SA: Simple 3-state Markov model in R

The DARTH workgroup

Developed by the Decision Analysis in R for Technologies in Health (DARTH) workgroup:

Fernando Alarid-Escudero, PhD (1)

Eva A. Enns, MS, PhD (2)

M.G. Myriam Hunink, MD, PhD (3,4)

Hawre J. Jalal, MD, PhD (5)

Eline M. Krijkamp, MSc (3)

Petros Pechlivanoglou, PhD (6,7)

Alan Yang, MSc (7)

In collaboration of:

1. Division of Public Administration, Center for Research and Teaching in Economics (CIDE), Aguascalientes, Mexico
2. University of Minnesota School of Public Health, Minneapolis, MN, USA
3. Erasmus MC, Rotterdam, The Netherlands
4. Harvard T.H. Chan School of Public Health, Boston, USA
5. University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA
6. University of Toronto, Toronto ON, Canada
7. The Hospital for Sick Children, Toronto ON, Canada

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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

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
```

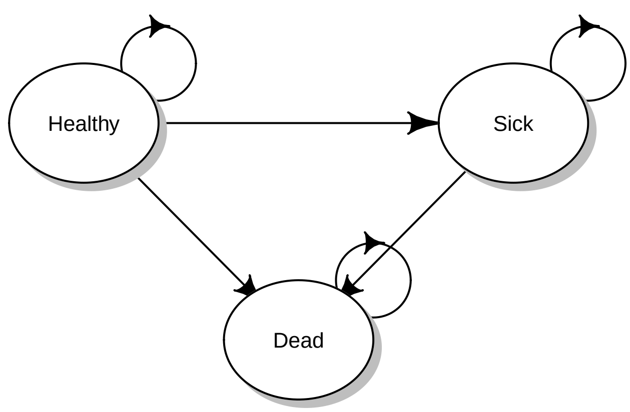
03 Input model parameters

```
# 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 ca
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     <- 8000                     # 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_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_n))

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_n, v_n))  # name the columns and rows of the matrix

# print the probability matrices
m_P_SoC  # 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_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
```

```r
# 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

```r
# 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

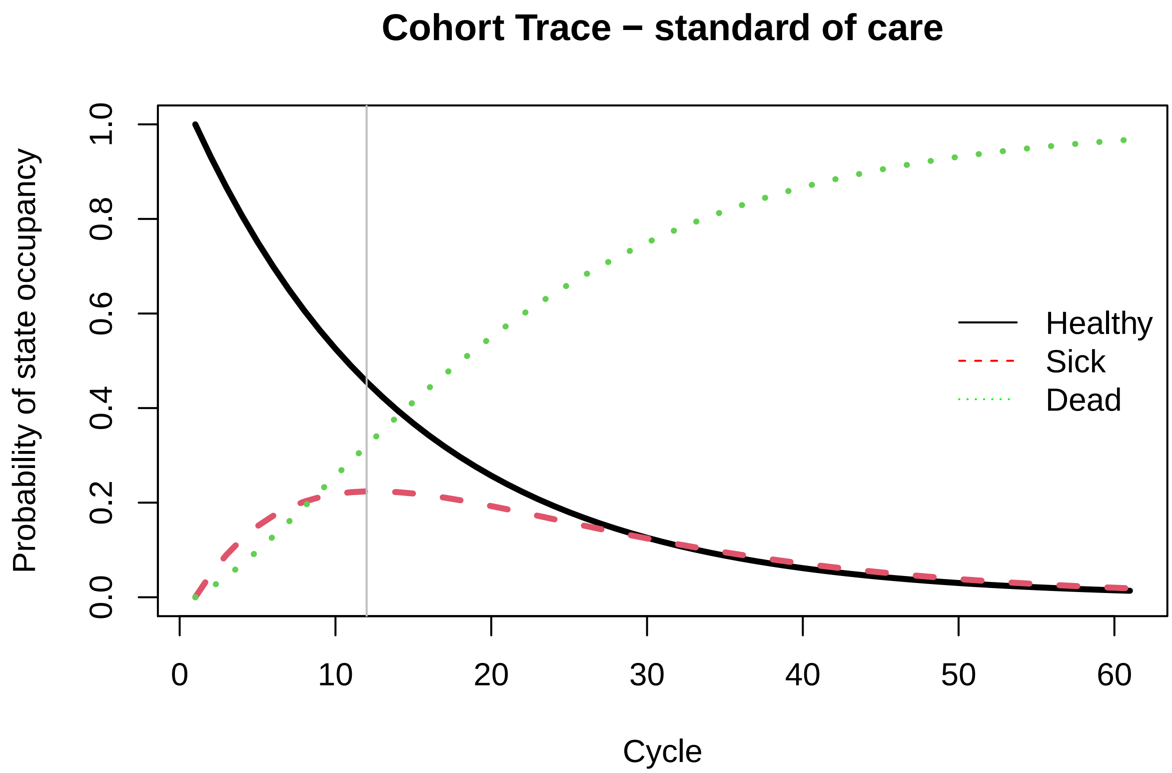
```r
for (t in 1:n_t){  # loop through the number of cycles
  m_M_SoC[t + 1, ] <- m_M_SoC[t, ] %*% m_P_SoC  # estimate the state vector for the next cycle (t + 1)
  m_M_trt[t + 1, ] <- m_M_trt[t, ] %*% m_P_trt  # for treatment
}
```

06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

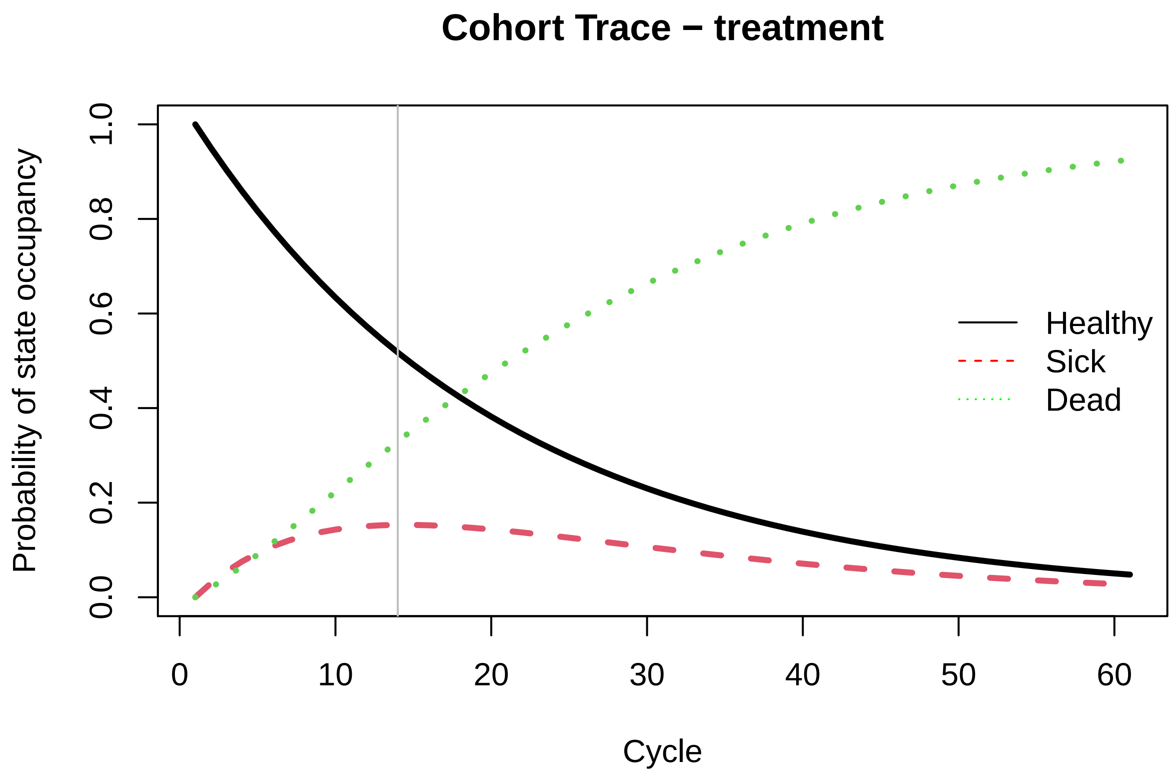
Standard of Care:

