# Microsimulation Sick-Sicker model with time dependency with PSA

Includes individual characteristics: age, age dependent mortality, individual treatment effect modifier, state-residency for the sick (S1) state, increasing change of death in the first 6 year of sickness

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)

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",
# 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
n_t   <- 30                       # time horizon, 30 cycles
n_i   <- 100000                   # number of simulated individuals
v_n   <- c("H", "S1", "S2", "D")  # the model states names
n_states <- length(v_n)           # the number of health states
d_r   <- 0.03                     # discount rate of 3% per cycle
v_dwe <- v_dwc <- 1 / ((1 + d_r) ^ (0:n_t))    # discount weight
v_names_str <- c("no treatment", "treatment")  # strategy names
n_str <- length(v_names_str)      # number of strategies

# Event probabilities (per cycle)
# Annual transition probabilities
# (all non-probabilities are conditional on survival)
p_HS1   <- 0.15   # probability of becoming sick when healthy
p_S1H   <- 0.5    # probability of recovering to healthy when sick
p_S1S2  <- 0.105  # probability of becoming sicker when sick

# Annual probabilities of death
# load age dependent probability
p_mort   <- read.csv("mortProb_age.csv")
# load age distribution
dist_Age <- read.csv("MyPopulation-AgeDistribution.csv")
```

```r
# probability to die in S1 by cycle (is increasing)
p_S1D    <- c(0.0149, 0.018, 0.021, 0.026, 0.031, rep(0.037, n_t - 5))
p_S2D    <- 0.048  # probability to die in S2

# Cost inputs
c_H     <- 2000    # cost of one cycle in the healthy state
c_S1    <- 4000    # cost of one cycle in the sick state
c_S2    <- 15000   # cost of one cycle in the sicker state
c_D     <- 0       # cost of one cycle in the dead state
c_trt   <- 12000   # cost of treatment (per cycle)

# Utility inputs
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 sick and being treated
```

# 04 Sample individual level characteristics

## 04.1 Static characteristics

```r
v_x     <- runif(n_i, min = 0.95, max = 1.05) # treatment effect modifier at baseline
# your turn
```

## 04.2 Dynamic characteristics

```r
# your turn
```

## 04.3 Create a dataframe with the individual characteristics

```r
# your turn
# HINT: df_X <- # data.frame(# ADD ALL CHARACTERISTICS)
```

# 05 Define Simulation Functions

*HINT*: There is no need to make two functions for each strategy. We recommend to make one `Probs()`, one `Costs()` and one `Effs()` function and have a function argument `Trt` which you "switch" on and off (i.e TRUE/FALSE - or 0/1) of the strategy of interest.

Please see a hypothetical example below :

```r
cost_stay <- function (days = 0, Trt = FALSE) {
  # Arguments:
    # days: days an individual is staying in a care facility
    # Trt: is the individual treated? (default is FALSE)
  # Returns:
    # costs accrued in this cycle

  c_stay_day <- 100   # the price to stay a day at the care facility
  c_trt      <- 3000   # the price of treatment, total price for drug. Drug requires one dose

  cost <- c_stay_day * days + Trt * c_trt # calculate total cost

  return(cost)       # return the price
}

cost_stay_noTrt <- cost_stay(days = 10, Trt = FALSE) # run the function for the no treatment strategy
cost_stay_Trt   <- cost_stay(days = 10, Trt = TRUE) # run the function for the treatment strategy

cost_stay_noTrt
cost_stay_Trt
```

### 05.1 Probability function

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

Please make sure you incorporate the time dependency

```r
# your turn
# HINT: In this function you have to incorporate age specific mortality and incorporate
# the change in probability of the years spend in the sick state
```

### 05.2 Cost function

The `Costs` function estimates the costs at every cycle.

```r
# your turn
# Make sure you incorporate the cost of the treatment in the treatment strategy for both sick and sicke
```

### 05.3 Health outcome function

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

```r
# your turn
# HINT: Make sure you incorporate the treatment effect modifier
# HINT: Remember treatment improves the quality of life for those in the Sick (S1) state but not for th
```

### 05.4 The Microsimulation function

You need to develop the main function `MicroSim()` that runs the microsimulation.

```r
# your turn
# HINT: Build your own `MicroSim` function here that calls the Effs() and Costs() functions and samples
```

## 06 Run Microsimulation

You have to run the `Microsim()` function twice. Once for the treatment strategy and once of the no-treatment strategy, as follows:

- `outcomes_no_trt  <- MicroSim(n_i, df_X, Trt = FALSE, seed = 1)`
- `outcomes_trt     <- MicroSim(n_i, df_X, Trt = TRUE,  seed = 1)`

## 07 Visualize results

```r
# your turn
# HINT: use pre-defined functions in "Functions.R" or check the example code
```

## 08 Cost Effectiveness Analysis

```r
# store the mean costs of each strategy in a new variable v_C (vector of costs)
# remove # below
# v_C <- c(outcomes_no_trt$tc_hat, outcomes_trt$tc_hat)

# store the mean QALYs of each strategy in a new variable v_E (vector of effects)
# remove # below
# v_E <- c(outcomes_no_trt$te_hat, outcomes_trt$te_hat)


# remove # below
# use dampack to calculate the ICER
# calculate_icers(cost       = v_C,
#                 effect     = v_E,
#                 strategies = v_names_str)
```

## 09 Probabilistic Sensitivity Analysis

```r
# your turn
```