

# 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/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")

# 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_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%

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)

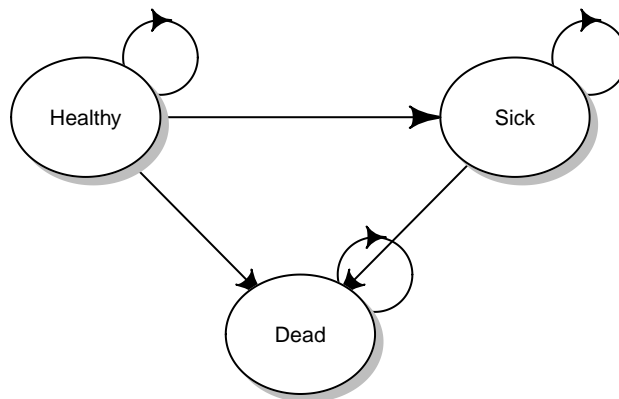
```

## 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 <- 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

# print the probability matrices
m_P # for standard of care
```

```
##           Healthy Sick Dead
## Healthy      0      0      0
## Sick         0      0      0
## Dead         0      0      0
```

```
m_P_trt # treatment
```

```
##           Healthy Sick Dead
## Healthy      0      0      0
## Sick         0      0      0
## Dead         0      0      0
```

Fill in the transition probability matrix:

```
# For Standard of Care
# 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
```

```

# Under treatment
m_P_trt <- m_P # Assign the matrix for standard of care to the transition probability matrix for treatment
# 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, verbose = TRUE)
check_transition_probability(m_P_trt, 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)
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){
  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)
  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:

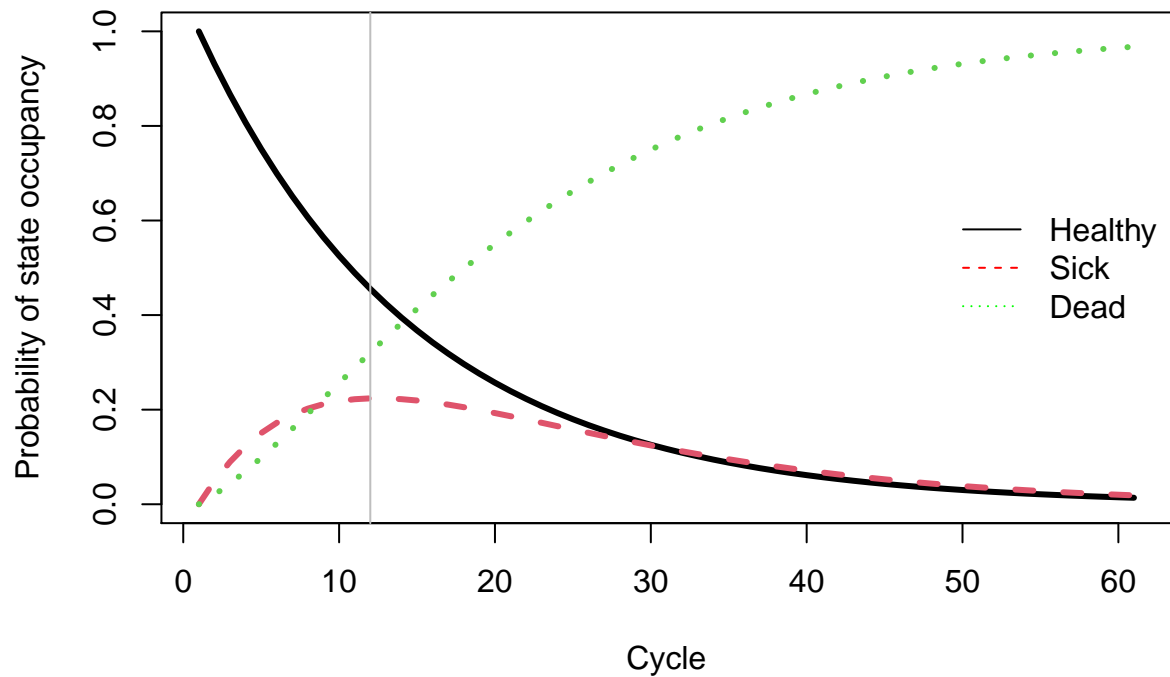
```

