# PSA: Three-strategy decision tree in R - HVE

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

## 01 Load packages

## 02 Load functions

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

## 03 Define parameter input values

```
v_names_str <- c("No Tx", "Tx All", "Biopsy") # names of strategies</pre>
n_str
          <- length(v_names_str)</pre>
                                               # number of strategies
wtp
            <- 100000
                                               # willingness to pay threshold
# Probabilities
            <- 0.52 # prevalence of HVE
p_{HVE}
p_HVE_comp <- 0.71 # complications with untreated HVE
p_OVE_comp <- 0.01 # complications with untreated OVE
p_HVE_comp_tx <- 0.36 # complications with treated HVE
p_OVE_comp_tx <- 0.20 # complications with treated OVE
p_biopsy_comp <- 0.05 # probability of complications due to biopsy</pre>
# Costs
         <- 1200 # cost of viral encephalitis care without complications
c_VE_comp <- 9000 # cost of viral encephalitis care with complications
c tx <- 9500 # cost of treatment
c_biopsy <- 25000 # cost of brain biopsy</pre>
# QALYs
a VE
                       # remaining QALYs for those without VE-related complications
             <- 19
                       # remaining QALYs for those with VE-related complications
q_loss_biopsy <- -0.01 # one-time QALY loss due to brain biopsy
# store the parameters into a list
l_params_all <- list(p_HVE, p_HVE_comp, p_OVE_comp, p_HVE_comp_tx,</pre>
                     p_OVE_comp_tx, p_biopsy_comp,
```