```r
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_n, 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 identifyi
```



Treatment:

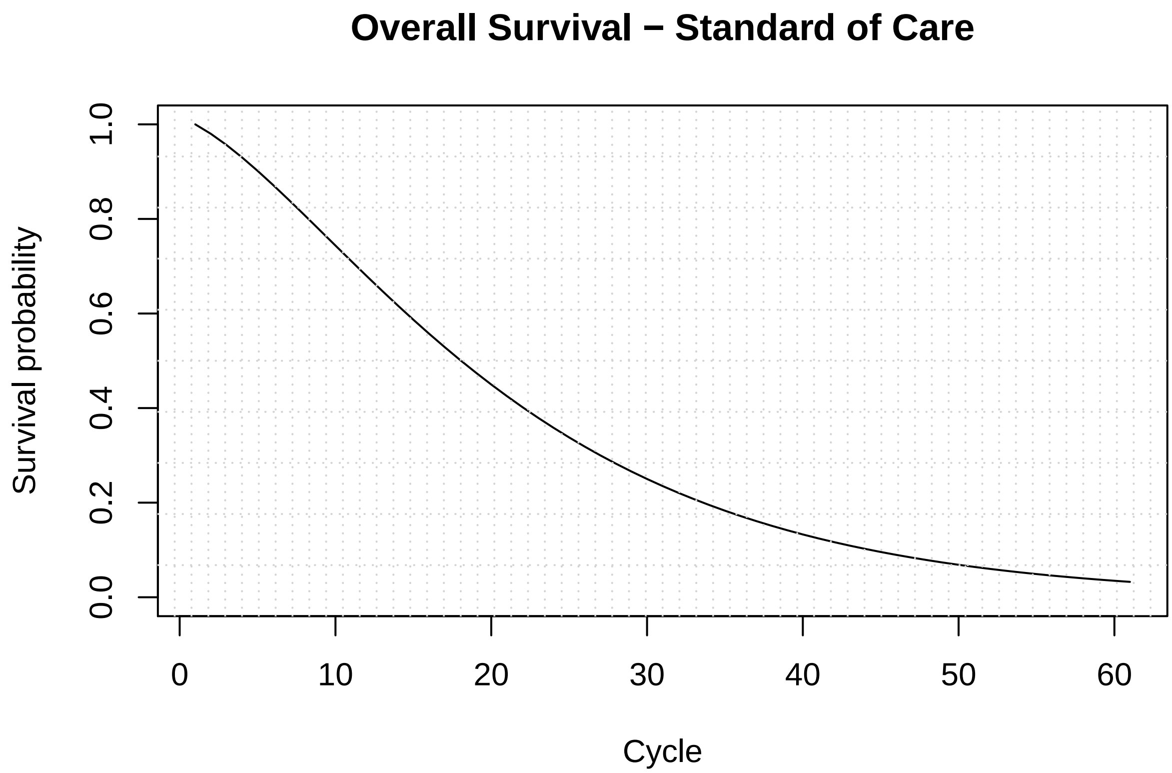
```
matplot(m_M_trt, type = 'l',
        ylab = "Probability of state occupancy",
        xlab = "Cycle",
        main = "Cohort Trace - treatment", lwd = 3)      # create a plot of the data
legend("right", v_n, col = c("black", "red", "green"),
       lty = 1:3, bty = "n")                          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

abline(v = which.max(m_M_trt[, "Sick"]), col = "gray")      # plot a vertical line that helps identifyi
```



06.2 Overall Survival (OS)

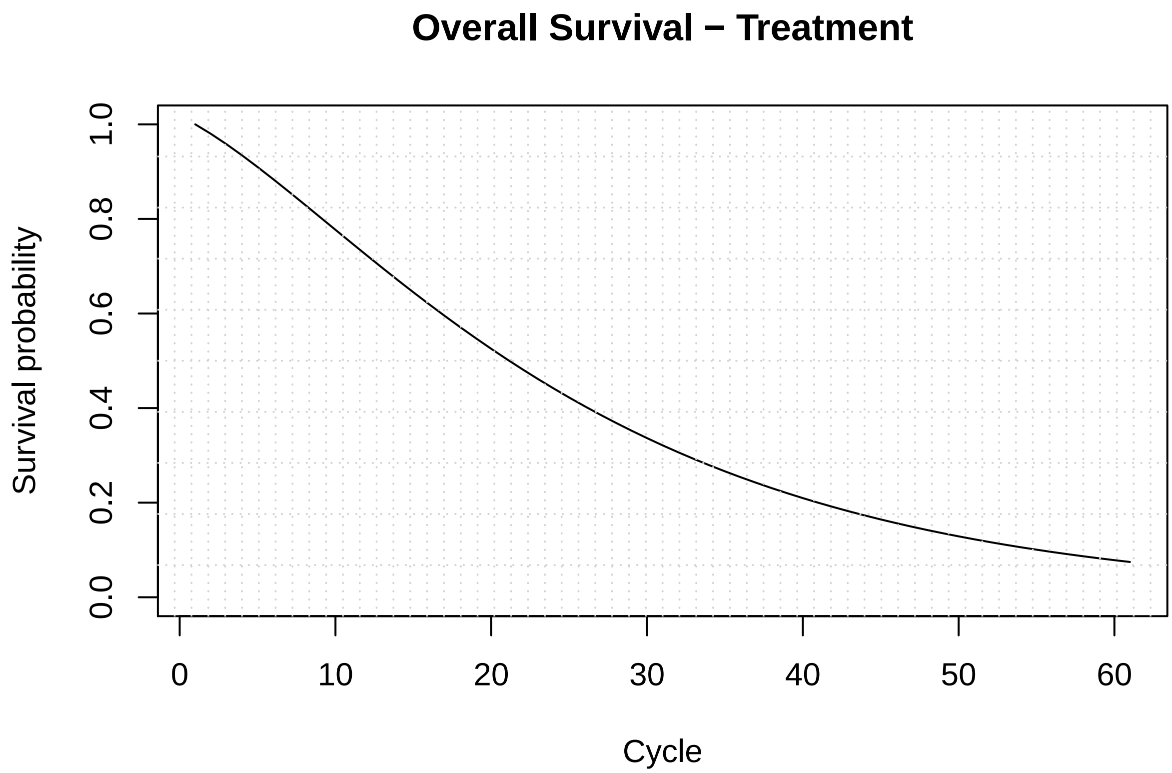
Standard of Care:

```
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)
```



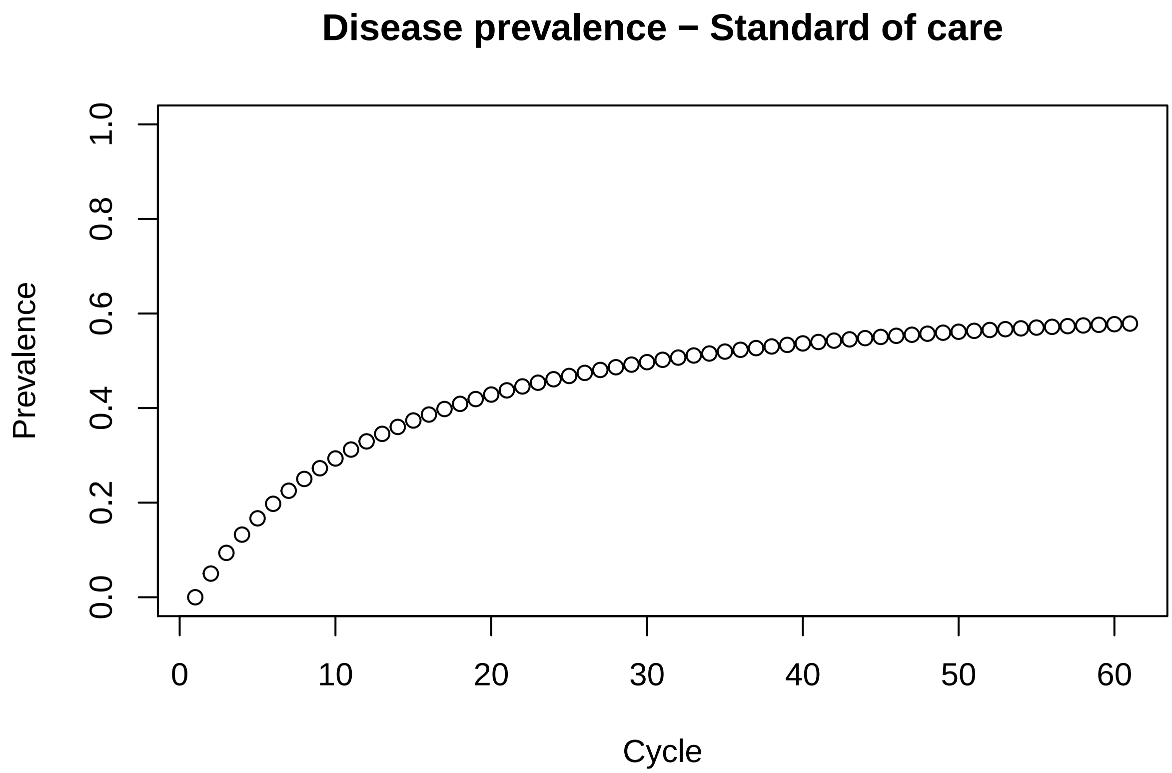
06.2.1 Life Expectancy (LE)

```
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

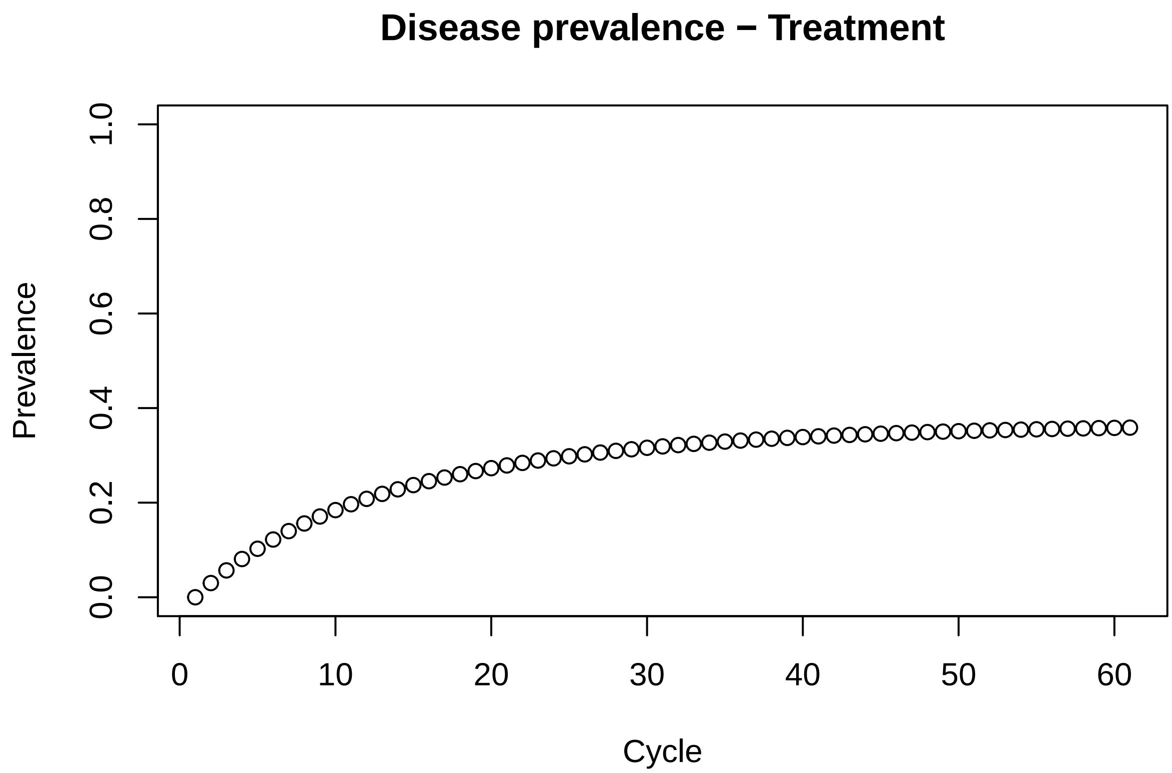
Standard of Care:

```
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_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_dwe  # Standard of Care
```

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

```
##           Strategy     Cost   Effect
## 1 Standard of Care 8043.139 10.25087
## 2        Treatment 8028.490 11.73928
```

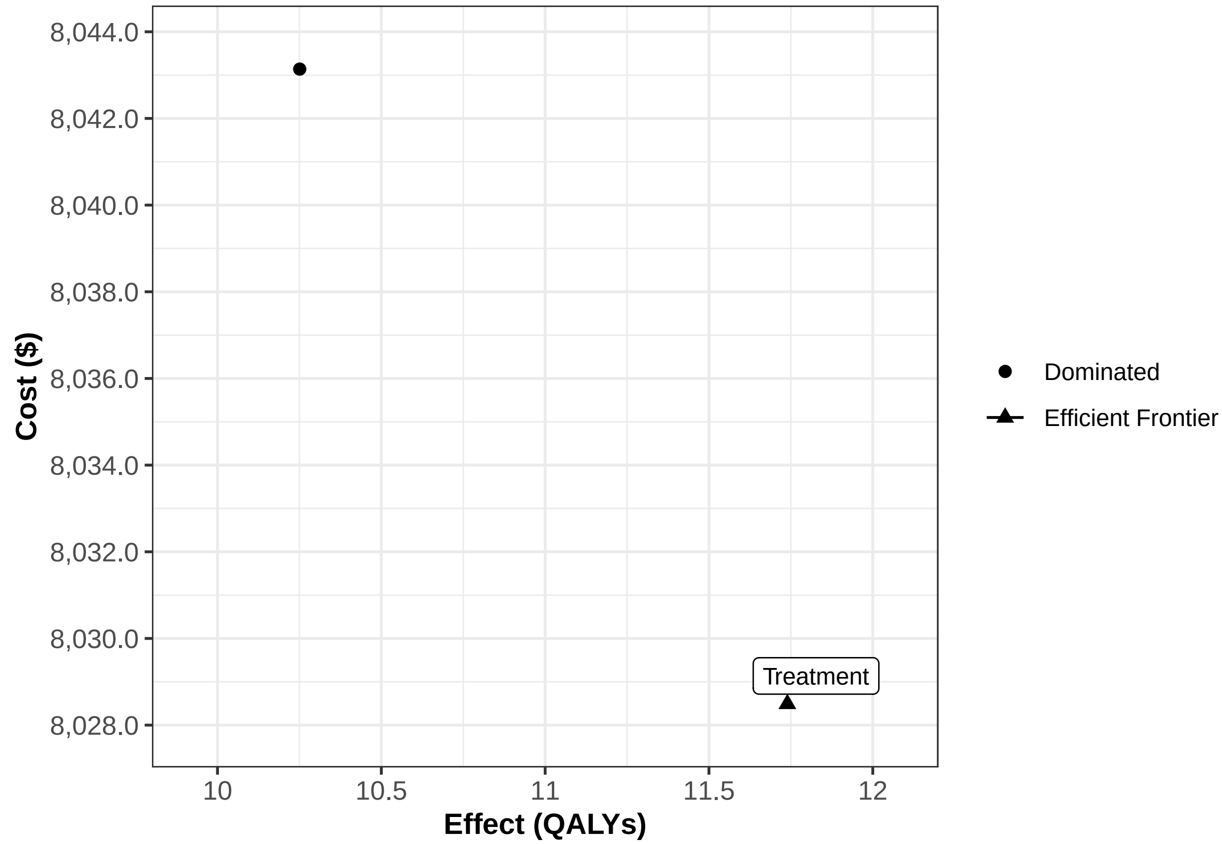
07.3 Compute ICERs of the Markov model

```r
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        Treatment 8028.490 11.73928       NA         NA   NA     ND
## 2 Standard of Care 8043.139 10.25087       NA         NA   NA      D
```