matplot(m_M, 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

```

## Cohort Trace – standard of care

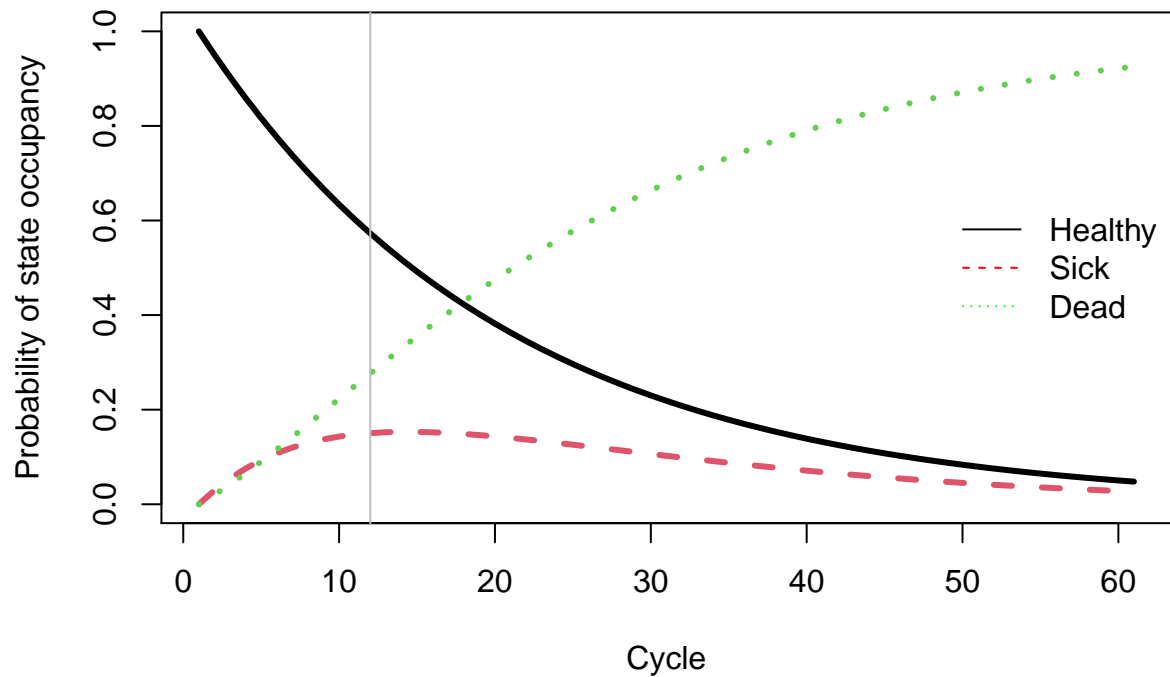


Treatment:

```
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
```

## Cohort Trace – treatment



## 06.2 Overall Survival (OS)

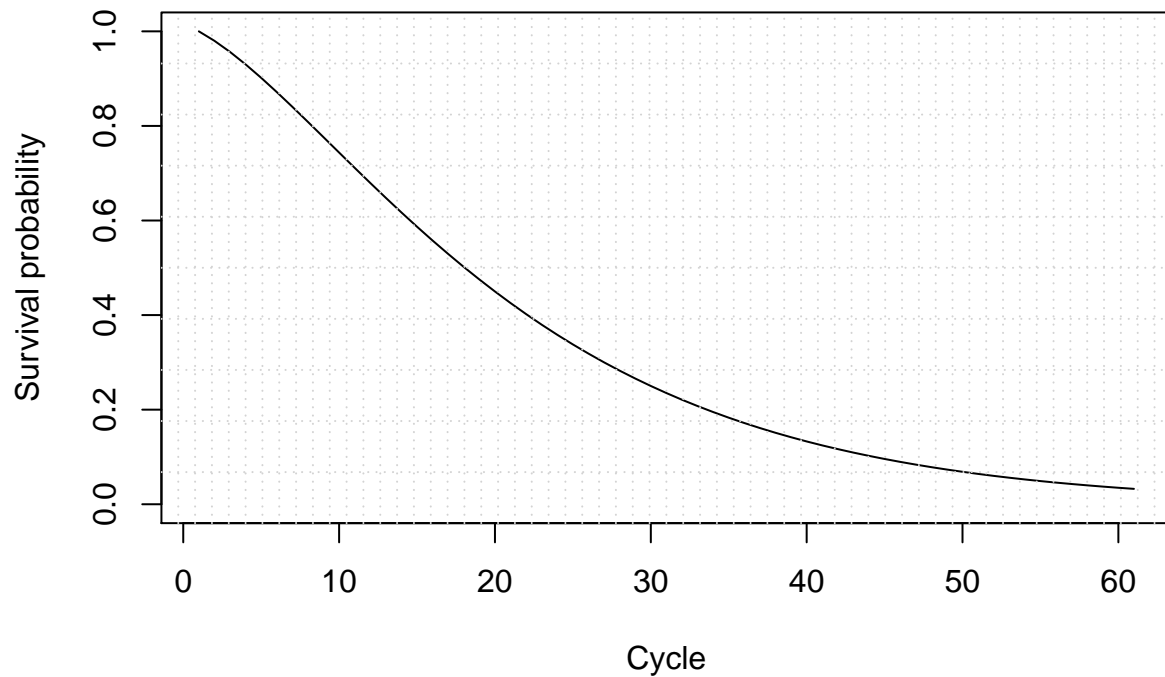
Standard of Care:

```
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 - 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)
```

## Overall Survival – Standard of Care



Treatment:

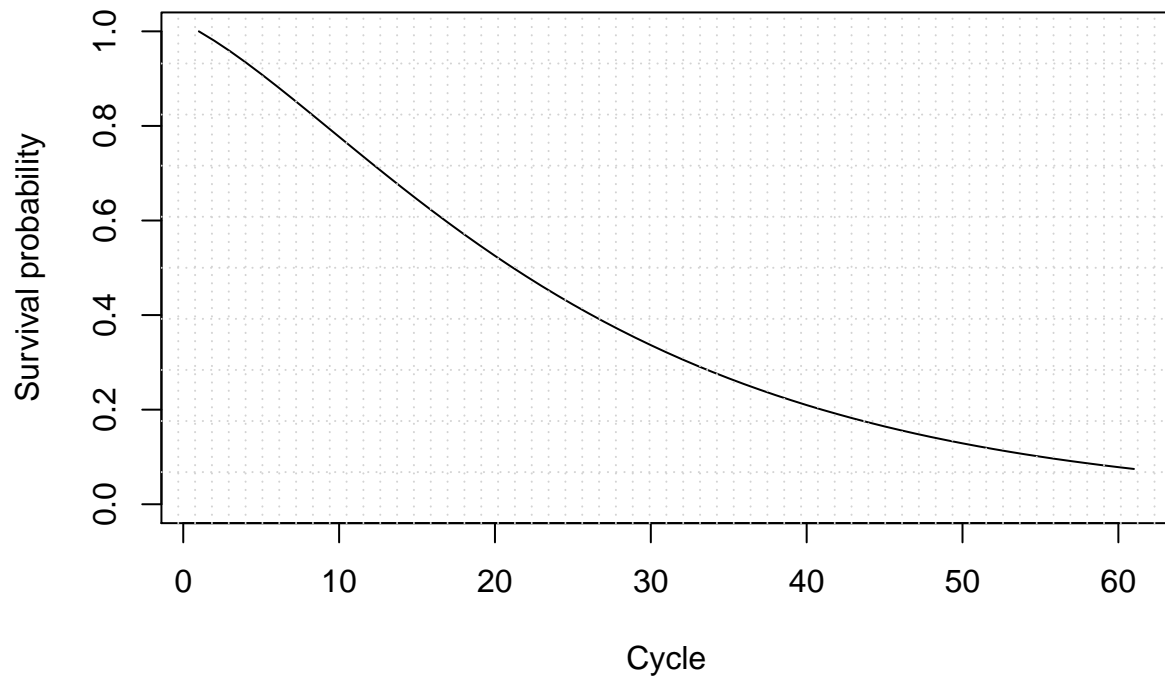
```
v_os_trt <- 1 - m_M_trt[, "Dead"]      # calculate the overall survival (OS) probability
v_os_trt <- rowSums(m_M_trt[, 1:2])    # alternative way of calculating the OS probability

