

# 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

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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. *Med Decis Mak*. 2020;40(2):242-248. <https://doi.org/10.1177/0272989X19893973>

Change eval to TRUE if you want to knit this document.

## 01 Load packages

```
if (!require('pacman')) install.packages('pacman'); library(pacman)
# load (install if required) packages from CRAN
p_load("devtools", "dplyr", "scales", "ellipse", "ggplot2", "lazyeval", "igraph", "truncnorm", "ggraph")
# load (install if required) packages from GitHub
# install_github("DARTH-git/darthtools", force = TRUE) # Uncomment if there is a newer version
p_load_gh("DARTH-git/darthtools")
```

## 02 Load functions

```
# No functions needed
```

## 03 Input model parameters

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

# Strategy names
v_names_str <- c("Standard of care")

# Model structure
v_names_states <- c("Healthy", "Sick", "Dead") # vector with state names
n_states <- length(v_names_states) # 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%

#### 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 # cost of one cycle in dead state
```

```

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

# 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)

```

## 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_names_states

# 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) # return costs accrued this cycle
}

```

## 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) # return the QALYs accrued this cycle
}

```

## 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_rows = n_i, n_cycles = n_t, verbose = TRUE)
  }
}

```

```

# sample the next 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] <- Efs (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

```

plot(density(outcomes$tc), main = paste("Total cost per person"), xlab = "Cost ($)")
plot(density(outcomes$te), main = paste("Total QALYs per person"), xlab = "QALYs")
plot_trace_microsim(outcomes$m_M) # health state trace

```

Small note: The difference between `paste()` and `paste0()` is that the argument sep by default is `" "` (`paste`) and `"` (`paste0`). In conclusion, `paste0()` is faster than `paste()` if our objective is concatenate strings without spaces because we don't have to specify the argument sep.