PSA: Markov Sick-Sicker model in R

The DARTH workgroup

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- 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 Online first. https://doi.org/10.1177/0272989X19893973

- Alarid-Escudero, F., Krijkamp, E. M., Enns, E. A., Hunink, M. G. M., Pechlivanoglou, P., & Jalal, H. (2020). Cohort state-transition models in R: From conceptualization to implementation. arXiv:2001.07824v1, 1–31. http://arxiv.org/abs/2001.07824

- Alarid-Escudero, F., Enns, E. A., Kuntz, K. M., Michaud, T. L., & Jalal, H. (2019). "Time Traveling Is Just Too Dangerous" But Some Methods Are Worth Revisiting: The Advantages of Expected Loss Curves Over Cost-Effectiveness Acceptability Curves and Frontier. Value in Health, 22(5), 611–618. https://doi.org/10.1016/j.jval.2019.02.008

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```r
rm(list = ls())        # clear memory (removes all the variables from the workspace)
```

01 Load packages

```r
if (!require('pacman')) {
  install.packages('pacman')
}
library(pacman) # use this package to conveniently install other packages
# load (install if required) packages from CRAN
p_load("here", "dplyr", "devtools", "scales", "ellipse", "ggplot2", "lazyeval",
       "igraph", "truncnorm", "ggraph", "reshape2", "knitr", "stringr", "reshape2")
# load (install if required) packages from GitHub
# install_github("DARTH-git/dampack", force = TRUE) Uncomment if there is a newer version
# install_github("DARTH-git/dectree", force = TRUE) Uncomment if there is a newer version
# install_github("annaheath/EVSI", force = TRUE) #Uncomment if there is a newer version
p_load_gh("DARTH-git/dampack", "DARTH-git/dectree")
p_load_gh("annaheath/EVSI")
```

02 Load functions

```r
source("Functions.R")
```

03 Input model parameters

```r
# Strategy names
v_names_str <- c("No Treatment", "Treatment")

# Number of strategies
n_str <- length(v_names_str)

# Markov model parameters
age     <- 25                    # age at baseline
max_age <- 55                    # maximum age of follow up
n_t     <- max_age - age         # time horizon, number of cycles
v_n     <- c("H", "S1", "S2", "D") # the 4 states of the model: Healthy (H),
                                 # Sick (S1), Sicker (S2), Dead (D)
n_s     <- length(v_n)           # number of health states

# Transition probabilities (per cycle)
p_HD    <- 0.005            # probability to die when healthy
p_HS1   <- 0.15            # probability to become sick when healthy
p_S1H   <- 0.5            # probability to become healthy when sick
p_S1S2  <- 0.105            # probability to become sicker when sick
hr_S1   <- 3            # hazard ratio of death in sick vs healthy
hr_S2   <- 10            # hazard ratio of death in sicker vs healthy
r_HD    <- - log(1 - p_HD) # rate of death in healthy
r_S1D   <- hr_S1 * r_HD     # rate of death in sick
r_S2D   <- hr_S2 * r_HD     # rate of death in sicker
p_S1D   <- 1 - exp(-r_S1D) # probability to die in sick
p_S2D   <- 1 - exp(-r_S2D) # probability to die in sicker
```

```r
# Cost and utility inputs
c_H      <- 2000    # cost of remaining one cycle in the healthy state
c_S1     <- 4000    # cost of remaining one cycle in the sick state
c_S2     <- 15000   # cost of remaining one cycle in the sicker state
c_trt    <- 12000   # cost of treatment(per cycle)
c_D      <- 0       # cost of being in the death state
u_H      <- 1       # utility when healthy
u_S1     <- 0.75    # utility when sick
u_S2     <- 0.5     # utility when sicker
u_D      <- 0       # utility when dead
u_trt    <- 0.95    # utility when being treated

# Discounting factor
d_r      <- 0.03 # 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_r) ^ (0:n_t)
# calculate discount weights for effectiveness for each cycle based on discount rate d_e
v_dwe    <- 1 / (1 + d_r) ^ (0:n_t)
```

04 Define and initialize matrices and vectors

04.1 Cohort trace

```r
# create the markov trace matrix M capturing the proportion of the cohort
# in each state at each cycle
m_M_notrt <- m_M_trt <- matrix(NA,
                               nrow     = n_t + 1, ncol = n_s,
                               dimnames = list(paste("cycle", 0:n_t, sep = " "), v_n))

head(m_M_notrt) # show first 6 rows of the matrix
```

```
##          H S1 S2  D
## cycle 0 NA NA NA NA
## cycle 1 NA NA NA NA
## cycle 2 NA NA NA NA
## cycle 3 NA NA NA NA
## cycle 4 NA NA NA NA
## cycle 5 NA NA NA NA
```

```r
# The cohort starts as healthy
m_M_notrt[1, ] <- m_M_trt[1, ] <- c(1, 0, 0, 0) # initiate first cycle of cohort trace
```

04.2 Transition probability matrix

```r
# create the transition probability matrix for NO treatment (notrt)
m_P_notrt  <- matrix(0,
                     nrow = n_s,
                     ncol = n_s,
                     dimnames = list(v_n, v_n)) # name the columns and rows of the matrix
m_P_notrt
```

```
##    H S1 S2 D
## H  0  0  0 0
```

```
## S1 0   0   0 0
## S2 0   0   0 0
## D  0   0   0 0
```

Fill in the transition probability matrix:

```
# from Healthy
m_P_notrt["H", "H"]    <- 1 - (p_HS1 + p_HD)
m_P_notrt["H", "S1"]  <- p_HS1
m_P_notrt["H", "D"]    <- p_HD
# from Sick
m_P_notrt["S1", "H"]  <- p_S1H
m_P_notrt["S1", "S1"] <- 1 - (p_S1H + p_S1S2 + p_S1D)
m_P_notrt["S1", "S2"] <- p_S1S2
m_P_notrt["S1", "D"]  <- p_S1D
# from Sicker
m_P_notrt["S2", "S2"] <- 1 - p_S2D
m_P_notrt["S2", "D"]   <- p_S2D
# from Dead
m_P_notrt["D", "D"]    <- 1

# check rows add up to 1
rowSums(m_P_notrt)
```

```
##  H S1 S2  D
##  1  1  1  1
```

```
# create transition probability matrix for treatment same as no treatment
m_P_trt <- m_P_notrt
```

05 Run Markov model

```
for (t in 1:n_t){      # loop through the number of cycles
  m_M_notrt[t + 1, ] <- t(m_M_notrt[t, ]) %*% m_P_notrt # estimate the Markov trace
                                                         # for the next cycle (t + 1)
  m_M_trt[t + 1, ]   <- t(m_M_trt[t, ])    %*% m_P_trt    # estimate the Markov trace
                                                         # for the next cycle (t + 1)
} # close the loop

head(m_M_notrt)  # show the first 6 lines of the matrix
```

```
##                   H        S1         S2          D
## cycle 0 1.0000000 0.0000000 0.00000000 0.00000000
## cycle 1 0.8450000 0.1500000 0.00000000 0.00500000
## cycle 2 0.7890250 0.1837612 0.01575000 0.01146377
## cycle 3 0.7586067 0.1881968 0.03427491 0.01892157
## cycle 4 0.7351211 0.1853199 0.05235988 0.02719916
## cycle 5 0.7138373 0.1807036 0.06925860 0.03620055
```
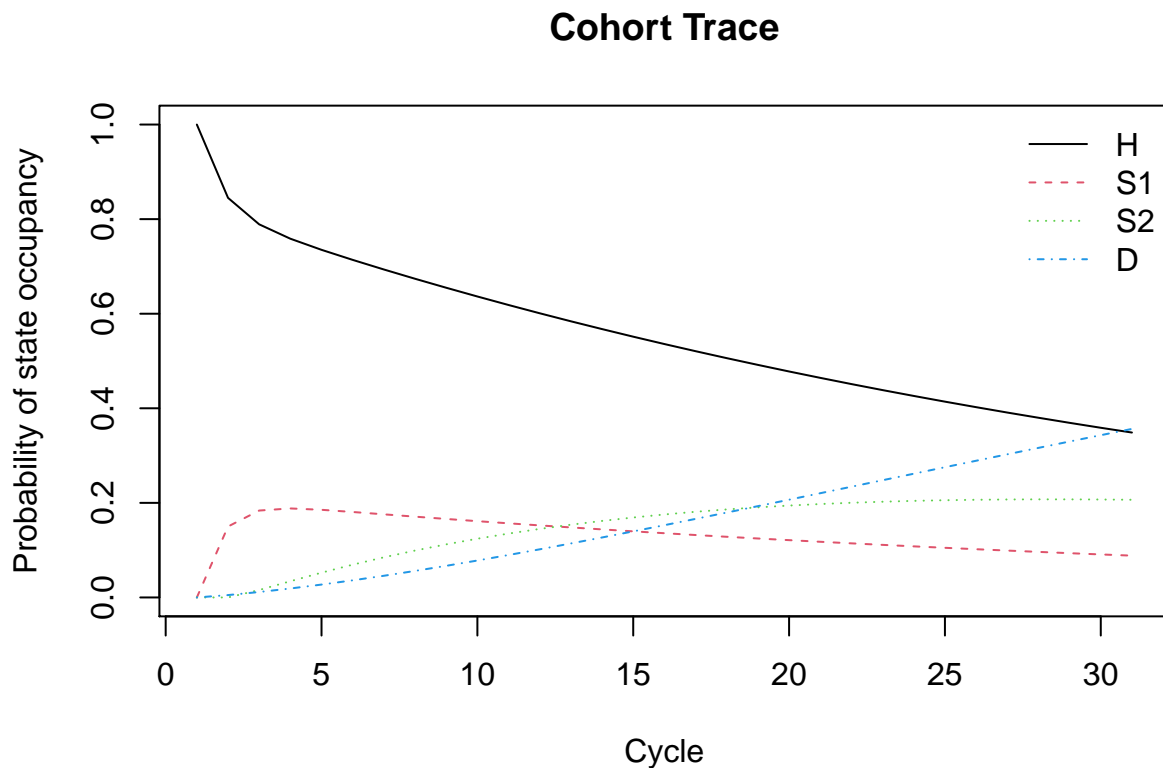
06 Compute and Plot Epidemiological Outcomes

06.1 Cohort trace

