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.(E. A. 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. Finaly, 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 anual 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"). Individuals that become sick incur a one-time utility decrement of 0.01 (`du.HS1`, disutility of transitioning from H to S1) and a one-time cost of $1000 (`ic.HS1`) that reflect the acute impacts of developing the illness. 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. When an individual dies, they incur a one-time cost of $200 (`ic.D`) that reflects the acute care that might be received immediately preceding death. 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 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
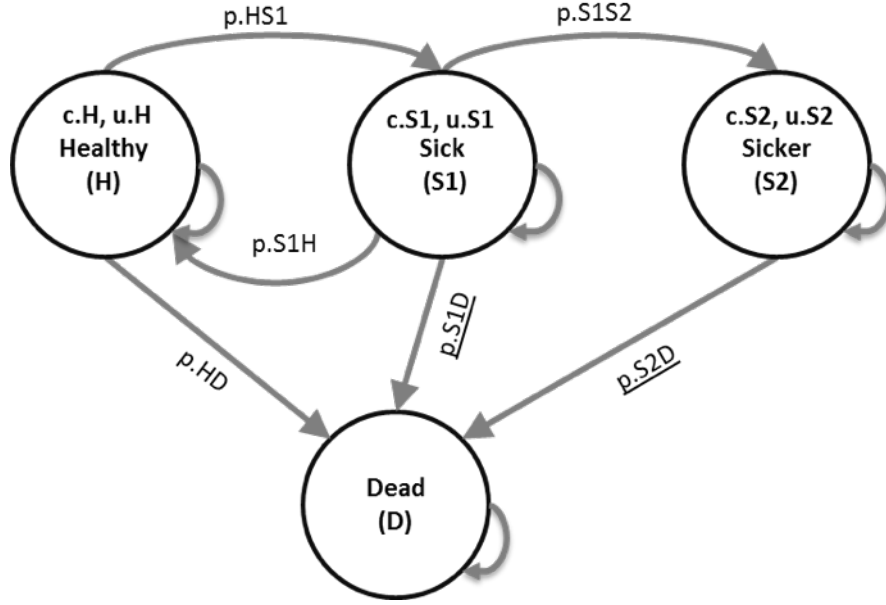
Figure 1: Sick-Sicker

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.

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 tabel 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 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 ratae fro 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		

Parameter	R name	Value
- 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
Transition rewards		
- Utility decrement of healthy individuals when transitioning to S1	du.HS1	0.01
- Cost of healthy individuals when transitioning to S1	ic.HS1	$1,000
- Cost of dying	ic.D	$2,000

