Markov_model_assignment

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In this document, we present the results from Assignment 4 where we conduct a cost-effectiveness analysis considering three strategies: 1) without treatment 2) with treatment but no end-of-life care, 3) with both treatment and end-of-life care. We then provide a table of cost and QALY of three strategies and report ICER for the three 2-way comparisons.

We have conducted a base case analysis. The structure of our model is as follows: 1. Define fixed variables and parameters for the model 2. Prepare state-specific per-cycle cost, qaly, and transitional cost matrix 3. Prepare transition probability matrix (this will change in simulation given age-specific mortality) 4. Prepare population matrix that keeps track of health state transition by cycle 5. Prepare a matrix ('trans') to record the transitional cost 6. Prepare empty matrices to record QALYs and Cost outcomes by cycle and by strategy 7. Define a function to calculate time-dependent transition probability based on age-specific mortality 8. Simulate a cohort for 'no drug' and 'drug' scenario 9. Calculate cost and qaly of each scenario 10. Calculate ICER 11. Plot

Basecase analysis

1. Define parameters

```r
t_names <- c("without_drug", "with_drug", "with_drug_eol")#t_names : strategy/scenario label ## modifie
n_treatments <- length(t_names)#n_treatment: number of strategies

s_names  <- c("Asymptomatic_disease", "Progressive_disease", "Dead")#s_names: vector of health states
n_states <- length(s_names)#n_states: number of health states

n_cohort <- 1000#n_cohort: cohort size
cycle <- 1#cycle: cycle length
n_cycles <- 46#n_cylces: total number of cycles

Initial_age <- 55#Initial_age: age at the beginning of simulation

cAsymp <- 500#cAsymp: cost of having asymptomatic disease (per-cycle cost)
cDeath <- 1000#cDeath: cost of death (transitional cost), only applies to the death among progressive d
cDrug <- 1000#cDrug: cost of drug
cProg <- 3000#cProg: cost of having progressive disease (per-cycle cost)
cEol <- 500 #cEndcare: cost of new end of life care ## modified code

uAsymp <- 0.95#uAsymp: utility of having asymptomatic disease
uProg <- 0.75#uProg: utility of having progressive disease
```

```
oDr <- 0.06#oDr: discount rate for qaly
cDr <- 0.06#cDr: discount rate for cost

tpDcm <- 0.15#tpDcm: excess mortality with progressive disease
tpDcm_r <- tpDcm*0.5 #excess mortality with progressive disease after EoL care
tpProg <- 0.01#tpProg: transition probability from asymptomatic to progressive disease
tpDn <- 0.0379  #pDn: baseline mortality <- mortality 0.0379  # over 65 year old

effect <- 0.5#effect: drug efficacy in decreasing the risk of progressing from asymptomatic to progress
```

2. Prepare cost, qaly, and transitional cost matrix. Note that the parameters defined in the previous block are used/called here cost and qaly matrix has the following structure row: strategies column: health states value: cost, qaly payoffs Transitional cost matrix has the following structure row: health states (departure state) column: health states(arrival state) value: transitional cost(toll)

```
# cost of staying in state
state_c_matrix <-
  matrix(c(cAsymp, cProg, 0,
           cAsymp + cDrug, cProg, 0,
           cAsymp + cDrug +cEol, cProg, 0), ##modified code
         byrow = TRUE,
         nrow = n_treatments,
         dimnames = list(t_names,
                         s_names))
state_c_matrix
```

```
##               Asymptomatic_disease Progressive_disease Dead
## without_drug                   500                3000    0
## with_drug                     1500                3000    0
## with_drug_eol                 2000                3000    0
```

```
# qaly when staying in state
state_q_matrix <-
  matrix(c(uAsymp, uProg, 0,
           uAsymp, uProg, 0,
           uAsymp, uProg, 0),
         byrow = TRUE,
         nrow = n_treatments,
         dimnames = list(t_names,
                         s_names))
state_q_matrix
```

```
##               Asymptomatic_disease Progressive_disease Dead
## without_drug                  0.95                0.75    0
## with_drug                     0.95                0.75    0
## with_drug_eol                 0.95                0.75    0
```

```
# cost of moving to a state
# same for both treatments
trans_c_matrix <-
  matrix(c(0, 0, 0,
           0, 0, cDeath,
           0, 0, 0),
         byrow = TRUE,
         nrow = n_states,
         dimnames = list(from = s_names,
                         to = s_names))
trans_c_matrix
```

```
##                         to
## from                     Asymptomatic_disease Progressive_disease Dead
##   Asymptomatic_disease                      0                   0    0
##   Progressive_disease                       0                   0 1000
##   Dead                                      0                   0    0
```