## 04 Create and run decision tree model

```
decision tree HVE output <- with(as.list(1 params all), {</pre>
 # Create vector of weights for each strategy
 v_w_no_tx <- c( p_HVE * p_HVE_comp , # HVE, complications</pre>
                   p_HVE * (1-p_HVE_comp) , # HVE, no complications
                 (1-p_HVE) * p_OVE_comp , # OVE, complications
                 (1-p_HVE) * (1-p_OVE_comp)) # OVE, no complications
            <- c( 1
                                              , # On treatment
 v_w_tx
                   p_HVE * p_HVE_comp_tx , # HVE w/tx, complications
                   p_HVE * (1-p_HVE_comp_tx) , # HVE w/tx, no complications
                 (1-p_HVE) * p_OVE_comp_tx , # OVE w/tx, complications
                 (1-p_HVE) * (1-p_OVE_comp_tx)) # OVE w/tx, no complications
 v w biopsy <- c(1
                                                       , # Undergo biopsy
                                                       , # biopsy complications
                 p_biopsy_comp
                 # no biopsy comp., HVE w/tx, complications
                 (1-p_biopsy_comp) * p_HVE * p_HVE_comp_tx ,
                 # no biopsy comp., HVE w/tx, no complications
                 (1-p_biopsy_comp) * p_HVE * (1-p_HVE_comp_tx),
                 # no biopsy comp., OVE, complications
                 (1-p\_biopsy\_comp) * (1-p\_HVE) *
                                                  p_OVE_comp
                 # no biopsy comp., OVE, no complications
                 (1-p\_biopsy\_comp) * (1-p\_HVE) * (1-p\_OVE\_comp))
 # Create vector of outcomes (QALYs) for each strategy
 v_qaly_no_tx <- c(q_VE_comp, # HVE, complications</pre>
                    q_VE , # HVE, no complications
                    q_VE_comp, # OVE, complications
                              # OVE, no complications
                    q_VE)
               <-c(0)
                             , # treatment does not directly add any QALYs
 v_qaly_tx
                    q_VE_comp , # HVE, complications
                    q_VE , # HVE, no complications
                    q_VE_comp , # OVE, complications
                               # OVE, no complications
                    q_VE)
 v_qaly_biopsy <- c(q_loss_biopsy, # loss due to biopsy</pre>
```

```
q_VE_comp , # biopsy complications
                               , # no biopsy comp., HVE w/tx, complications
                  q_VE_comp
                              , # no biopsy comp., HVE w/tx, no complications
                  q VE
                               , # no biopsy comp., OVE, complications
                  q_VE_comp
                                # no biopsy comp., OVE, no complications
                  q VE)
# Create vector of costs for each strategy
v_cost_no_tx <- c(c_VE_comp , # HVE, complications</pre>
                  c_VE , # HVE, no complications
                  c_VE_comp , # OVE, complications
                             # OVE, no complications
                          , # cost of treatment
v_cost_tx
            <- c(c_tx
                  c_VE_comp , # HVE, complications
                  c_VE , # HVE, no complications
                  c_VE_comp , # OVE, complications
                             # OVE, no complications
                                 , # cost of biopsy procedure
v_cost_biopsy <- c(c_biopsy</pre>
                                 , # biopsy complications
                  c VE comp
                  c_VE_comp + c_tx , # no biopsy comp., HVE w/tx, complications
                  c_{VE} + c_{tx} , # no biopsy comp., HVE w/tx, no complications
                                 , # no biopsy comp., OVE, complications
                  c_VE_comp
                  c VE)
                                    # no biopsy comp., OVE, no complications
# Calculate total utilities for each strategy
total_qaly_no_tx <- v_w_no_tx %*% v_qaly_no_tx
total_qaly_tx
              total_qaly_biopsy <- v_w_biopsy %*% v_qaly_biopsy</pre>
# Calculate total costs for each strategy
total_cost_no_tx <- v_w_no_tx %*% v_cost_no_tx
total_cost_tx <- v_w_tx %*% v_cost_tx
total_cost_biopsy <- v_w_biopsy %*% v_cost_biopsy</pre>
# vector of total QALYs
v_total_qaly <- c(total_qaly_no_tx, total_qaly_tx, total_qaly_biopsy)</pre>
# vector of total costs
v_total_cost <- c(total_cost_no_tx, total_cost_tx, total_cost_biopsy)</pre>
# calculate vector of nmb
            <- v_total_qaly * wtp - v_total_cost
v_nmb
# Name outcomes
names(v_total_qaly) <- v_names_str # names for the elements of the total QALYs vector</pre>
names(v_total_cost) <- v_names_str # names for the elements of the total cost vector</pre>
                  <- v_names_str # names for the elements of the nmb vector
names(v_nmb)
df_output <- data.frame(Strategy = v_names_str,</pre>
                       Cost = v_total_cost,
                       Effect = v_total_qaly,
                       NMB
                               = v_nmb)
```

```
return(df_output)
})

# model output
decision_tree_HVE_output

## Strategy Cost Effect NMB
## No Tx No Tx 4117.20 19.6260 1958483
## Tx All Tx All 12908.96 19.7168 1958771
## Biopsy Biopsy 32705.72 19.7576 1943054
```

#### 04.1 Plot the decision tree

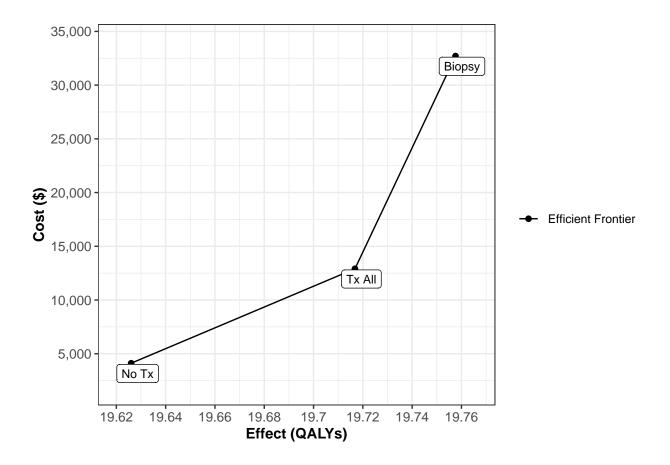
```
# branches <- read.csv(here('data', 'decision_tree_HVE_branches.csv'),
# stringsAsFactors = F, header = T)
# tree <- create_tree(branches)
# plot_tree(tree, font.size = 5)</pre>
```