```r
# create a plot of the data
matplot(m_M_notrt, type = 'l',
        ylab = "Probability of state occupancy",
        xlab = "Cycle",
        main = "Cohort Trace")
# add a legend to the graph
legend("topright", v_n, col = 1:n_s, lty = 1:n_s, bty = "n")
```


Cohort Trace

06.2 Overall Survival (OS)

```r
# calculate the overall survival (OS) probability for no treatment
v_os_notrt <- 1 - m_M_notrt[, "D"]
# alternative way of calculating the OS probability
v_os_notrt <- rowSums(m_M_notrt[, 1:3])
# create a simple plot showing the OS
plot(0:n_t, v_os_notrt, type = 'l',
     ylim = c(0, 1),
     ylab = "Survival probability",
     xlab = "Cycle",
     main = "Overall Survival")
# add grid
grid(nx = n_t, ny = 10, col = "lightgray", lty = "dotted", lwd = par("lwd"),
     equilogs = TRUE)
```
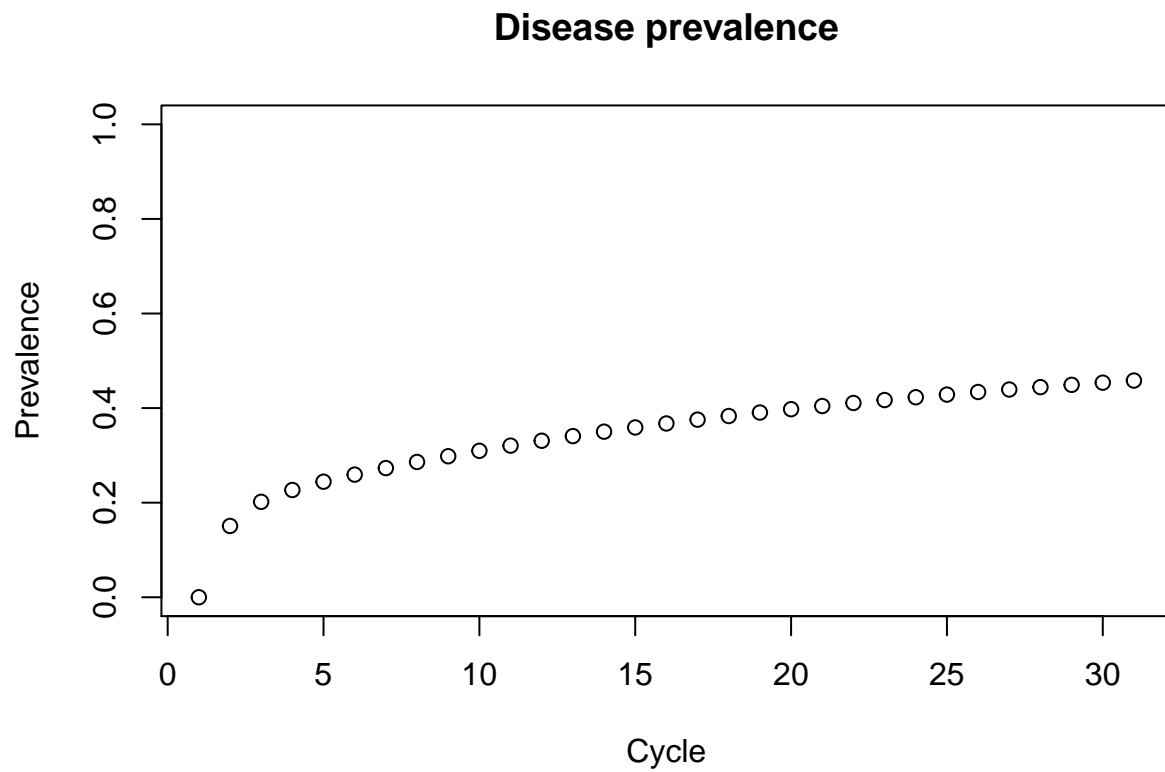
Overall Survival
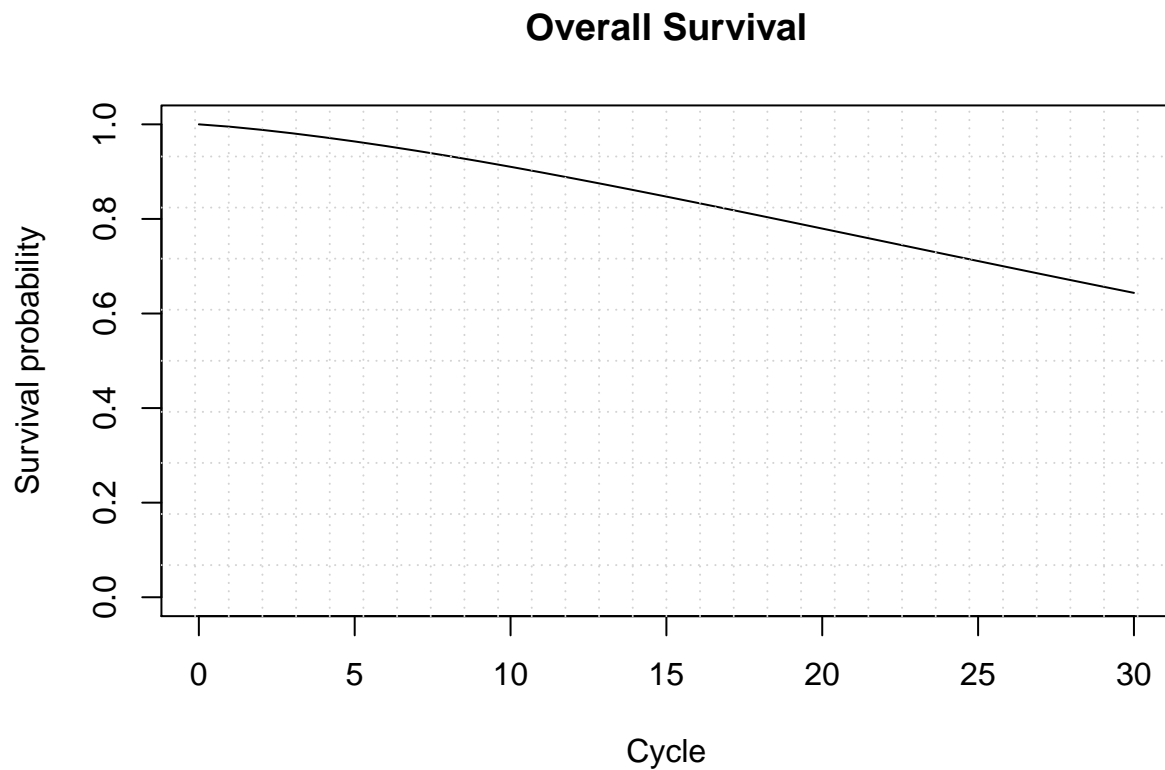
06.2.1 Life Expectancy (LE)

```r
v_le <- sum(v_os_notrt)      # summing probablity of OS over time  (i.e. life expectancy)
```

06.3 Disease prevalence