02 Model implementation

```
###############################################################################
# This script runs the cohort implementation of the Sick-Sicker        #
# state-transition model (STM)                                          #
#                                                                       #
# Depends on:                                                           #
#   01_model-inputs.R                                                   #
#   02_simulation-model_functions.R                                     #
#                                                                       #
# Author: Fernando Alarid-Escudero                                      #
# E-mail: fernando.alarid@cide.edu                                      #
###############################################################################
# The structure of this code is according to the DARTH framework        #
# https://github.com/DARTH-git/Decision-Modeling-Framework              #
###############################################################################


# rm(list = ls()) # to clean the workspace

#### 02.1 Load packages and functions ####
#### 02.1.1 Load packages and functions ####
library(dplyr) # For data manipulation

#### 02.1.2 Load inputs ####
#source("../R/01_model-inputs.R")

#### 02.1.3 Load functions ####
source("../functions/02_simulation-model_functions.R")

#### 02.2 Run STM ####
### Create list of model output
l.out.stm <- f.decision_model(v.params = v.params.init)
```

```
l.out.stm
```

```
## $m.M
##              H            S1          S2           D
## 0  1.000000000 0.0000000000 0.000000e+00 0.000000000
## 1  0.848986514 0.1500000000 0.000000e+00 0.001013486
## 2  0.795790823 0.1861491001 1.575000e-02 0.002310077
## 3  0.768645709 0.1923009374 3.512803e-02 0.003925325
## 4  0.748664257 0.1906296546 5.493985e-02 0.005766235
## 5  0.730810003 0.1869349741 7.432126e-02 0.007933762
## 6  0.713803632 0.1828075002 9.308715e-02 0.010301723
## 7  0.697271518 0.1786154798 1.111596e-01 0.012953395
## 8  0.681090327 0.1744544700 1.284906e-01 0.015964624
## 9  0.665248084 0.1703778568 1.451094e-01 0.019264638
## 10 0.649735713 0.1663851050 1.610175e-01 0.022861687
## 11 0.634545938 0.1624751804 1.762176e-01 0.026761241
## 12 0.619656868 0.1586349437 1.906714e-01 0.031036832
## 13 0.605066086 0.1548733929 2.043954e-01 0.035665116
## 14 0.590765872 0.1511858939 2.173806e-01 0.040667607
## 15 0.576765850 0.1475836287 2.296828e-01 0.045967694
## 16 0.563036056 0.1440389484 2.412014e-01 0.051723599
## 17 0.549530245 0.1405312472 2.517812e-01 0.058157319
## 18 0.536239852 0.1370769264 2.614231e-01 0.065260154
## 19 0.523178354 0.1336906657 2.701967e-01 0.072934283
## 20 0.510295420 0.1303274411 2.778399e-01 0.081537254
## 21 0.497610651 0.1270269593 2.845045e-01 0.090857846
## 22 0.485087699 0.1237520439 2.899674e-01 0.101192883
## 23 0.472736360 0.1205279786 2.943268e-01 0.112408867
## 24 0.460509349 0.1173141238 2.972885e-01 0.124888071
## 25 0.448383767 0.1141163184 2.987734e-01 0.138726518
## 26 0.436356449 0.1109435497 2.987966e-01 0.153903359
## 27 0.424419908 0.1077917798 2.973265e-01 0.170461836
## 28 0.412576130 0.1046661963 2.944126e-01 0.188345033
## 29 0.400815675 0.1015587579 2.900264e-01 0.207599193
## 30 0.389152309 0.0984844269 2.843306e-01 0.228032641
## 31 0.377595899 0.0954439461 2.774368e-01 0.249523402
## 32 0.366128921 0.0924194267 2.692846e-01 0.272167038
## 33 0.354721760 0.0893972628 2.597935e-01 0.296087435
## 34 0.343422625 0.0864276868 2.494583e-01 0.320691367
## 35 0.332244277 0.0834970149 2.383934e-01 0.345865305
## 36 0.321187921 0.0806000451 2.266990e-01 0.371513027
## 37 0.310220109 0.0777115283 2.142750e-01 0.397793348
## 38 0.299316094 0.0748292504 2.011617e-01 0.424692992
## 39 0.288445213 0.0719425458 1.873739e-01 0.452238356
## 40 0.277755221 0.0691739561 1.740091e-01 0.479061688
## 41 0.267182780 0.0664076358 1.605696e-01 0.505840032
## 42 0.256701937 0.0636548687 1.471346e-01 0.532508630
## 43 0.246278163 0.0609027824 1.337041e-01 0.559114911
## 44 0.235943699 0.0581907304 1.206357e-01 0.585229867
## 45 0.225591512 0.0554271982 1.075407e-01 0.611440615
## 46 0.215274181 0.0526994991 9.496707e-02 0.637059246
## 47 0.204866139 0.0498946798 8.253767e-02 0.662701512
## 48 0.194442029 0.0471232724 7.087235e-02 0.687562353
## 49 0.184053070 0.0443864455 6.019142e-02 0.711369062
```