#### 05 Cost-Effectiveness Analysis

```
# create the transition probability matrix for NO treatment
strategies = decision_tree_HVE_output$Strategy)
decision_tree_HVE_cea
##
   Strategy
             Cost Effect Inc_Cost Inc_Effect
                                          ICER Status
     No Tx 4117.20 19.6260
## 1
                         NA
                                            NA
## 2
    Tx All 12908.96 19.7168 8791.76
                                0.0908 96825.55
                                                 ND
     Biopsy 32705.72 19.7576 19796.76 0.0408 485214.71
                                                 ND
```

#### 05.1 Plot frontier of Decision Tree

```
plot(decision_tree_HVE_cea, effect_units = "QALYs")
```



# 06 Deterministic Sensitivity Analysis

# 06.1 List of input parameters

```
## $p_HVE
## [1] 0.52
## $p_HVE_comp
## [1] 0.71
##
## $p_OVE_comp
## [1] 0.01
##
## $p_HVE_comp_tx
## [1] 0.36
## $p_OVE_comp_tx
## [1] 0.2
##
## $p_biopsy_comp
## [1] 0.05
##
## $c_VE
```

1\_params\_all

```
## [1] 1200
##
## $c VE comp
## [1] 9000
## $c tx
## [1] 9500
##
## $c_biopsy
## [1] 25000
## $q_VE
## [1] 20
##
## $q_VE_comp
## [1] 19
##
## $q loss biopsy
## [1] -0.01
```

## 06.2 Load decision tree model function

```
#### We wrapped the decision tree in a function which we called calculate_ce_out
# This function is stored in "Functions_decision_tree_HVE.R" and needes the list of parameters
source("Functions_decision_tree_HVE.R")
# Test function to see if it gives the CE results
calculate_ce_out(l_params_all)

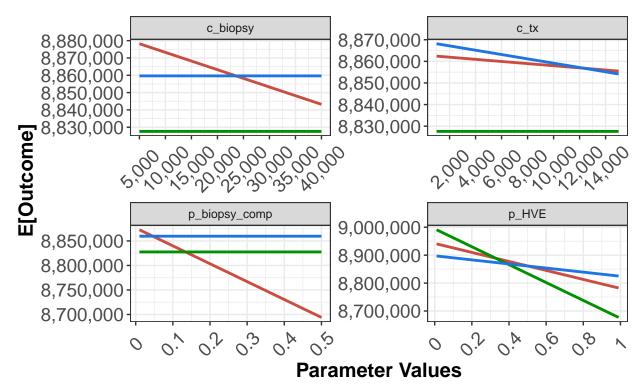
## Strategy Cost Effect NMB
## No Tx No Tx 4117.20 19.6260 1958483
## Tx All Tx All 12908.96 19.7168 1958771
## Biopsy Biopsy 32705.72 19.7576 1943054
```

#### 06.3 One-way sensitivity analysis (OWSA)

```
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_HVE", "p_biopsy_comp", "c_tx", "c_biopsy"),</pre>
                            min = c(0.01, 0.01, 1000, 5000), # min parameter values
                            \max = c(0.99, 0.50, 15000, 40000) # 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
                                  = 450000
                                                        # extra argument to pass to FUN
                        n_wtp
```

