Final Case Study

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2023-04-19

Basic dependencies:

- R>=4.1 # https://www.r-project.org/

- RStudio>=1.4.1717 # https://posit.co/download/rstudio-desktop/

R Package Dependencies

```r
options(warn=-1)
if (!require(pacman)) install.packages("pacman")
```

```
## Loading required package: pacman
```

```r
pacman::p_load(tidyverse, glmnet, iregnet, penAFT,
               survival, mice, ggsurvfit, dplyr, xtable, ggplot2)

dir.create("plots", showWarnings = F)
theme_set(theme_classic(base_size = 12))
```

System Information

```r
sessionInfo()
```

```
## R version 4.1.3 (2022-03-10)
## Platform: x86_64-redhat-linux-gnu (64-bit)
## Running under: Fedora Linux 36 (MATE-Compiz)
##
## Matrix products: default
## BLAS/LAPACK: /usr/lib64/libflexiblas.so.3.3
##
## locale:
##  [1] LC_CTYPE=en_US.UTF-8       LC_NUMERIC=C
##  [3] LC_TIME=en_US.UTF-8        LC_COLLATE=en_US.UTF-8
##  [5] LC_MONETARY=en_US.UTF-8    LC_MESSAGES=en_US.UTF-8
##  [7] LC_PAPER=en_US.UTF-8       LC_NAME=C
##  [9] LC_ADDRESS=C               LC_TELEPHONE=C
## [11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
##  [1] xtable_1.8-4       ggsurvfit_0.3.0    mice_3.15.0        survival_3.5-5
##  [5] penAFT_0.3.0       iregnet_0.1.0.9000 glmnet_4.1-7       Matrix_1.5-4
```

```
##  [9] lubridate_1.9.2    forcats_1.0.0     stringr_1.5.0       dplyr_1.1.2
## [13] purrr_1.0.1        readr_2.1.4       tidyr_1.3.0         tibble_3.2.1
## [17] ggplot2_3.4.2      tidyverse_2.0.0   pacman_0.5.1
##
## loaded via a namespace (and not attached):
##  [1] shape_1.4.6         tidyselect_1.2.0   xfun_0.39
##  [4] listenv_0.9.0       splines_4.1.3      lattice_0.21-8
##  [7] colorspace_2.1-0    vctrs_0.6.2        generics_0.1.3
## [10] htmltools_0.5.5     yaml_2.3.7         utf8_1.2.3
## [13] rlang_1.1.0         pillar_1.9.0       glue_1.6.2
## [16] withr_2.5.0         foreach_1.5.2      lifecycle_1.0.3
## [19] munsell_0.5.0       gtable_0.3.3       future_1.32.0
## [22] codetools_0.2-19    evaluate_0.20      knitr_1.42
## [25] tzdb_0.3.0          fastmap_1.1.1      irlba_2.3.5.1
## [28] parallel_4.1.3      fansi_1.0.4        broom_1.0.4
## [31] Rcpp_1.0.10         backports_1.4.1    scales_1.2.1
## [34] parallelly_1.35.0   RhpcBLASctl_0.23-42 hms_1.1.3
## [37] digest_0.6.31       stringi_1.7.12     grid_4.1.3
## [40] cli_3.6.1           tools_4.1.3        magrittr_2.0.3
## [43] future.apply_1.10.0 pkgconfig_2.0.3    timechange_0.2.0
## [46] rmarkdown_2.21      rstudioapi_0.14    iterators_1.0.14
## [49] R6_2.5.1            globals_0.16.2     compiler_4.1.3
```

Load data

```r
data = read.csv('METABRIC_RNA_Mutation.csv')

sum(is.na(data))
```

```
## [1] 638
```

```r
# drop the patient with sarcoma
sum(data$cancer_type == "Breast Sarcoma")
```

```
## [1] 1
```

```r
# only keep patients with Breast Invasive Ductal Carcinoma
data = data[data$cancer_type_detailed == 'Breast Invasive Ductal Carcinoma',]

# Drop the rare claudin low subtype
data = data[data$pam50_._claudin.low_subtype != 'NC',]

# drop: patient_id
data = data %>% select(-c('patient_id', 'cancer_type', 'cancer_type_detailed', 'cohort', 'overall_surviv

sum(is.na(data))
```

```
## [1] 498
```

```r
# select only the ones for which we know the surgery type
data_sel = data[data$type_of_breast_surgery != "",]

sum(is.na(data_sel$overall_survival_months))
```

```
## [1] 0
```

```r
data_sel = Filter(function(x)(length(unique(x))>1), data_sel)
data_BIDC = data_sel
```

```
#print(names(data_BIDC))

#sum(is.na(data_sel))

num_cols = ncol(data_sel)
for (i in 1:num_cols)
{
  if (sum(is.na(data_sel[,i])) > 0)
  {
    print(i)
    print(colnames(data_sel[i]))
  }
}
```

```
## [1] 8
## [1] "neoplasm_histologic_grade"
## [1] 17
## [1] "mutation_count"
## [1] 23
## [1] "tumor_size"
## [1] 24
## [1] "tumor_stage"
```

```
# Recode the treatment prodecures: 0 - breast conserving, 1 - mastectomy
data_BIDC$treatment = 1*(data_BIDC$type_of_breast_surgery == "MASTECTOMY")
unique(data_BIDC$type_of_breast_surgery)
```

```
## [1] "MASTECTOMY"       "BREAST CONSERVING"
```

```
data_BIDC$primary_tumor_laterality[data_BIDC$primary_tumor_laterality == ""] = NA
data_BIDC$inferred_menopausal_state[data_BIDC$inferred_menopausal_state == ""] = NA
data_BIDC$er_status_measured_by_ihc[data_BIDC$er_status_measured_by_ihc == ""] = NA


sum(is.na(data_BIDC$primary_tumor_laterality))
```

```
## [1] 83
```

```
sum(is.na(data_BIDC$inferred_menopausal_state))
```

```
## [1] 0
```

```
sum(is.na(data_BIDC$er_status_measured_by_ihc))
```

```
## [1] 22
```

```
sum(is.na(data_BIDC[,26:514]))
```

```
## [1] 0
```