4

```
## 50 0.173777134 0.0417156831 5.071666e-02 0.733790523
## 51 0.163481934 0.0389873723 4.206222e-02 0.755468474
## 52 0.153239505 0.0363098042 3.451153e-02 0.775939156
## 53 0.142992638 0.0336129365 2.789474e-02 0.795499681
## 54 0.132848117 0.0309932977 2.237079e-02 0.813787794
## 55 0.122750461 0.0283699901 1.772037e-02 0.831159180
## 56 0.112685011 0.0257604335 1.386449e-02 0.847690063
## 57 0.102767158 0.0232428471 1.080579e-02 0.863184202
## 58 0.092997428 0.0207723932 8.376124e-03 0.877854054
## 59 0.083440560 0.0183917967 6.483640e-03 0.891684003
## 60 0.074164749 0.0161170660 5.022996e-03 0.904695189
## 61 0.065246744 0.0139689983 3.900379e-03 0.916883879
## 62 0.056783576 0.0119753205 3.040609e-03 0.928200494
## 63 0.048646557 0.0100390225 2.332470e-03 0.938981950
## 64 0.041080389 0.0083312316 1.791957e-03 0.948796423
## 65 0.034280772 0.0068589608 1.391578e-03 0.957468689
## 66 0.028153123 0.0055279655 1.070730e-03 0.965248181
## 67 0.022671628 0.0043594423 8.095748e-04 0.972159355
## 68 0.017860515 0.0033623813 6.021403e-04 0.978174964
## 69 0.013711597 0.0025231033 4.394935e-04 0.983325807
## 70 0.010289758 0.0018633894 3.173351e-04 0.987529518
## 71 0.007452129 0.0013129700 2.233838e-04 0.991011518
## 72 0.005289890 0.0009269966 1.546055e-04 0.993628508
## 73 0.003637040 0.0006236112 1.060324e-04 0.995633317
## 74 0.002416730 0.0004096192 6.995842e-05 0.997103692
## 75 0.001563922 0.0002627741 4.536471e-05 0.998127940
##
## $a.P
## , , 0
##
##             H         S1        S2          D
## H  0.8489865 0.1500000 0.0000000 0.001013486
## S1 0.5000000 0.3919626 0.1050000 0.003037378
## S2 0.0000000 0.0000000 0.9899112 0.010088764
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 1
##
##             H         S1        S2          D
## H  0.8490015 0.1500000 0.0000000 0.0009985012
## S1 0.5000000 0.3920075 0.1050000 0.0029925135
## S2 0.0000000 0.0000000 0.9900597 0.0099402657
## D  0.0000000 0.0000000 0.0000000 1.0000000000
##
## , , 2
##
##             H         S1       S2          D
## H  0.8489306 0.1500000 0.000000 0.001069428
## S1 0.5000000 0.3917951 0.105000 0.003204853
## S2 0.0000000 0.0000000 0.989357 0.010642959
## D  0.0000000 0.0000000 0.000000 1.000000000
##
## , , 3
##
```

```
##             H        S1        S2           D
## H  0.8489136 0.1500000 0.0000000 0.001086409
## S1 0.5000000 0.3917443 0.1050000 0.003255689
## S2 0.0000000 0.0000000 0.9891889 0.010811135
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 4
##
##             H        S1        S2           D
## H  0.8488387 0.1500000 0.0000000 0.001161325
## S1 0.5000000 0.3915201 0.1050000 0.003479931
## S2 0.0000000 0.0000000 0.9884473 0.011552749
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 5
##
##             H        S1        S2           D
## H  0.8488337 0.1500000 0.0000000 0.001166319
## S1 0.5000000 0.3915051 0.1050000 0.003494879
## S2 0.0000000 0.0000000 0.9883978 0.011602170
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 6
##
##             H        S1        S2           D
## H  0.8487877 0.1500000 0.0000000 0.001212265
## S1 0.5000000 0.3913676 0.1050000 0.003632387
## S2 0.0000000 0.0000000 0.9879433 0.012056728
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 7
##
##             H        S1        S2           D
## H  0.8487118 0.1500000 0.0000000 0.001288170
## S1 0.5000000 0.3911405 0.1050000 0.003859533
## S2 0.0000000 0.0000000 0.9871927 0.012807280
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 8
##
##             H       S1        S2           D
## H  0.8486699 0.150000 0.0000000 0.001330115
## S1 0.5000000 0.391015 0.1050000 0.003985039
## S2 0.0000000 0.000000 0.9867782 0.013221814
## D  0.0000000 0.000000 0.0000000 1.000000000
##
## , , 9
##
##             H        S1        S2           D
## H  0.8486259 0.1500000 0.0000000 0.001374055
## S1 0.5000000 0.3908835 0.1050000 0.004116504
## S2 0.0000000 0.0000000 0.9863441 0.013655901
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
```

```