#### 06.3.1 Plot OWSA

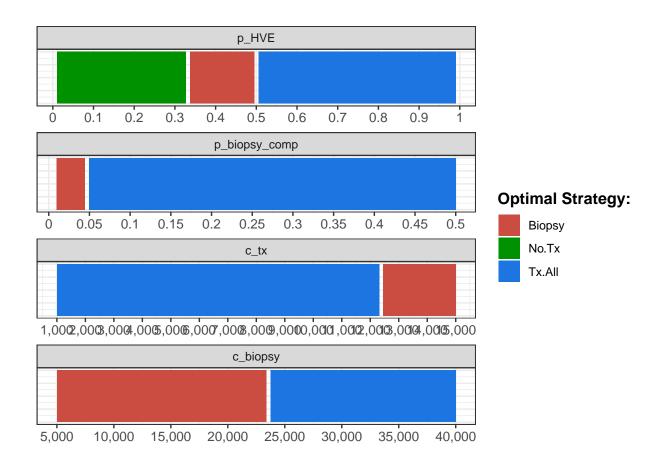
```
plot(owsa_nmb, txtsize = 16, n_x_ticks = 5, n_y_ticks = 3,
    facet_scales = "free") +
    theme(legend.position = "bottom",
        axis.text.x = element_text(angle = 45, vjust = 0.5))
```



**Strategy** — Biopsy — No.Tx — Tx.All

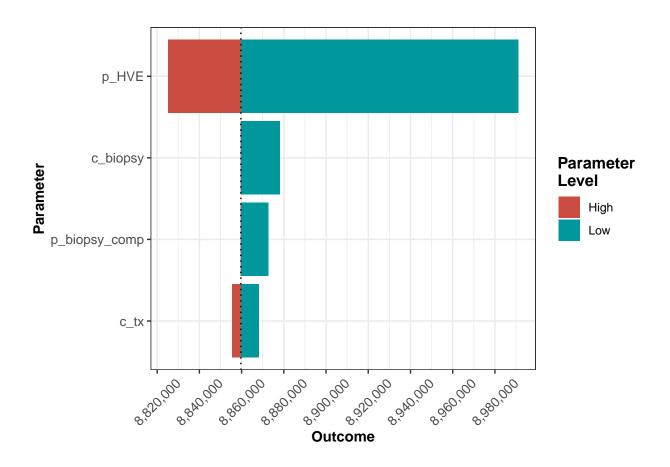
#### 06.3.2 Optimal strategy with OWSA

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



# 06.3.3 Tornado plot

```
owsa_tornado(owsa = owsa_nmb) +
theme(axis.text.x = element_text(angle = 45, vjust = 0.5))
```



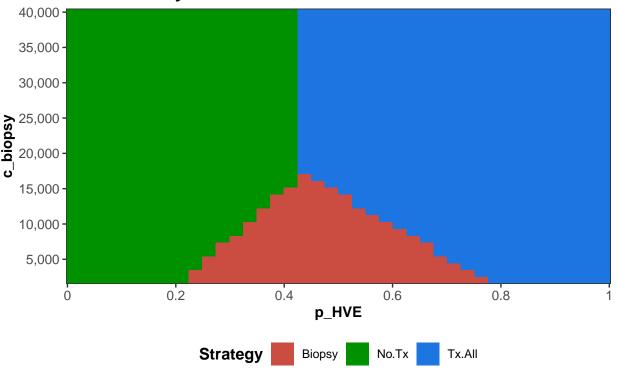
## 06.4 Two-way sensitivity analysis (TWSA)

```
# 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("p_HVE", "c_biopsy"),</pre>
                             min = c(0.01, 2000), # min parameter values
                             max = c(0.99, 40000) # 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
                                                       # number of parameter values
                        nsamp
                                   = 40,
                                   = calculate_ce_out, # function to compute outputs
                        FUN
                        outcomes = c("NMB"),
                                                    # output to do the twsa on
                                                      # names of the strategies
                        strategies = v_names_str,
                                 = 200000)
                                                     # extra argument to pass to FUN
                        n_wtp
```