3. Prepare transition probability matrix p_matrix is a time-dependent transition probability matrix when incorporating age-specific mortality, meaning that transition probability will depend on the age/cycle. Here we define p_matrix with a set of parameters.

Note: array is useful to create a multidimensional matrix. Here p_matrix has 3-dimensional matrix with (health states x health states) x strategies

```
# Transition probabilities ----

# time-homogeneous
p_matrix <- array(data = c(1 - tpProg - tpDn, 0, 0,
                           tpProg, 1 - tpDcm - tpDn, 0,
                           tpDn, tpDcm + tpDn, 1,
                           1 - tpProg*(1-effect) - tpDn, 0, 0,
                           tpProg*(1-effect), 1 - tpDcm - tpDn, 0,
                           tpDn, tpDcm + tpDn, 1,
                           1 - tpProg*(1-effect) - tpDn, 0, 0,
                           tpProg*(1-effect), 1 - tpDcm_r - tpDn, 0,
                           tpDn, tpDcm_r + tpDn, 1),
                  dim = c(n_states, n_states, n_treatments),
                  dimnames = list(from = s_names,
                                  to = s_names,
                                  t_names))
p_matrix
```

```
## , ,  = without_drug
##
##                         to
## from                     Asymptomatic_disease Progressive_disease   Dead
##   Asymptomatic_disease                 0.9521              0.0100 0.0379
##   Progressive_disease                  0.0000              0.8121 0.1879
##   Dead                                 0.0000              0.0000 1.0000
##
## , ,  = with_drug
##
##                         to
## from                     Asymptomatic_disease Progressive_disease   Dead
##   Asymptomatic_disease                 0.9571              0.0050 0.0379
##   Progressive_disease                 0.0000              0.8121 0.1879
##   Dead                                0.0000              0.0000 1.0000
## 
## , ,  = with_drug_eol
## 
##                        to
## from                    Asymptomatic_disease Progressive_disease   Dead
##   Asymptomatic_disease                0.9571              0.0050 0.0379
##   Progressive_disease                 0.0000              0.8871 0.1129
##   Dead                                0.0000              0.0000 1.0000
```

4. Prepare population matrix that keeps track of health state transition by cycle 'pop' matrix will record health state distribution in the population for each cycle by strategy (3-dimensional matrix: (n__states x n__cycles) x n__treatments)

