state from those in the Sicker state, so under a treatment strategy, individuals in both sick states must be treated (and incur the costs of treatment), while only those in the sick state benefit from it.

In summary, the model assumes the following:

i) The mortality rates depend on age

ii) Probability of dying when sick depends on state-residence in the Sick (S1) state.

iii) The improvement on quality of life by the treatment varies across individuals through a characteristic that acts as a treatment effect modifier.

All model parameter values and `R` variable names are presented in Table 1.

Tasks

There are quite some steps you need to take in order to create a microsimulation reflecting this case. Start by download all the materials as a folder or collect all the files in one folder. If there is an R projects in the folder, a file ending on `.Rproj`, double click on this file to open an Rstudio environoment. Working from a Rproject avoid struggles with working directories.

1. Open the file `microsim_Sick-Sicker_time_full_template.Rmd`. This is a template to load the data for the time dependency and the necessary data. Start making the functions `Probs()`, `Costs()` and `Effs()`.

2. Build your microsimulation model (function). Then, simulate a population of 100,000 individuals and plot the resulting distributions of remaining lifetime costs and QALYs. Please be reminded that the probabilities of transitioning from one state to the other (except to the Dead state) are conditional on staying alive.

3. Expand your microsimulation model to include the possibility of the hypothetical treatment for the disease in the Sick-Sicker model (and its impact on costs and quality of life). Remember treatment is given to both individuals in Sick and Sicker but only improved the quality of life of those in Sick. Create a new variable within the model function that can be used to turn treatment on and off in the model.

4. Simulate a population of 100,000 individuals under a treatment strategy where anyone who is sick (in the Sick or Sicker states) receives treatment. Plot the resulting distributions of remaining lifetime costs and QALYs.

5. Calculate the incremental cost-effectiveness ratio (ICER) of treatment compared to no treatment (see code template).

Table 1: Input parameters for the time dependent Sick-Sicker Microsimulation

Parameter	R name	Value
Time horizon	`n_t`	30 years
Cycle length		1 year
Names of simulated individuals	`n_i`	1000
Names of health states	`v_n`	H, S1, S2, D
Annual discount rate (costs/QALYs)	`d_e d_c`	3%
Population characteristics		
- Age distribution	–	Range:25-55 distributed as in `MyPopulation-AgeDistribution.csv`
Annual transition probabilities conditional on survival		
- Disease onset (H to S1)	`p_HS1`	0.15
- Recovery (S1 to H)	`p_S1H`	0.5
- Disease progression (S1 to S2)	`p_S1S2`	0.105
Annual mortality		
- All-cause mortality (H to D)	`p_HD`	Human Mortality Database (`mortProb_age.csv`): age dependent from 2015
- Probability of death is S1 (S1 to D)	`p_S1D`	*(in template)
- Probability of death in S2 (S2 to D)	`p_S2D`	0.048
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
Time varying extension of Sick-Sicker model		
- Treatment effect modifier at baseline	`v_x`	Uniform(0.95, 1.05)

