

PSA: Markov Sick-Sicker model in R

with age-specific mortality

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 Mak*. 2020;40(2):242-248. <https://doi.org/10.1177/0272989X19893973>

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Change eval to TRUE if you want to knit this document.

```
rm(list = ls()) # clear memory (removes all the variables from the workspace)
```

01 Load packages

```
if (!require('pacman')) install.packages('pacman'); library(pacman) # use this package to conveniently
# load (install if required) packages from CRAN
p_load("here", "dplyr", "devtools", "scales", "ellipse", "ggplot2", "lazyeval", "igraph", "ggraph",
       "reshape2", "knitr")
# load (install if required) packages from GitHub
# install_github("DARTH-git/dampack", force = TRUE) Uncomment if there is a newer version
# install_github("DARTH-git/darthtools", force = TRUE) Uncomment if there is a newer version
p_load_gh("DARTH-git/dampack", "DARTH-git/darthtools")
```

02 Load functions

```
# No functions needed
```

03 Input model parameters

```
# Strategy names
v_names_str <- c("No Treatment", "Treatment")

# Number of strategies
n_str <- length(v_names_str)

# Markov model parameters
age      <- 25 # age at baseline
max_age  <- 55 # maximum age of follow up
n_t      <- max_age - age # time horizon, number of cycles
v_names_states <- c("H", "S1", "S2", "D") # the 4 states of the model: Healthy (H), Sick (S1),
# Sicker (S2), Dead (D)
n_s      <- length(v_names_states) # number of health states

# Transition probabilities (per cycle)
p_HD     <- 0.005 # probability to die when healthy
p_HS1    <- 0.15  # probability to become sick when healthy
p_S1H    <- 0.5    # probability to become healthy when sick
p_S1S2   <- 0.105  # probability to become sicker when sick
hr_S1    <- 3      # hazard ratio of death in sick vs healthy
hr_S2    <- 10     # hazard ratio of death in sicker vs healthy
r_HD     <- - log(1 - p_HD) # rate of death in healthy
r_S1D    <- hr_S1 * r_HD   # rate of death in sick
r_S2D    <- hr_S2 * r_HD   # rate of death in sicker
```

```

p_S1D <- 1 - exp(-r_S1D)      # probability to die in sick
p_S2D <- 1 - exp(-r_S2D)      # probability to die in sicker

# Cost and utility inputs
c_H <- 2000                    # cost of remaining one cycle in the healthy state
c_S1 <- 4000                   # cost of remaining one cycle in the sick state
c_S2 <- 15000                  # cost of remaining one cycle in the sicker state
c_trt <- 12000                 # cost of treatment(per cycle)
c_D <- 0                       # cost of being in the death state
u_H <- 1                       # utility when healthy
u_S1 <- 0.75                   # utility when sick
u_S2 <- 0.5                   # utility when sicker
u_D <- 0                       # utility when dead
u_trt <- 0.95                 # utility when being treated

# Discounting factor
d_r <- 0.03                    # equal discount of costs and QALYs by 3%
# calculate discount weights for costs for each cycle based on discount rate d_c
v_dwc <- 1 / (1 + d_r) ^ (0:n_t)
# calculate discount weights for effectiveness for each cycle based on discount rate d_e
v_dwe <- 1 / (1 + d_r) ^ (0:n_t)

```

04 Define and initialize matrices and vectors

04.1 Cohort trace

```

# create the markov trace matrix M capturing the proportion of the cohort in each state
# at each cycle
m_M_notrt <- m_M_trt <- matrix(NA,
                                nrow = n_t + 1, ncol = n_s,
                                dimnames = list(paste("cycle", 0:n_t, sep = " "), v_names_states))

head(m_M_notrt) # show first 6 rows of the matrix

# The cohort starts as healthy
m_M_notrt[1, ] <- m_M_trt[1, ] <- c(1, 0, 0, 0) # initiate first cycle of cohort trace

