

Simple 3-state microsimulation model with PSA

Includes sex specific probability of dying when healthy and state occupation: probability of dying when sick depends on the time of being sick

The DARTH workgroup

Developed by the Decision Analysis in R for Technologies in Health (DARTH) workgroup:

Fernando Alarid-Escudero, PhD (1)

Eva A. Enns, MS, PhD (2)

M.G. Myriam Hunink, MD, PhD (3,4)

Hawre J. Jalal, MD, PhD (5)

Eline M. Krijkamp, MSc (3)

Petros Pechlivanoglou, PhD (6,7)

Alan Yang, MSc (7)

In collaboration of:

1. Drug Policy Program, Center for Research and Teaching in Economics (CIDE) - CONACyT, Aguascalientes, Mexico
2. University of Minnesota School of Public Health, Minneapolis, MN, USA
3. Erasmus MC, Rotterdam, The Netherlands
4. Harvard T.H. Chan School of Public Health, Boston, USA
5. University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA
6. University of Toronto, Toronto ON, Canada
7. The Hospital for Sick Children, Toronto ON, Canada

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 Making*. 2020 Online first. <https://doi.org/10.1177/0272989X19893973>

Copyright 2017, THE HOSPITAL FOR SICK CHILDREN AND THE COLLABORATING INSTITUTIONS. All rights reserved in Canada, the United States and worldwide. Copyright, trademarks, trade names and any and all associated intellectual property are exclusively owned by THE HOSPITAL FOR SICK CHILDREN and the collaborating institutions. These materials may be used, reproduced, modified, distributed and adapted with proper attribution.

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", "r
# 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

```
set.seed(1) # set the seed

# Model structure
v_n  <- c("healthy", "sick", "dead")      # vector with state names
n_states <- length(v_n)                   # number of states
n_t  <- 60                                # number of cycles
n_i  <- 10000                             # number of individuals
d_e <- d_c <- 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_e) ^ (0:n_t)
# calculate discount weights for effectiveness for each cycle based on discount rate d_e
v_dwe <- 1 / (1 + d_c) ^ (0:n_t)

#### Deterministic analysis ####

# Transition probabilities
p_HS <- 0.05      # probability healthy -> sick
p_HD_female <- 0.0382 # probability health -> dead when female
p_HD_male <- 0.0463 # probability health -> dead when male
m_p_HD <- data.frame(Sex = c("Female", "Male"), p_HD = c(p_HD_female, p_HD_male)) # combine the pr

# probability to die in sick state by cycle of being sick
p_SD <- c(0.1, 0.2, 0.3, 0.4, 0.5, rep(0.7, n_t - 5))
```

```

# Costs inputs
c_H <- 1500      # cost of one cycle in healthy state
c_S <- 5000      # cost of one cycle in sick state
c_D <- 0

# utility inputs
u_H <- 1         # utility when healthy
u_S <- 0.85      # utility when sick
u_D <- 0         # utility when dead

```

04 Sample individual level characteristics

04.1 Static characteristics

```

# randomly sample the sex of an individual (50% female)
v_sex <- sample(x = c("Female", "Male"), prob = c(0.5, 0.5), size = n_i, replace = TRUE)
df_X <- data.frame(ID = 1:n_i, Sex = v_sex) # Make a data frame of the individual characteristics

```

04.2 Dynamic characteristics

```

# Specify the initial health state of the individuals
# everyone begins in the healthy state (in this example)
v_M_init <- rep("healthy", times = n_i)
v_Ts_init <- rep(0, n_i) # a vector with the time of being sick at the start of the model

```

05 Define Simulation Functions

05.1 Probability function

The function that updates the transition probabilities of every cycle is shown below.

```

Probs <- function(M_t, df_X, v_Ts) {
  # Arguments:
  # M_t: health state occupied at cycle t (character variable)
  # df_X: data frame with individual characteristics data
  # v_Ts: vector with the duration of being sick
  # Returns:
  # transition probabilities for that cycle

  # create matrix of state transition probabilities
  m_p_t <- matrix(0, nrow = n_states, ncol = n_i)
  # give the state names to the rows
  rownames(m_p_t) <- v_n

  # lookup baseline probability and rate of dying based on individual characteristics
  p_HD_all <- inner_join(df_X, m_p_HD, by = c("Sex") )
}

