

# Simple 3-state Markov model in R

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*. 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

```
# all functions are in the darthtools package
```

## 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 <- 0.02                        # probability of dying when healthy
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%

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)

```

## Draw the state-transition cohort model

```

m_P_diag <- matrix(0, nrow = n_states, ncol = n_states, dimnames = list(v_n, v_n))
m_P_diag["Healthy", "Sick" ]      = ""
m_P_diag["Healthy", "Dead" ]      = ""
m_P_diag["Healthy", "Healthy" ]   = ""
m_P_diag["Sick" , "Dead" ]        = ""
m_P_diag["Sick" , "Sick" ]        = ""
m_P_diag["Dead" , "Dead" ]        = ""
layout.fig <- c(2, 1)
plotmat(t(m_P_diag), t(layout.fig), self.cex = 0.5, curve = 0, arr.pos = 0.8,
        latex = T, arr.type = "curved", relsize = 0.85, box.prop = 0.8,
        cex = 0.8, box.cex = 0.7, lwd = 1)

```

## 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, ] <- v_init           # initialize first cycle of Markov trace

```

### 04.2 Transition probability matrix

```

# create the transition probability matrix
m_P <- matrix(0,
              nrow = n_states, ncol = n_states,
              dimnames = list(v_n, v_n)) # name the columns and rows of the transition
                                          # probability matrix

m_P

```

Fill in the transition probability matrix:

```

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

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

# from Dead
m_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(m_P, verbose = TRUE)
# Check that all rows sum to 1
check_sum_of_transition_array(m_P, n_states = n_states, n_cycles = n_t, verbose = TRUE)

```

## 05 Run Markov model

```

for (t in 1:n_t){
  m_M[t + 1, ] <- m_M[t, ] %*% m_P # loop through the number of cycles
}                                     # estimate the state vector for the next cycle (t + 1)

```

## 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 = 3, # line widths
        col = c(3, 1, 2)) # colors
legend("right", v_n, col = c("green", "black", "red"),
       lty = 1:3, bty = "n") # add a legend to the graph

abline(v = which.max(m_M[, "Sick"]), col = "gray") # plot a vertical line that helps identifying at whi

```

### 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

plot(v_os, type = 'l',
     ylim = c(0, 1),
     ylab = "Survival probability",
     xlab = "Cycle",
     main = "Overall Survival")      # create a simple plot showing the OS

# 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_dw

```

```
# 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
```