07.4 Plot frontier of the Markov model

```r
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 yo
```

08 Probabilistic Sensitivity Analysis (PSA)

08.1 List of input parameters

Create list `l_params_all` with all input probabilities, cost and utilities.

```
l_params_all <- as.list(data.frame(
  p_HD     = 0.02,  # probability of dying when healthy
  p_HS     = 0.05,  # probability of becoming sick when healthy, conditioned on not dying
  p_HS_trt = 0.03,  # probability of becoming sick when healthy, conditioned on not dying
  p_SD     = 0.1,   # probability of dying when sick
  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,   # one-time cost of treatment (at first cycle)
  u_H      = 0.8,   # utility when healthy
  u_S      = 0.5,   # utility when sick
  u_D      = 0,     # utility when dead
  d_e      = 0.03,  # discount factor for effectiveness
  d_c      = 0.03   # discount factor for costs
))
```

```
# store the parameter names into a vector
v_names_params <- names(l_params_all)
```

08.2 Load Sick-Sicker Markov model function

```
source("Functions_markov_3state.R")
# Test function
calculate_ce_out(l_params_all)
```

```
##           Strategy      Cost   Effect       NMB
## 1 Standard of Care  8043.139 10.25087  94465.51
## 2        Treatment 10331.262 11.73928 107061.54
```

08.3 Generate PSA datasets

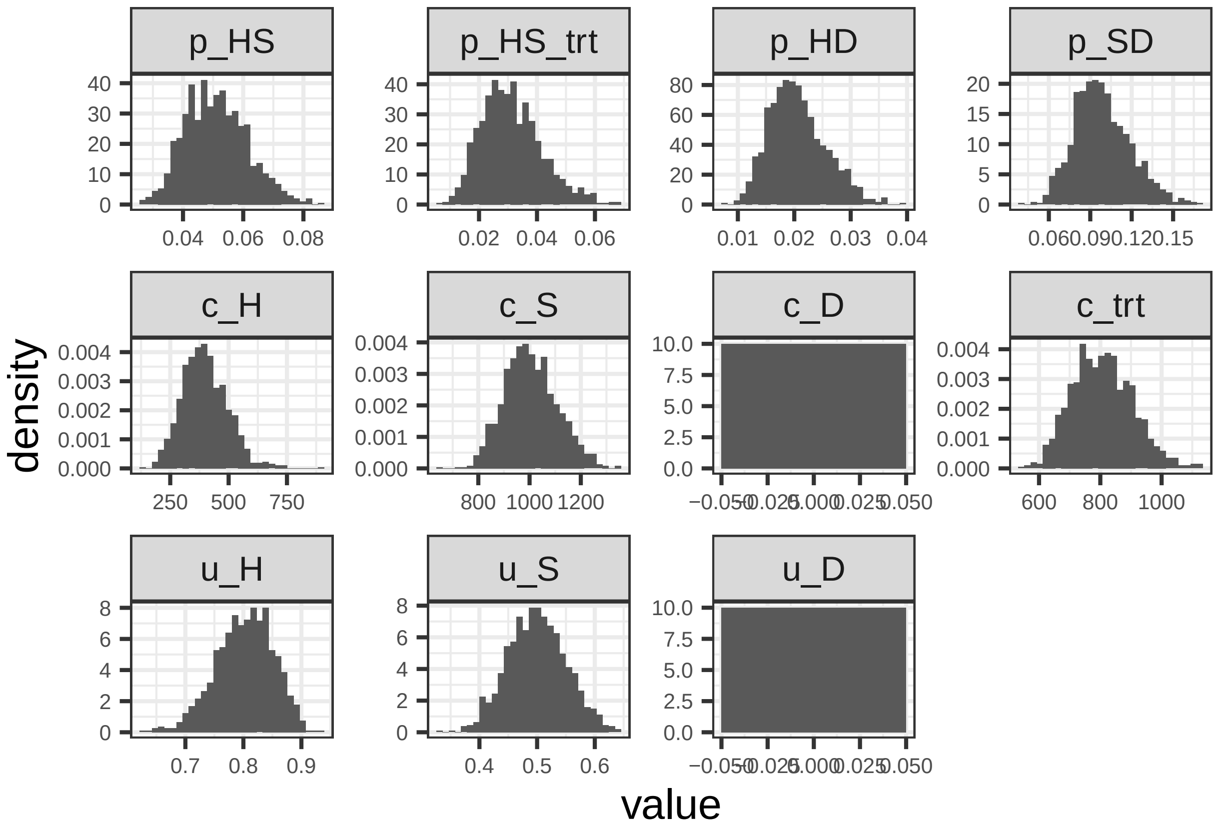
```
# Function to generate PSA input dataset
gen_psa <- function(n_sim = 1000, seed = 071818){
  set.seed(seed) # set a seed to be able to reproduce the same results
  df_psa <- data.frame(
    # Transition probabilities (per cycle)
    # probability to become sick when healthy
    p_HS     = rbeta(n_sim, shape1 = 24, shape2 = 450),
    p_HS_trt = rbeta(n_sim, shape1 = 9,  shape2 = 281),   # under treatment
    # probability of dying when healthy
    p_HD     = rbeta(n_sim, shape1 = 16, shape2 = 767),
    # probability of dying when sick
    p_SD     = rbeta(n_sim, shape1 = 22.4, shape2 = 201.6),

    # Cost vectors with length n_sim
    # cost of remaining one cycle in state H
    c_H      = rgamma(n_sim, shape = 16, scale = 25),
    # cost of remaining one cycle in state S1
    c_S      = rgamma(n_sim, shape = 100, scale = 10),
    # cost of being in the death state
    c_D      = 0,
    # cost of treatment (per cycle)
    c_trt    = rgamma(n_sim, shape = 64, scale = 12.5),

    # Utility vectors with length n_sim
    # utility when healthy
    u_H      = rbeta(n_sim, shape1 =  50.4, shape2 = 12.6),
    # utility when sick
    u_S      = rbeta(n_sim, shape1 = 49.5, shape2 = 49.5),
    # utility when dead
    u_D      = 0
  )
  return(df_psa)
}
# Try it
gen_psa(10)
```

```
##           p_HS    p_HS_trt        p_HD        p_SD       c_H        c_S c_D     c_trt
## 1  0.05116365 0.02717469 0.02650780 0.09350365 331.7253 1001.3478   0 621.7035
## 2  0.04095451 0.01181545 0.02787410 0.15823599 535.2239  995.9279   0 937.7706
## 3  0.05334926 0.01972404 0.01561002 0.12357583 334.2034  955.0140   0 659.1331
## 4  0.03627100 0.03901602 0.02620191 0.08771020 352.7561  990.4764   0 865.2337
## 5  0.04782122 0.02128019 0.01998096 0.10799984 260.4642  943.7245   0 855.5065
## 6  0.07206924 0.02272066 0.01521342 0.12685251 291.1215  983.1453   0 860.4577
## 7  0.04803791 0.04457119 0.01499307 0.08911761 483.8274 1050.5295   0 994.2503
## 8  0.04335723 0.02882206 0.02131098 0.05814786 541.4731  864.3322   0 601.8085
## 9  0.05302297 0.03409499 0.01709267 0.15922549 551.1535 1080.4473   0 757.1225
## 10 0.03096171 0.01553948 0.01983932 0.10406523 315.7027  984.6521   0 787.5281
##           u_H       u_S u_D
## 1  0.8559721 0.4815761   0
## 2  0.7783084 0.5349337   0
## 3  0.8628224 0.5227023   0
## 4  0.8968823 0.4871518   0
## 5  0.8179546 0.5294793   0
## 6  0.6717953 0.5249675   0
## 7  0.8177386 0.5600215   0
## 8  0.8145828 0.5243320   0
## 9  0.8153981 0.5503887   0
## 10 0.8835447 0.5837644   0
```

```r
# Number of simulations
n_sim <- 1000

# Generate PSA input dataset
df_psa_input <- gen_psa(n_sim = n_sim)
# First six observations
head(df_psa_input)
```

```
##          p_HS    p_HS_trt        p_HD        p_SD       c_H        c_S c_D     c_trt
## 1 0.05116365 0.01954245 0.02621456 0.13853135 307.8380  899.5153   0  687.5154
## 2 0.04095451 0.04346716 0.01760834 0.13075427 466.9600 1066.1617   0  875.5292
## 3 0.05334926 0.03357981 0.02404573 0.08454761 235.2890  955.0145   0  658.2810
## 4 0.03627100 0.03806155 0.02716409 0.10457346 306.5100  789.6969   0  702.7446
## 5 0.04782122 0.03737024 0.01716697 0.14474739 535.1188  868.0570   0  566.1605
## 6 0.07206924 0.04257367 0.01710648 0.12289879 353.6715  991.6205   0 1096.0742
##          u_H       u_S u_D
## 1 0.7965014 0.4473598   0
## 2 0.7659582 0.4644020   0
## 3 0.7593770 0.4215045   0
## 4 0.8338376 0.5052819   0
## 5 0.8798517 0.5181703   0
## 6 0.7306958 0.5905503   0
```

```r
# Histogram of parameters
ggplot(melt(df_psa_input, variable.name = "Parameter"), aes(x = value)) +
       facet_wrap(~Parameter, scales = "free") +
       geom_histogram(aes(y = ..density..)) +
       theme_bw(base_size = 16) +
       theme(axis.text = element_text(size=8))
```




```
# Initialize dataframes with PSA output
# Dataframe of costs
df_c <- as.data.frame(matrix(0,
                      nrow = n_sim,
                      ncol = n_str))
colnames(df_c) <- v_names_str
# Dataframe of effectiveness
df_e <- as.data.frame(matrix(0,
                      nrow = n_sim,
                      ncol = n_str))
colnames(df_e) <- v_names_str
```