```r
v_prev <- rowSums(m_M_notrt[, c("S1", "S2")]) / v_os_notrt
plot(v_prev,
     ylim = c(0, 1),
     ylab = "Prevalence",
     xlab = "Cycle",
     main = "Disease prevalence")
```
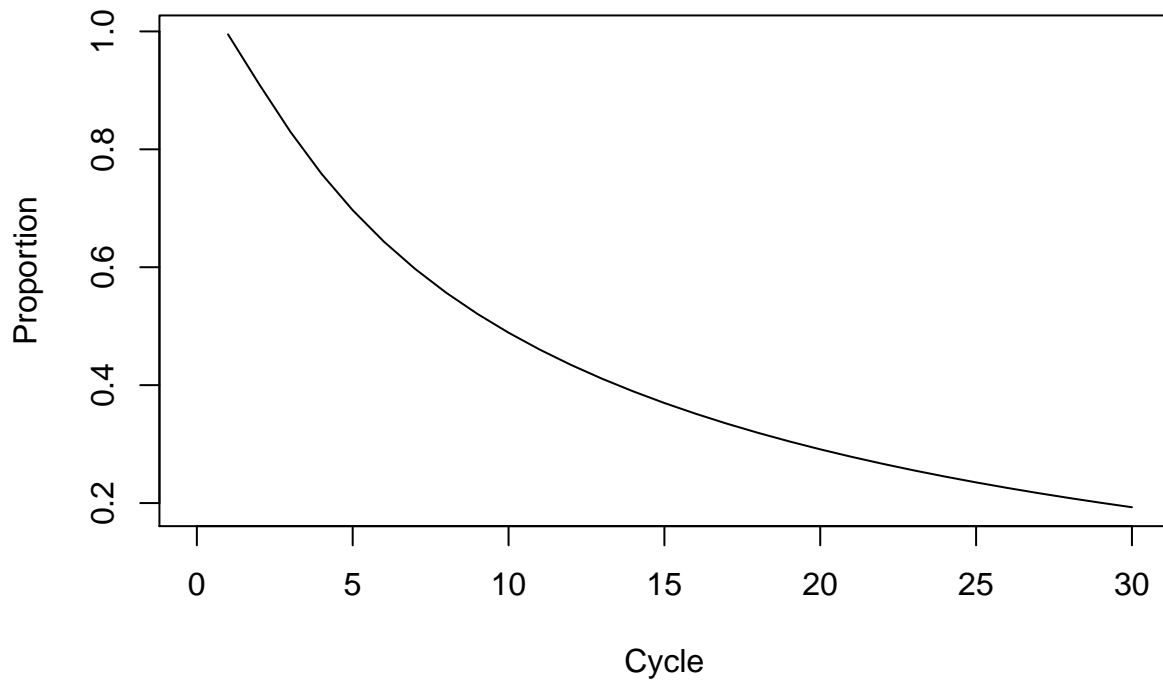
Disease prevalence

06.4 Proportion of sick in S1 state

```
v_prop_S1 <- m_M_notrt[, "S1"] / v_prev
plot(0:n_t, v_prop_S1,
     xlab = "Cycle",
     ylab = "Proportion",
     main = "Proportion of sick in S1 state",
     col  = "black", type = "l")
```

Proportion of sick in S1 state

07 Compute Cost-Effectiveness Outcomes

```r
# Vectors with costs and utilities by treatment
v_u_notrt   <- c(u_H, u_S1, u_S2, u_D)
v_u_trt     <- c(u_H, u_trt, u_S2, u_D)

v_c_notrt   <- c(c_H, c_S1, c_S2, c_D)
v_c_trt     <- c(c_H, c_S1 + c_trt, c_S2 + c_trt, c_D)
```

07.1 Mean Costs and QALYs for Treatment and NO Treatment

```r
v_tu_notrt  <- m_M_notrt    %*%  v_u_notrt
v_tu_trt    <- m_M_trt      %*%  v_u_trt

v_tc_notrt  <- m_M_notrt    %*%  v_c_notrt
v_tc_trt    <- m_M_trt      %*%  v_c_trt
```

07.2 Discounted Mean Costs and QALYs

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

tc_d_notrt  <- t(v_tc_notrt)    %*%  v_dwc
tc_d_trt    <- t(v_tc_trt)      %*%  v_dwc
```

```
# store them into a vector
v_tc_d     <- c(tc_d_notrt, tc_d_trt)
v_tu_d     <- c(tu_d_notrt, 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 No Treatment  75976.15 15.83885
## 2    Treatment 141623.03 16.40041
```

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 No Treatment  75976.15 15.83885       NA         NA        NA     ND
## 2    Treatment 141623.03 16.40041 65646.88  0.5615578 116901.4     ND
```
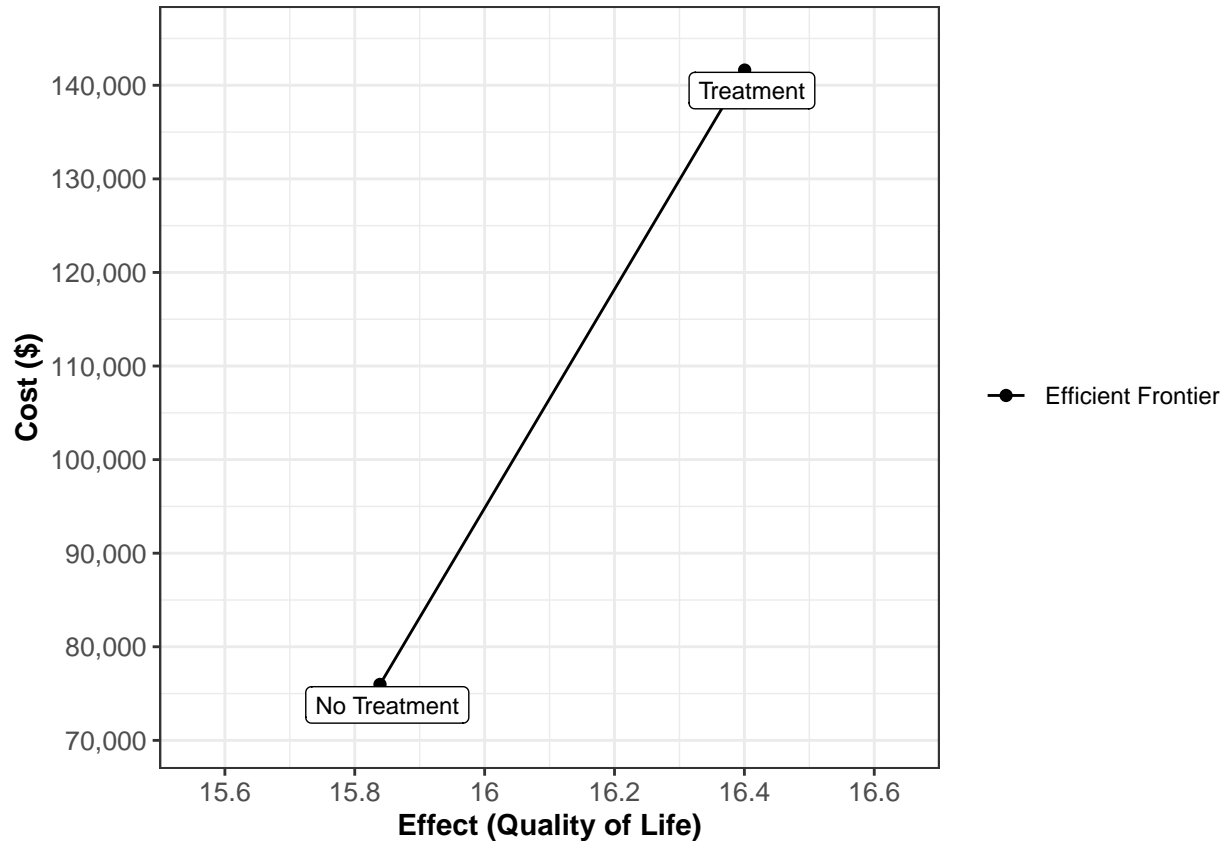
07.4 Plot frontier of the Markov model

```
plot(df_cea, effect_units = "Quality of Life", xlim = c(15.6, 16.6))
```

08 Deterministic Sensitivity Analysis

08.1 List of input parameters

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

```r
l_params_all <- list(
  p_HD    = 0.005,   # probability to die when healthy
  p_HS1   = 0.15,    # probability to become sick when healthy
  p_S1H   = 0.5,     # probability to become healthy when sick
  p_S1S2  = 0.105,   # probability to become sicker when sick
  hr_S1   = 3,       # hazard ratio of death in sick vs healthy
  hr_S2   = 10,      # hazard ratio of death in sicker vs healthy
  c_H     = 2000,    # cost of remaining one cycle in the healthy state
  c_S1    = 4000,    # cost of remaining one cycle in the sick state
  c_S2    = 15000,   # cost of remaining one cycle in the sicker state
  c_trt   = 12000,   # cost of treatment(per cycle)
  c_D     = 0,       # cost of being in the death state
  u_H     = 1,       # utility when healthy
  u_S1    = 0.75,    # utility when sick
  u_S2    = 0.5,     # utility when sicker
  u_D     = 0,       # utility when dead
  u_trt   = 0.95,    # utility when treated
  d_e     = 0.03,    # discount factor for effectiveness
  d_c     = 0.03     # discount factor for costs
)
```

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

08.2 Load Sick-Sicker Markov model function

```r
source("Functions_markov_sick-sicker.R")
# Test function
calculate_ce_out(l_params_all)
```

