Sick-Sicker case study

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In this document we showcase the framework via a fully functional decision model. In this case-study we perform a cost-effectiveness analysis (CEA) using a previously published 4-state model called the Sick-Sicker model.(Enns et al. 2015) The model is used to quantify the expected costs and quality-adjusted life years (QALYs) for individuals with a hypothetical disease with two different stages, "Sick" and "Sicker". We calibrate the model using three targets, survival, prevalence and the proportion who are "Sick" among all those afflicted "Sick + Sicker". We then evaluate the cost-effectiveness of a hypothetical treatment that increases quality of life (QoL) in one of the disease states.(Krijkamp et al. 2018) We identify the uncertainty around our decision based on the CEA using sensitivity analysis. Finally, we perform a value of information (VoI) analysis to see if it is worth investing in extra research projects with the aim to eliminate the uncertainty around our decision.

The Sick-Sicker model

In the Sick-Sicker model, we simulate a hypothetical cohort of 25-year-old individuals over a lifetime (or reaching age 100 years old) using 75 annual cycles, represented with `n.t`. The cohort start in the "Healthy" health state (denoted "H"). Healthy individuals are at risk of developing the illness, at which point they would transition to the first stage of the disease (the "Sick" health state, denoted "S1"). Sick individuals are at risk of further progressing to a more severe stage (the "Sicker" health state, denoted "S2"), which is constant in this case example. There is a chance that individuals in the Sick state eventually recover and return back to the Healthy state. However, once an individual reaches the Sicker health state, they cannot recover; that is, the probability of transitioning to the Sick or Healthy health states from the Sicker health state is zero. Individuals in the Healthy state face background mortality that is age-specific (i.e., time-dependent). Sick and Sicker individuals face an increased mortality in the form of a hazard rate ratio (HR) of 3 and 10 times, respectively, on the background mortality rate. Sick and Sicker individuals also experience increased health care costs and reduced QoL compared to healthy individuals. Once simulated individuals die, they transition to the "Dead" health state (denoted "D"), where they remain. The state-transition diagram of the Sick-Sicker model is shown in Figure 1. The evolution of the cohort is simulated in one-year discrete-time cycles. Both costs and QALYs are discounted at an annual rate of 0.03%.

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 assuming a willingness to pay of $80000.

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.

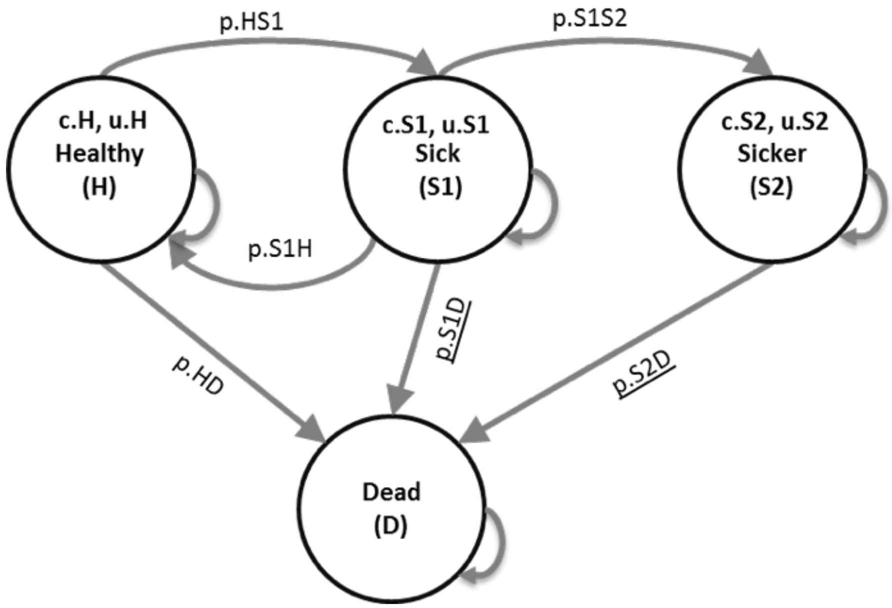

Figure 1: Sick-Sicker

01 Define model inputs

The input for the Sick-Sicker model is informed by external data. All model parameter values and R variable names, for both the general set up and the external data, are presented in Table 1. This table is informed via the files `01_Model-inputs_function.R`, that generates the base-case parameter set including these external values from the `01_basecase-params.csv` dataset in the data folder and the `01_model-inputs.R`. The age specific mortality rated are derived from the Human Mortality data base and include the all-cause mortality rate for the USA population based on 2015 data. This information is stored in the `01_all-cause-mortality-USA-2015.csv` file.

Table 1: Description of parameters with their R name and value.

Parameter	**R name**	**Value**
Time horizon (n_t)	`n.t`	75 years
Names of health states (n)	`v.n`	H, S1, S2, D
Annual discount rate (costs/QALYs)	`d.c`/`d.e`	3%
Annual transition probabilities		
- Disease onset (H to S1)	`p.HS1`	0.15
- Recovery (S1 to H)	`p.S1H`	0.5
- Disease progression (S1 to S2) in the time-homogenous model	`p.S1S2`	0.105
Annual mortality		
- All-cause mortality (H to D)	`p.HD`	age-specific
- Hazard ratio of death in S1 vs H	`hr.S1`	3
- Hazard ratio of death in S2 vs H	`hr.S2`	3
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		

Parameter	**R name**	**Value**
- 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

Enns, EA, LE Cipriano, CT Simons, and CY Kong. 2015. "Identifying Best-Fitting Inputs in Health-Economic Model Calibration: A Pareto Frontier Approach." *Medical Decision Making* 35 (2): 170–82. doi:10.1177/0272989X14528382.

Krijkamp, EM, F Alarid-Escudero, EA Enns, H Jalal, MGM Hunink, and P Pechlivanoglou. 2018. "Microsimulation Modeling for Health Decision Sciences Using R: A Tutorial." *Medical Decision Making : An International Journal of the Society for Medical Decision Making* 38 (3): 400–422. doi:10.1177/0272989X18754513.