

# 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*