08.4 Conduct probabilistic sensitivity analysis

```
# Run Markov model on each parameter set of PSA input dataset
for(i in 1:n_sim){
  l_out_temp <- calculate_ce_out(df_psa_input[i, ])
  df_c[i, ] <- l_out_temp$Cost
  df_e[i, ] <- l_out_temp$Effect
  # Display simulation progress
  if(i/(n_sim/10) == round(i/(n_sim/10), 0)) { # display progress every 10%
    cat('\r', paste(i/n_sim * 100, "% done", sep = " "))
  }
}
```

```
##  10 % done 20 % done 30 % done 40 % done 50 % done 60 % done 70 % done 80 % done 90 % done 100 % done
```

08.4.1 Create PSA object for dampack

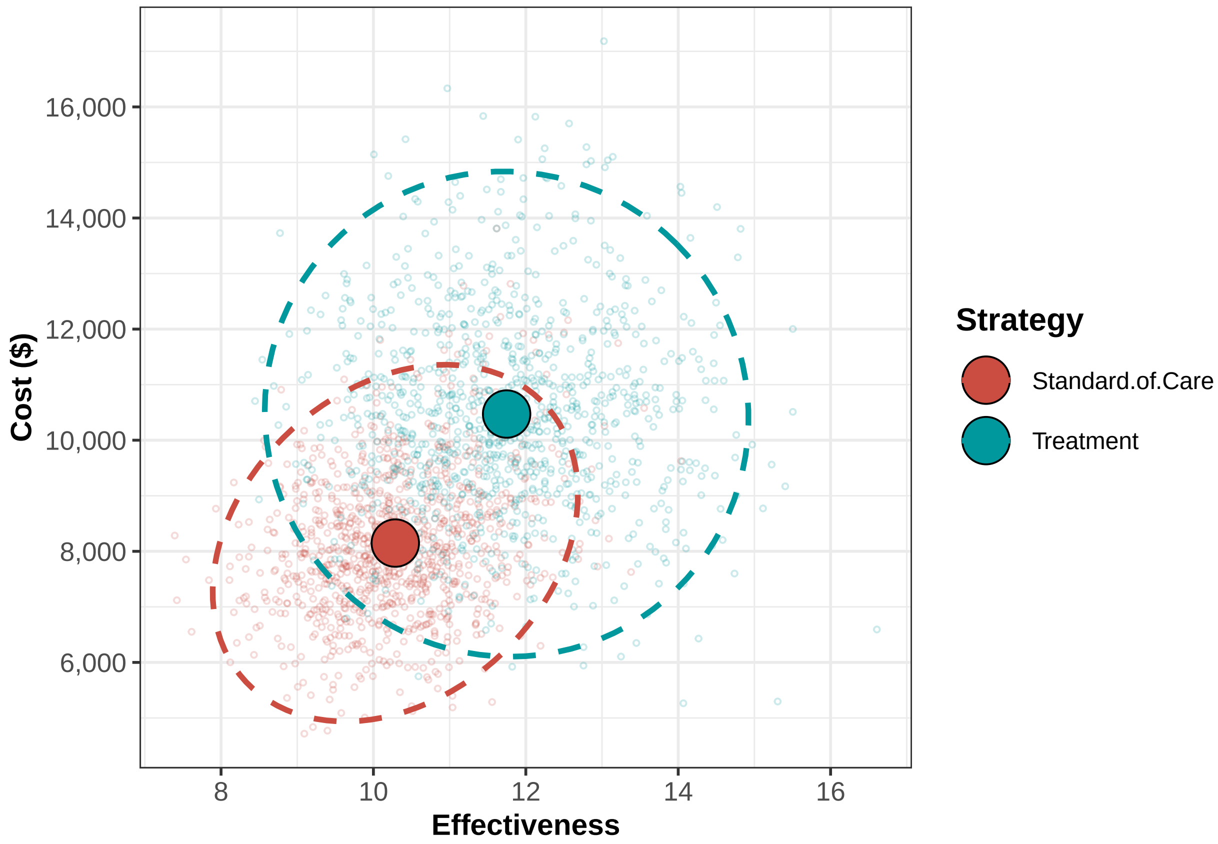
```
l_psa <- make_psa_obj(cost          = df_c,
                      effectiveness = df_e,
                      parameters    = df_psa_input,
                      strategies    = v_names_str)
```

Vector with willingness-to-pay (WTP) thresholds.

```
v_wtp <- seq(0, 5000, by = 1000)
```