```
##        Strategy     Cost    Effect      NMB
## 1 No Treatment  75976.15 15.83885 1507909
## 2    Treatment 141623.03 16.40041 1498418
```

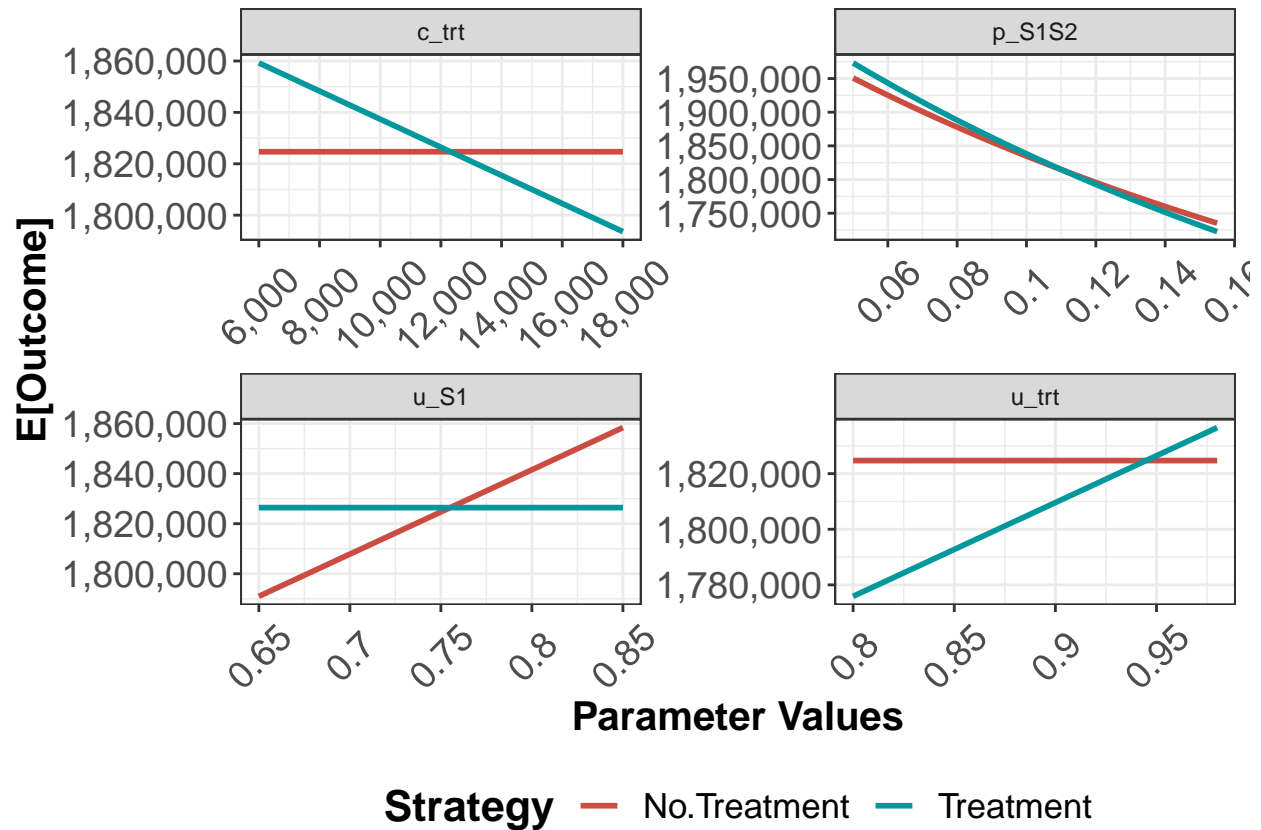## 08.3 One-way sensitivity analysis (OWSA)

```r
options(scipen = 999) # disabling scientific notation in R
# dataframe containing all parameters, their basecase values, and the min and
# max values of the parameters of interest
df_params_owsa <- data.frame(pars = c("p_S1S2", "c_trt", "u_S1", "u_trt"),
                             min  = c(0.05 ,  6000 , 0.65, 0.80), # min parameter values
                             max  = c(0.155, 18000 , 0.85, 0.98)  # max parameter values
                             )

owsa_nmb  <- run_owsa_det(params_range     = df_params_owsa,   # dataframe with parameters for owsa
                          params_basecase  = l_params_all,     # list with all parameters
                          nsamp            = 100,              # number of parameter values
                          FUN              = calculate_ce_out, # function to compute outputs
                          outcomes         = c("NMB"),          # output to do the OWSA on
                          strategies       = v_names_str,       # names of the strategies
                          n_wtp            = 120000)            # extra argument to pass to FUN
```

```
## Warning: strategy name 'No Treatment' was converted to 'No.Treatment' for
## compatibility. See ?make.names
```
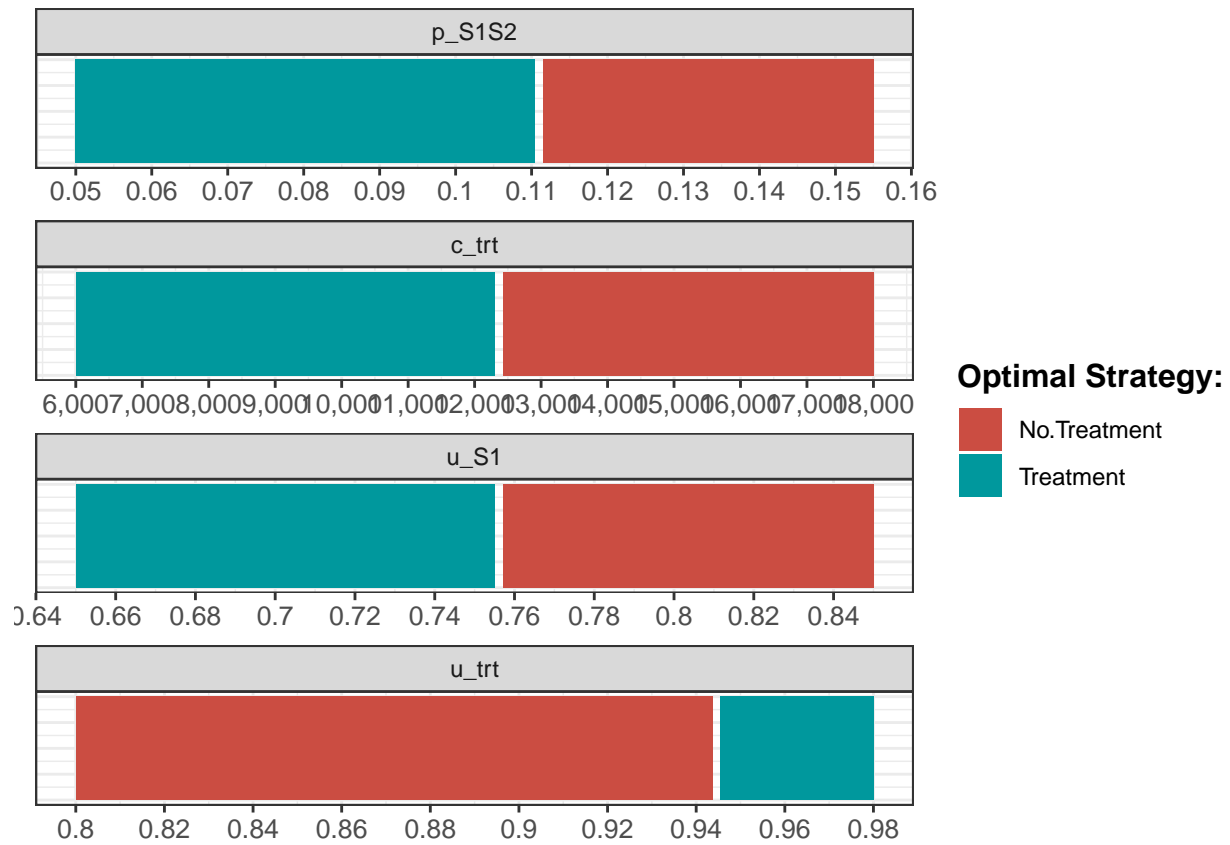
08.3.1 Plot OWSA

