

# Simple 3-state Markov model in R

The DARTH workgroup

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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>
- 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("dplyr", "devtools", "scales", "ellipse", "ggplot2", "lazyeval", "igraph", "ggraph", "reshape2")
# 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

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

## 03 Input model parameters

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

# Number of strategies
n_str <- length(v_names_str)

# Markov model parameters
v_n <- c("Healthy", "Sick", "Dead") # state names
n_states <- length(v_n)             # number of states
n_t <- 60                           # number of cycles
v_init <- c(1, 0, 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_HS_trt <- 0.03                    # probability of becoming sick when healthy, under treatment
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
c_trt <- 800                        # cost of treatment (per cycle)
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%

# 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)

```

## 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 <- m_M_trt <- 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, ] <- m_M_trt[1, ] <- v_init      # initialize first cycle of Markov trace

```

### 04.2 Transition probability matrix

```

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

m_P

```

Fill in the transition probability matrix:

```

# from Healthy
m_P["Healthy", "Healthy"] <- 1 - p_HS - p_HD
m_P["Healthy", "Sick"]    <- 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

# Under treatment
m_P_trt <- m_P
m_P_trt["Healthy", "Healthy"] <- 1 - p_HS_trt - p_HD
m_P_trt["Healthy", "Sick"]    <- p_HS_trt

```

## 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
  m_M_trt[t + 1, ] <- m_M_trt[t, ] %*% m_P_trt # estimate the state vector for the next cycle (t + 1)
  # for treatment
}

```

## 06 Compute and Plot Epidemiological Outcomes

### 06.1 Cohort trace

Standard of Care:

```

matplot(m_M, type = 'l',
  ylab = "Probability of state occupancy",
  xlab = "Cycle",
  main = "Cohort Trace - standard of care", lwd = 3) # create a plot of the data
legend("right", v_n, col = c("black", "red", "green"),
  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 a

```

Treatment:

```

matplot(m_M_trt, type = 'l',
  ylab = "Probability of state occupancy",
  xlab = "Cycle",
  main = "Cohort Trace - treatment", lwd = 3) # create a plot of the data
legend("right", v_n, col = c("black", "red", "green"),
  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 a

```

## 06.2 Overall Survival (OS)

Standard of Care:

```
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)
```

Treatment:

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

plot(v_os_trt, 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)
v_le_trt  <- sum(v_os_trt)           # summing probability of OS over time (i.e. life expectancy), treatment
```

## 06.3 Disease prevalence

Standard of Care:

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

Treatment:

```
v_prev_trt <- m_M_trt[, "Sick"]/v_os_trt
plot(v_prev_trt,
     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)      # Standard of Care
v_tc_trt  <- m_M_trt  %*% c(c_H, c_S + c_trt, c_D) # Treatment
# 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)      # Standard of Care
v_tu_trt  <- m_M_trt  %*% c(u_H, u_S, u_D)      # Treatment
```

### 07.2 Discounted Mean Costs and QALYs

```
# Discount costs by multiplying the cost vector with discount weights
tc_d      <- t(v_tc)      %*% v_dwc      # Standard of Care
tc_d_trt  <- t(v_tc_trt) %*% v_dwc      # Treatment
# Discount QALYS by multiplying the QALYs vector with discount weights
tu_d      <- t(v_tu)      %*% v_dwc      # Standard of Care
tu_d_trt  <- t(v_tu_trt) %*% v_dwc      # Treatment

# store them into a vector
v_tc_d    <- c(tc_d, tc_d_trt)
v_tu_d    <- c(tu_d, tu_d_trt)

# Dataframe with discounted costs and effectiveness
df_ce     <- data.frame(Strategy = v_names_str,
                        Cost      = v_tc_d,
                        Effect    = v_tu_d
                        )
df_ce
```

### 07.3 Compute ICERs of the Markov model

```
df_cea <- calculate_icers(cost      = df_ce$Cost,
                          effect    = df_ce$Effect,
                          strategies = df_ce$Strategy)
```

```
df_cea
```

## 07.4 Plot frontier of the Markov model

```
plot(df_cea, effect_units = "QALYs", xlim = c(10, 12))
```