08.4.2 Cost-Effectiveness Scatter plot

```
plot(l_psa)
```



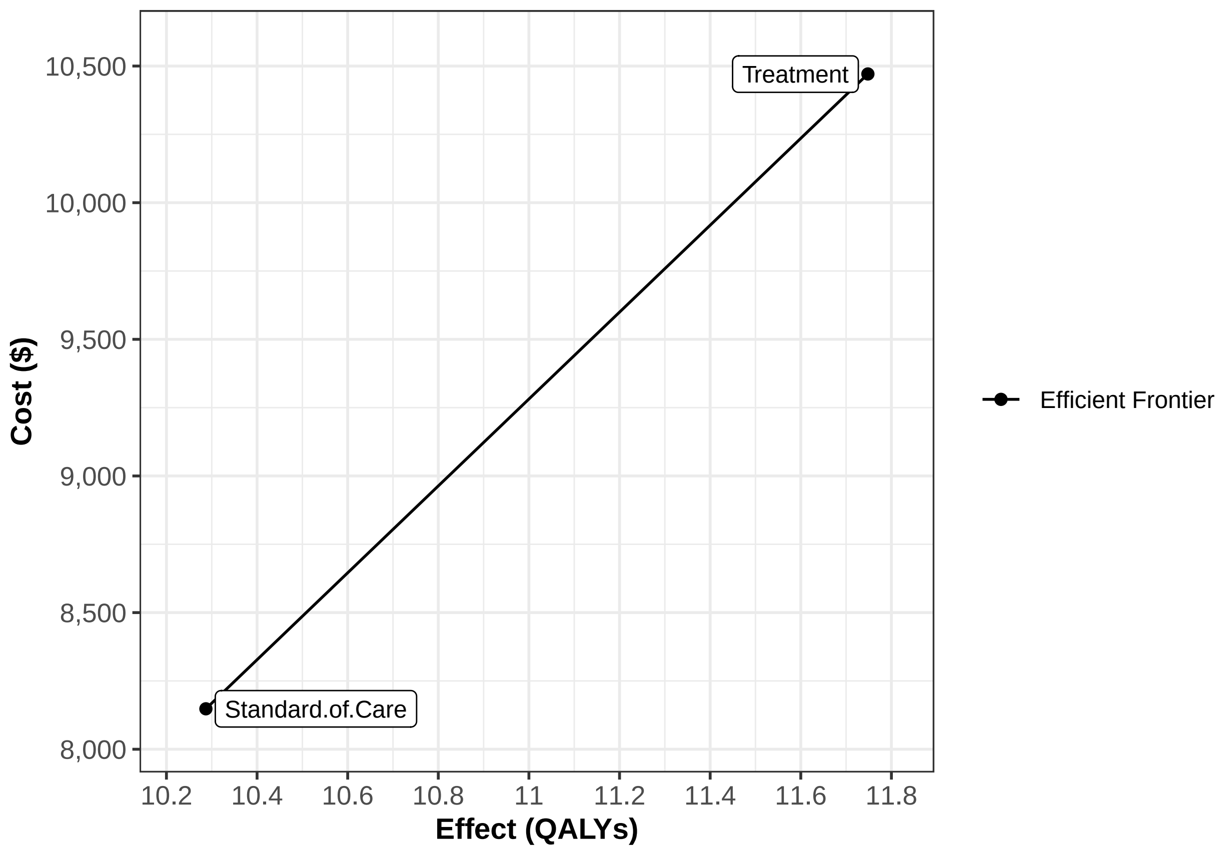
08.4.3 Conduct CEA with probabilistic output

```r
# Compute expected costs and effects for each strategy from the PSA
df_out_ce_psa <- summary(l_psa)

# Calculate incremental cost-effectiveness ratios (ICERs)
df_cea_psa <- calculate_icers(cost       = df_out_ce_psa$meanCost,
                              effect     = df_out_ce_psa$meanEffect,
                              strategies = df_out_ce_psa$Strategy)
df_cea_psa
```

```
##           Strategy      Cost   Effect Inc_Cost Inc_Effect     ICER Status
## 1 Standard.of.Care  8148.004 10.28706       NA         NA       NA     ND
## 2        Treatment 10470.998 11.74808 2322.994   1.461028 1589.972     ND
```

08.4.4 Plot cost-effectiveness frontier

```r
plot(df_cea_psa)
```

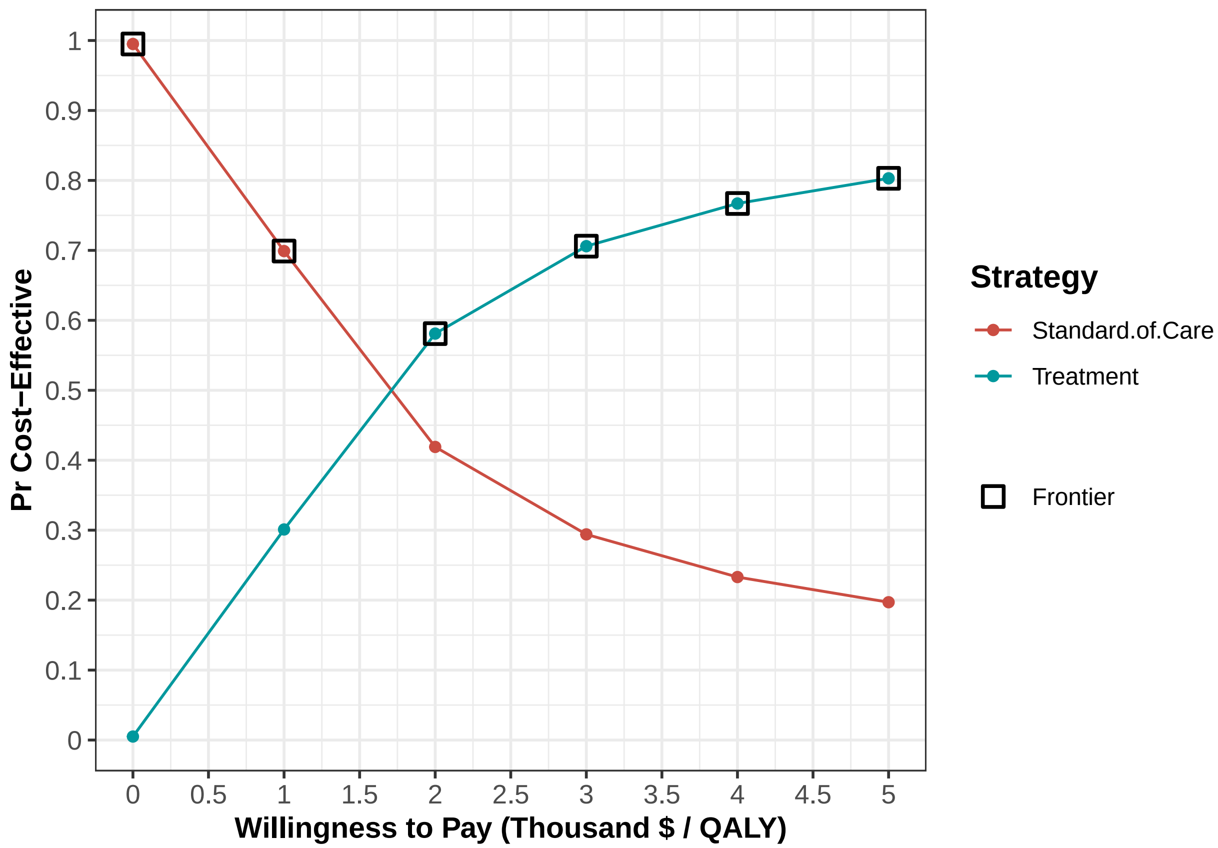


08.4.5 Cost-effectiveness acceptability curves (CEACs) and frontier (CEAF)

```r
ceac_obj <- ceac(wtp = v_wtp, psa = l_psa)
# Regions of highest probability of cost-effectiveness for each strategy
summary(ceac_obj)
```

```
##   range_min range_max   cost_eff_strat
## 1         0      2000 Standard.of.Care
## 2      2000      5000        Treatment
```

```r
# CEAC & CEAF plot
plot(ceac_obj)
```