```r
plot(owsa_nmb, txtsize = 16, n_x_ticks = 5, n_y_ticks = 3,
     facet_scales = "free") +
     theme(legend.position = "bottom",
           axis.text.x = element_text(angle = 45, vjust = 0.5))
```
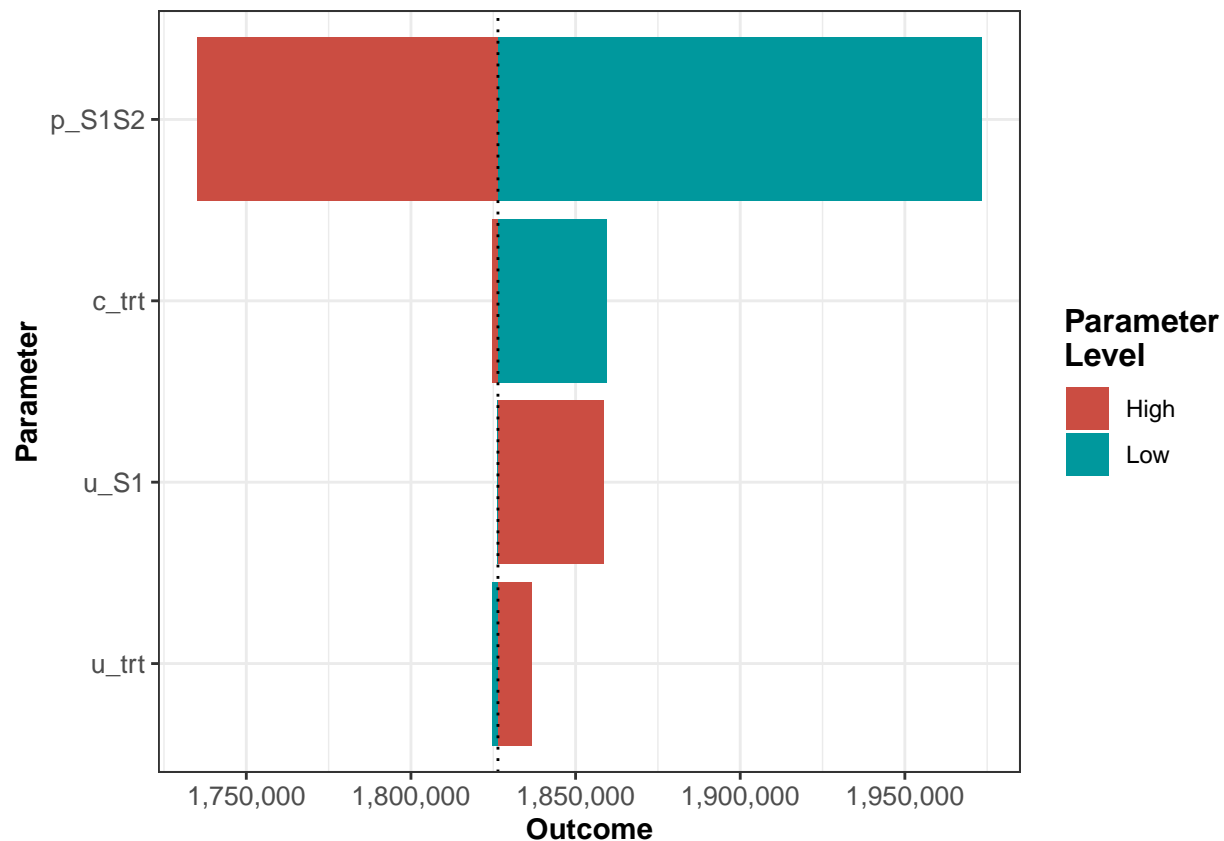
08.3.2 Optimal strategy with OWSA

```
owsa_opt_strat(owsa = owsa_nmb)
```

08.3.3 Tornado plot

```
owsa_tornado(owsa = owsa_nmb)
```

08.4 Two-way sensitivity analysis (TWSA)

```
# dataframe containing all parameters, their basecase values, and the min and
# max values of the parameters of interest
df_params_twsa <- data.frame(pars = c("c_trt", "u_trt"),
                             min  = c(6000, 0.80), # min parameter values
                             max  = c(18000, 0.98) # max parameter values
                             )

twsa_nmb <- run_twsa_det(params_range    = df_params_twsa,  # dataframe with parameters for twsa
                         params_basecase = l_params_all,    # list with all parameters
                         nsamp           = 40,              # number of parameter values
                         FUN             = calculate_ce_out, # function to compute outputs
                         outcomes        = c("NMB"),         # output to do the twsa on
                         strategies      = v_names_str,      # names of the strategies
                         n_wtp           = 120000)           # extra argument to pass to FUN
```
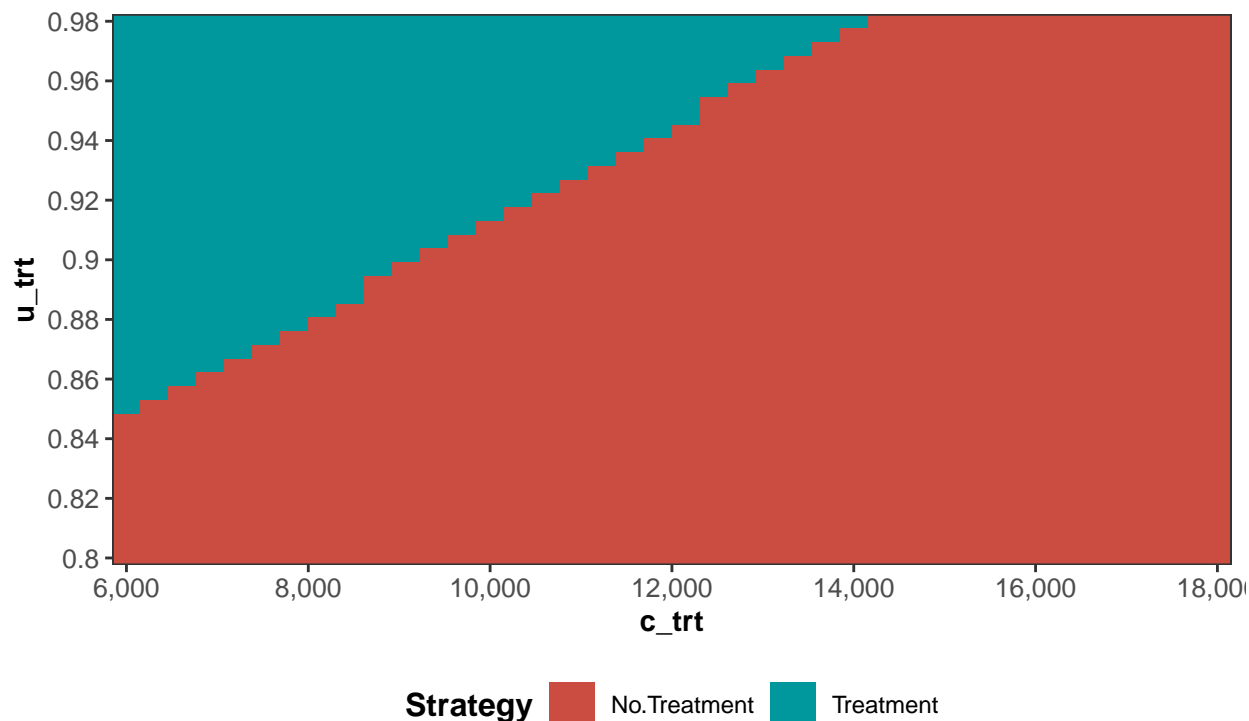
08.4.1 Plot TWSA

```
plot(twsa_nmb) +
  ggtitle(label = "Two-way sensitivity analysis",
          subtitle = "Net monetary benefit") +
          theme(legend.position = "bottom")
```

Two–way sensitivity analysis
Net monetary benefit

Strategy — No.Treatment — Treatment

09 Probabilistic Sensitivity Analysis (PSA)

```r
# Function to generate PSA input dataset
generate_psa_params <- 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)
    p_HS1   = rbeta(n_sim, 30, 170) , # probability to become sick when healthy
    p_S1H   = rbeta(n_sim, 60, 60)  , # probability to become healthy when sick
    p_S1S2  = rbeta(n_sim, 84, 716) , # probability to become sicker when sick
    p_HD    = rbeta(n_sim, 10, 1990), # probability to die when healthy
    hr_S1   = rlnorm(n_sim, log(3),  0.01), # rate ratio of death in S1 vs healthy
    hr_S2   = rlnorm(n_sim, log(10), 0.02), # rate ratio of death in S2 vs healthy

    # State rewards
    # Costs
    c_H   = rgamma(n_sim, shape = 100, scale = 20)     , # cost of remaining one cycle in state H
    c_S1  = rgamma(n_sim, shape = 177.8, scale = 22.5), # cost of remaining one cycle in state S1
    c_S2  = rgamma(n_sim, shape = 225, scale = 66.7)   , # cost of remaining one cycle in state S2
    c_Trt = rgamma(n_sim, shape = 73.5, scale = 163.3), # cost of treatment (per cycle)
    c_D   = 0                                          , # cost of being in the death state

    # Utilities
    u_H   = rbeta(n_sim, shape1 = 200, shape2 = 3)  , # utility when healthy
    u_S1  = rbeta(n_sim, shape1 = 130, shape2 = 45) , # utility when sick
```

```
    u_S2  = rbeta(n_sim, shape1 = 230, shape2 = 230), # utility when sicker
    u_D   = 0                                       , # utility when dead
    u_Trt = rbeta(n_sim, shape1 = 300, shape2 = 15) , # utility when being treated
    d_e   = 0.03,  # discount factor for effectiveness
    d_c   = 0.03   # discount factor for costs
  )
    return(df_psa)
}
# Try it
generate_psa_params(10)
```