Data Imputation with MICE

```
# categorical_vars <- c("cellularity", "pam50_._claudin.low_subtype",
#                       "neoplasm_histologic_grade", "tumor_other_histologic_subtype",
#                       "integrative_cluster", "X3.gene_classifier_subtype")
#
# other_categorical = c("inferred_menopausal_state",
```

```
#                       "primary_tumor_laterality",
#                       "pr_status",
#                       "tumor_stage",
#                       "her2_status",
#                       "er_status_measured_by_ihc",
#                       "radio_therapy", "hormone_therapy", "chemotherapy")


categorical_vars <- c("cellularity", "pam50_._claudin.low_subtype",
                      "neoplasm_histologic_grade", "tumor_other_histologic_subtype",
                      "integrative_cluster", "X3.gene_classifier_subtype")

other_categorical = c("inferred_menopausal_state",
                      "primary_tumor_laterality",
                      "pr_status",
                      "tumor_stage",
                      "her2_status",
                      "er_status_measured_by_ihc",
                      "radio_therapy", "hormone_therapy", "chemotherapy")

data_mice <- data_BIDC %>% mutate(across(all_of(unlist(c(categorical_vars, other_categorical))), factor)

data_BIDC_2 = data_BIDC
data_BIDC_3 = data_BIDC
data_BIDC_4 = data_BIDC
data_BIDC_5 = data_BIDC

data_mice = data_mice[,1:24]
#sum(is.na(data_mice))
names(data_mice)
```

```
##  [1] "age_at_diagnosis"              "type_of_breast_surgery"
##  [3] "cellularity"                   "chemotherapy"
##  [5] "pam50_._claudin.low_subtype"   "er_status_measured_by_ihc"
##  [7] "er_status"                     "neoplasm_histologic_grade"
##  [9] "her2_status_measured_by_snp6"  "her2_status"
## [11] "tumor_other_histologic_subtype" "hormone_therapy"
## [13] "inferred_menopausal_state"     "integrative_cluster"
## [15] "primary_tumor_laterality"      "lymph_nodes_examined_positive"
## [17] "mutation_count"                "nottingham_prognostic_index"
## [19] "overall_survival_months"       "pr_status"
## [21] "radio_therapy"                 "X3.gene_classifier_subtype"
## [23] "tumor_size"                    "tumor_stage"
```

```
set.seed(5)
mice_obj <- mice(data = data_mice, m = 5)
```

```
##
##  iter imp variable
##   1   1  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   1   2  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   1   3  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   1   4  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   1   5  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
```

```
##   2   1  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   2   2  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   2   3  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   2   4  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   2   5  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   3   1  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   3   2  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   3   3  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   3   4  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   3   5  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   4   1  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   4   2  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   4   3  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   4   4  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   4   5  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   5   1  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   5   2  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   5   3  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   5   4  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
##   5   5  er_status_measured_by_ihc  neoplasm_histologic_grade  primary_tumor_laterality  mutation_cou
```

```r
data_full <- complete(mice_obj,1)
data_full_2 <- complete(mice_obj,2)
data_full_3 <- complete(mice_obj,3)
data_full_4 <- complete(mice_obj,4)
data_full_5 <- complete(mice_obj,5)

data_BIDC[,1:24] = data_full
data_BIDC_2[,1:24] = data_full_2
data_BIDC_3[,1:24] = data_full_3
data_BIDC_4[,1:24] = data_full_4
data_BIDC_5[,1:24] = data_full_5

data_BIDC$tumor_stage = 0*(data_BIDC$tumor_stage == 0) + 1*(data_BIDC$tumor_stage == 1) + 2*(data_BIDC$

data_BIDC_2$tumor_stage = 0*(data_BIDC_2$tumor_stage == 0) + 1*(data_BIDC_2$tumor_stage == 1) + 2*(data_

data_BIDC_3$tumor_stage = 0*(data_BIDC_3$tumor_stage == 0) + 1*(data_BIDC_3$tumor_stage == 1) + 2*(data_

data_BIDC_4$tumor_stage = 0*(data_BIDC_4$tumor_stage == 0) + 1*(data_BIDC_4$tumor_stage == 1) + 2*(data_

data_BIDC_5$tumor_stage = 0*(data_BIDC_5$tumor_stage == 0) + 1*(data_BIDC_5$tumor_stage == 1) + 2*(data_

# sum(data_BIDC$tumor_stage == 0)
# sum(data$tumor_stage == 4,na.rm = TRUE)

# Drop patients with stage 0 or stage 4 tumor
# data_full_2 = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4,]
# data_full_3 = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4,]
# data_full_4 = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4,]
# data_full_5 = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4,]


# 0 - pre, 1 - post menopause
```

```r
data_BIDC$menopause = 1*(data_BIDC$inferred_menopausal_state == "Post")

# 0 - left, 1 - right
data_BIDC$tumor_laterality = 1*(data_BIDC$primary_tumor_laterality == "Right")

# Recode more variables
data_BIDC$progesterone_status = 1*(data_BIDC$pr_status == "Positive")
data_BIDC$HER2_status = 1*(data_BIDC$her2_status == "Positive")
data_BIDC$er_status_ihc = 1*(data_BIDC$er_status_measured_by_ihc == "Positive")

#####################################################
# 0 - pre, 1 - post menopause
data_BIDC_2$menopause = 1*(data_BIDC_2$inferred_menopausal_state == "Post")

# 0 - left, 1 - right
data_BIDC_2$tumor_laterality = 1*(data_BIDC_2$primary_tumor_laterality == "Right")

# Recode more variables
data_BIDC_2$progesterone_status = 1*(data_BIDC_2$pr_status == "Positive")
data_BIDC_2$HER2_status = 1*(data_BIDC_2$her2_status == "Positive")
data_BIDC_2$er_status_ihc = 1*(data_BIDC_2$er_status_measured_by_ihc == "Positive")
#####################################################

#####################################################
# 0 - pre, 1 - post menopause
data_BIDC_3$menopause = 1*(data_BIDC_3$inferred_menopausal_state == "Post")

# 0 - left, 1 - right
data_BIDC_3$tumor_laterality = 1*(data_BIDC_3$primary_tumor_laterality == "Right")

# Recode more variables
data_BIDC_3$progesterone_status = 1*(data_BIDC_3$pr_status == "Positive")
data_BIDC_3$HER2_status = 1*(data_BIDC_3$her2_status == "Positive")
data_BIDC_3$er_status_ihc = 1*(data_BIDC_3$er_status_measured_by_ihc == "Positive")
#####################################################

#####################################################
# 0 - pre, 1 - post menopause
data_BIDC_4$menopause = 1*(data_BIDC_4$inferred_menopausal_state == "Post")

# 0 - left, 1 - right
data_BIDC_4$tumor_laterality = 1*(data_BIDC_4$primary_tumor_laterality == "Right")

# Recode more variables
data_BIDC_4$progesterone_status = 1*(data_BIDC_4$pr_status == "Positive")
data_BIDC_4$HER2_status = 1*(data_BIDC_4$her2_status == "Positive")
data_BIDC_4$er_status_ihc = 1*(data_BIDC_4$er_status_measured_by_ihc == "Positive")
#####################################################

#####################################################
# 0 - pre, 1 - post menopause
data_BIDC_5$menopause = 1*(data_BIDC_5$inferred_menopausal_state == "Post")
```

```r
# 0 - left, 1 - right
data_BIDC_5$tumor_laterality = 1*(data_BIDC_5$primary_tumor_laterality == "Right")

# Recode more variables
data_BIDC_5$progesterone_status = 1*(data_BIDC_5$pr_status == "Positive")
data_BIDC_5$HER2_status = 1*(data_BIDC_5$her2_status == "Positive")
data_BIDC_5$er_status_ihc = 1*(data_BIDC_5$er_status_measured_by_ihc == "Positive")
####################################################

data_BIDC_excl = data_BIDC[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4,]

data_BIDC_excl_2 = data_BIDC[data_BIDC_2$tumor_stage != 0 & data_BIDC_2$tumor_stage != 4,]
data_BIDC_excl_3 = data_BIDC[data_BIDC_3$tumor_stage != 0 & data_BIDC_3$tumor_stage != 4,]
data_BIDC_excl_4 = data_BIDC[data_BIDC_4$tumor_stage != 0 & data_BIDC_4$tumor_stage != 4,]
data_BIDC_excl_5 = data_BIDC[data_BIDC_5$tumor_stage != 0 & data_BIDC_5$tumor_stage != 4,]

# Mutation indicators
gene_expr_names = names(data_BIDC)[26:514]
mutation_names = names(data_BIDC)[515:687]

for (var in mutation_names) {
  data_BIDC[[var]] <- as.integer(data_BIDC[[var]] != 0)

  data_BIDC_2[[var]] <- as.integer(data_BIDC_2[[var]] != 0)
  data_BIDC_3[[var]] <- as.integer(data_BIDC_3[[var]] != 0)
  data_BIDC_4[[var]] <- as.integer(data_BIDC_4[[var]] != 0)
  data_BIDC_5[[var]] <- as.integer(data_BIDC_5[[var]] != 0)
}




# Exclude patients with rare mutations
p = ncol(data_BIDC)
n = nrow(data_BIDC)
include = rep(FALSE, n)

n_2 = nrow(data_BIDC_2)
n_3 = nrow(data_BIDC_3)
n_4 = nrow(data_BIDC_4)
n_5 = nrow(data_BIDC_5)

include_2 = rep(FALSE, nrow(data_BIDC_2))
include_3 = rep(FALSE, nrow(data_BIDC_3))
include_4 = rep(FALSE, nrow(data_BIDC_4))
include_5 = rep(FALSE, nrow(data_BIDC_5))

for (i in 1:n)
{
  if (sum(as.numeric(data_BIDC[i,c(608, 611:614, 616:687)]))  == 0)
  {
    include[i] = TRUE
  }
}
```

```
# for (i in 1:n_2)
# {
#   print(i)
#   if (sum(as.numeric(data_BIDC_2[i,c(608, 611:614, 616:687)])) == 0)
#   {
#     include_2[i] = TRUE
#   }
# }
#
# for (i in 1:n_3)
# {
#   if (sum(as.numeric(data_BIDC_3[i,c(608, 611:614, 616:687)])) == 0)
#   {
#     include_3[i] = TRUE
#   }
# }
#
# for (i in 1:n_4)
# {
#   if (sum(as.numeric(data_BIDC_4[i,c(608, 611:614, 616:687)])) == 0)
#   {
#     include_4[i] = TRUE
#   }
# }
#
# for (i in 1:n_5)
# {
#   if (sum(as.numeric(data_BIDC_5[i,c(608, 611:614, 616:687)])) == 0)
#   {
#     include_5[i] = TRUE
#   }
# }

sum(include)
```

```
## [1] 889
```

```
data_BIDC_common = data_BIDC[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & include,]

data_BIDC_common_2 = data_BIDC_2[data_BIDC_2$tumor_stage != 0 & data_BIDC_2$tumor_stage != 4 & include,]
data_BIDC_common_3 = data_BIDC_3[data_BIDC_3$tumor_stage != 0 & data_BIDC_3$tumor_stage != 4 & include,]
data_BIDC_common_4 = data_BIDC_4[data_BIDC_4$tumor_stage != 0 & data_BIDC_4$tumor_stage != 4 & include,]
data_BIDC_common_5 = data_BIDC_5[data_BIDC_5$tumor_stage != 0 & data_BIDC_5$tumor_stage != 4 & include,]
```

```
nrow(data_BIDC_common)
```

```
## [1] 879
```