## , , 10
##
##           H        S1        S2           D
## H  0.848581 0.1500000 0.0000000 0.001418992
## S1 0.500000 0.3907491 0.1050000 0.004250939
## S2 0.000000 0.0000000 0.9859003 0.014099656
## D  0.000000 0.0000000 0.0000000 1.000000000
##
## , , 11
##
##            H       S1        S2           D
## H  0.8485111 0.15000 0.0000000 0.001488891
## S1 0.5000000 0.39054 0.1050000 0.004460024
## S2 0.0000000 0.00000 0.9852105 0.014789544
## D  0.0000000 0.00000 0.0000000 1.000000000
##
## , , 12
##
##            H        S1        S2           D
## H  0.8484512 0.1500000 0.0000000 0.001548799
## S1 0.5000000 0.3903608 0.1050000 0.004639205
## S2 0.0000000 0.0000000 0.9846195 0.015380493
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 13
##
##            H        S1        S2           D
## H  0.8483853 0.1500000 0.0000000 0.001614695
## S1 0.5000000 0.3901637 0.1050000 0.004836267
## S2 0.0000000 0.0000000 0.9839699 0.016030128
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 14
##
##            H        S1        S2           D
## H  0.8483444 0.1500000 0.0000000 0.001655628
## S1 0.5000000 0.3900413 0.1050000 0.004958665
## S2 0.0000000 0.0000000 0.9835665 0.016433473
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 15
##
##            H        S1        S2           D
## H  0.8482545 0.1500000 0.0000000 0.001745475
## S1 0.5000000 0.3897727 0.1050000 0.005227290
## S2 0.0000000 0.0000000 0.9826817 0.017318284
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 16
##
##            H        S1        S2           D
## H  0.8480998 0.1500000 0.0000000 0.001900192
## S1 0.5000000 0.3893102 0.1050000 0.005689752
## S2 0.0000000 0.0000000 0.9811597 0.018840261
```

```
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 17
##
##             H         S1        S2          D
## H  0.8479501 0.1500000 0.0000000 0.002049896
## S1 0.5000000 0.3888629 0.1050000 0.006137091
## S2 0.0000000 0.0000000 0.9796891 0.020310898
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 18
##
##             H         S1        S2          D
## H  0.8478294 0.1500000 0.0000000 0.002170641
## S1 0.5000000 0.3885022 0.1050000 0.006497797
## S2 0.0000000 0.0000000 0.9785044 0.021495604
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 19
##
##             H         S1        S2          D
## H  0.8476079 0.1500000 0.0000000 0.002392134
## S1 0.5000000 0.3878408 0.1050000 0.007159250
## S2 0.0000000 0.0000000 0.9763345 0.023665475
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 20
##
##             H         S1        S2          D
## H  0.8474443 0.1500000 0.0000000 0.002555729
## S1 0.5000000 0.3873524 0.1050000 0.007647607
## S2 0.0000000 0.0000000 0.9747346 0.025265351
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 21
##
##             H         S1        S2          D
## H  0.8471969 0.1500000 0.0000000 0.002803064
## S1 0.5000000 0.3866144 0.1050000 0.008385643
## S2 0.0000000 0.0000000 0.9723203 0.027679698
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 22
##
##             H         S1        S2          D
## H  0.8469816 0.150000 0.0000000 0.003018435
## S1 0.5000000 0.385972 0.1050000 0.009028001
## S2 0.0000000 0.000000 0.9702224 0.029777643
## D  0.0000000 0.000000 0.0000000 1.000000000
##
## , , 23
##
##             H         S1        S2          D
## H  0.8466566 0.1500000 0.0000000 0.003343398
```

```
## S1 0.5000000 0.3850033 0.1050000 0.009996697
## S2 0.0000000 0.0000000 0.9670646 0.032935418
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 24
##
##            H        S1        S2           D
## H  0.8462949 0.1500000 0.0000000 0.003705119
## S1 0.5000000 0.3839258 0.1050000 0.011074224
## S2 0.0000000 0.0000000 0.9635605 0.036439499
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 25
##
##            H        S1        S2           D
## H  0.8459233 0.1500000 0.0000000 0.004076668
## S1 0.5000000 0.3828198 0.1050000 0.012180213
## S2 0.0000000 0.0000000 0.9599731 0.040026885
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 26
##
##            H        S1        S2           D
## H  0.8455201 0.1500000 0.0000000 0.004479935
## S1 0.5000000 0.3816203 0.1050000 0.013379686
## S2 0.0000000 0.0000000 0.9560931 0.043906914
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 27