```
##        p_HS1      p_S1H      p_S1S2         p_HD     hr_S1      hr_S2       c_H
## 1  0.15132349 0.4820445 0.08485456 0.003973762 3.055410 10.148768 1887.449
## 2  0.12522484 0.4392546 0.11683397 0.004813328 3.005252  9.928044 1966.291
## 3  0.15673720 0.5311020 0.11925841 0.004491843 2.982392 10.021998 2101.059
## 4  0.11276858 0.4493088 0.09393848 0.010646056 2.981918 10.167486 1728.664
## 5  0.14292946 0.5825087 0.11628065 0.007045338 3.024975 10.006505 2160.895
## 6  0.20088601 0.4580278 0.10403415 0.004058637 2.971345 10.012715 1969.304
## 7  0.14347796 0.5492245 0.09294048 0.005658464 2.989181 10.001860 1641.192
## 8  0.13149270 0.4899896 0.12838861 0.007354969 2.984080  9.919332 2276.032
## 9  0.15593267 0.5705602 0.09237907 0.004162148 2.988974 10.142331 1717.867
## 10 0.09824029 0.5127637 0.10683148 0.002141140 2.968692  9.749869 2132.549
##        c_S1     c_S2    c_Trt c_D       u_H       u_S1      u_S2 u_D     u_Trt
## 1  4173.600 14607.88 10673.74   0 0.9829120 0.7252701 0.4757751   0 0.9435773
## 2  4188.264 14714.84 13380.61   0 0.9693926 0.7610392 0.4591563   0 0.9501528
## 3  4578.682 16664.54 12522.58   0 0.9910033 0.7076433 0.5032719   0 0.9670124
## 4  3395.922 15669.87 13833.65   0 0.9928844 0.7124119 0.5132492   0 0.9649128
## 5  3878.562 15302.70 13154.65   0 0.9748972 0.7344718 0.4895693   0 0.9325969
## 6  3970.522 15303.55 13914.95   0 0.9832065 0.7169406 0.4628316   0 0.9456881
## 7  3680.588 15378.20 12117.86   0 0.9917677 0.7851270 0.4504530   0 0.9093339
## 8  3781.956 15614.73 12070.99   0 0.9727485 0.7582961 0.4727426   0 0.9390084
## 9  3448.146 15401.50 11760.17   0 0.9836544 0.7648816 0.4851046   0 0.9537789
## 10 4656.666 15198.97 10216.98   0 0.9915345 0.7751203 0.5311969   0 0.9577708
##     d_e  d_c
## 1  0.03 0.03
## 2  0.03 0.03
## 3  0.03 0.03
## 4  0.03 0.03
## 5  0.03 0.03
## 6  0.03 0.03
## 7  0.03 0.03
## 8  0.03 0.03
## 9  0.03 0.03
## 10 0.03 0.03
```

```
# Number of simulations
n_sim <- 1000

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

```
##        p_HS1      p_S1H      p_S1S2         p_HD     hr_S1      hr_S2       c_H
```

```
## 1 0.1513235 0.5617628 0.1033817 0.006269864 2.962948  9.820157 1658.447
## 2 0.1252248 0.4380343 0.1152594 0.005371105 3.014068 10.100813 2050.281
## 3 0.1567372 0.5458102 0.1274505 0.004301015 3.018588  9.825985 2094.425
## 4 0.1127686 0.5106953 0.1015742 0.005319105 2.979709  9.697122 2135.411
## 5 0.1429295 0.5277308 0.1020384 0.004225209 3.025490 10.254387 1665.257
## 6 0.2008860 0.5252364 0.1030676 0.008319206 2.979175 10.366400 2049.794
##        c_S1      c_S2     c_Trt c_D       u_H       u_S1      u_S2 u_D      u_Trt
## 1 4191.109 15165.80 10292.050   0 0.9816602 0.7395884 0.5106656   0 0.9496993
## 2 4133.823 15042.66 10779.006   0 0.9906084 0.7240259 0.4927761   0 0.9731185
## 3 3567.033 15052.49 12811.443   0 0.9834960 0.6910869 0.5024542   0 0.9598494
## 4 3726.226 16084.60 10072.741   0 0.9919197 0.7065183 0.5118351   0 0.9357411
## 5 3654.486 15201.84 14917.228   0 0.9953850 0.6838064 0.5021483   0 0.9635901
## 6 3927.001 17060.57  9581.097   0 0.9813330 0.7766346 0.5035428   0 0.9506926
##    d_e  d_c
## 1 0.03 0.03
## 2 0.03 0.03
## 3 0.03 0.03
## 4 0.03 0.03
## 5 0.03 0.03
## 6 0.03 0.03
```

```r
# Histogram of parameters
ggplot(reshape2::melt(df_psa_input, variable.name = "Parameter",
                      value.name = "Parameter value"),
                      aes(x = `Parameter value`)) +
                      facet_wrap(~Parameter, scales = "free") +
                      geom_histogram(aes(y = ..density..), alpha = 0.8) +
                      scale_x_continuous(breaks = number_ticks(2)) +
                      ylab("") +
                      theme_bw(base_size = 14) +
                      theme(axis.text.y = element_blank(), text = element_text(size=10))
```

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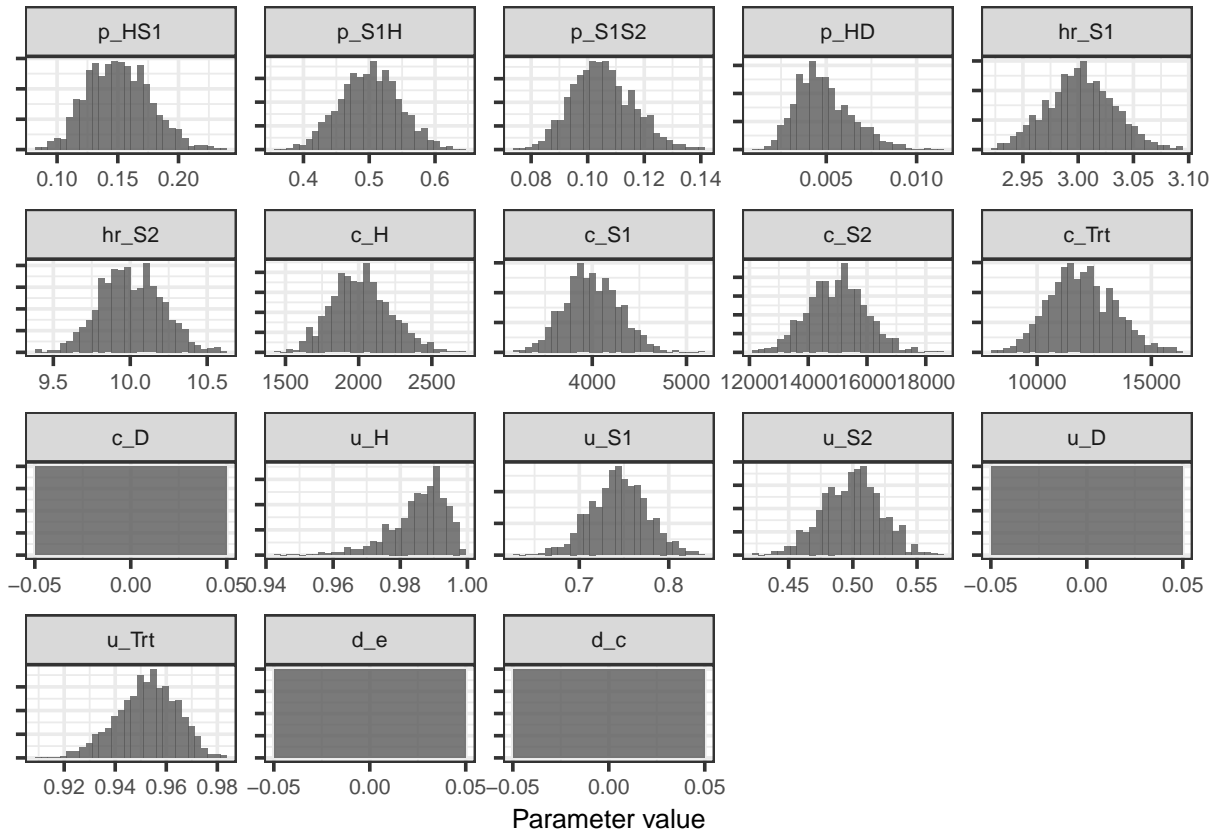
```r
# Initialize dataframes with PSA output
# Dataframe of costs
df_c <- as.data.frame(matrix(0,
                      nrow = n_sim,
                      ncol = n_str))
colnames(df_c) <- v_names_str
# Dataframe of effectiveness
df_e <- as.data.frame(matrix(0,
                      nrow = n_sim,
  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

09.1 Conduct probabilistic sensitivity analysis

```r
# Run Markov model on each parameter set of PSA input dataset
for(i in 1:n_sim){
  l_psa_input <- update_param_list(l_params_all, df_psa_input[i,])
  df_out_psa  <- calculate_ce_out(l_psa_input)
  df_c[i, ] <- df_out_psa$Cost
  df_e[i, ] <- df_out_psa$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 = " "))
  }
}
```

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09.2 Create PSA object for dampack

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

09.2.1 Save PSA objects