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)
```



## Overall Survival – Treatment



### 06.2.1 Life Expectancy (LE)

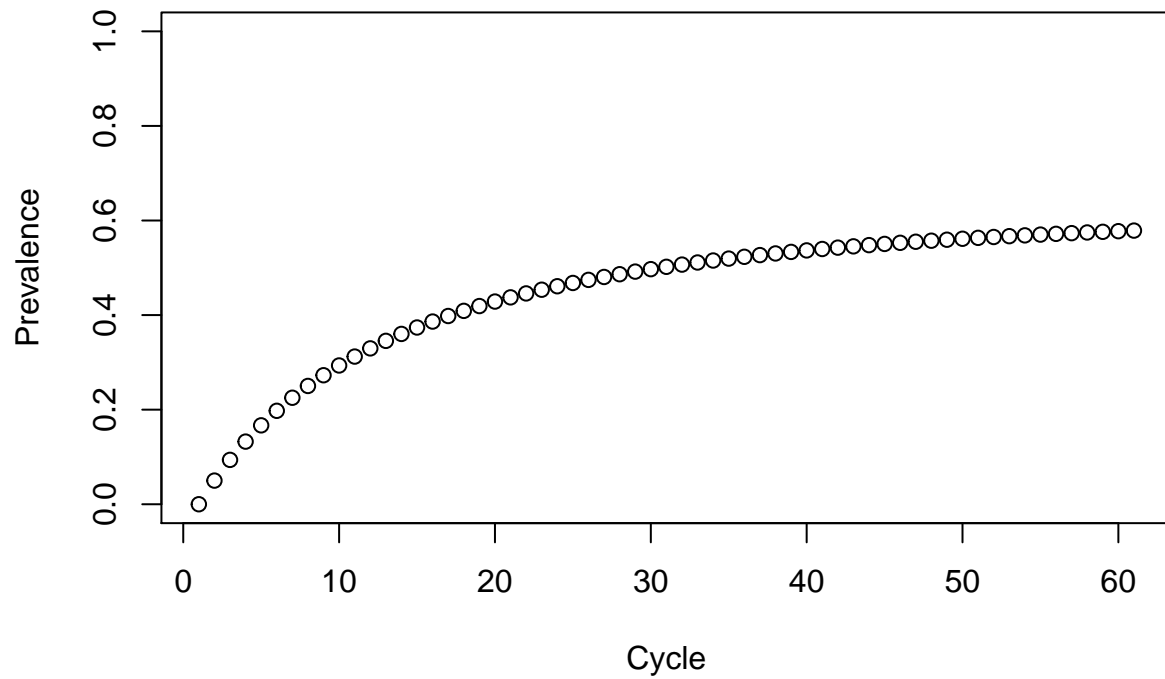
```
v_le      <- sum(v_os)      # summing probability of OS over time (i.e. life expectancy)
v_le_trt  <- sum(v_os_trt)  # summing probability of OS over time (i.e. life expectancy), treatment
```

### 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 - Standard of care")
```

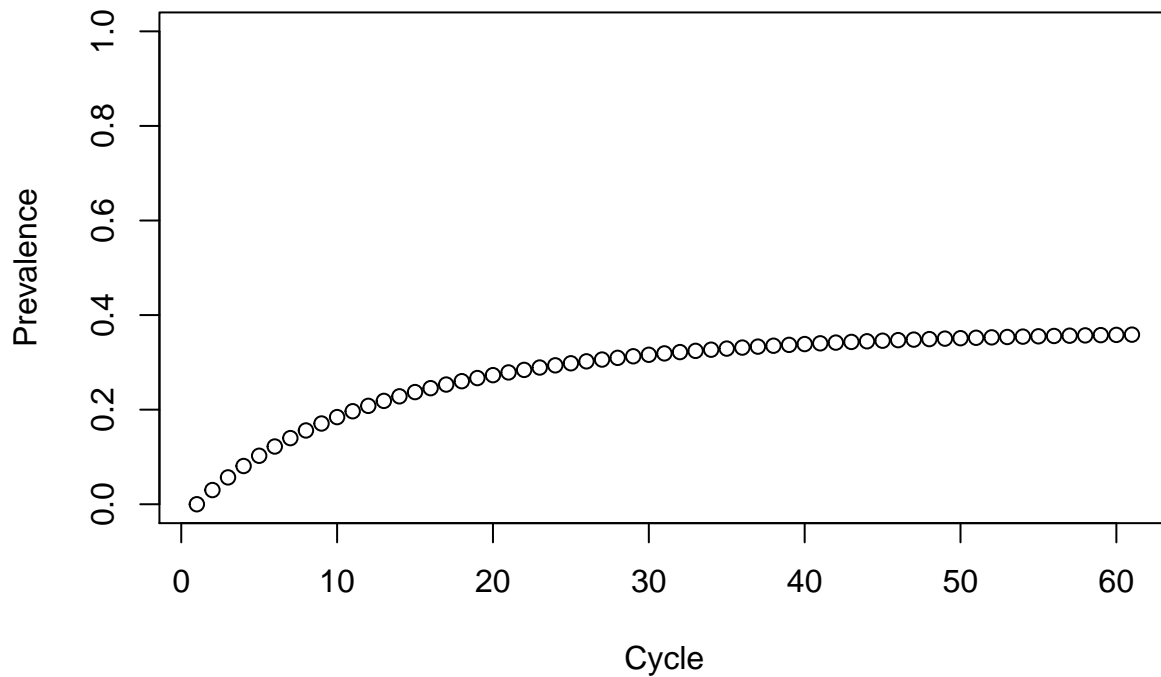
## Disease prevalence – Standard of care