##
##           H        S1        S2          D
## H  0.845107 0.1500000 0.0000000 0.00489299
## S1 0.500000 0.3803927 0.1050000 0.01460726
## S2 0.000000 0.0000000 0.9521335 0.04786648
## D  0.000000 0.0000000 0.0000000 1.00000000
##
## , , 28
##
##            H        S1        S2           D
## H  0.8446504 0.1500000 0.0000000 0.005349639
## S1 0.5000000 0.3790368 0.1050000 0.015963215
## S2 0.0000000 0.0000000 0.9477732 0.052226757
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 29
##
##            H        S1        S2           D
## H  0.8442108 0.1500000 0.0000000 0.005789178
## S1 0.5000000 0.3777328 0.1050000 0.017267184
## S2 0.0000000 0.0000000 0.9435933 0.056406670
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 30
##
```

```
##             H         S1         S2          D
## H  0.8437665 0.1500000 0.0000000 0.006233491
## S1 0.5000000 0.3764159 0.1050000 0.018584145
## S2 0.0000000 0.0000000 0.9393849 0.060615119
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 31
##
##             H         S1         S2          D
## H  0.8432479 0.1500000 0.0000000 0.006752101
## S1 0.5000000 0.3748802 0.1050000 0.020119840
## S2 0.0000000 0.0000000 0.9344941 0.065505932
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 32
##
##             H         S1         S2          D
## H  0.8426323 0.1500000 0.0000000 0.007367724
## S1 0.5000000 0.3730593 0.1050000 0.021940723
## S2 0.0000000 0.0000000 0.9287181 0.071281871
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 33
##
##             H         S1         S2          D
## H  0.8421361 0.1500000 0.0000000 0.007863916
## S1 0.5000000 0.3715933 0.1050000 0.023406712
## S2 0.0000000 0.0000000 0.9240861 0.075913872
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 34
##
##             H         S1         S2          D
## H  0.8416173 0.1500000 0.0000000 0.008382668
## S1 0.5000000 0.3700622 0.1050000 0.024937785
## S2 0.0000000 0.0000000 0.9192658 0.080734227
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 35
##
##             H         S1         S2          D
## H  0.8410661 0.1500000 0.0000000 0.008933854
## S1 0.5000000 0.3684372 0.1050000 0.026562833
## S2 0.0000000 0.0000000 0.9141688 0.085831162
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
## , , 36
##
##             H         S1         S2          D
## H  0.8403806 0.1500000 0.0000000 0.009619434
## S1 0.5000000 0.3664184 0.1050000 0.028581593
## S2 0.0000000 0.0000000 0.9078646 0.092135372
## D  0.0000000 0.0000000 0.0000000 1.000000000
##
```

```
## , , 37
##
##            H        S1        S2          D
## H  0.8395985 0.1500000 0.0000000 0.01040153
## S1 0.5000000 0.3641189 0.1050000 0.03088113
## S2 0.0000000 0.0000000 0.9007208 0.09927925
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 38
##
##            H        S1        S2          D
## H  0.8386806 0.1500000 0.0000000 0.01131945
## S1 0.5000000 0.3614246 0.1050000 0.03357540
## S2 0.0000000 0.0000000 0.8924007 0.10759927
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 39
##
##            H        S1        S2          D
## H  0.8382318 0.1500000 0.0000000 0.01176821
## S1 0.5000000 0.3601092 0.1050000 0.03489078
## S2 0.0000000 0.0000000 0.8883584 0.11164159
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 40
##
##            H        S1        S2          D
## H  0.8374129 0.150000 0.0000000 0.01258711
## S1 0.5000000 0.357712 0.1050000 0.03728802
## S2 0.0000000 0.000000 0.8810244 0.11897564
## D  0.0000000 0.000000 0.0000000 1.00000000
##
## , , 41
##
##           H        S1        S2          D
## H  0.836499 0.1500000 0.0000000 0.01350103
## S1 0.500000 0.3550413 0.1050000 0.03995872
## S2 0.000000 0.0000000 0.8729037 0.12709627
## D  0.000000 0.0000000 0.0000000 1.00000000
##
## , , 42
##
##            H        S1       S2          D
## H  0.8354075 0.1500000 0.000000 0.01459248
## S1 0.5000000 0.3518583 0.105000 0.04314173
## S2 0.0000000 0.0000000 0.863294 0.13670602
## D  0.0000000 0.0000000 0.000000 1.00000000
##
## , , 43
##
##            H        S1        S2          D
## H  0.8343911 0.1500000 0.0000000 0.01560890
## S1 0.5000000 0.3489004 0.1050000 0.04609959
## S2 0.0000000 0.0000000 0.8544306 0.14556940
```

```
## D   0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 44
##
##             H         S1        S2          D
## H  0.8328095 0.1500000 0.0000000 0.01719053
## S1 0.5000000 0.3443099 0.1050000 0.05069012
## S2 0.0000000 0.0000000 0.8408012 0.15919877
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 45