Sensitivity analysis data

```
# data_BIDC_2 = data_BIDC[include,]
# data_BIDC_3 = data_BIDC[include,]
```

```
# data_BIDC_4 = data_BIDC[include,]
# data_BIDC_5 = data_BIDC[include,]
#
# unique(data_BIDC_2$tumor_stage)

# data_BIDC_3 = data_BIDC[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & include,]
# data_BIDC_4 = data_BIDC[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & include,]
# data_BIDC_5 = data_BIDC[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & include,]

#colnames(data_BIDC)[1:24]
#colnames(x)[1:24]

# data_BIDC_2[,c(8,17,23,24)] = data_full_2[data_full_2$tumor_stage != 0 & data_full_2$tumor_stage != 4
#
# unique(data_BIDC_2$tumor_stage)
#
# data_BIDC_3[,c(8,17,23,24)] = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & i
#
# data_BIDC_4[,c(8,17,23,24)] = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & i
#
# data_BIDC_5[,c(8,17,23,24)] = data_full_2[data_BIDC$tumor_stage != 0 & data_BIDC$tumor_stage != 4 & i


# data_BIDC_common_2 = data_BIDC_2
# data_BIDC_common_3 = data_BIDC_3
# data_BIDC_common_4 = data_BIDC_4
# data_BIDC_common_5 = data_BIDC_5

# delete mutations which did not occur
mutation_names = setdiff(mutation_names, c("hras_mut", "siah1_mut", "smarcb1_mut", "stmn2_mut", "foxo1_m

# delete rare mutations
mutation_names = setdiff(mutation_names, names(data_BIDC)[c(608, 611:614, 616:685)])
```

Creating model matrix

```
# Convert the mutation variables, categorical variables, and treatment to factors

categorical_vars <- c("cellularity", "pam50_._claudin.low_subtype",
                      "neoplasm_histologic_grade", "tumor_other_histologic_subtype",
                      "integrative_cluster", "X3.gene_classifier_subtype", 'tumor_stage')

categorical_recoded <- c("menopause", "HER2_status", "progesterone_status", "tumor_laterality", "radio_
#data_BIDC_2 <- mutate_at(data_BIDC, vars(mutation_names, categorical_vars, "treatment"), as.factor)

data_BIDC_common <- data_BIDC_common %>% mutate(across(all_of(unlist(c(categorical_vars))), as.factor))

#######################
data_BIDC_common_2 <- data_BIDC_common_2 %>% mutate(across(all_of(unlist(c(categorical_vars))), as.facto
data_BIDC_common_3 <- data_BIDC_common_3 %>% mutate(across(all_of(unlist(c(categorical_vars))), as.facto
data_BIDC_common_4 <- data_BIDC_common_4 %>% mutate(across(all_of(unlist(c(categorical_vars))), as.facto
data_BIDC_common_5 <- data_BIDC_common_5 %>% mutate(across(all_of(unlist(c(categorical_vars))), as.facto
```

```r
###########################
# sum(data_BIDC_common$pam50_._claudin.low_subtype == 'NC')
# unique(data_BIDC_common$pam50_._claudin.low_subtype)
#
# unique(data_BIDC$cellularity)
# unique(data_BIDC$pam50_._claudin.low_subtype)
# unique(data_BIDC$neoplasm_histologic_grade)
# sum(is.na(data_BIDC$neoplasm_histologic_grade))
#
# unique(data_BIDC$tumor_other_histologic_subtype)
#
# unique(data_BIDC$integrative_cluster)
#
# unique(data_BIDC$X3.gene_classifier_subtype)


# Create the interaction terms
interaction_terms <- lapply(1:length(gene_expr_names), function(i) {
  if (paste0(gene_expr_names[i], "_mut") %in% mutation_names) {
    return(paste0(gene_expr_names[i], ":", gene_expr_names[i], "_mut"))
  }
})
interaction_terms <- unlist(interaction_terms)

# Define the main effects variables
main_effects <- c("age_at_diagnosis", "lymph_nodes_examined_positive", "tumor_size")

# Create the formula for the model matrix
# formula <- paste(" ~ ", paste(main_effects, collapse = " + "), " + ",
#                  paste(categorical_vars, collapse = " + "), " + ",
#                  paste(gene_expr_names, collapse = " + "), " + ",
#                  paste(interaction_terms, collapse = " + "), " + ",
#                  paste("treatment", "(", paste(main_effects, categorical_vars, gene_expr_names, colla
#                  " -1")

# Create the model matrix
#model_matrix <- model.matrix(as.formula(formula), data = data_BIDC)

#cat(formula, "\n")


vars1 = paste(main_effects, collapse = " + ")
vars2 = paste(categorical_vars, collapse = " + ")
vars3 = paste(categorical_recoded, collapse = " + ")
vars3 = paste(gene_expr_names, collapse = " + ")
vars4 = paste(interaction_terms, collapse = " + ")


vars_all = paste(vars1, vars2, vars3, vars4, sep = " + ")
form = paste(" ~  ", "treatment + ", vars_all, " + treatment:(", vars_all, ")")

# STANDARDIZE THE VARIABLES FOLLOWING GELMAN
data_BIDC_common_std = data_BIDC_common
```

```
data_BIDC_common_std_2 = data_BIDC_common_2
data_BIDC_common_std_3 = data_BIDC_common_3
data_BIDC_common_std_4 = data_BIDC_common_4
data_BIDC_common_std_5 = data_BIDC_common_5

cont.names = c(main_effects, gene_expr_names)

for (i in 1:ncol(data_BIDC_common))
{
  if (names(data_BIDC_common)[i] %in% cont.names)
  {
    data_BIDC_common_std[,i] = (data_BIDC_common[,i] - mean(data_BIDC_common[,i]))/ (2*sd(data_BIDC_comm

    data_BIDC_common_std_2[,i] = (data_BIDC_common_2[,i] - mean(data_BIDC_common_2[,i]))/ (2*sd(data_BI

    data_BIDC_common_std_3[,i] = (data_BIDC_common_3[,i] - mean(data_BIDC_common_3[,i]))/ (2*sd(data_BI

        data_BIDC_common_std_4[,i] = (data_BIDC_common_4[,i] - mean(data_BIDC_common_4[,i]))/ (2*sd(data

          data_BIDC_common_std_5[,i] = (data_BIDC_common_5[,i] - mean(data_BIDC_common_5[,i]))/ (2*sd

  }
}



model_matrix <- model.matrix(as.formula(form), data = data_BIDC_common_std)

model_matrix_2 <- model.matrix(as.formula(form), data = data_BIDC_common_std_2)
model_matrix_3 <- model.matrix(as.formula(form), data = data_BIDC_common_std_3)
model_matrix_4 <- model.matrix(as.formula(form), data = data_BIDC_common_std_4)
model_matrix_5 <- model.matrix(as.formula(form), data = data_BIDC_common_std_5)


delta_2 = 1*(data_BIDC_common_2$death_from_cancer == "Died of Disease")
delta_3 = 1*(data_BIDC_common_3$death_from_cancer == "Died of Disease")
delta_4 = 1*(data_BIDC_common_4$death_from_cancer == "Died of Disease")
delta_5 = 1*(data_BIDC_common_5$death_from_cancer == "Died of Disease")

y_2 = Surv(data_BIDC_common_2$overall_survival_months, delta_2)
y_3 = Surv(data_BIDC_common_3$overall_survival_months, delta_3)
y_4 = Surv(data_BIDC_common_4$overall_survival_months, delta_4)
y_5 = Surv(data_BIDC_common_5$overall_survival_months, delta_5)

treatment_2 = data_BIDC_common_2$treatment
treatment_3 = data_BIDC_common_3$treatment
treatment_4 = data_BIDC_common_4$treatment
treatment_5 = data_BIDC_common_5$treatment

dataX = model_matrix[,2:ncol(model_matrix)]
logY = log(data_BIDC_common$overall_survival_months)
delta = 1*(data_BIDC_common$death_from_cancer == "Died of Disease")
```

```r
x = model_matrix
y = Surv(data_BIDC_common$overall_survival_months, delta)

p = ncol(dataX)

#weight.set <- list("w" = c(0, rep(1, p-1)))
set.seed(3)
fit.en.cv <- penAFT.cv(dataX, logY, delta, alpha = 0.5, nlambda = 30, nfolds = 5)
```

```
## CV through:   ###                     20 %
## CV through:   ### ###                 40 %
## CV through:   ### ### ###             60 %
## CV through:   ### ### ### ###         80 %
## CV through:   ### ### ### ### ###     100 %
```

