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

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- 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

```r
rm(list = ls())      # clear memory (removes all the variables from the workspace)
```

01 Load packages

```r
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
 p_load_gh("DARTH-git/dampack")
```

02 Load functions

```r
source("Functions.R")  # This line only works when you "Function.R" file is in the same folder
```

03 Input model parameters

```r
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
```

```r
u_S  <- 0.85      # utility when sick
u_D  <- 0         # utility when dead
```

04 Sample individual level characteristics

04.1 Static characteristics

```r
# 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 cahracteristics
```

04.2 Dynamic characteristics

```r
# 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.

```r
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 if 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 illnes 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)
    # 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]  <- 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) 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)
```

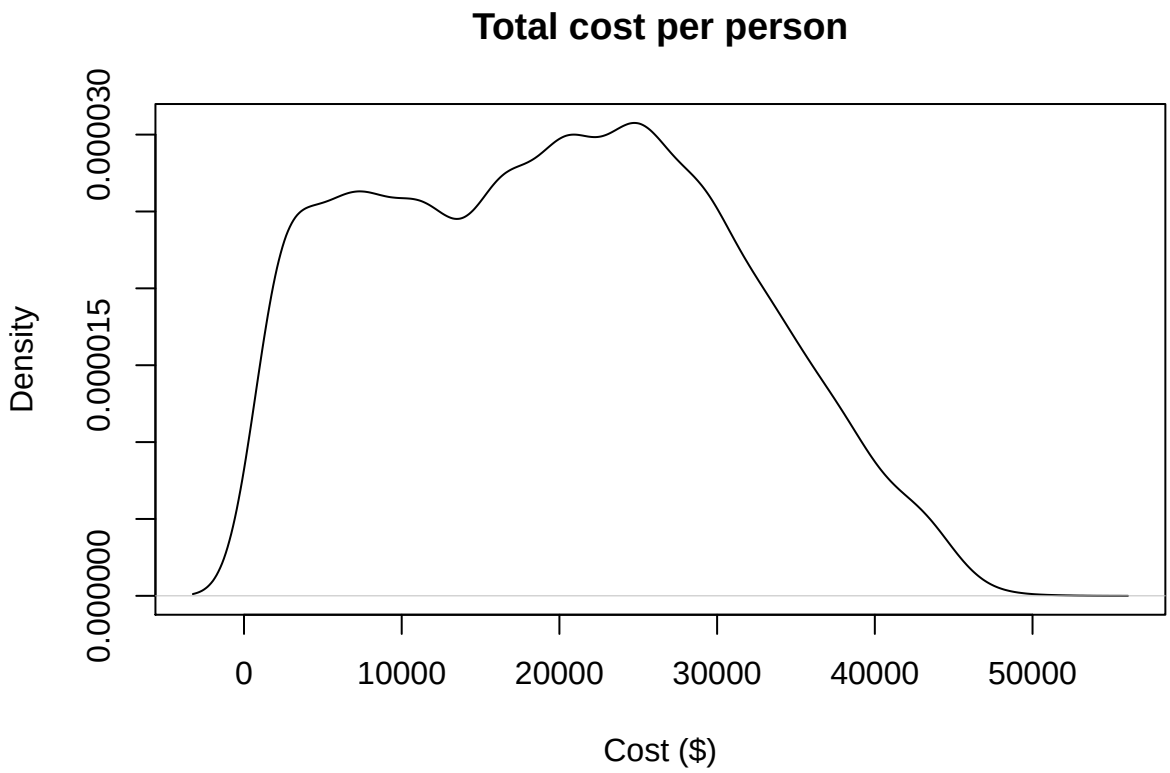
```
##  10 % done 20 % done 30 % done 40 % done 50 % done 60 % done 70 % done 80 % done 90 % done 100 % done
```

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

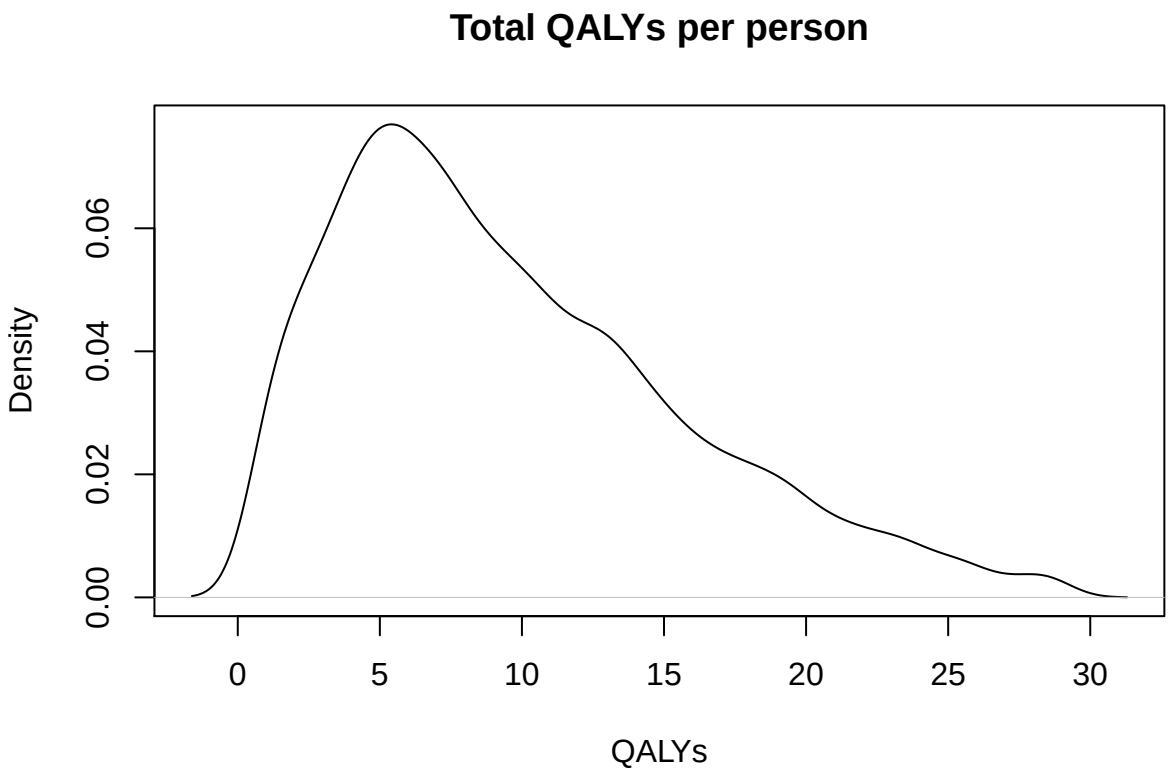
```
##   Total.Cost Total.QALYs
## 1   19755.09    9.643643
```

07 Visualize results

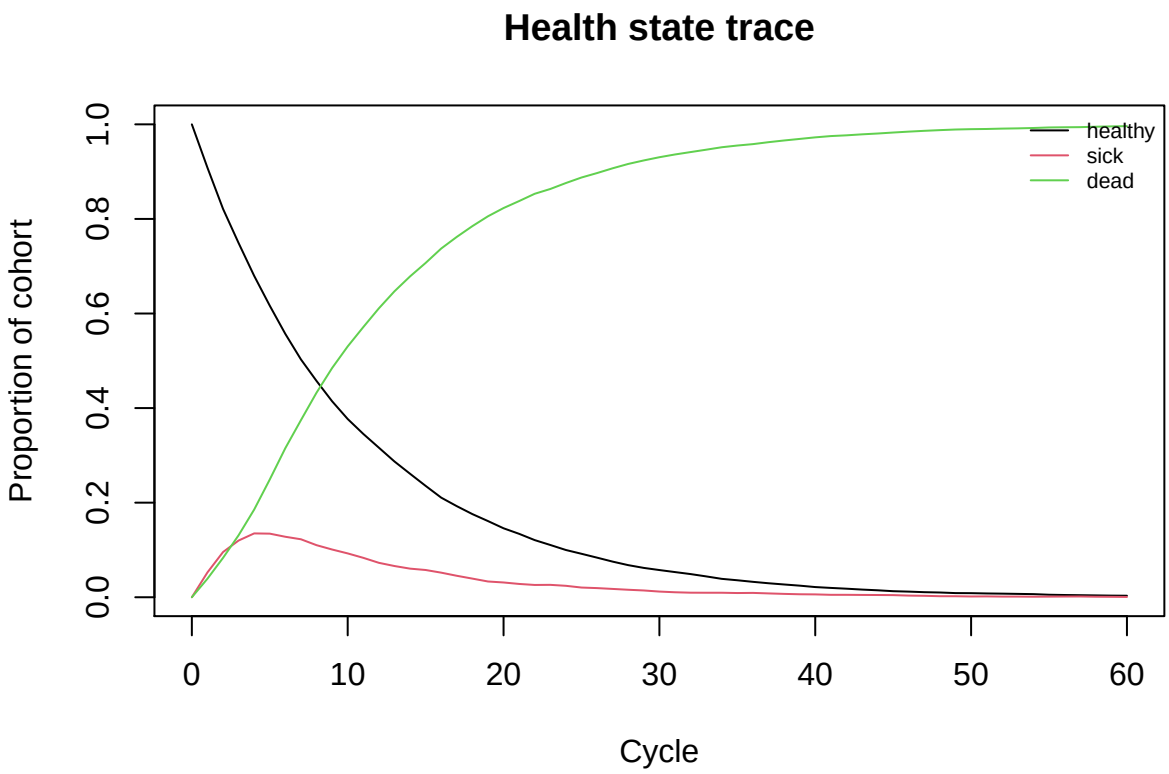
```
options(scipen = 999)  # disabling scientific notation in R
plot(density(outcomes$tc), main = paste("Total cost per person"), xlab = "Cost ($)")
```




```
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
```


Health state trace
Proportion of cohort
0.0
0.2
0.4
0.6
0.8
1.0
0
10
20
30
40
50
60
Cycle
healthy
sick
dead