##
##             H         S1        S2          D
## H  0.8314168 0.1500000 0.0000000 0.01858316
## S1 0.5000000 0.3402801 0.1050000 0.05471991
## S2 0.0000000 0.0000000 0.8289628 0.17103720
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 46
##
##             H         S1        S2          D
## H  0.8292513 0.1500000 0.0000000 0.02074872
## S1 0.5000000 0.3340364 0.1050000 0.06096357
## S2 0.0000000 0.0000000 0.8108518 0.18914822
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 47
##
##             H         S1        S2          D
## H  0.8273436 0.1500000 0.0000000 0.02265640
## S1 0.5000000 0.3285591 0.1050000 0.06644089
## S2 0.0000000 0.0000000 0.7951933 0.20480666
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 48
##
##             H         S1        S2          D
## H  0.8253948 0.1500000 0.0000000 0.02460523
## S1 0.5000000 0.3229857 0.1050000 0.07201434
## S2 0.0000000 0.0000000 0.7794786 0.22052137
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 49
##
##             H         S1        S2          D
## H  0.8235881 0.1500000 0.0000000 0.02641194
## S1 0.5000000 0.3178385 0.1050000 0.07716147
## S2 0.0000000 0.0000000 0.7651602 0.23483976
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 50
##
##             H         S1        S2          D
## H  0.8207299 0.1500000 0.000000 0.02927008
```

```
## S1 0.5000000 0.3097349 0.105000 0.08526512
## S2 0.0000000 0.0000000 0.742992 0.25700800
## D  0.0000000 0.0000000 0.000000 1.00000000
##
## , , 51
##
##            H         S1        S2          D
## H  0.8181076 0.1500000 0.0000000 0.03189236
## S1 0.5000000 0.3023418 0.1050000 0.09265815
## S2 0.0000000 0.0000000 0.7231635 0.27683654
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 52
##
##            H         S1        S2          D
## H  0.8146577 0.1500000 0.0000000 0.03534234
## S1 0.5000000 0.2926761 0.1050000 0.10232393
## S2 0.0000000 0.0000000 0.6978019 0.30219808
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 53
##
##            H         S1        S2          D
## H  0.8115218 0.1500000 0.0000000 0.03847816
## S1 0.5000000 0.2839503 0.1050000 0.11104974
## S2 0.0000000 0.0000000 0.6754474 0.32455260
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 54
##
##            H         S1        S2          D
## H  0.8073416 0.1500000 0.0000000 0.0426584
## S1 0.5000000 0.2724064 0.1050000 0.1225936
## S2 0.0000000 0.0000000 0.6466501 0.3533499
## D  0.0000000 0.0000000 0.0000000 1.0000000
##
## , , 55
##
##            H         S1        S2          D
## H  0.8024411 0.1500000 0.0000000 0.04755889
## S1 0.5000000 0.2590013 0.1050000 0.13599870
## S2 0.0000000 0.0000000 0.6143011 0.38569885
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 56
##
##            H         S1        S2          D
## H  0.7976832 0.1500000 0.0000000 0.05231679
## S1 0.5000000 0.2461176 0.1050000 0.14888243
## S2 0.0000000 0.0000000 0.5842946 0.41570542
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 57
##
```

```
##             H        S1        S2         D
## H  0.7918484 0.1500000 0.0000000 0.05815165
## S1 0.5000000 0.2304933 0.1050000 0.16450674
## S2 0.0000000 0.0000000 0.5493003 0.45069970
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 58
##
##             H        S1       S2         D
## H  0.7855525 0.1500000 0.000000 0.06444749
## S1 0.5000000 0.2138503 0.105000 0.18114970
## S2 0.0000000 0.0000000 0.513667 0.48633296
## D  0.0000000 0.0000000 0.000000 1.00000000
##
## , , 59
##
##             H        S1        S2         D
## H  0.7786243 0.1500000 0.0000000 0.07137567
## S1 0.5000000 0.1957928 0.1050000 0.19920717
## S2 0.0000000 0.0000000 0.4768706 0.52312935
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 60
##
##             H        S1        S2         D
## H  0.7710969 0.1500000 0.0000000 0.07890307
## S1 0.5000000 0.1764767 0.1050000 0.21852334
## S2 0.0000000 0.0000000 0.4395956 0.56040437
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 61
##
##             H        S1        S2         D
## H  0.7632423 0.1500000 0.0000000 0.08675766
## S1 0.5000000 0.1566547 0.1050000 0.23834532
## S2 0.0000000 0.0000000 0.4035157 0.59648435
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 62