08.4.6 Expected Loss Curves (ELCs)

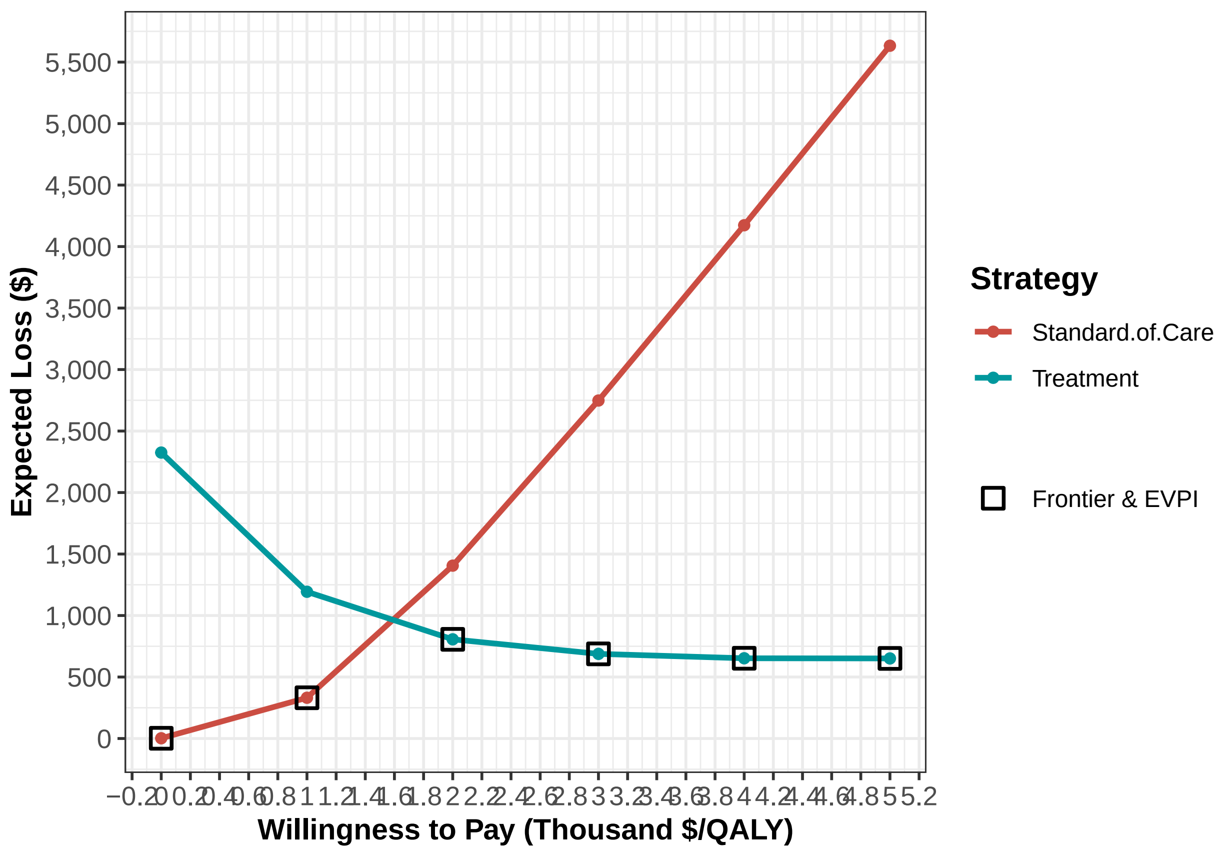
The expected loss is the the quantification of the foregone benefits when choosing a suboptimal strategy given current evidence.

```r
elc_obj <- calc_exp_loss(wtp = v_wtp, psa = l_psa)
elc_obj
```

```
##      WTP         Strategy Expected_Loss On_Frontier
## 1      0 Standard.of.Care       1.92815        TRUE
## 2      0        Treatment    2324.92196       FALSE
```

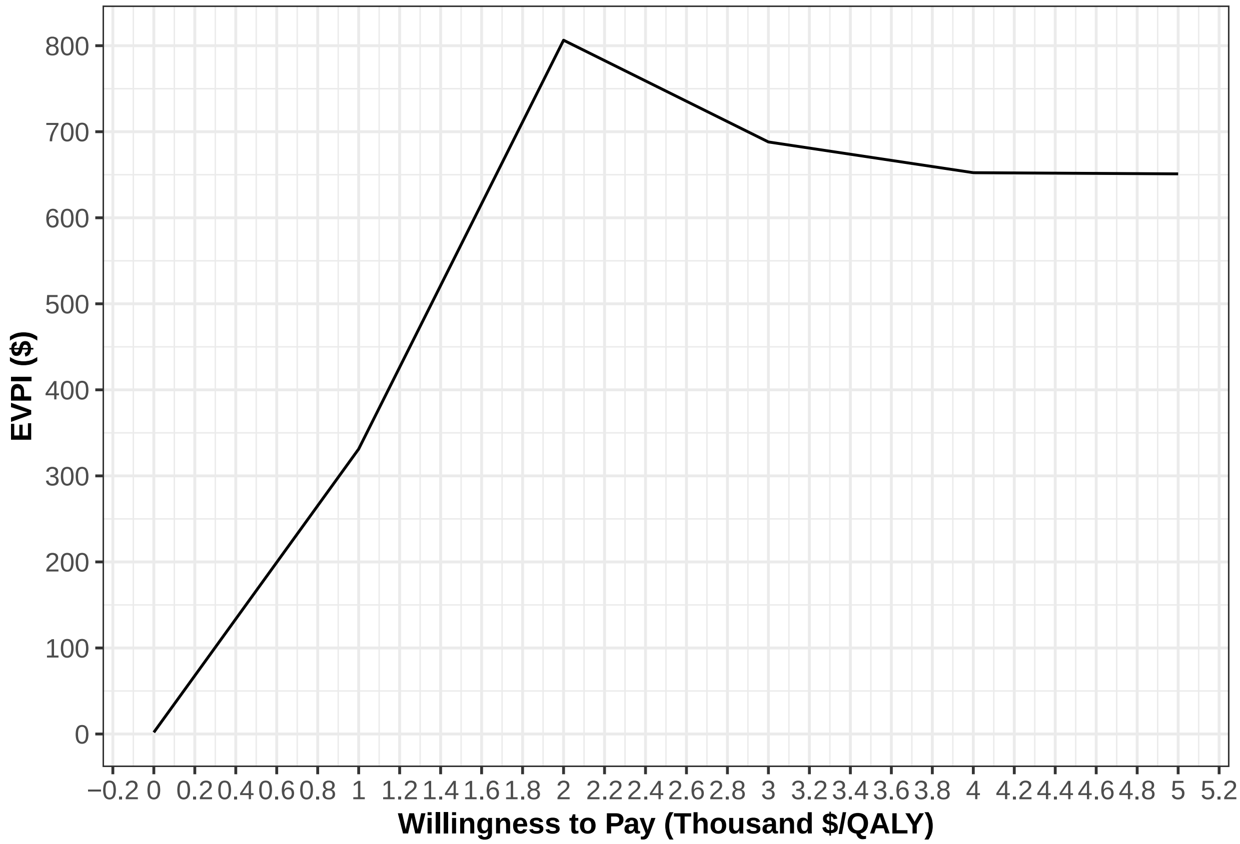
```
## 3  1000 Standard.of.Care      331.23937        TRUE
## 4  1000          Treatment    1193.20487       FALSE
## 5  2000 Standard.of.Care     1405.42678       FALSE
## 6  2000          Treatment     806.36395        TRUE
## 7  3000 Standard.of.Care     2748.21166       FALSE
## 8  3000          Treatment     688.12052        TRUE
## 9  4000 Standard.of.Care     4173.51938       FALSE
## 10 4000          Treatment     652.39992        TRUE
## 11 5000 Standard.of.Care     5633.16928       FALSE
## 12 5000          Treatment     651.02150        TRUE
```

```
# ELC plot
plot(elc_obj, log_y = FALSE)
```



08.4.7 Expected value of perfect information (EVPI)

```
evpi <- calc_evpi(wtp = v_wtp, psa = l_psa)
# EVPI plot
plot(evpi, effect_units = "QALY")
```



09 Using `R` package `hesim`

```
p_load("hesim")
```

09.1 Model setup

Here we define target population and intervention strategies.

