

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*. 2020 Feb;40(2):242-248. <https://journals.sagepub.com/doi/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/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", "Treatment")

# Markov model parameters
v_names_states <- 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, conditional on surviving, unde
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 <- 1 # 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%, separate
```

```

n_str      <- length(v_names_str)      # Number of strategies
n_states   <- length(v_names_states)   # 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)

```

03.1 Draw the state-transition cohort model

```

m_P_diag <- matrix(0, nrow = n_states, ncol = n_states, dimnames = list(v_names_states, v_names_states))
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_SoC <- 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_names_states))

m_M_SoC[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_SoC <- m_P_trt <- matrix(0,
                             nrow = n_states, ncol = n_states,
                             dimnames = list(v_names_states, v_names_states)) # name the columns and

# print the probability matrices
m_P_SoC # for standard of care
m_P_trt # treatment

```

Fill in the transition probability matrix:

```

# For Standard of Care
# from Healthy
m_P_SoC["Healthy", "Healthy"] <- (1 - p_HD) * (1 - p_HS)
m_P_SoC["Healthy", "Sick"]     <- (1 - p_HD) * p_HS
m_P_SoC["Healthy", "Dead"]     <- p_HD

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

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

# Under treatment
m_P_trt <- m_P_SoC # Assign the matrix for standard of care to the transition probability matrix for t
# replace values that are different under treatment
m_P_trt["Healthy", "Healthy"] <- (1 - p_HD) * (1 - p_HS_trt)
m_P_trt["Healthy", "Sick"]     <- (1 - p_HD) * p_HS_trt

```

04.3 Check if transition probability structure and probabilities are valid

```

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

```

05 Run Markov model

```

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

```

06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

Standard of Care:

```

matplot(m_M_SoC, 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_names_states, col = c("black", "red", "green"),

```

```

    lty = 1:3, bty = "n") # add a legend to the graph
abline(v = which.max(m_M_SoC[, "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_names_states, col = c("black", "red", "green"),
      lty = 1:3, bty = "n") # add a legend to the graph
abline(v = which.max(m_M_trt[, "Sick"]), col = "gray") # plot a vertical line that helps identifying a

```

06.2 Overall Survival (OS)

Standard of Care:

```

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

plot(v_os_SoC, type = 'l',
     ylim = c(0, 1),
     ylab = "Survival probability",
     xlab = "Cycle",
     main = "Overall Survival - Standard of Care") # 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 - Treatment") # 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_SoC <- sum(v_os_SoC) # 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_SoC <- m_M_SoC[, "Sick"]/v_os_SoC
plot(v_prev_SoC,
     ylim = c(0, 1),
     ylab = "Prevalence",
     xlab = "Cycle",
     main = "Disease prevalence - Standard of care")
```

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 - Treatment")
```

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_SoC <- m_M_SoC %*% 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_SoC <- m_M_SoC %*% 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_SoC <- t(v_tc_SoC) %*% 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_SoC <- t(v_tu_SoC) %*% 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_SoC, tc_d_trt)
v_tu_d    <- c(tu_d_SoC, 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))

# note: you need to adjust the xlim values to values that are covering the range of effect values in your data

```