Out-of-sample performance - concordance

```r
########################################
####### OUT OF SAMPLE PERFORMANCE ######
########################################

get.concordance = function(pred_test, truth_test, death)
{
  nvalid = length(pred_test)
  agree.count = 0
  pair.count = 0
  for (i in 2:nvalid)
  {
    for (j in 1:(i-1))
    {
      pair.count = pair.count + death[j]
      agree.count = agree.count + death[j]*((pred_test[i] >= pred_test[j]) == (truth_test[i] >= truth_te
    }
  }

  concord = agree.count / pair.count
  return(concord)
}

ndata = nrow(data_BIDC_common)
nvalid = floor(0.3*nrow(data_BIDC_common))

#ndata = nrow(dataX)
#nvalid = floor(0.3*nrow(dataX))

#set.seed(4)

set.seed(4)
index = sample(1:ndata, size = nvalid, replace = FALSE)
test_data = data_BIDC_common[index,]
train_data = data_BIDC_common[-index,]

#en.gehan = penAFT(dataX[-index,], logY[-index], delta[-index], alpha = 0.6, lambda = c(lambda.gehan))
```

```
set.seed(8)
en.gehan.cv = penAFT.cv(dataX[-index,], logY[-index], delta[-index], alpha = 0.5, nlambda = 30, nfold =
```

```
## CV through:  ###                     20 %
## CV through:  ### ###                 40 %
## CV through:  ### ### ###             60 %
## CV through:  ### ### ### ###         80 %
## CV through:  ### ### ### ### ###     100 %
```

```
##############################################################
###### Change after fixing package #########################

lambda = en.gehan.cv$full.fit$lambda
cv.err.linPred = en.gehan.cv$cv.err.linPred
lambda[which(cv.err.linPred == min(cv.err.linPred))]
```

```
## [1] 0.02274304
```

```
best.ind = which.min(cv.err.linPred)
lambda.min = lambda[which.min(cv.err.linPred)]
lambda.gehan = lambda.min

#beta.gehan = fit.en.cv$full.fit$beta[,best.ind]
##############################################################

#saveRDS(en.gehan.cv, file = 'gehan_train.RDS')
#en.gehan = penAFT(dataX[-index,], logY[-index], delta[-index], alpha = 0.6, nlambda = 10)

x = model_matrix

set.seed(6)
p = ncol(x)
penalty = c(0, rep(1, p-1))
en.cox.cv =  cv.glmnet(x[-index,], y[-index,], family = "cox", alpha = 0.5, nlambda = 30, nfold = 5)
```

```
en.cox.cv$index
```

```
##      Lambda
## min       6
## 1se       3
```

```
beta.cox = en.cox.cv$glmnet.fit$beta[,8]
lambda.cox = en.cox.cv$glmnet.fit$lambda[8]
preds.cox <- x[index,]%*%beta.cox

truth_test = logY[index]
death = delta[index]


preds.gehan <- penAFT.predict(en.gehan.cv, Xnew = dataX[index,], lambda = lambda.gehan)

get.concordance(-preds.cox, truth_test, death)
```

```
## [1] 0.677399
```

```
get.concordance(preds.gehan, truth_test, death)
```

```
## [1] 0.6635101
```

Causal Inference

Propensity Scores

```r
x = model_matrix

delta = 1*(data_BIDC_common$death_from_cancer == "Died of Disease")
y = Surv(data_BIDC_common$overall_survival_months, delta)

# PROPENSITY SCORES

vars1 = paste(main_effects, collapse = " + ")
vars2 = paste(categorical_vars, collapse = " + ")
vars3 = paste(categorical_recoded, collapse = " + ")
vars3 = paste(gene_expr_names, collapse = " + ")
vars4 = paste(interaction_terms, collapse = " + ")

x = model_matrix

vars_all = paste(vars1, vars2, vars3, vars4, sep = " + ")
form_2 = paste("treatment ~  ", vars_all)

x_prop <- model.matrix(as.formula(form_2), data = data_BIDC_common_std)
treatment = data_BIDC_common$treatment

# ridge regression
set.seed(3)
prop.cv  = cv.glmnet(x_prop, treatment, family = "binomial", alpha = 0, nlambda = 30, nfold = 5)
e.vec = predict(prop.cv, newx = x_prop, s = prop.cv$lambda.min, type = 'response')
omega = 1
W.vec = omega / (treatment*e.vec + (1-treatment)*e.vec)
W.vec = c(W.vec)
```

EDA

```r
data_EDA = data_BIDC_common
data_EDA$prop_score = e.vec

data_EDA$death = ifelse(delta, "Yes", "No")


print(nrow(data_EDA))
```

```
## [1] 879
```

```r
print(sum(delta))
```

```
## [1] 303
```

```r
data_EDA$treatment_name = data_EDA$type_of_breast_surgery


g1 <- ggplot(data_EDA, aes(x = treatment_name, fill = death)) +
```

```r
  geom_bar(position = "fill") +
  ggtitle("Censoring by Treatment") +
  theme(axis.title.x = element_blank()) +
  labs(fill = "Death Observed", y = "Proportion")


pdf("plots/censoring_by_trt.pdf", height = 3.5, width = 6)
g1
dev.off()
```