```

```

p_HD      <- p_HD_all[M_t == "healthy", "p_HD"]

# update m_p_t with the appropriate probabilities
# transition probabilities when healthy
m_p_t[, M_t == "healthy"] <- rbind(1 - p_HD - p_HS, p_HS, p_HD)
# transition probabilities when sick
m_p_t[, M_t == "sick"]    <- rbind(0, 1 - p_SD[v_Ts], p_SD[v_Ts])
# transition probabilities when dead
m_p_t[, M_t == "dead"]    <- rbind(0, 0, 1)
return(t(m_p_t))
}

```

05.2 Cost function

The Costs function estimates the costs at every cycle.

```

Costs <- function (M_t) {
  # M_t: current health state
  c_t <- c()
  c_t[M_t == "dead"]    <- c_D      # costs at dead state
  c_t[M_t == "healthy"] <- c_H      # costs accrued by being healthy this cycle
  c_t[M_t == "sick"]    <- c_S      # costs accrued by being sick this cycle

  return(c_t) # return costs accrued this cycle
}

```

05.3 Health outcome function

The Effs function to update the utilities at every cycle.

```

Effs <- function (M_t) {
  # M_t: current health state
  q_t <- c()
  q_t[M_t == "dead"]    <- u_D      # QALYs at dead state
  q_t[M_t == "healthy"] <- u_H      # QALYs accrued by being healthy this cycle
  q_t[M_t == "sick"]    <- u_S      # QALYs accrued by being sick this cycle

  return(q_t) # return the QALYs accrued this cycle
}

```

06 Run Microsimulation

```

MicroSim <- function(n_i, df_X, seed = 1) {
  # Arguments:
  # n_i:      number of individuals
  # df_X:     data frame with individual data
  # seed:     default is 1
  # Returns:

```

```

# results: a list of microsimulation results

set.seed(seed) # set the seed

# create three matrices called m_M, m_C and m_E
# number of rows is equal to the n_i, the number of columns is equal to n_t
# (the initial state and all the n_t cycles)
# m_M is used to store the health state information over time for every individual
# m_C is used to store the costs information over time for every individual
# m_E is used to store the effects information over time for every individual

m_M <- m_C <- m_E <- matrix(nrow = n_i, ncol = n_t + 1,
                             dimnames = list(paste("ind" , 1:n_i, sep = " "),
                                                paste("cycle", 0:n_t, sep = " ")))

m_M[, 1] <- v_M_init           # initial health state
v_Ts      <- v_Ts_init         # initialize time since illness onset
m_C[, 1] <- Costs(m_M[, 1])    # costs accrued during cycle 0
m_E[, 1] <- Efts(m_M[, 1])     # QALYs accrued during cycle 0

# open a loop for time running cycles 1 to n_t
for (t in 1:n_t) {
  # calculate the transition probabilities for the cycle based on health state t
  m_P <- Probs(m_M[, t], df_X, v_Ts)
  # sample the current health state and store that state in matrix m_M
  m_M[, t + 1] <- samplev(m_P, 1)
  # calculate costs per individual during cycle t + 1
  m_C[, t + 1] <- Costs(m_M[, t + 1])
  # calculate QALYs per individual during cycle t + 1
  m_E[, t + 1] <- Efts (m_M[, t + 1])

  # update time since illness onset for t + 1
  v_Ts <- if_else(m_M[, t + 1] == "sick", v_Ts + 1, 0)

  # Display simulation progress
  if(t/(n_t/10) == round(t/(n_t/10), 0)) { # display progress every 10%
    cat('\r', paste(t/n_t * 100, "% done", sep = " "))
  }
} # close the loop for the time points

# calculate
tc <- m_C %>% v_dwc # total (discounted) cost per individual
te <- m_E %>% v_dwe # total (discounted) QALYs per individual
tc_hat <- mean(tc)  # average (discounted) cost
te_hat <- mean(te)  # average (discounted) QALYs

# store the results from the simulation in a list
results <- list(m_M = m_M, m_C = m_C, m_E = m_E, tc = tc , te = te, tc_hat = tc_hat,
               te_hat = te_hat)

return(results) # return the results

```

```

} # end of the MicroSim function

# By specifying all the arguments in the `MicroSim()` the simulation can be started

# Run the simulation model
outcomes <- MicroSim(n_i, df_X, seed = 1)

# Show results
results <- data.frame("Total Cost" = outcomes$tc_hat, "Total QALYs" = outcomes$te_hat)
results

```

07 Visualize results

```

options(scipen = 999) # disabling scientific notation in R
plot(density(outcomes$tc), main = paste("Total cost per person"), xlab = "Cost ($)")
plot(density(outcomes$te), main = paste("Total QALYs per person"), xlab = "QALYs")
plot_m_TR(outcomes$m_M) # health state trace, function from the "Function.R"-file

```