In cycle = 1, everyone is in the asymptomatic disease state. The third dimension is not specified to apply the same operation to both treatment strategies

```r
# Store population output for each cycle

# state populations
pop <- array(data = NA,
             dim = c(n_states, n_cycles, n_treatments),
             dimnames = list(state = s_names,
                             cycle = NULL,
                             treatment = t_names))

pop["Asymptomatic_disease", cycle = 1, ] <- n_cohort
pop["Progressive_disease", cycle = 1, ] <- 0
pop["Dead", cycle = 1, ] <- 0

head(pop)
```

```
## , , treatment = without_drug
## 
##                        cycle
## state                   [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10] [,11]
##   Asymptomatic_disease 1000   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##   Progressive_disease     0   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##   Dead                    0   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##                        cycle
## state                   [,12] [,13] [,14] [,15] [,16] [,17] [,18] [,19] [,20]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                   [,21] [,22] [,23] [,24] [,25] [,26] [,27] [,28] [,29]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                   [,30] [,31] [,32] [,33] [,34] [,35] [,36] [,37] [,38]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                  [,39] [,40] [,41] [,42] [,43] [,44] [,45] [,46]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA
##
## , , treatment = with_drug
##
##                        cycle
## state                  [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10] [,11]
##   Asymptomatic_disease 1000   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##   Progressive_disease     0   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##   Dead                    0   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##                        cycle
## state                  [,12] [,13] [,14] [,15] [,16] [,17] [,18] [,19] [,20]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                  [,21] [,22] [,23] [,24] [,25] [,26] [,27] [,28] [,29]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                  [,30] [,31] [,32] [,33] [,34] [,35] [,36] [,37] [,38]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                  [,39] [,40] [,41] [,42] [,43] [,44] [,45] [,46]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA
##
## , , treatment = with_drug_eol
##
##                        cycle
## state                  [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10] [,11]
##   Asymptomatic_disease 1000   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##   Progressive_disease     0   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##   Dead                    0   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA
##                        cycle
## state                  [,12] [,13] [,14] [,15] [,16] [,17] [,18] [,19] [,20]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                  [,21] [,22] [,23] [,24] [,25] [,26] [,27] [,28] [,29]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                        cycle
## state                  [,30] [,31] [,32] [,33] [,34] [,35] [,36] [,37] [,38]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                         cycle
## state                  [,39] [,40] [,41] [,42] [,43] [,44] [,45] [,46]
##   Asymptomatic_disease    NA    NA    NA    NA    NA    NA    NA    NA
##   Progressive_disease     NA    NA    NA    NA    NA    NA    NA    NA
##   Dead                    NA    NA    NA    NA    NA    NA    NA    NA
```

5. Prepare a matrix (‘trans’) to record total transitional cost per cycle by state ‘pop’ matrix records total number of people in each health state, whereas trans records the number of people who ‘enter’ the state and the cost imposed to those who newly enter the state

dimension: n_states x n_cycles x n_treatments (here n_states indicate ‘destination state’) For example, trans[“asymptomatic”, cycle=10, treatment=‘without drug’] indicates the “toll” or “transitional costs” imposed to those who arrived in the asymptomatic state at cycle 10 under the ‘without drug’ scenario

```
# _arrived_ state populations
trans <- array(data = NA,
               dim = c(n_states, n_cycles, n_treatments),
               dimnames = list(state = s_names,
                               cycle = NULL,
                               treatment = t_names))

trans[, cycle = 1, ] <- 0
```

6. Prepare empty matrices to record QALYs and Costs outcomes by cycle and by strategy by cycle: cycle_costs, cycle_QALYs, cycle_QALE, LE, LYs (dimension: n_treatments, cycles) total: total_costs, total_QALYs (1xn_treatments)

```
# Sum costs and QALYs for each cycle at a time for each drug
cycle_empty_array <-
  array(NA,
        dim = c(n_treatments, n_cycles),
        dimnames = list(treatment = t_names,
                        cycle = NULL)) # per-cycle outcome template matrix

cycle_empty_array
```

```
##                 cycle
## treatment        [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10] [,11] [,12]
##   without_drug     NA   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA    NA
##   with_drug        NA   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA    NA
##   with_drug_eol    NA   NA   NA   NA   NA   NA   NA   NA   NA    NA    NA    NA
##                 cycle
## treatment        [,13] [,14] [,15] [,16] [,17] [,18] [,19] [,20] [,21] [,22]
##   without_drug      NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   with_drug         NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   with_drug_eol     NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                 cycle
## treatment        [,23] [,24] [,25] [,26] [,27] [,28] [,29] [,30] [,31] [,32]
##   without_drug     NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   with_drug        NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   with_drug_eol    NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                 cycle
## treatment       [,33] [,34] [,35] [,36] [,37] [,38] [,39] [,40] [,41] [,42]
##   without_drug     NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   with_drug        NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##   with_drug_eol    NA    NA    NA    NA    NA    NA    NA    NA    NA    NA
##                 cycle
## treatment       [,43] [,44] [,45] [,46]
##   without_drug     NA    NA    NA    NA
##   with_drug        NA    NA    NA    NA
##   with_drug_eol    NA    NA    NA    NA
```

```
cycle_state_costs <- cycle_trans_costs <- cycle_empty_array
cycle_costs <- cycle_QALYs <- cycle_empty_array
LE <- LYs <- cycle_empty_array    # life expectancy; life-years
cycle_QALE <- cycle_empty_array   # quality-adjusted life expectancy

total_costs <- setNames(c(NA, NA, NA), t_names)
total_QALYs <- setNames(c(NA, NA, NA), t_names)
```