#### 06.4.1 Plot TWSA

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

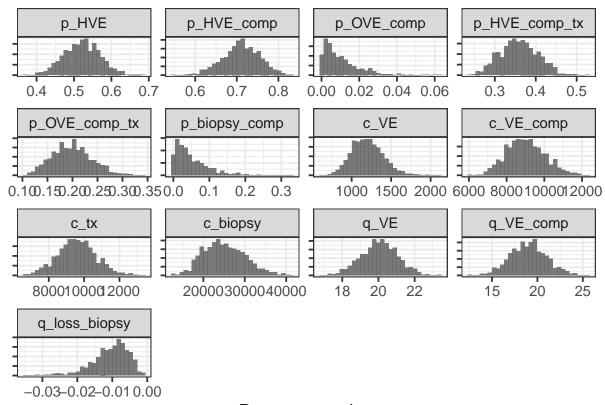
# Two-way sensitivity analysis Net monetary benefit



# 07 Probabilistic Sensitivity Analysis (PSA)

```
# Function to generate PSA input dataset
generate_psa_params <- function(n_sim = 1000, seed = 071518){</pre>
  set.seed(seed)
  # Dataframe of input parameters
  df_psa_params <- data.frame(</pre>
    # Transition probabilities (per cycle)
                 = rbeta(n_sim, 52, 48), # prevalence of HVE
   p_HVE
                 = rbeta(n_sim, 71, 29), # complications with untreated HVE
   p_HVE_comp
               = rbeta(n_sim, 1, 99), # complications with untreated OVE
   p_OVE_comp
   p_HVE_comp_tx = rbeta(n_sim, 36, 64), # complications with treated HVE
   p_OVE_comp_tx = rbeta(n_sim, 20, 80), # complications with treated OVE
   p_biopsy_comp = rbeta(n_sim, 1, 19), # probability of complications due to biopsy
    # Costs
             = rgamma(n_sim, shape = 36.0, scale = 33.33), # cost of remaining one cycle in state H
    c_VE_comp = rgamma(n_sim, shape = 81.0, scale = 111.1), # cost of remaining one cycle in state S1
    c_tx = rgamma(n_sim, shape = 74.6, scale = 127.4), # cost of remaining one cycle in state S2
   c_biopsy = rgamma(n_sim, shape = 25.0, scale = 1000), # cost of treatment (per cycle)
    # Utilities
                 = rnorm(n_sim, mean = 20, sd = 1), # utility when healthy
   q_VE
               = rnorm(n_sim, mean = 19, sd = 2), # utility when sick
   q_VE_comp
```

```
q_loss_biopsy = -rbeta(n_sim, shape1 = 4, shape2 = 380)
  )
  return(df_psa_params)
}
# Try it
generate_psa_params(10)
##
          p_HVE p_HVE_comp p_OVE_comp p_HVE_comp_tx p_OVE_comp_tx p_biopsy_comp
## 1 0.4749320 0.7235430 0.013378726
                                           0.3348038
                                                         0.1780884
                                                                     0.011999941
## 2
     0.5026526 0.6775784 0.009708085
                                           0.3681839
                                                         0.2114838
                                                                     0.025238361
## 3
     0.5843657 0.7484966 0.005812847
                                           0.4176749
                                                         0.1890676
                                                                     0.097321243
     0.4724143 0.7862144 0.005562199
                                           0.4084075
                                                         0.1854461
                                                                     0.075889209
     0.5111739 0.7476649 0.002928047
## 5
                                           0.4391065
                                                         0.2861042
                                                                     0.020872239
## 6
     0.5009217
                 0.7436646 0.028676511
                                           0.3770443
                                                         0.1986550
                                                                     0.008250482
## 7
     0.4738643
                0.7818476 0.002355727
                                           0.4088189
                                                         0.2726996
                                                                     0.005996830
     0.5040218
                0.7169040 0.027213835
                                           0.3016436
                                                         0.1915582
                                                                     0.005243219
## 9
     0.6019221
                0.6970007 0.003126903
                                           0.3837506
                                                         0.2331747
                                                                     0.054704895
## 10 0.5841529
                 0.7237498 0.016735953
                                                         0.2517606
                                                                     0.050570658
                                           0.3926275
##
           c_VE c_VE_comp
                               c_tx c_biopsy
                                                 q_VE q_VE_comp q_loss_biopsy
       966.2249 9544.065
## 1
                           8252.200 22888.59 21.17721
                                                       15.82956
                                                                 -0.022057880
    1353.3774 9563.488 9070.115 33952.29 19.59487