```
save(df_psa_input, df_c, df_e, v_names_str, n_str, l_psa,
     file = "markov_sick-sicker_PSA_dataset.RData")
```

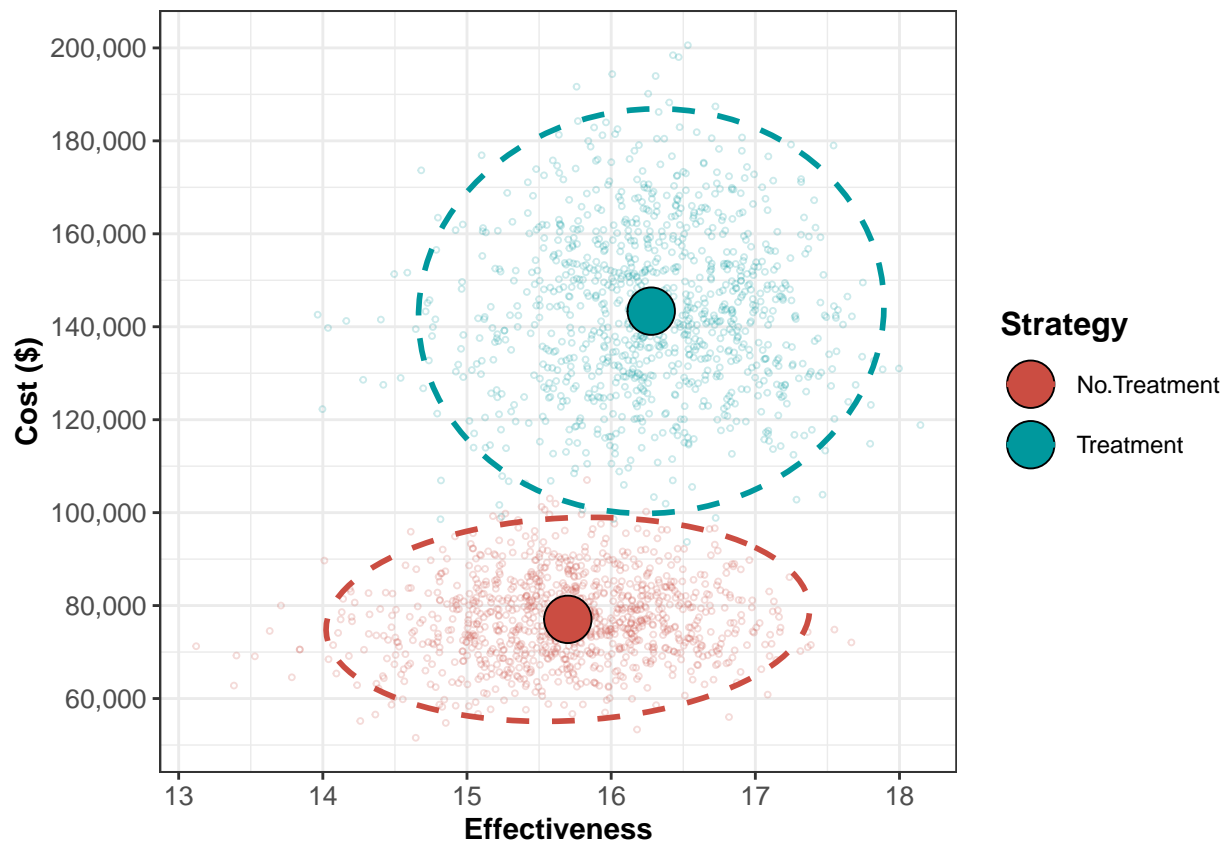## 09.3 Create probabilistic analysis graphs

```
load(file = "markov_sick-sicker_PSA_dataset.RData")
```

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

```
v_wtp <- seq(0, 200000, by = 10000)
```

09.3.1 Cost-Effectiveness Scatter plot

```
plot(l_psa)
```

09.4 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 No.Treatment   77033.8 15.69937       NA         NA        NA     ND
## 2    Treatment  143354.8 16.27791    66321  0.5785414 114634.8     ND
```

```r
# Save CEA table with ICERs
# As .RData
save(df_cea_psa,
     file = "markov_sick-sicker_probabilistic_CEA_results.RData")
# As .csv
write.csv(df_cea_psa,
          file = "markov_sick-sicker_probabilistic_CEA_results.csv")
```