```

04.2 Transition probability matrix

```

# create the transition probability matrix for NO treatment
m_P_notrt <- matrix(0,
                    nrow = n_s,
                    ncol = n_s,
                    dimnames = list(v_names_states, v_names_states)) # name the columns and rows

m_P_notrt

```

Fill in the transition probability matrix:

```
# from Healthy
# from Sick
# from Sicker
# from Dead

# create transition probability matrix for treatment same as no treatment
m_P_trt <- m_P_notrt
```

05 Run Markov model

```
# your turn
```

06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

```
# your turn
```

06.2 Overall Survival (OS)

```
# your turn
```

06.2.1 Life Expectancy (LE)

```
# your turn
```

06.3 Disease prevalence

```
# your turn
```

06.4 ratio of sick(S1) vs sicker(S2)

```
# your turn
```

07 Compute Cost-Effectiveness Outcomes

07.1 Mean Costs and QALYs for Treatment and NO Treatment

```
# your turn
```

07.2 Discounted Mean Costs and QALYs

```
# your turn
```

07.3 Compute ICERs of the Markov model

```
# your turn
```

07.4 Plot frontier of the Markov model

```
# your turn
```

08 Deterministic Sensitivity Analysis

08.1 List of input parameters

Create list “l_params_all” with all input probabilities, cost and utilities.

```
l_params_all <- as.list(data.frame(  
  p_HD    = 0.005, # probability to die when healthy  
  p_HS1   = 0.15,  # probability to become sick when healthy  
  p_S1H   = 0.5,   # probability to become healthy when sick  
  p_S1S2  = 0.105, # probability to become sicker when sick  
  hr_S1   = 3,     # hazard ratio of death in sick vs healthy  
  hr_S2   = 10,    # hazard ratio of death in sicker vs healthy  
  c_H     = 2000,  # cost of remaining one cycle in the healthy state  
  c_S1    = 4000,  # cost of remaining one cycle in the sick state  
  c_S2    = 15000, # cost of remaining one cycle in the sicker state  
  c_trt   = 12000, # cost of treatment(per cycle)  
  c_D     = 0,     # cost of being in the death state  
  u_H     = 1,     # utility when healthy  
  u_S1    = 0.75,  # utility when sick  
  u_S2    = 0.5,   # utility when sicker  
  u_D     = 0,     # utility when dead  
  u_trt   = 0.95,  # utility when treated  
  d_e     = 0.03,  # discount factor for effectiveness  
  d_c     = 0.03   # discount factor for costs  
))
```

08.2 Load Sick-Sicker Markov model function

```
source("Functions_markov_sick-sicker_tunnels.R")
```

08.3 One-way sensitivity analysis (OWSA)

```
# your turn
```

08.3.1 Plot OWSA

```
# your turn
```

08.3.2 Optimal strategy with OWSA

```
# your turn
```

08.3.3 Tornado plot

```
# your turn
```

08.4 Two-way sensitivity analysis (TWSA)

```
# your turn
```

08.4.1 Plot TWSA

```
# your turn
```

09 Probabilistic Sensitivity Analysis (PSA)

```
# Function to generate PSA input dataset
```

09.1 Conduct probabilistic sensitivity analysis

your turn

09.2 Create PSA object for dampack

your turn

09.2.1 Save PSA objects

your turn

09.3 Create probabilistic analysis graphs

your turn

Vector with willingness-to-pay (WTP) thresholds.

your turn

09.3.1 Cost-Effectiveness Scatter plot

your turn

09.4 Conduct CEA with probabilistic output

your turn

09.4.1 Plot cost-effectiveness frontier

your turn

09.4.2 Cost-effectiveness acceptability curves (CEACs) and frontier (CEAF)

your turn

09.4.3 Expected Loss Curves (ELCs)

your turn

09.4.4 Expected value of perfect information (EVPI)

your turn