                                                       20.84448
                                                                 -0.005446182
     1389.0181 10085.773 10345.118 35437.55 21.30693
                                                       16.97661
                                                                 -0.011560750
       857.6754 7906.581 8965.302 29412.51 20.52500
                                                       18.02876
                                                                 -0.008128747
## 4
## 5
    1105.0702 6985.411 11056.538 19986.71 18.42311
                                                       21.49919
                                                                 -0.011470230
       991.2847 8706.526 11945.426 30449.68 20.15380
## 6
                                                       21.99035
                                                                 -0.014261496
     1238.2001 9339.254 9207.500 28529.47 19.14336
                                                       16.66124
                                                                 -0.008557772
## 8 1252.5362 10690.522 9711.167 24510.61 20.69662
                                                       16.55107
                                                                 -0.008861377
## 9 1012.6053 8943.545 9355.705 24554.44 20.55443
                                                       20.63643
                                                                 -0.015265554
## 10 1159.7220 8964.960 11193.358 27584.24 21.47903 16.81484
                                                                 -0.013003072
# Generate PSA dataset for CEA
# Number of simulations
n_sim <- 1000
# Generate PSA input dataset
df_psa_input <- generate_psa_params(n_sim = n_sim)</pre>
# First six observations
head(df_psa_input)
         p_HVE p_HVE_comp p_OVE_comp p_HVE_comp_tx p_OVE_comp_tx p_biopsy_comp
## 1 0.4749320 0.6840178 0.003715272
                                          0.4004084
                                                        0.2440951
                                                                     0.10028887
## 2 0.5026526  0.6826655  0.001535613
                                          0.3892561
                                                        0.2877619
                                                                     0.04649270
## 3 0.5843657 0.6605204 0.003732674
                                          0.3718509
                                                        0.1478400
                                                                     0.03177914
## 4 0.4724143 0.6661886 0.011322197
                                          0.4107147
                                                        0.2033657
                                                                     0.10379519
## 5 0.5111739 0.6564449 0.028811840
                                          0.4090270
                                                        0.1869370
                                                                     0.04914194
## 6 0.5009217 0.7018521 0.027931389
                                          0.3483384
                                                        0.1992983
                                                                     0.03061638
          c_VE c_VE_comp
                              c_tx c_biopsy
                                                q_VE q_VE_comp q_loss_biopsy
## 1 1012.0528 8231.366
                          9665.090 19841.40 20.77157 17.27182 -0.013827874
## 2 1129.2054
                8696.403 8719.779 17944.24 19.83319
                                                     17.79020 -0.024366690
## 3 1250.6772
               8697.659
                          7019.244 22204.50 21.98852 19.54381
                                                                -0.011710122
## 4 1031.9902
                6771.872
                          9423.112 25499.04 21.35562
                                                      17.96397
                                                                -0.013048945
## 5 980.5815
               7284.947 11432.434 19903.18 20.19028
                                                      17.82056
                                                                -0.001471185
## 6 1148.3751 9205.581 9920.907 32975.68 20.31572 17.02939
                                                                -0.012723213
```



#### Parameter value

#### 07.1 Conduct probabilistic sensitivity analysis

```
# Run decision tree 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 = " "))
    }
}</pre>
```