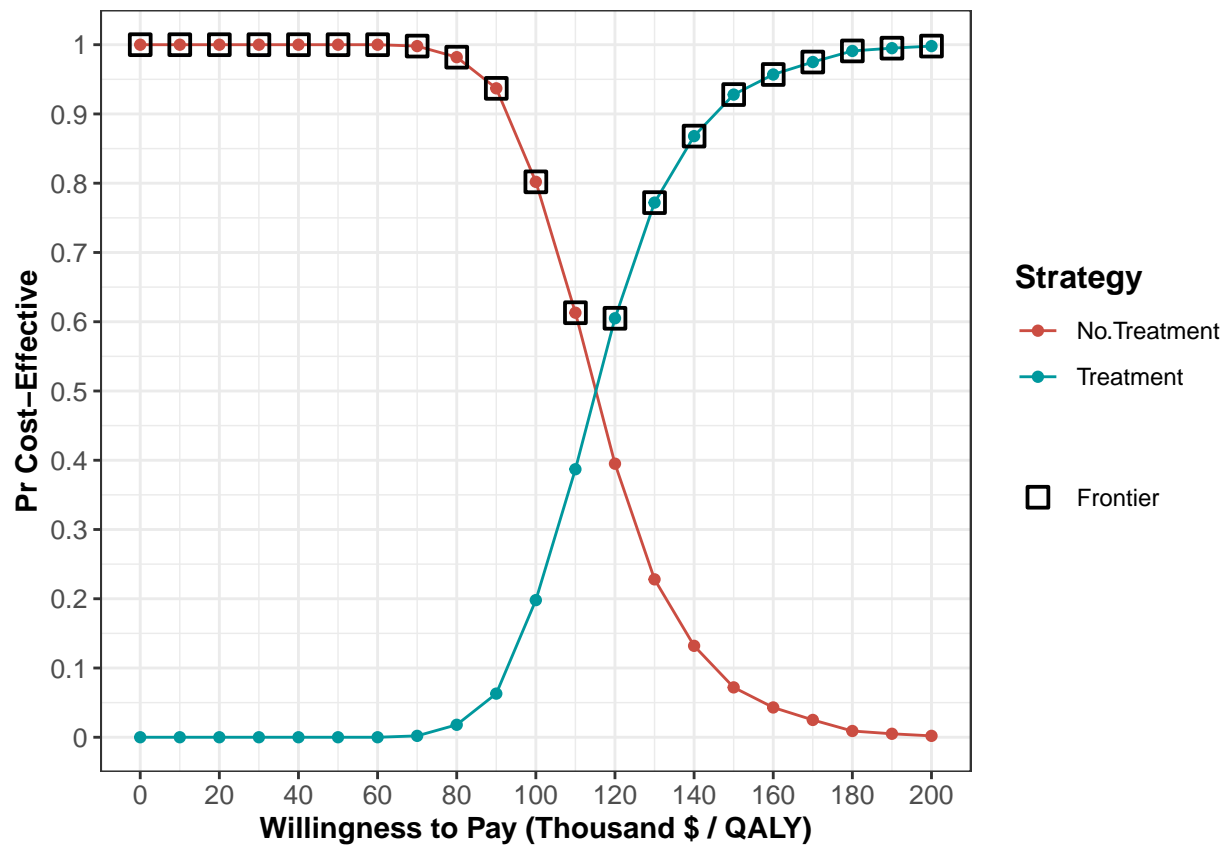## 09.4.1 Plot cost-effectiveness frontier

```r
plot(df_cea_psa)
```
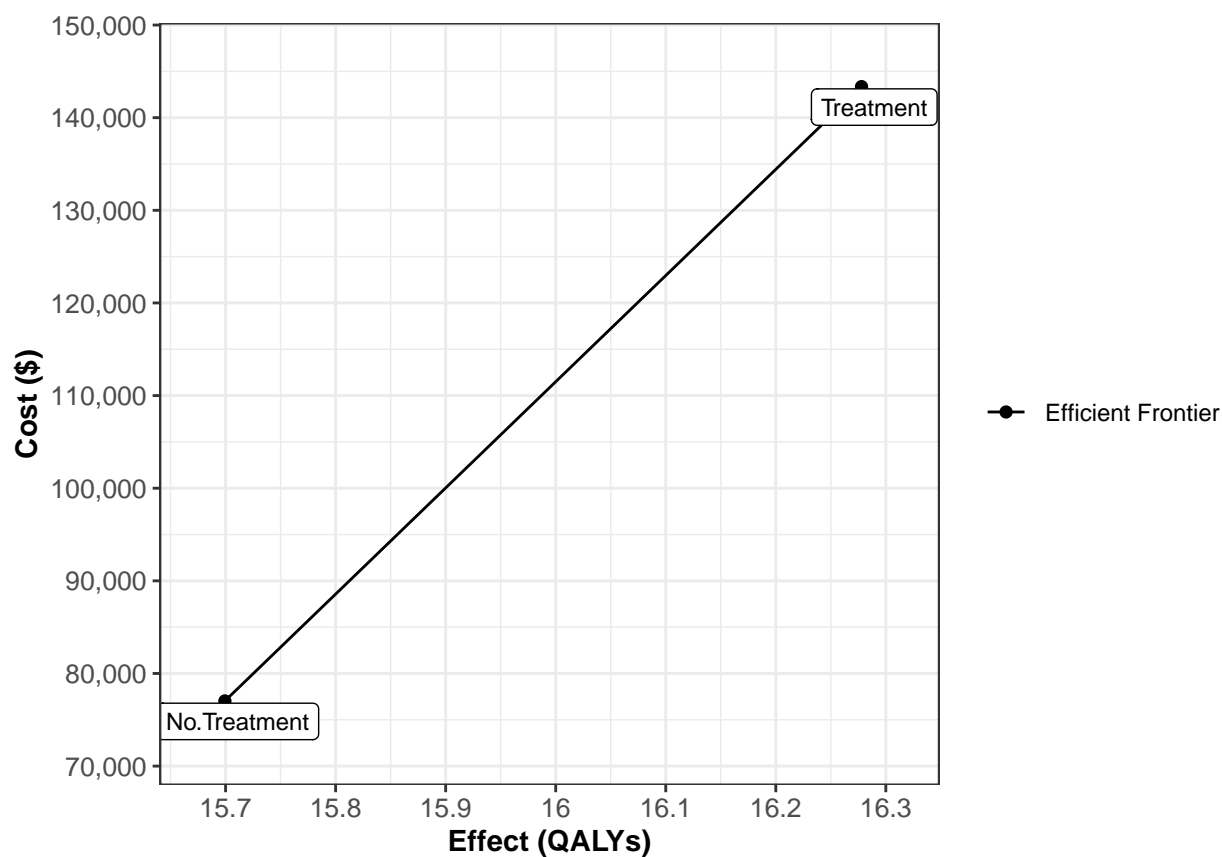
09.4.2 Cost-effectiveness acceptability curves (CEACs) and frontier (CEAF)

```
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    120000    No.Treatment
## 2    120000    200000       Treatment
# CEAC & CEAF plot
plot(ceac_obj)
```
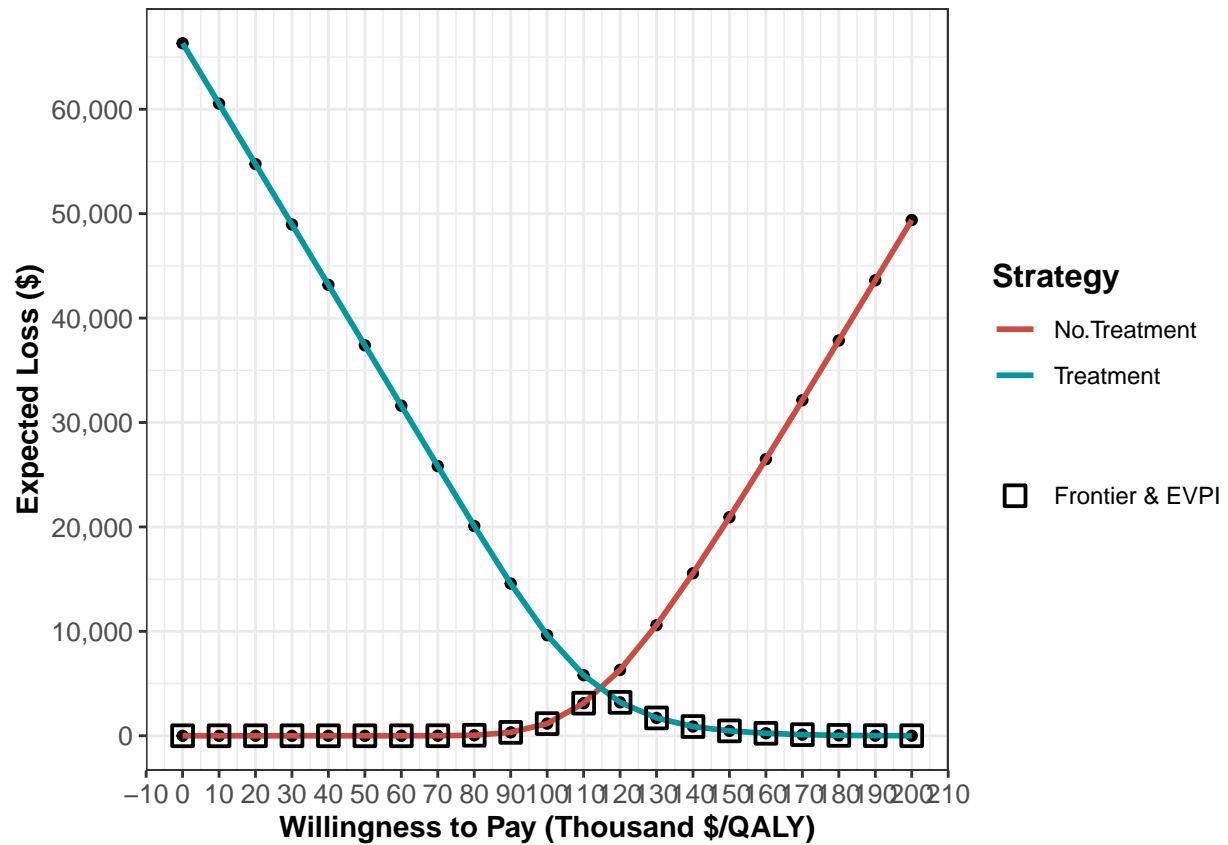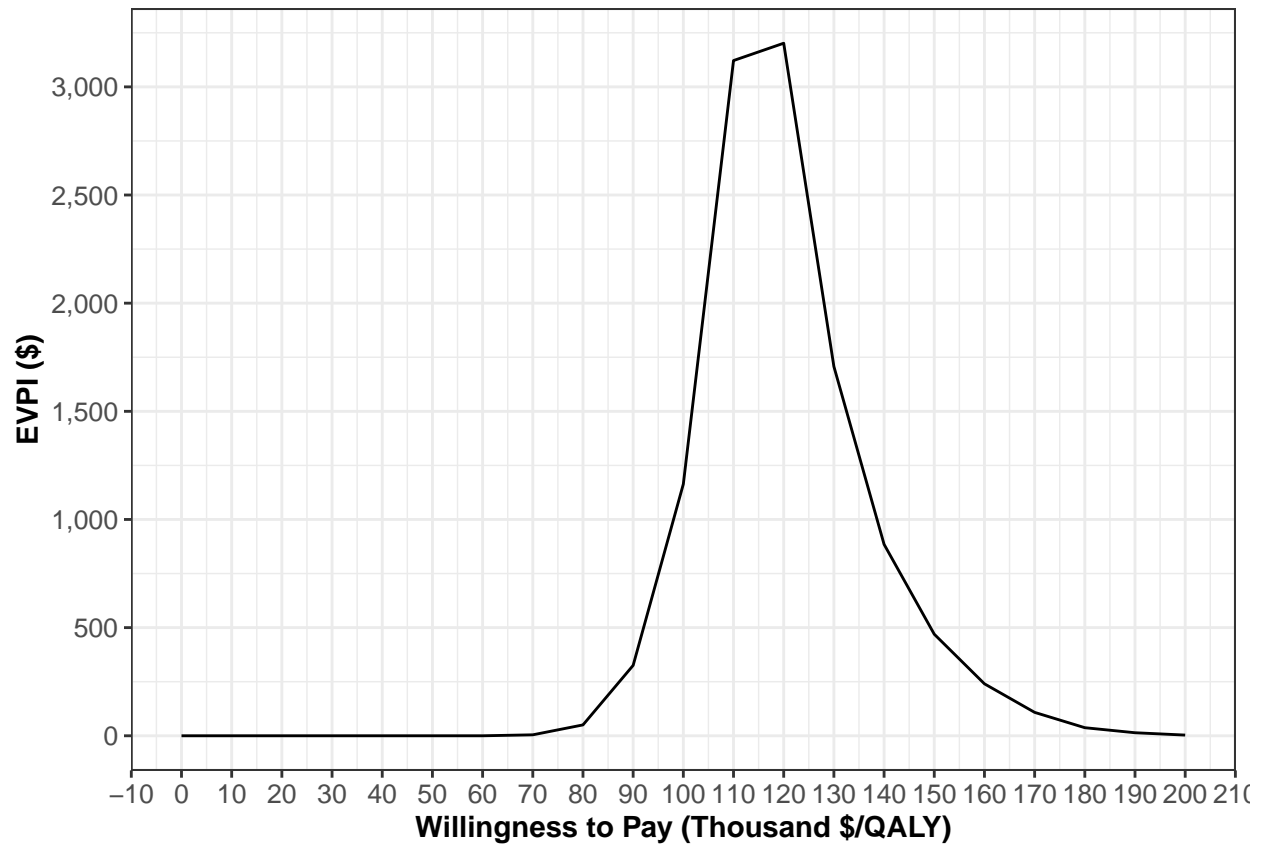

09.4.3 Expected Loss Curves (ELCs)

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

```
elc_obj <- calc_exp_loss(wtp = v_wtp, psa = l_psa)
# ELC plot
plot(elc_obj, log_y = FALSE)
```

09.4.4 Expected value of perfect information (EVPI)

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

07.4.5 Expected value of partial perfect information (EVPPI)

```
evppi <- calc_evppi(psa = l_psa,
                    wtp = v_wtp,
                    params = c("p_S1S2"),
                    outcome = c("nmb"),
                    type = c("gam", "poly"),
                    poly.order = 2,
                    k = -1,
                    pop = 1
)
# EVPPI plot
dampack:::plot.evppi(evppi)
```