We have one representative patient here of age 25, we can think of this as a cohort of homogenous patients instead of one individual patient.

```
# define strategies
strategies <- data.frame(
  strategy_id   = 1:n_str,
  strategy_name = v_names_str
  )
# define patient cohort
patients <- data.frame(
  patient_id = 1,
  age        = 25
)
# create dataset with
```

```r
hesim_dat <- hesim_data(
  strategies = strategies,
  patients   = patients
)
hesim_dat
```

```
## $strategies
##   strategy_id    strategy_name
## 1           1 Standard of Care
## 2           2        Treatment
##
## $patients
##   patient_id age
## 1          1  25
##
## attr(,"class")
## [1] "hesim_data"
```

09.2 parameters

```r
params <- list(
  # medical costs
  c_medical    = c(Healthy = c_H, Sick = c_S),
  c_medical_se = c(Healthy = 100, Sick = 100),
  # treatment costs (embedded in medical costs since only those who are sick get treated)
  c_trt   = c_trt,
  # state utilities
  u_mean = c(Healthy = u_H,  Sick = u_S),
  u_se   = c(Healthy = 0.05, Sick = 0.05)
)
```

09.3 PSA setup

rng_def()

```r
rng_def <- define_rng({
  list( # Parameters to return
    # medical costs
    c_medical = gamma_rng(mean = c_medical, sd = c_medical_se),
    c_trt     = gamma_rng(mean = c_trt,     sd = 1000),
    # state utilities
    u = beta_rng(mean = u_mean, sd = u_se)
  )
}, n = 1000)
```

09.4 Transform parameters

```r
input_data <- hesim::expand(hesim_dat, by = c("strategies", "patients"))
head(input_data)
```

```
##    strategy_id patient_id    strategy_name age
## 1:           1          1 Standard of Care  25
## 2:           2          1        Treatment  25
```

The function `define_tparams()` returns:

- `tpmatrix`: The transition probability matrix
- `utility`: Utility assigned to each health state
- `costs`: Costs assigned to each health state or each cost category

Your task: write mathematical expressions

The function: automatically loops over PSA iterations (running the model on each sampled parameter set)

```r
tparams_def <- define_tparams({
  # treatment reduces the risk of getting sick
  rr <- ifelse(strategy_name == "Standard of Care", 1, p_HS_trt / p_HS) # relative risk

  list(
    tpmatrix = tpmatrix(
      (1 - p_HD) * (1 - p_HS * rr),  (1 - p_HD) * (p_HS * rr),  p_HD,
       0,   C,   p_SD,
       0,   0,   1
    ),

    utility = u,
    costs = list(
      treatment = ifelse(strategy_name == "Standard of Care", 0, c_trt),
      medical   = c_medical
    )
  )
})
```

09.5 Simulation

Construct model:

```r
mod_def <- define_model(tparams_def = tparams_def,
                        rng_def     = rng_def,
                        params      = params)
```

Initialize-model:

```r
cost_args <- list(
  treatment = list(method = "starting"),
  medical   = list(method = "wlos")
)
econmod <- create_CohortDtstm(mod_def, input_data, cost_args = cost_args)
```

Simulate outcomes:

```
econmod$sim_stateprobs(n_cycles = n_t)
head(econmod$stateprobs_)
```

```
##    sample strategy_id patient_id grp_id state_id t      prob
## 1:      1           1          1      1        1 0 1.0000000
## 2:      1           1          1      1        1 1 0.9310000
## 3:      1           1          1      1        1 2 0.8667610
## 4:      1           1          1      1        1 3 0.8069545
## 5:      1           1          1      1        1 4 0.7512746
## 6:      1           1          1      1        1 5 0.6994367
```

```
econmod$sim_qalys(dr = d_e, lys = TRUE, integrate_method = "riemann_right")
head(econmod$qalys_)
```

```
##    sample strategy_id patient_id grp_id state_id   dr    qalys       lys
## 1:      1           1          1      1        1 0.03 6.484607  9.339850
## 2:      1           1          1      1        2 0.03 1.841271  3.861427
## 3:      1           2          1      1        1 0.03 8.199613 11.809992
## 4:      1           2          1      1        2 0.03 1.361197  2.854639
## 5:      2           1          1      1        1 0.03 8.063655  9.339850
## 6:      2           1          1      1        2 0.03 1.849052  3.861427
```

```
econmod$sim_costs(dr = d_c, integrate_method = "riemann_right")
head(econmod$costs_)
```

```
##    sample strategy_id patient_id grp_id state_id   dr  category    costs
## 1:      1           1          1      1        1 0.03 treatment    0.000
## 2:      1           1          1      1        2 0.03 treatment    0.000
## 3:      1           2          1      1        1 0.03 treatment 7819.843
## 4:      1           2          1      1        2 0.03 treatment    0.000
## 5:      2           1          1      1        1 0.03 treatment    0.000
## 6:      2           1          1      1        2 0.03 treatment    0.000
```

09.6 Cost-effectivess analysis

```
ce_sim <- econmod$summarize()
cea_pw_out <- cea_pw(ce_sim,
                     comparator = 1,
                     dr_qalys = 0.03, dr_costs = 0.03,
                     k = seq(0, 5000, 1000))

## @knitr icer
icer_tbl(cea_pw_out, colnames = strategies$strategy_name)
```

```
##                     Standard of Care Treatment
## Incremental QALYs "-"              "1.47 (1.21, 1.72)"
## Incremental costs "-"              "7,990 (6,070, 10,233)"
## Incremental NMB   "-"              "65,685 (52,214, 77,821)"
## ICER              "-"              "5,422"
## Conclusion        "-"              "Cost-effective"
```

10 Overview of `hesim`

Advantages:

- Easy to build models without having to program the complete model structure (easier for novice modelers).
- A lot of the modeling code are implemented for you in the back end.
- Suitable for modelers who are not familiar with `R` programming and functionality.
- Code written in `C++` in the back end, which offers enhanced computational speed.

Disadvantages:

- Its rigid function structure inhibits its ability tweak models or incorporate more complex model components (e.g. tunnel states, transition rewards).
- Does not provide the option for running deterministic analysis or one-way and two-way sensitivity analyses.
- Does not provide the ability to capture information about the specific transitions among health states (transition dynamics).
- Does not provide the ability to easily compute epidemiological outcomes.
- Does not allow costs to be applied to certain health states (at least not easily).

References

```
citation("hesim")
```

```
##
## To cite package 'hesim' in publications use:
##
##   Devin Incerti and Jeroen P. Jansen (2020). hesim: Health-Economic
##   Simulation Modeling and Decision Analysis. R package version 0.4.1.
##   https://CRAN.R-project.org/package=hesim
##
## A BibTeX entry for LaTeX users is
##
##   @Manual{,
##     title = {hesim: Health-Economic Simulation Modeling and Decision Analysis},
##     author = {Devin Incerti and Jeroen P. Jansen},
##     year = {2020},
##     note = {R package version 0.4.1},
##     url = {https://CRAN.R-project.org/package=hesim},
##   }
```