

Simple 3-state Markov model in R

with age 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>
- Alarid-Escudero F, Krijkamp EM, Enns EA, Yang A, Hunink MGM, Pechlivanoglou P, Jalal H. Cohort State-Transition Models in R: A Tutorial. *arXiv:200107824v2*. 2020:1-48. <http://arxiv.org/abs/2001.07824>
- 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>

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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) # use this package to conveniently
# load (install if required) packages from CRAN
p_load("diagram")
# 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

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

# Markov model parameters
v_n <- c("Healthy", "Sick", "Dead") # state names
n_t <- 60                          # number of cycles

v_init <- c("Healthy" = 1,
            "Sick"    = 0,
            "Dead"    = 0)          # initial cohort distribution (everyone allocated to the
                                   # "healthy" state)

# Transition probabilities
p_HD_min <- 0.003                  # probability of dying when healthy at t = 0
p_HD_max <- 0.01                   # probability of dying when health at t = n.t
p_HS <- 0.05                       # probability of becoming sick when healthy, under standard of care
p_SD <- 0.1                        # probability of dying when sick

# Costs and utilities
c_H <- 400                         # cost of one cycle in healthy state
c_S <- 1000                        # cost of one cycle in sick state
c_D <- 0                           # cost of one cycle in dead state
u_H <- 0.8                         # utility when healthy
u_S <- 0.5                         # utility when sick
u_D <- 0                           # utility when dead
d_e <- d_c <- 0.03                 # discount rate per cycle equal discount of costs and QALYs by 3%
```

```

p_HD <- seq(p_HD_min, p_HD_max, length.out = n_t) # probabilities of dying when healthy (age-dependent)
# this is now a sequence of numbers, officially v_p_

n_str <- length(v_names_str) # Number of strategies
n_states <- length(v_n) # number of states

# Discount weights for costs and effects
v_dwc <- 1 / (1 + d_c) ^ (0:n_t)
v_dwe <- 1 / (1 + d_e) ^ (0:n_t)

```

04 Define and initialize matrices and vectors

04.1 Cohort trace

```

# create the cohort trace
m_M <- matrix(NA,
              nrow = n_t + 1, # create Markov trace (n.t + 1 because R doesn't
                              # understand cycle 0)
              ncol = n_states,
              dimnames = list(0:n_t, v_n))

m_M[1, ] <- c(1, 0, 0) # initialize first cycle of Markov trace

```

04.2 Transition probability array

```

# create the transition probability array
a_P <- array(0, # Create 3-D array
             dim = c(n_states, n_states, n_t),
             dimnames = list(v_n, v_n, 0:(n_t - 1))) # name the dimensions of the array

```

Fill in the transition probability array:

```

# from Healthy
a_P["Healthy", "Healthy", ] <- (1 - p_HD) * (1 - p_HS)
a_P["Healthy", "Sick", ] <- (1 - p_HD) * p_HS
a_P["Healthy", "Dead", ] <- p_HD

# from Sick
a_P["Sick", "Sick", ] <- 1 - p_SD
a_P["Sick", "Dead", ] <- p_SD

# from Dead
a_P["Dead", "Dead", ] <- 1

```

04.3 Check if transition array and probabilities are valid

```
# Check that transition probabilities are in [0, 1]
check_transition_probability(a_P, verbose = TRUE)
# Check that all rows sum to 1
check_sum_of_transition_array(a_P, n_states = n_states, n_cycles = n_t, verbose = TRUE)
```

05 Run Markov model

```
for (t in 1:n_t){ # t<-1                                # loop through the number of cycles
  m_M[t + 1, ] <- m_M[t, ] %*% a_P[, , t] # estimate the Markov trace for cycle t + 1
                                                    # using the t-th matrix from the
                                                    # probability array
}
head(m_M) # print the first lines of the matrix
```

06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

```
# create a plot of the data
matplot(m_M, type = 'l',
        ylab = "Probability of state occupancy",
        xlab = "Cycle",
        main = "Cohort Trace", lwd = 2)
# add a legend to the graph
legend("right", v_n, col = c("black", "red", "green"), lty = 1:3, bty = "n")
```

06.2 Overall Survival (OS)

```
v_os <- 1 - m_M[, "Dead"] # calculate the overall survival (OS) probability
v_os <- rowSums(m_M[, 1:2]) # alternative way of calculating the OS probability

# create a simple plot showing the OS
plot(v_os, type = 'l',
     ylim = c(0, 1),
     ylab = "Survival probability",
     xlab = "Cycle",
     main = "Overall Survival")
# add grid
grid(nx = n_t, ny = 10,
     col = "lightgray", lty = "dotted", lwd = par("lwd"),
     equilogs = TRUE)
```

06.2.1 Life Expectancy (LE)

```
v_le <- sum(v_os) # summing probability of OS over time (i.e. life expectancy)
```

06.3 Disease prevalence

```
v_prev <- m_M[, "Sick"]/v_os  
plot(v_prev,  
      ylim = c(0, 1),  
      ylab = "Prevalence",  
      xlab = "Cycle",  
      main = "Disease prevalence")
```

07 Compute Cost-Effectiveness Outcomes

07.1 Mean Costs and QALYs

```
# per cycle  
# calculate expected costs by multiplying m_M with the cost vector for the different  
# health states  
v_tc <- m_M %*% c(c_H, c_S, c_D)  
# calculate expected QALYs by multiplying m_M with the utilities for the different  
# health states  
v_tu <- m_M %*% c(u_H, u_S, u_D)
```

07.2 Discounted Mean Costs and QALYs

```
# Discount costs by multiplying the cost vector with discount weights (v_dw)  
v_tc_d <- t(v_tc) %*% v_dwc  
# Discount QALYs by multiplying the QALYs vector with discount weights (v_dw)  
v_te_d <- t(v_tu) %*% v_dwe
```

07.3 Store Results

```
df_ce <- data.frame("Total Discounted Cost" = v_tc_d,  
                   "Life Expectancy"      = v_le,  
                   "Total Discounted QALYs" = v_te_d,  
                   check.names = F)  
df_ce
```