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 5 years of sickness

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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

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.

```
# 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

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

08 Cost Effectiveness Analysis

```
# 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

```
# your turn
```