7. Define a function to calculate time-dependent transition probability based on age-specific mortality Because non-mortality transition probabilities can change based on mortality, we will update the transition probability matrix given age by calling the following function.

```
# Time-dependent probability matrix ----

p_matrix_cycle <- function(p_matrix, age, cycle,
                           tpProg = 0.01,
                           tpDcm = 0.15,
                           tpDcm_r = 0.075,
                           effect = 0.5) {
  tpDn_lookup <-
    c("(34,44]" = 0.0017,
      "(44,54]" = 0.0044,
      "(54,64]" = 0.0138,
      "(64,74]" = 0.0379,
      "(74,84]" = 0.0912,
      "(84,100]" = 0.1958)

  age_grp <- cut(age, breaks = c(34,44,54,64,74,84,100)) # find the age group that this age falls into
  tpDn <- tpDn_lookup[age_grp] # look up mortality table using age_grp label

  # Matrix containing transition probabilities for without_drug
  p_matrix["Asymptomatic_disease", "Progressive_disease", "without_drug"] <- tpProg*cycle
  p_matrix["Asymptomatic_disease", "Dead", "without_drug"] <- tpDn
  p_matrix["Asymptomatic_disease", "Asymptomatic_disease", "without_drug"] <- 1 - tpProg*cycle - tpDn
  p_matrix["Progressive_disease", "Dead", "without_drug"] <- tpDcm + tpDn
  p_matrix["Progressive_disease", "Progressive_disease", "without_drug"] <- 1 - tpDcm - tpDn
  p_matrix["Dead", "Dead", "without_drug"] <- 1

  # Matrix containing transition probabilities for with_drug
  p_matrix["Asymptomatic_disease", "Progressive_disease", "with_drug"] <- tpProg*(1 - effect)*cycle
  p_matrix["Asymptomatic_disease", "Dead", "with_drug"] <- tpDn
  p_matrix["Asymptomatic_disease", "Asymptomatic_disease", "with_drug"] <-
    1 - tpProg*(1 - effect)*cycle - tpDn
  p_matrix["Progressive_disease", "Dead", "with_drug"] <- tpDcm + tpDn
  p_matrix["Progressive_disease", "Progressive_disease", "with_drug"] <- 1 - tpDcm - tpDn
  p_matrix["Dead", "Dead", "with_drug"] <- 1

    # Matrix containing transition probabilities for with_drug
  p_matrix["Asymptomatic_disease", "Progressive_disease", "with_drug_eol"] <- tpProg*(1 - effect)*cycle
  p_matrix["Asymptomatic_disease", "Dead", "with_drug_eol"] <- tpDn
  p_matrix["Asymptomatic_disease", "Asymptomatic_disease", "with_drug_eol"] <-
    1 - tpProg*(1 - effect)*cycle - tpDn
  p_matrix["Progressive_disease", "Dead", "with_drug_eol"] <- tpDcm_r + tpDn
  p_matrix["Progressive_disease", "Progressive_disease", "with_drug_eol"] <- 1 - tpDcm_r - tpDn ## modi
  p_matrix["Dead", "Dead", "with_drug_eol"] <- 1

  return(p_matrix)
}
```