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

```r
data_EDA = data_BIDC_common
data_EDA$prop_score = e.vec
data_EDA$Mastectomy = as.factor(data_EDA$treatment)

p_prop_score <- ggplot(data_EDA, aes(x = prop_score, fill = Mastectomy,
                                     color = Mastectomy)) +
  geom_density(alpha = 0.5) +
  labs(x = "Propensity Score",
       y = "Density",
       fill = "Treatment:") +
  scale_color_discrete(guide = "none")
p_prop_score
```
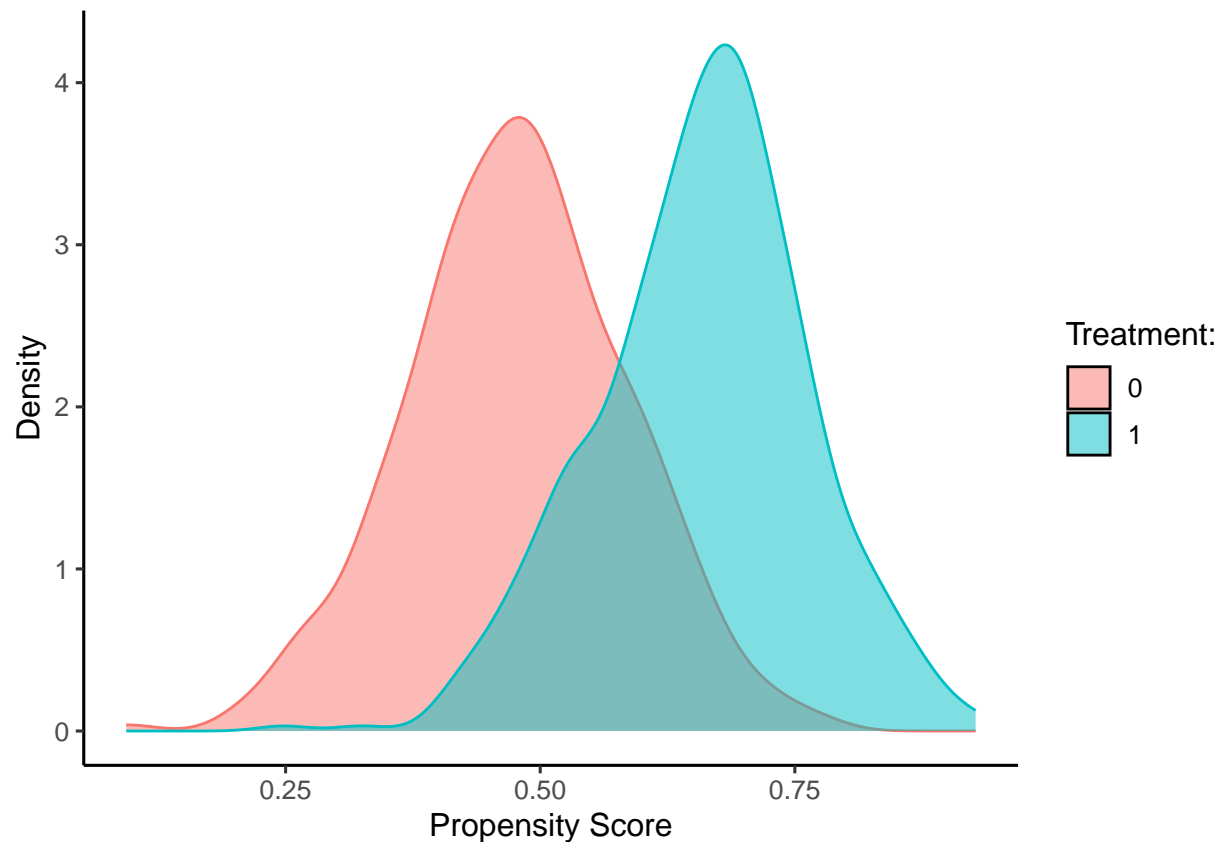


```r
PlotKMCurve <- function(group_var, var_name = NULL, data, y) {
  if (is.null(var_name)) var_name <- group_var
```

```
  survfit2(y ~ get(group_var), data = data) %>%
    ggsurvfit() +
    add_confidence_interval() +
    labs(
      x = "Days",
      y = "Survival probability",
      fill = element_blank(), color = element_blank()
    )
}

fig1 <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA, y) +
  labs(subtitle = "") +
  scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
  scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))

pdf("plots/surv_curve.pdf", height = 3.5, width = 6)
fig1
dev.off()
```

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

```
fig_stage1 <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA[data_EDA$tumor_stage == 1,], y[data_EI
  labs(subtitle = "Stage I Tumor Patients") +
  scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
  scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))

fig_stage2 <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA[data_EDA$tumor_stage == 2,], y[data_EI
  labs(subtitle = "Stage II Tumor Patients") +
  scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
  scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))


fig_stage3 <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA[data_EDA$tumor_stage == 3,], y[data_EI
  labs(subtitle = "Stage III Tumor Patients") +
  scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
  scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))


fig_stage1
```