#### 07.2 Create PSA object for dampack

## 07.2.1 Save PSA objects

#### 07.3 Create probabilistic analysis graphs

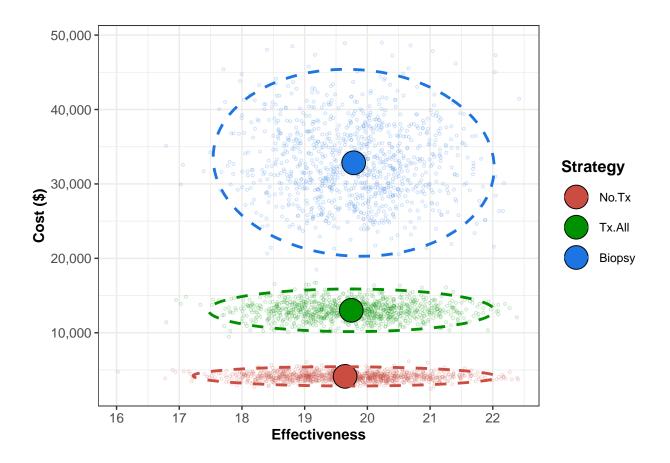
```
load(file = "decision_tree_HVE_PSA_dataset.RData")
```

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

```
v_{wtp} \leftarrow seq(0, 600000, by = 10000)
```

#### 07.3.1 Cost-Effectiveness Scatter plot

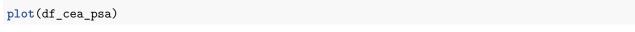
```
plot(l_psa)
```

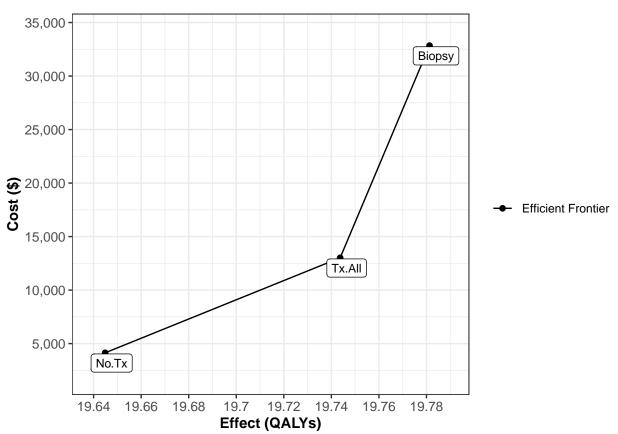


#### 07.4 Conduct CEA with probabilistic output

```
# Compute expected costs and effects for each strategy from the PSA
df_out_ce_psa <- summary(l_psa)</pre>
df_out_ce_psa
##
     Strategy meanCost meanEffect
## 1
       No.Tx 4141.093
                          19.64486
## 2
       Tx.All 13018.905
                          19.74369
       Biopsy 32842.806
                          19.78128
# Calculate incremental cost-effectiveness ratios (ICERs)
df_cea_psa <- calculate_icers(cost</pre>
                                       = df_out_ce_psa$meanCost,
                                         = df_out_ce_psa$meanEffect,
                              effect
                              strategies = df_out_ce_psa$Strategy)
df_cea_psa
##
                          Effect Inc Cost Inc Effect
                                                            ICER Status
    Strategy
                   Cost
       No.Tx 4141.093 19.64486
## 1
                                        NA
                                                                     ND
       Tx.All 13018.905 19.74369 8877.813 0.09883105 89828.17
                                                                     ND
       Biopsy 32842.806 19.78128 19823.901 0.03758512 527440.16
# Save CEA table with ICERs
# As .RData
save(df_cea_psa,
     file = "decision_tree_HVE_probabilistic_CEA_results.RData")
# As .csv
```