8. Simulate a cohort for ‘no drug’ and ‘drug’ scenario two for loops are implemented in this block

(1) given strategy (outer loop)
(2) given cycle # (inner loop)

- calculate age-specific transition probability matrix
- update pop matrix in the current cycle given pop matrix in last cycle and transition probability matrix (matrix multiplication)
- calculate trans matrix to count the number of people move from one to another state within a cycle

A * B: element-wise multiplication A %*% B: matrix multiplication (take the row of A, column of B and sum the product)

To calculate the transitional cost per cycle to arrive in each state, For example, the transitional cost of arriving in “progressive disease (state #2)” is N_1P_12C_12 + N_2P_22C_22 + N3P_32C_32 = N_1C_12P_12 + N_2C_22P_22 + N3C_32P_32 = c(N_1, N_2, N_3) %% t(c(C_12P_12, C_22P_22, C_32P_32)) = c(N_1, N_2, N_3) %% t(c(C_12,C_22,C_32) c(P_12,P_22,P_32))

trans_c_matrix * p_matrix -> transition probability-weighted transitional cost c(1,1,1) %*% column vector() -> sum of elements in the column vector

```
## Run model ----

for (i in 1:n_treatments) { # outer loop: over strategies

  age <- Initial_age

  for (j in 2:n_cycles) { # inner loop: over cycles
    # update cycle and age specific transition probability matrix
    p_matrix <- p_matrix_cycle(p_matrix, age, j - 1)
    #print(p_matrix[,,'with_drug']) # Uncomment this line to see how transition probability matrix chan
    # calculate population health state distribution in the next cycle
    pop[, cycle = j, treatment = i] <-
```

```
      pop[, cycle = j - 1, treatment = i] %*% p_matrix[, , treatment = i]
    # calculate the total transitional costs per cycle
    trans[, cycle = j, treatment = i] <-
      pop[, cycle = j - 1, treatment = i] %*% (trans_c_matrix * p_matrix[, , treatment = i])

    age <- age + 1
  }
  # calculate cycle-specific state costs given a treatment strategy
  cycle_state_costs[i, ] <-
    (state_c_matrix[treatment = i, ] %*% pop[, , treatment = i]) * 1/(1 + cDr)^(1:n_cycles - 1)

  # discounting at _previous_ cycle
  cycle_trans_costs[i, ] <-
    (c(1,1,1) %*% trans[, , treatment = i]) * 1/(1 + cDr)^(1:n_cycles - 2) # dot product with c(1,1,1)
  # per-cycle cost is the summ of state cost and transitional cost
  cycle_costs[i, ] <- cycle_state_costs[i, ] + cycle_trans_costs[i, ]

  # life expectancy
  LE[i, ] <- c(1,1,0) %*% pop[, , treatment = i]

  # life-years
  LYs[i, ] <- LE[i, ] * 1/(1 + oDr)^(1:n_cycles - 1)

  # quality-adjusted life expectancy
  cycle_QALE[i, ] <-
    state_q_matrix[treatment = i, ] %*% pop[, , treatment = i]

  # quality-adjusted life-years
  cycle_QALYs[i, ] <- cycle_QALE[i, ] * 1/(1 + oDr)^(1:n_cycles - 1)
  # calculate the total cost and qaly (sum of per-cycle costs and qalys) of each scenario
  total_costs[i] <- sum(cycle_costs[treatment = i, -1])
  total_QALYs[i] <- sum(cycle_QALYs[treatment = i, -1])
}
```

9. Incremental cost and qaly between two strategies

```
## Plot results ----
results_combined <- rbind(Costs = unlist(total_costs), QALYs = unlist(total_QALYs))
results_combined
```

```
##       without_drug    with_drug with_drug_eol
## Costs  9331448.374 16210619.637  21687012.080
## QALYs     7755.952     8624.738      8993.777
```

```
# Incremental costs and QALYs of with_drug vs to without_drug
c_incr_21 <- total_costs["with_drug"] - total_costs["without_drug"]
c_incr_32 <- total_costs["with_drug_eol"] - total_costs["with_drug"]
c_incr_31 <- total_costs["with_drug_eol"] - total_costs["without_drug"]

q_incr_21 <- total_QALYs["with_drug"] - total_QALYs["without_drug"]
q_incr_32 <- total_QALYs["with_drug_eol"] - total_QALYs["with_drug"]
q_incr_31 <- total_QALYs["with_drug_eol"] - total_QALYs["without_drug"]
```