Stage I Tumor Patients

fig_stage2

Stage II Tumor Patients

```
fig_stage3
```

Stage III Tumor Patients
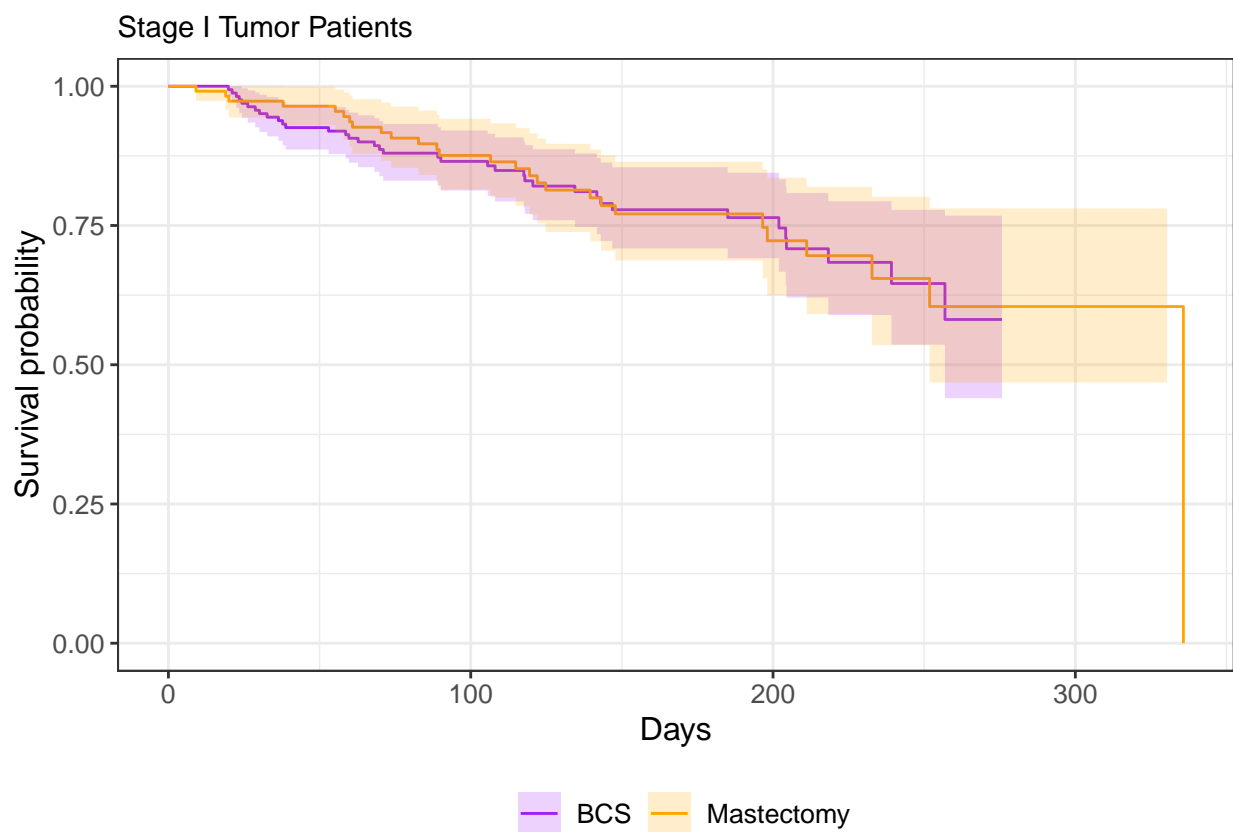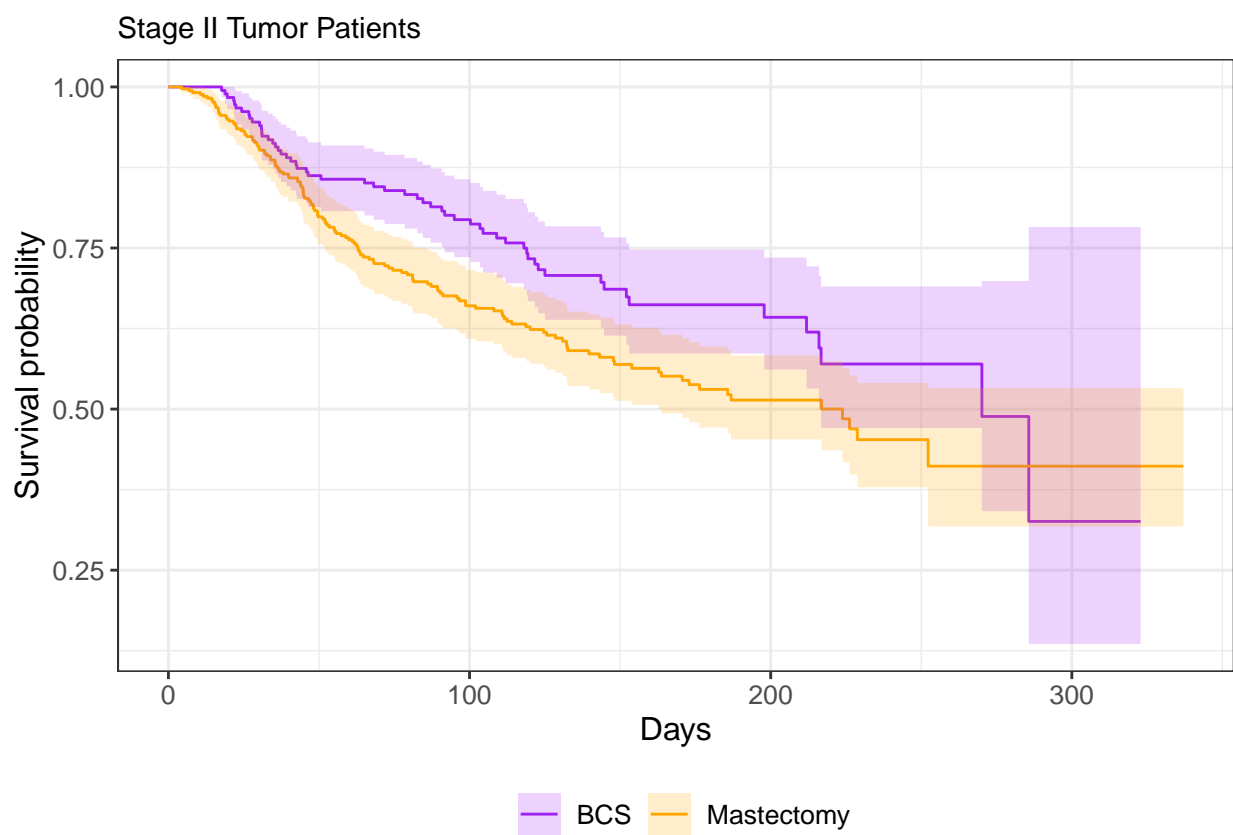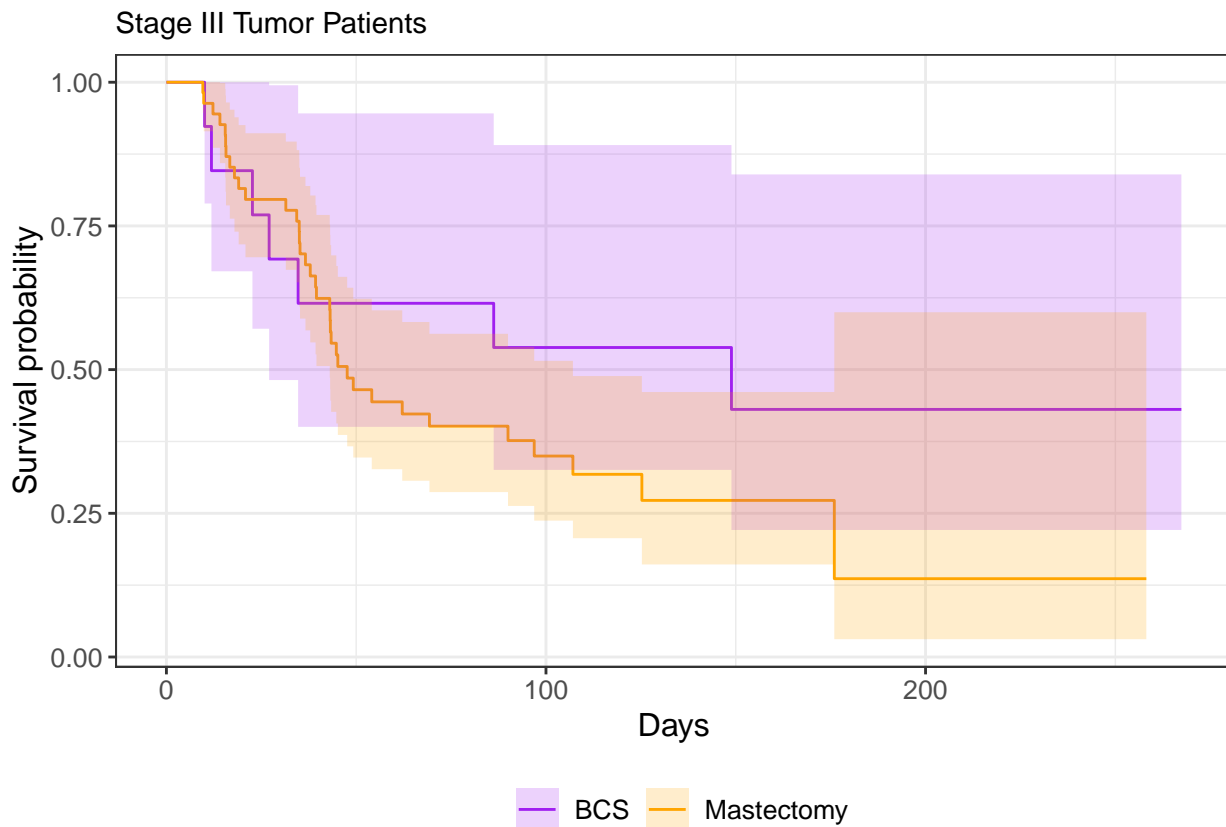

```
pdf("plots/stage1_diff.pdf", height = 3.5, width = 6)
fig_stage1
dev.off()

## pdf
##   2

pdf("plots/stage2_diff.pdf", height = 3.5, width = 6)
fig_stage2
dev.off()

## pdf
##   2

pdf("plots/stage3_diff.pdf", height = 3.5, width = 6)
fig_stage3
dev.off()

## pdf
##   2

data_EDA$hormone_therapy

##   [1] 1 1 1 1 1 0 1 1 1 1 1 0 1 1 1 1 1 0 1 1 1 1 1 1 1 1 1 1 1 1 0 1 1 1 1 1 1 1 1 1 1 0
##  [38] 1 1 1 0 0 1 1 1 1 1 1 0 1 1 1 0 1 1 0 0 1 1 1 0 0 1 1 1 0 1 0 0 0 1 1 1 1
##  [75] 0 1 0 0 1 1 0 1 1 1 1 1 1 0 0 0 1 1 1 0 0 1 1 0 1 1 1 1 1 1 1 1 1 1 1 0 1 0
## [112] 1 1 1 1 1 1 1 1 0 0 1 1 1 1 1 1 1 1 1 1 0 1 1 1 1 1 1 1 1 1 0 1 0 1 1 0 0 0 1 1 1
## [149] 1 1 0 1 0 1 1 1 0 0 1 1 1 1 1 1 1 1 1 1 1 1 0 1 1 0 1 0 1 1 0 1 1 0 1 1 0 1 1
```