#### 07.4.1 Plot cost-effectiveness frontier

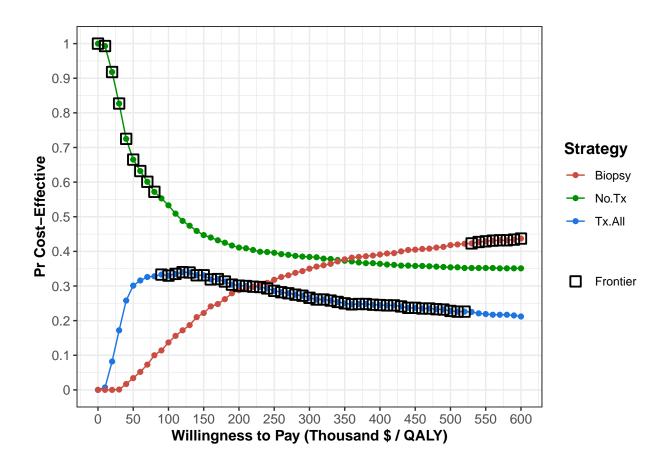




## 07.4.2 Cost-effectiveness acceptability curves (CEACs) and frontier (CEAF)

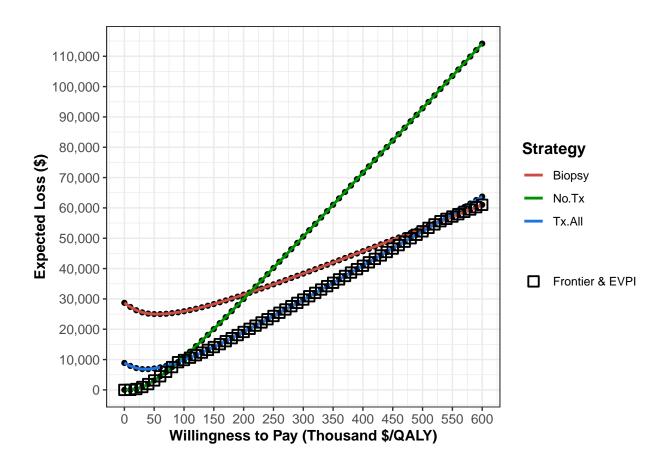
```
ceac_obj <- ceac(wtp = v_wtp, psa = l_psa)</pre>
# Regions of highest probability of cost-effectiveness for each strategy
summary(ceac_obj)
    range_min range_max cost_eff_strat
                   90000
## 1
             0
                                  No.Tx
## 2
             0
                  530000
                                  Tx.All
## 3
                  600000
                                  Tx.All
        90000
## 4
        530000
                  600000
                                  Biopsy
        530000
                                  Biopsy
## 5
                      NA
```

# CEAC & CEAF plot
plot(ceac\_obj)



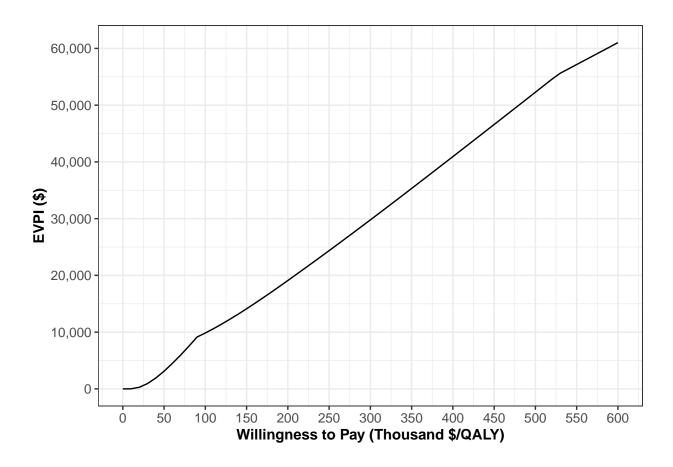
# 07.4.3 Expected Loss Curves (ELCs)

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



## 07.4.4 Expected value of perfect information (EVPI)

```
evpi <- calc_evpi(wtp = v_wtp, psa = 1_psa)
# EVPI plot
plot(evpi, effect_units = "QALY")</pre>
```



# 07.4.5 Expected value of partial perfect information (EVPPI)