10. Calculate ICER

```
# Incremental cost-effectiveness ratio
ICER_21 <- c_incr_21/q_incr_21
ICER_32 <- c_incr_32/q_incr_32
ICER_31 <- c_incr_31/q_incr_31

ICER_21
```

```
## with_drug
##  7918.141
```

```
ICER_32
```

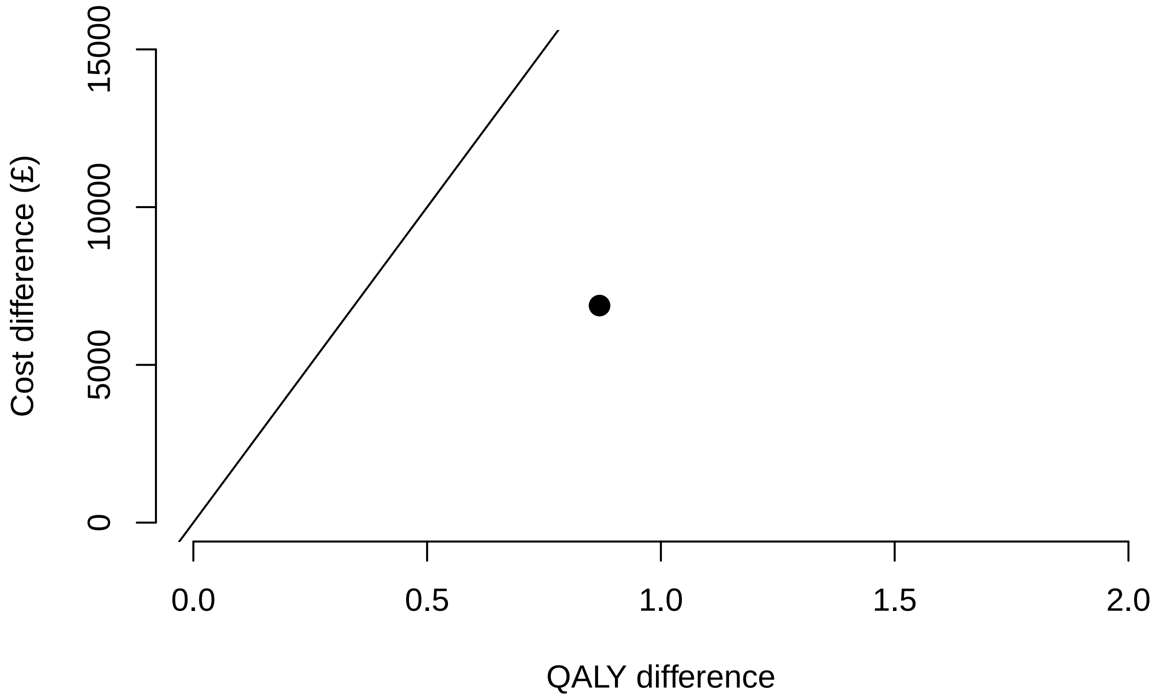
```
## with_drug_eol
##      14839.58
```

```
ICER_31
```

```
## with_drug_eol
##      9981.667
```

11. Plot 1

```
wtp <- 20000
plot(x = q_incr_21/n_cohort, y = c_incr_21/n_cohort,
     xlim = c(0, 2),
     ylim = c(0, 15e3),
     pch = 16, cex = 1.5,
     xlab = "QALY difference",
     ylab = paste0("Cost difference (", enc2utf8("\u00A3"), ")"),
     frame.plot = FALSE)
abline(a = 0, b = wtp) # willingness-to-pay threshold
```