18

```
## [186] 0 1 1 1 1 0 1 1 1 1 1 1 1 0 1 1 1 1 1 1 1 1 1 1 1 1 0 1 1 1 1 1 1 1 1 1 1 1
## [223] 0 1 1 1 1 1 1 1 1 1 1 1 0 1 1 1 1 0 1 1 1 1 1 1 1 0 1 1 1 1 1 1 0 1 1 1 1 1
## [260] 1 0 0 0 1 1 1 1 1 0 1 0 1 1 1 0 0 1 1 1 0 0 0 1 0 0 0 0 1 1 1 1 1 0 1 1 0
## [297] 1 1 1 1 0 1 1 0 1 0 1 0 0 0 0 0 1 0 0 0 0 0 1 1 0 0 1 1 1 1 0 0 0 1 0 0 1
## [334] 1 1 1 0 0 1 0 1 1 0 1 1 0 1 1 0 1 1 1 0 0 0 1 1 0 1 1 1 1 1 0 0 0 1 0 0 1 1 1 0
## [371] 0 0 1 0 0 1 0 1 1 1 1 1 0 1 0 1 1 0 0 0 1 0 0 1 0 1 0 1 0 1 0 0 1 1 0 0 1
## [408] 0 1 1 1 1 1 1 0 0 1 1 1 0 0 1 0 1 1 0 0 1 0 1 1 0 1 1 1 0 0 0 0 1 1 1 0 0
## [445] 0 1 1 0 0 1 0 1 0 0 0 1 1 1 0 0 0 0 1 0 0 0 0 0 0 1 0 0 1 0 1 0 0 1 0 0 1
## [482] 0 1 0 0 0 1 0 1 0 1 0 1 0 1 0 1 0 1 1 0 1 0 1 0 1 0 0 0 1 0 0 0 1 1 1 1 1 1 0 1 0
## [519] 0 0 0 0 1 1 1 1 0 0 1 1 1 1 0 1 0 1 0 1 1 0 0 1 0 0 0 0 1 0 1 0 0 0 1 1 1
## [556] 1 0 1 1 0 1 1 1 0 0 1 0 0 1 0 0 1 0 0 1 0 1 0 1 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1
## [593] 1 0 1 0 1 0 1 0 1 0 1 1 1 1 1 0 0 1 0 0 0 0 1 0 1 1 0 0 1 1 0 1 1 0 1 1 1 0 0
## [630] 0 1 0 1 1 0 1 1 1 1 0 1 1 0 1 1 1 1 1 1 1 1 1 0 1 0 0 1 0 0 0 0 0 0 1 1 1 1 0
## [667] 1 1 1 0 0 1 1 0 0 1 1 1 0 1 0 1 1 1 0 1 0 0 1 1 0 0 1 1 1 0 1 1 1 1 0 0 0
## [704] 1 0 0 1 1 1 0 1 0 0 0 0 1 0 1 1 1 1 1 0 0 1 0 0 0 0 0 0 1 0 0 0 1 0 1 0 1
## [741] 0 1 0 1 1 1 0 1 1 0 0 0 0 0 0 0 0 0 1 0 1 1 0 1 1 1 1 1 0 0 0 1 1 1 1 1 0 0
## [778] 1 1 1 0 1 0 1 0 0 0 1 1 1 1 0 1 0 0 0 1 1 0 0 1 0 1 1 0 1 1 1 0 0 1 1 1 1
## [815] 1 0 1 1 1 1 1 1 1 1 1 1 1 0 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 0 1 1 1
## [852] 1 1 1 0 1 1 1 1 1 0 1 0 0 0 1 1 1 1 1 1 1 1 1 1 1 0 1 1
## Levels: 0 1
```

```
unique(data_EDA$hormone_therapy)
```

```
## [1] 1 0
## Levels: 0 1
```

```
#
# hist(data_EDA$tumor_size, breaks = 50)
#
# data_EDA$tumor_size_cat = 1 + 1*(data_EDA$tumor_size > 20) + 1*(data_EDA$tumor_size > 26)
#
# fig_size_small <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA[data_EDA$tumor_size_cat == 1,],
#   labs(subtitle = "") +
#   scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
#   scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))
#
# fig_size_small
#
# fig_size_med <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA[data_EDA$tumor_size_cat == 2,], y
#   labs(subtitle = "") +
#   scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
#   scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))
#
# fig_size_med
#
# fig_size_large <- PlotKMCurve("Mastectomy", var_name = NULL, data_EDA[data_EDA$tumor_size_cat == 3,],
#   labs(subtitle = "") +
#   scale_color_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy")) +
#   scale_fill_manual(values = c("purple", "orange"), labels = c("BCS", "Mastectomy"))
#
# fig_size_large
#
#
# quantile(data_EDA$tumor_size, c(0.33, 0.66))
```

```r
# Exclude treatment from the penalized predictors
p = ncol(x)
penalty = c(0, 0, rep(1, p-2))


set.seed(4)
cox.cv = cv.glmnet(x, y, weights = W.vec, penalty.factor = penalty, family = "cox", alpha = 0.5, nlambd
lambda.cox = cox.cv$lambda.min

cox.fit =  glmnet(x, y, weights = W.vec, family = "cox", alpha = 0.5, penalty.factor = penalty, lambda =

cox.fit$beta[,1]['treatment']

## treatment
## 0.3477823
cox.en.beta = cox.fit$beta[,1]
cox.en.beta.nonzero = cox.fit$beta[,1][abs(cox.fit$beta[,1]) > 1e-10][order(cox.fit$beta[,1][abs(cox.fi
```