##
##             H        S1        S2         D
## H  0.7512541 0.1500000 0.0000000 0.09874586
## S1 0.5000000 0.1270518 0.1050000 0.26794820
## S2 0.0000000 0.0000000 0.3535678 0.64643219
## D  0.0000000 0.0000000 0.0000000 1.00000000
##
## , , 63
##
##             H        S1        S2        D
## H  0.7412833 0.1500000 0.0000000 0.1087167
## S1 0.5000000 0.1030228 0.1050000 0.2919772
## S2 0.0000000 0.0000000 0.3163424 0.6836576
## D  0.0000000 0.0000000 0.0000000 1.0000000
##
```

```
## , , 64
##
##           H          S1         S2         D
## H  0.7330787 0.15000000 0.0000000 0.1169213
## S1 0.5000000 0.08364939 0.1050000 0.3113506
## S2 0.0000000 0.00000000 0.2883991 0.7116009
## D  0.0000000 0.00000000 0.0000000 1.0000000
##
## , , 65
##
##           H          S1         S2         D
## H  0.7212102 0.15000000 0.0000000 0.1287898
## S1 0.5000000 0.05625482 0.1050000 0.3387452
## S2 0.0000000 0.00000000 0.2519008 0.7480992
## D  0.0000000 0.00000000 0.0000000 1.0000000
##
## , , 66
##
##           H          S1        S2         D
## H  0.7071203 0.15000000 0.000000 0.1428797
## S1 0.5000000 0.02468789 0.105000 0.3703121
## S2 0.0000000 0.00000000 0.214002 0.7859980
## D  0.0000000 0.00000000 0.000000 1.0000000
##
## , , 67
##
##           H           S1         S2         D
## H  0.6916483  0.150000000 0.0000000 0.1583517
## S1 0.5000000 -0.008799942 0.1050000 0.4037999
## S2 0.0000000  0.000000000 0.1783638 0.8216362
## D  0.0000000  0.000000000 0.0000000 1.0000000
##
## , , 68
##
##           H           S1        S2         D
## H  0.6735755  0.15000000 0.0000000 0.1764245
## S1 0.5000000 -0.04638792 0.1050000 0.4413879
## S2 0.0000000  0.00000000 0.1435603 0.8564397
## D  0.0000000  0.00000000 0.0000000 1.0000000
##
## , , 69
##
##           H           S1        S2         D
## H  0.6584358  0.15000000 0.0000000 0.1915642
## S1 0.5000000 -0.07663186 0.1050000 0.4716319
## S2 0.0000000  0.00000000 0.1192492 0.8807508
## D  0.0000000  0.00000000 0.0000000 1.0000000
##
## , , 70
##
##          H          S1         S2         D
## H  0.633682  0.1500000 0.00000000 0.2163180
## S1 0.500000 -0.1236959 0.10500000 0.5186959
## S2 0.000000  0.0000000 0.08737728 0.9126227
```

```
## D   0.000000   0.0000000 0.00000000 1.0000000
##
## , , 71
##
##             H          S1         S2          D
## H  0.6217559   0.1500000 0.0000000 0.2282441
## S1 0.5000000 -0.1453367 0.1050000 0.5403367
## S2 0.0000000   0.0000000 0.0749548 0.9250452
## D  0.0000000   0.0000000 0.0000000 1.0000000
##
## , , 72
##
##             H          S1          S2          D
## H  0.5999258   0.1500000 0.00000000 0.2500742
## S1 0.5000000 -0.1832502 0.10500000 0.5782502
## S2 0.0000000   0.0000000 0.05625783 0.9437422
## D  0.0000000   0.0000000 0.00000000 1.0000000
##
## , , 73
##
##             H          S1          S2          D
## H  0.5787468   0.1500000 0.00000000 0.2712532
## S1 0.5000000 -0.2179831 0.10500000 0.6129831
## S2 0.0000000   0.0000000 0.04224412 0.9577559
## D  0.0000000   0.0000000 0.00000000 1.0000000
##
## , , 74
##
##             H          S1          S2          D
## H  0.5623763   0.1500000 0.00000000 0.2876237
## S1 0.5000000 -0.2434833 0.10500000 0.6384833
## S2 0.0000000   0.0000000 0.03365849 0.9663415
## D  0.0000000   0.0000000 0.00000000 1.0000000
```

```r
head(l.out.stm$m.M)  # prin
```

```
##           H         S1         S2          D
## 0 1.0000000 0.0000000 0.00000000 0.000000000
## 1 0.8489865 0.1500000 0.00000000 0.001013486
## 2 0.7957908 0.1861491 0.01575000 0.002310077
## 3 0.7686457 0.1923009 0.03512803 0.003925325
## 4 0.7486643 0.1906297 0.05493985 0.005766235
## 5 0.7308100 0.1869350 0.07432126 0.007933762
```

```r
tail(l.out.stm$m.M)
```

```
##              H           S1           S2          D
## 70 0.010289758 0.0018633894 3.173351e-04 0.9875295
## 71 0.007452129 0.0013129700 2.233838e-04 0.9910115
## 72 0.005289890 0.0009269966 1.546055e-04 0.9936285
## 73 0.003637040 0.0006236112 1.060324e-04 0.9956333
## 74 0.002416730 0.0004096192 6.995842e-05 0.9971037
## 75 0.001563922 0.0002627741 4.536471e-05 0.9981279
```