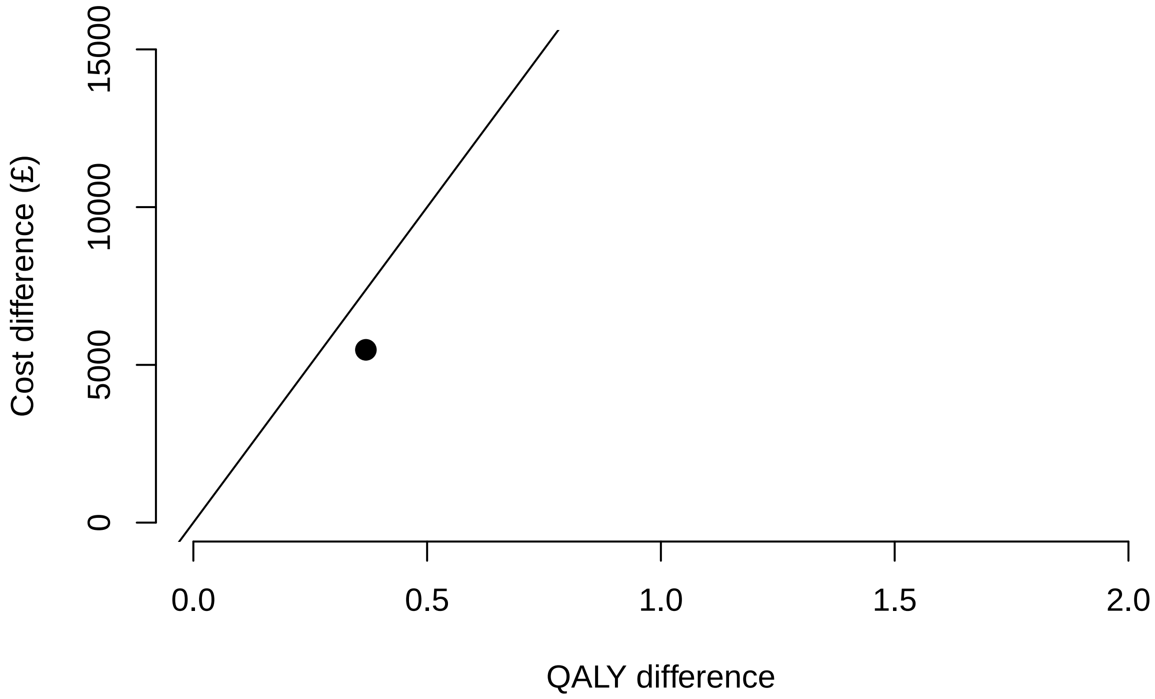


```r
png("ceplane_point.png", width = 4, height = 4, units = "in", res = 640)
plot(x = q_incr_21/n_cohort, y = c_incr_21/n_cohort,
     xlim = c(0, 2),
     ylim = c(0, 15e3),
     pch = 16, cex = 1.5,
     xlab = "QALY difference",
     ylab = paste0("Cost difference (", enc2utf8("\u00A3"), ")"),
     frame.plot = FALSE)
abline(a = 0, b = wtp) # willingness-to-pay threshold
dev.off()
```

```
## pdf
##   2
```

12. Plot 2

```r
wtp <- 20000
plot(x = q_incr_32/n_cohort, y = c_incr_32/n_cohort,
     xlim = c(0, 2),
     ylim = c(0, 15e3),
     pch = 16, cex = 1.5,
     xlab = "QALY difference",
     ylab = paste0("Cost difference (", enc2utf8("\u00A3"), ")"),
     frame.plot = FALSE)
abline(a = 0, b = wtp) # willingness-to-pay threshold
```

