

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. *BioRxiv* 670612 2019.<https://www.biorxiv.org/content/10.1101/670612v1>

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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
p_load_gh("DARTH-git/dampack")
```

02 Load functions

```
source(here::here("functions", "Functions.R"))
```

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_n      <- c("H", "S1", "S2", "D") # the 4 states of the model: Healthy (H), Sick (S1),
                                   # Sicker (S2), Dead (D)
n_s      <- length(v_n)      # number of health states

# Transition probabilities (per cycle) and hazard ratios
# Read age-specific mortality rates from csv file
lt_usa_2005 <- read.csv(here::here("data", "HMD_USA_Mx_2015.csv"))
v_r_HD <- lt_usa_2005 %>%
  filter(Age >= age & Age <= (max_age-1)) %>%
  select(Total) %>%
  as.matrix()

p_HD      <- 1 - exp(- v_r_HD) # 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_n))

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 array

```

# create transition probability array for NO treatment
a_P_notrt <- array(0, # Create 3-D array
                  dim = c(n_s, n_s, n_t),
                  dimnames = list(v_n, v_n, 0:(n_t-1))) # name dimensions of the array

```

Fill in the transition probability array:

```
# from Healthy  
# from Sick  
# from Sicker  
# from Dead  
  
# create transition probability matrix for treatment same as NO treatment  
a_P_trt <- a_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_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(here::here("functions", "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