To compute the mortality risks from the Sick and Sicker states, we transform `p.HD` to a rate assuming a constant exponential rate, $-log(1-p.HD)$, multiply it by the hazard rate ratios `hr.S1` and `hr.S2`, respectively,

and then convert them back to a probability $p = -e^{-rt}$. See the R code below for more details on the calculations.

```r
p.S1D  <- 1 - exp(log(1 - v.params.init$p.HD) * v.params.init$hr.S1) # probability of dying in Sick
p.S2D  <- 1 - exp(log(1 - v.params.init$p.HD) * v.params.init$hr.S2) # probability of dying in Sicker
```

03 Model calibration

The Sick-Sicker model results need to be calibrated against data containing information about survival, the prevalence of both sick and sicker and the proportion who are sick among those afflicted (sick and sicker). This data is stored in the 03_calibration-tarted.RData. The function to calibrate the model are stored in the 03_calibration_functions.R file stored in the functions folder. This file also contains a Goodness of fit function for calibration form a parameter set. The calibration function makes sure of the Nelder-Mead method.

04 Analysis

04a Validation

04b Deterministic analysis

04c Deterministic analysis

References

Enns, E A, L E Cipriano, C T Simons, and C Y 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, Eline M., Fernando Alarid-Escudero, Eva A. Enns, Hawre J. Jalal, M G Myriam Hunink, and Petros 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.