

Simple 3-state microsimulation model

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>

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)

# load (install if required) packages from CRAN
p_load("here", "devtools", "dplyr", "scales", "ellipse", "ggplot2", "lazyeval", "igraph", "truncnorm", "rstanarm")
# 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
# (all non-dead probabilities are conditional on survival)
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))

# 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)

```

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

```

04.3 Create a dataframe with the individual characteristics

```

# create a data frame with each individual's
# ID number, treatment effect modifier, age and initial time in sick state
df_X <- data.frame(ID = 1:n_i, Sex = v_sex, Ts_init = v_Ts_init, M_init = v_M_init)
head(df_X) # print the first rows of the dataframe

```

05 Define Simulation Functions

05.1 Probability function

The Probs function 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
# (all non-death probabilities are conditional on survival)
# transition probabilities when healthy
m_p_t[, M_t == "healthy"] <- rbind((1 - p_HD) * (1 - p_HS) ,
                                   (1 - p_HD) * 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) {
  # Arguments:
  # M_t: health state occupied at cycle t (character variable)
  # Returns:
  # costs accrued in this cycle

  c_t <- c()
  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
  c_t[M_t == "dead"]    <- c_D # costs at dead state

  return(c_t)
}

```

05.3 Health outcome function

The `Effs` function to update the utilities at every cycle.

```

Effs <- function (M_t) {
  # Arguments:
  # M_t: health state occupied at cycle t (character variable)
  # Returns:
  # QALYs accrued this cycle

  q_t <- c()
  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
  q_t[M_t == "dead"] <- u_D # QALYs at dead state

  return(q_t)
}

```

05.4 Microsimulation function

Below we develop the microsimulation function that allows the model to be run.

```

MicroSim <- function(n_i, df_X, seed = 1) {
  # Arguments:
  # n_i: number of individuals
  # df_X: data frame with individual data
  # seed: seed for the random number generator, default is 1
  # Returns:
  # results: data frame with total cost and QALYs

  set.seed(seed) # set a seed to be able to reproduce the same results

  # 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] <- as.character(df_X$M_init) # initial health state
  v_Ts <- df_X$Ts_init # initialize time since illness onset
  m_C[, 1] <- Costs(m_M[, 1]) # costs accrued during cycle 0
  m_E[, 1] <- Effs(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)
    # check if transition probabilities are between 0 and 1
    check_transition_probability(m_P, verbose = TRUE)
    # check if each of the rows of the transition probabilities matrix sum to one
    check_sum_of_transition_array(m_P, n_states = n_i, n_t = n_t, verbose = TRUE)
  }
}

```

```

# sample the next health state and store that state in matrix m_M
m_M[, t + 1] <- samplev(m_P)
# 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] <- Effs (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) QAL
# 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

```

06 Run Microsimulation

```

# 06 Run Microsimulation

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

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

```