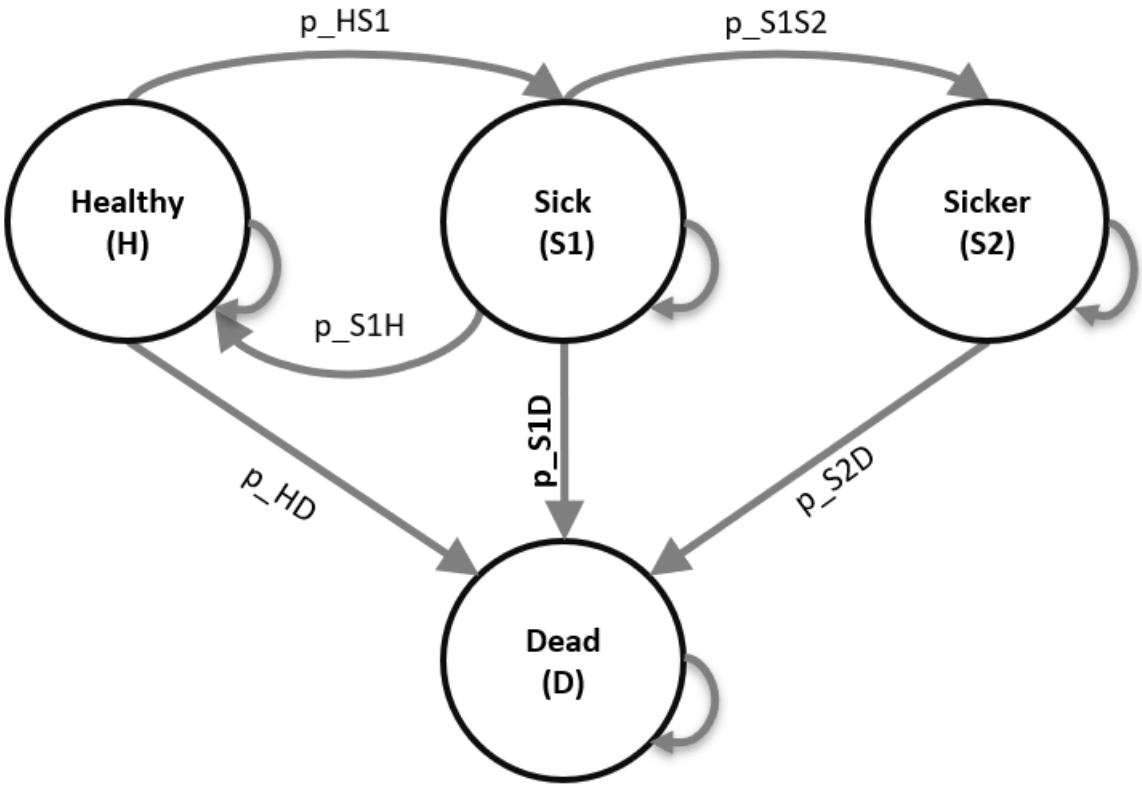

Figure 1: Schematic representation of the Sick-Sicker model

Exercise II: Probabilistic sensitivity analysis of the Sick-Sicker microsimulation model

This exercise continues based on the microsimulation model of the Sick-Sicker model from Exercise I. For the Sick-Sicker model you just created, you will develop a probabilistic sensitivity analysis (PSA) with 1000 simulations (`n_sim`). The Table describes the distributions for the variables you used in the previous exercise.

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)	Beta	$\alpha = 84,\ \beta = 716$
- Probability of death in S2 (S2 to D)	Beta	$\alpha = 22,\ \beta = 434$
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	Beta	$\alpha = 200,\ \beta = 3$
- Sick individuals in S1	Beta	$\alpha = 130,\ \beta = 45$
- Sick individuals in S2	Beta	$\alpha = 230,\ \beta = 230$
Intervention effect		
- Utility for treated individuals in S1	Beta	$\alpha = 300,\ \beta = 15$

Tasks

The tasks below help you to develop a probabilistic sensitivity analysis (PSA). Please note that these tasks are very similar to what was demonstrated in the 3-state microsimulation model example and that you can use the Sick-Sicker model you already created.

6. Create the `calculate_ce_out R` function of the Sick-Sicker microsimulation model and store in a separate `R` file `Function_Microsim_Sick-Sicker_time.R`.
7. Create a function called `gen_psa` to sample values for the uncertain parameters using the appropriate distributions.
8. Open the file `microsim_Sick-Sicker_time_template.R` and conduct a probabilistic Cost-Effectiveness analysis of treatment vs no-treatment.
9. Create histograms of model inputs.
10. Create a cost-effectiveness plane to present discounted costs and QALYs.

Extra 1: The solutions will provide you code to create a cost-effectiveness acceptability curves (CEAC) and frontier (CEAF) for the treatment comparison assuming WTP thresholds of \$0 to \$300,000.

Extra 2: The solutions will provide code to calculate the expected value of perfect information (EVPI)