Markov Sick-Sicker model in R

with dependency for time-since model start AND with state-residency dependency

The DARTH workgroup

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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. BioRxiv 670612 2019.https://www.biorxiv.org/content/10.1101/670612v1

```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", "truncnorm",
       "reshape2", "knitr")
# 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(here::here("functions","Functions.R"))
```

03 Input model parameters

```r
# Strategy names
v_names_str <- c("No Treatment", "Treatment")

# Number of strategies
n_str <- length(v_names_str)

# Markov model parameters
age      <- 25                        # age at baseline
max_age  <- 55                        # maximum age of follow up
n_t      <- max_age - age             # time horizon, number of cycles
v_n      <- c("H", "S1", "S2", "D")  # the 4 states of the model: Healthy (H), Sick (S1),
                                      # Sicker (S2), Dead (D)
n_states <- length(v_n)               # number of health states

# Tunnels
n_tunnel_size  <- n_t
# Sick state
v_Sick_tunnels <- paste("S1_", seq(1, n_tunnel_size), "Yr", sep = "")
### Create variables for time-dependent model
v_n_tunnels    <- c("H", v_Sick_tunnels, "S2", "D")   # state names
n_s_tunnels    <- length(v_n_tunnels)                 # number of states

# Transition probabilities (per cycle) and hazard ratios
# Read age-specific mortality rates from csv file
lt_usa_2005 <- read.csv(here::here("data", "HMD_USA_Mx_2015.csv"))
v_r_HD <- lt_usa_2005 %>%
  filter(Age >= age & Age <= (max_age - 1)) %>%
  select(Total) %>%
  as.matrix()

p_HD    <- 1 - exp(- v_r_HD)          # probability to die when healthy
p_HS1   <- 0.15                         # probability to become sick when healthy
```

```r
p_S1H   <- 0.5                          # probability to become healthy when sick

# Weibull parameters
l       <- 0.08 # scale
g       <- 1.1  # shape
# Weibull function
p_S1S2  <- l * g * (1:n_tunnel_size) ^ {g-1} # probability to become sicker when sick
                                      # (time-dependent)

hr_S1   <- 3                            # hazard ratio of death in sick vs healthy
hr_S2   <- 10                           # hazard ratio of death in sicker vs healthy
r_HD    <- - log(1 - p_HD)            # rate of death in healthy
r_S1D   <- hr_S1 * r_HD                 # rate of death in sick
r_S2D   <- hr_S2 * r_HD                 # rate of death in sicker
p_S1D   <- 1 - exp(-r_S1D)            # probability to die in sick
p_S2D   <- 1 - exp(-r_S2D)            # probability to die in sicker

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

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)
```

04 Define and initialize matrices and vectors

04.1 Cohort trace

```r
# create the markov trace matrix M capturing the proportion of the cohort in each state
# at each cycle
m_M_notrt <- m_M_trt  # <-  your turn






head(m_M_notrt) # show first 6 rows of the matrix

# The cohort starts as healthy
# initialize first cycle of Markov trace accounting for the tunnels
m_M_notrt[1, ] <- m_M_trt[1, ] <- c(1, rep(0, n_tunnel_size), 0, 0)
```

```

```

04.2 Transition probability array

```
# create the transition probability array for NO treatment
a_P_notrt # <- your turn
```

Fill in the transition probability array:

```
# from Healthy

# from Sick

# from Sicker

# from Dead

# create transition probability matrix for treatment same as NO treatment
a_P_trt <- a_P_notrt
```

05 Run Markov model

```
# your turn
```

06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

```
# your turn
```

06.2 Overall Survival (OS)

```
# your turn
```

06.2.1 Life Expectancy (LE)

```
# your turn
```

06.3 Disease prevalence

```
# your turn
```

06.4 ratio of sick(S1) vs sicker(S2)

```
# your turn
```

07 Compute Cost-Effectiveness Outcomes

07.1 Mean Costs and QALYs for Treatment and NO Treatment

```
# your turn
```

07.2 Discounted Mean Costs and QALYs

```
# your turn
```

07.3 Compute ICERs of the Markov model

```
# your turn
```

07.4 Plot frontier of the Markov model

```
# your turn
```