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")
```

## 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      <- 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_dwe      # Standard of Care
```

```

tu_d_trt <- t(v_tu_trt) %*% v_dwe      # 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

```

```

##           Strategy      Cost    Effect
## 1 Standard of Care  8043.139  10.25087
## 2           Treatment 10331.262  11.73928

```

### 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

```

```

##           Strategy      Cost    Effect Inc_Cost Inc_Effect      ICER Status
## 1 Standard of Care  8043.139  10.25087      NA      NA      NA      ND
## 2           Treatment 10331.262  11.73928 2288.123  1.488415 1537.288      ND

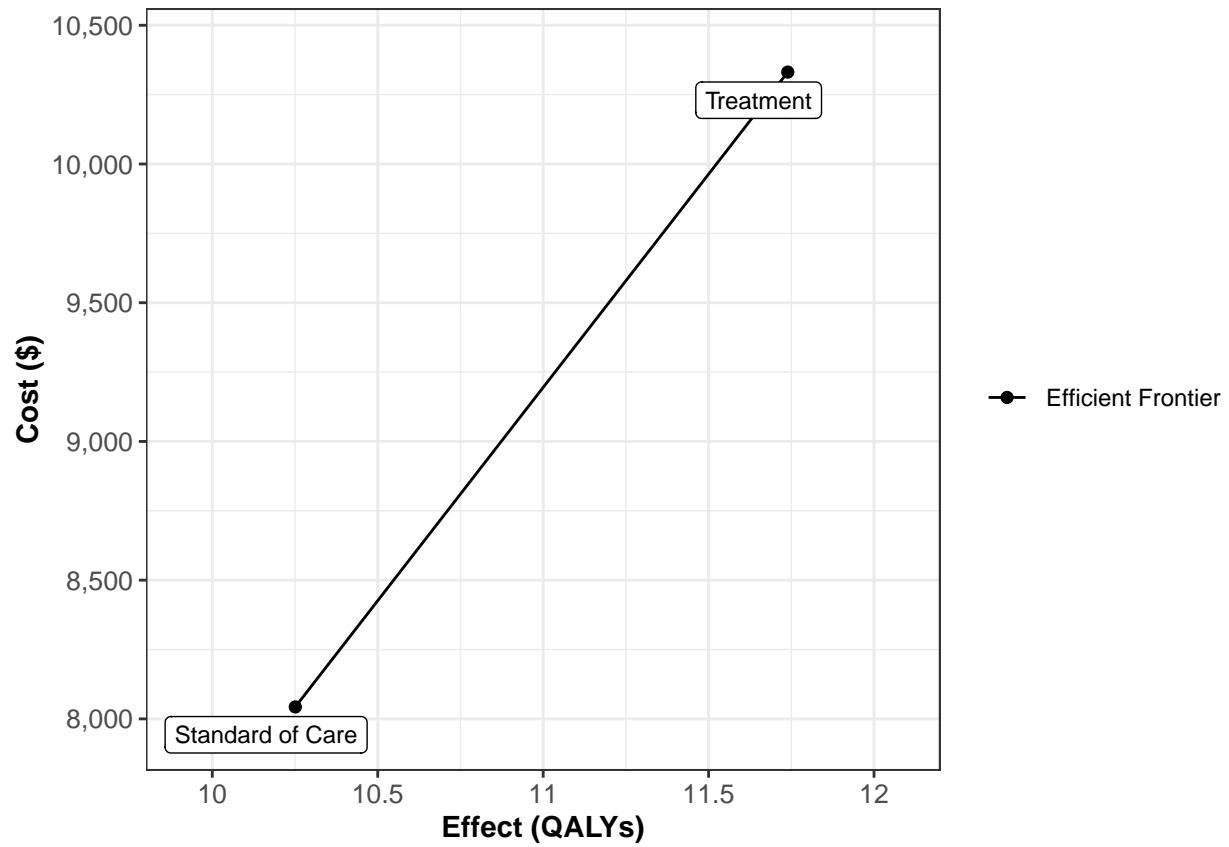
```

### 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