

# 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", "truncnorm",
# 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/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_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

# Tunnels
tunnel_size <- n_t
# Sick state
Sick_tunnel <- paste("S1_", seq(1, tunnel_size), "Yr", sep = "")
### Create variables for time-dependent model
v_n_td     <- c("H", Sick_tunnel, "S2", "D") # state names
n_s_td     <- length(v_n_td)                # number of states

# Transition probabilities (per cycle) and hazard ratios
# Read age-specific mortality rates from csv file
```

```

lt_usa_2005 <- read.csv("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

# Weibull parameters
l <- 0.08 # scale
g <- 1.1 # shape
# Weibull function
p_S1S2 <- l*g*(1:tunnel_size)^(g-1) # probability to become sicker when sick
# (time-dependent)

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_td,
                                dimnames = list(paste("cycle", 0:n_t, sep = " "), v_n_td))

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

# The cohort starts as healthy
# initialize first cycle of Markov trace accounting for the tunnels
m_M_notrt[1, ] <- m_M_trt[1, ] <- c(1, rep(0, tunnel_size), 0, 0)

```

## 04.2 Transition probability array

```

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

```

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
  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*