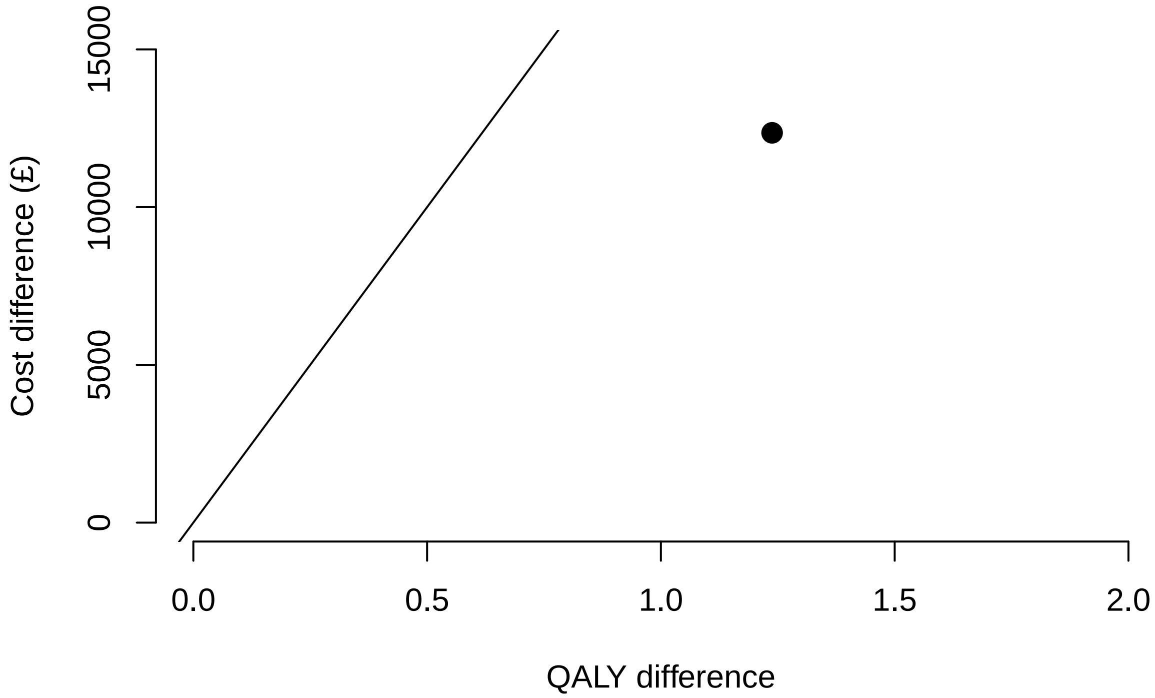


```
png("ceplane_point.png", width = 4, height = 4, units = "in", res = 640)
plot(x = q_incr_32/n_cohort, y = c_incr_32/n_cohort,
     xlim = c(0, 2),
     ylim = c(0, 15e3),
     pch = 16, cex = 1.5,
     xlab = "QALY difference",
     ylab = paste0("Cost difference (", enc2utf8("\u00A3"), ")"),
     frame.plot = FALSE)
abline(a = 0, b = wtp) # willingness-to-pay threshold
dev.off()
```

```
## pdf
##   2
```

13. Plot 3

```
wtp <- 20000
plot(x = q_incr_31/n_cohort, y = c_incr_31/n_cohort,
     xlim = c(0, 2),
     ylim = c(0, 15e3),
     pch = 16, cex = 1.5,
     xlab = "QALY difference",
     ylab = paste0("Cost difference (", enc2utf8("\u00A3"), ")"),
     frame.plot = FALSE)
abline(a = 0, b = wtp) # willingness-to-pay threshold
```



```
png("ceplane_point.png", width = 4, height = 4, units = "in", res = 640)
plot(x = q_incr_31/n_cohort, y = c_incr_31/n_cohort,
     xlim = c(0, 2),
     ylim = c(0, 15e3),
     pch = 16, cex = 1.5,
     xlab = "QALY difference",
     ylab = paste0("Cost difference (", enc2utf8("\u00A3"), ")"),
     frame.plot = FALSE)
abline(a = 0, b = wtp) # willingness-to-pay threshold
dev.off()
```

```
## pdf
##   2
```