Sensitivity Anaysis - different MICE imputations

```r
x_2 = model_matrix_2
x_3 = model_matrix_3
x_4 = model_matrix_4
x_5 = model_matrix_5


x_prop_2 <- model.matrix(as.formula(form_2), data = data_BIDC_common_std_2)
x_prop_3 <- model.matrix(as.formula(form_2), data = data_BIDC_common_std_3)
x_prop_4 <- model.matrix(as.formula(form_2), data = data_BIDC_common_std_4)
x_prop_5 <- model.matrix(as.formula(form_2), data = data_BIDC_common_std_5)

# ridge regression
set.seed(3)
prop.cv_2  = cv.glmnet(x_prop_2, treatment_2, family = "binomial", alpha = 0, nlambda = 30, nfold = 5)
e.vec_2 = predict(prop.cv_2, newx = x_prop_2, s = prop.cv_2$lambda.min, type = 'response')
omega = 1
W.vec_2 = omega / (treatment_2*e.vec_2 + (1-treatment_2)*e.vec_2)

set.seed(3)
prop.cv_3  = cv.glmnet(x_prop_3, treatment_3, family = "binomial", alpha = 0, nlambda = 30, nfold = 5)
e.vec_3 = predict(prop.cv_3, newx = x_prop_3, s = prop.cv_3$lambda.min, type = 'response')
omega = 1
W.vec_3 = omega / (treatment_3*e.vec_3 + (1-treatment_3)*e.vec_3)

set.seed(3)
prop.cv_4  = cv.glmnet(x_prop_4, treatment_4, family = "binomial", alpha = 0, nlambda = 30, nfold = 5)
e.vec_4 = predict(prop.cv_4, newx = x_prop_4, s = prop.cv_4$lambda.min, type = 'response')
omega = 1
W.vec_4 = omega / (treatment_4*e.vec_4 + (1-treatment_4)*e.vec_4)

set.seed(3)
prop.cv_5  = cv.glmnet(x_prop_5, treatment_5, family = "binomial", alpha = 0, nlambda = 30, nfold = 5)
e.vec_5 = predict(prop.cv_5, newx = x_prop_5, s = prop.cv_5$lambda.min, type = 'response')
omega = 1
```

```
W.vec_5 = omega / (treatment_5*e.vec_5 + (1-treatment_5)*e.vec_5)



set.seed(4)
cox.cv_2 = cv.glmnet(x_2, y_2, weights = W.vec_2, penalty.factor = penalty, family = "cox", alpha = 0.5
lambda.cox_2 = cox.cv_2$lambda.min

cox.fit_2 =  glmnet(x_2, y_2, weights = W.vec_2, family = "cox", alpha = 0.5, penalty.factor = penalty,

set.seed(4)
cox.cv_3 = cv.glmnet(x_3, y_3, weights = W.vec_3, penalty.factor = penalty, family = "cox", alpha = 0.5
lambda.cox_3 = cox.cv_3$lambda.min

cox.fit_3 =  glmnet(x_3, y_3, weights = W.vec_3, family = "cox", alpha = 0.5, penalty.factor = penalty,

set.seed(4)
cox.cv_4 = cv.glmnet(x_4, y_4, weights = W.vec_4, penalty.factor = penalty, family = "cox", alpha = 0.5
lambda.cox_4 = cox.cv_4$lambda.min

cox.fit_4 =  glmnet(x_4, y_4, weights = W.vec_4, family = "cox", alpha = 0.5, penalty.factor = penalty,

set.seed(4)
cox.cv_5 = cv.glmnet(x_5, y_5, weights = W.vec_5, penalty.factor = penalty, family = "cox", alpha = 0.5
lambda.cox_5 = cox.cv_5$lambda.min

cox.fit_5 =  glmnet(x_5, y_5, weights = W.vec_5, family = "cox", alpha = 0.5, penalty.factor = penalty,

cox.en.beta
```

```
##                                          (Intercept)
##                                          0.000000000
##                                            treatment
##                                          0.347782309
##                                      age_at_diagnosis
##                                          0.000000000
##                        lymph_nodes_examined_positive
##                                          0.429991335
##                                           tumor_size
##                                          0.039285186
##                                      cellularityHigh
##                                          0.000000000
##                                       cellularityLow
##                                          0.000000000
##                                  cellularityModerate
##                                          0.000000000
##                 pam50_._claudin.low_subtypeclaudin-low
##                                          0.000000000
##                        pam50_._claudin.low_subtypeHer2
##                                          0.000000000
##                        pam50_._claudin.low_subtypeLumA
##                                         -0.152032481
##                        pam50_._claudin.low_subtypeLumB
##                                          0.000000000
```

```
##                          pam50_._claudin.low_subtypeNormal
##                                                  0.000000000
##                               neoplasm_histologic_grade2
##                                                  0.000000000
##                               neoplasm_histologic_grade3
##                                                  0.000000000
##               tumor_other_histologic_subtypeMedullary
##                                                  0.000000000
##       tumor_other_histologic_subtypeTubular/ cribriform
##                                                  0.000000000
##                                     integrative_cluster10
##                                                  0.000000000
##                                      integrative_cluster2
##                                                  0.000000000
##                                      integrative_cluster3
##                                                 -0.036916691
##                                  integrative_cluster4ER-
##                                                  0.000000000
##                                  integrative_cluster4ER+
##                                                  0.000000000
##                                      integrative_cluster5
##                                                  0.261403318
##                                      integrative_cluster6
##                                                  0.000000000
##                                      integrative_cluster7
##                                                  0.000000000
##                                      integrative_cluster8
##                                                  0.000000000
##                                      integrative_cluster9
##                                                  0.000000000
##                       X3.gene_classifier_subtypeER-/HER2-
##                                                  0.000000000
##            X3.gene_classifier_subtypeER+/HER2- High Prolif
##                                                  0.000000000
##             X3.gene_classifier_subtypeER+/HER2- Low Prolif
##                                                  0.000000000
##                         X3.gene_classifier_subtypeHER2+
##                                                  0.000000000
##                                                tumor_stage2
##                                                  0.000000000
##                                                tumor_stage3
##                                                  0.000000000
##                                                       brca1
##                                                  0.000000000
##                                                       brca2
##                                                 -0.042959447
##                                                       palb2
##                                                  0.000000000
##                                                        pten
##                                                  0.000000000
##                                                        tp53
##                                                  0.000000000
##                                                         atm
##                                                  0.000000000
```

```
##                                                        cdh1
##                                                 0.000000000
##                                                       chek2
##                                                 0.000000000
##                                                         nbn
##                                                 0.000000000
##                                                         nf1
##                                                 0.000000000
##                                                       stk11
##                                                 0.000000000
##                                                       bard1
##                                                 0.000000000
##                                                        mlh1
##                                                 0.000000000
##                                                        msh2
##                                                 0.000000000
##                                                        msh6
##                                                 0.000000000
##                                                        pms2
##                                                 0.000000000
##                                                       epcam
##                                                 0.000000000
##                                                      rad51c
##                                                 0.000000000
##                                                      rad51d
##                                                 0.000000000
##                                                       rad50
##                                                 0.000000000
##                                                         rb1
##                                                 0.000000000
##                                                        rbl1
##                                                 0.000000000
##                                                        rbl2
##                                                 0.000000000
##                                                       ccna1
##                                                 0.000000000
##                                                       ccnb1
##                                                 0.000000000
##                                                        cdk1
##                                                 0.000000000
##                                                       ccne1
##                                                 0.000000000
##                                                        cdk2
##                                                 0.000000000
##                                                      cdc25a
##                                                 0.000000000
##                                                       ccnd1
##                                                 0.000000000
##                                                        cdk4
##                                                 0.000000000
##                                                        cdk6
##                                                 0.000000000
##                                                       ccnd2
##                                                 0.000000000
```

```
##                                                        cdkn2a
##                                                   0.000000000
##                                                        cdkn2b
##                                                   0.000000000
##                                                           myc
##                                                   0.000000000
##                                                        cdkn1a
##                                                   0.000000000
##                                                        cdkn1b
##                                                   0.000000000
##                                                          e2f1
##                                                  -0.057084879
##                                                          e2f2
##                                                   0.000000000
##                                                          e2f3
##                                                   0.000000000
##                                                          e2f4
##                                                   0.000000000
##                                                          e2f5
##                                                   0.000000000
##                                                          e2f6
##                                                   0.000000000
##                                                          e2f7
##                                                   0.060377905
##                                                          e2f8
##                                                   0.000000000
##                                                           src
##                                                   0.000000000
##                                                          jak1
##                                                   0.000000000
##                                                          jak2
##                                                   0.000000000
##                                                         stat1
##                                                   0.000000000
##                                                         stat2
##                                                   0.000000000
##                                                         stat3
##                                                   0.000000000
##                                                        stat5a
##                                                  -0.111515329
##                                                        stat5b
##                                                   0.000000000
##                                                          mdm2
##                                                   0.000000000
##                                                       tp53bp1
##                                                   0.000000000
##                                                        adam10
##                                                   0.000000000
##                                                        adam17
##                                                   0.000000000
##                                                         aph1a
##                                                   0.000000000
##                                                         aph1b
##                                                   0.000000000
```

```
##                                                   arrdc1
##                                               0.000000000
##                                                      cir1
##                                               0.000000000
##                                                     ctbp1
##                                               0.000000000
##                                                     ctbp2
##                                               0.000000000
##                                                      cul1
##                                              -0.106889044
##                                                      dll1
##                                               0.000000000
##                                                      dll3
##                                               0.054955479
##                                                      dll4
##                                               0.000000000
##                                                      dtx1
##                                               0.000000000
##                                                      dtx2
##                                               0.000000000
##                                                      dtx3
##                                               0.000000000
##                                                      dtx4
##                                               0.000000000
##                                                     ep300
##                                               0.000000000
##                                                     fbxw7
##                                               0.000000000
##                                                     hdac1
##                                               0.000000000
##                                                     hdac2
##                                               0.000000000
##                                                      hes1
##                                               0.000000000
##                                                      hes5
##                                               0.000000000
##                                                      heyl
##                                               0.000000000
##                                                      itch
##                                               0.000000000
##                                                      jag1
##                                               0.000000000
##                                                      jag2
##                                               0.000000000
##                                                     kdm5a
##                                               0.000000000
##                                                      lfng
##                                               0.000000000
##                                                     maml1
##                                               0.000000000
##                                                     maml2
##                                               0.000000000
##                                                     maml3
##                                               0.000000000
```

```
##                                                       ncor2
##                                                  0.000000000
##                                                        ncstn
##                                                  0.000000000
##                                                       notch1
##                                                  0.000000000
##                                                       notch2
##                                                  0.000000000
##                                                       notch3
##                                                  0.000000000
##                                                        nrarp
##                                                  0.000000000
##                                                         numb
##                                                  0.000000000
##                                                        numbl
##                                                  0.000000000
##                                                        psen1
##                                                  0.000000000
##                                                        psen2
##                                                  0.000000000
##                                                       psenen
##                                                  0.000000000
##                                                         rbpj
##                                                  0.000000000
##                                                        rbpjl
##                                                  0.000000000
##                                                         rfng
##                                                  0.000000000
##                                                         snw1
##                                                  0.000000000
##                                                         spen
##                                                  0.000000000
##                                                         hes2
##                                                  0.000000000
##                                                         hes4
##                                                  0.000000000
##                                                         hes7
##                                                  0.000000000
##                                                         hey1
##                                                  0.000000000
##                                                         hey2
##                                                  0.000000000
##                                                        acvr1
##                                                  0.000000000
##                                                       acvr1b
##                                                  0.000000000
##                                                       acvr1c
##                                                 -0.105162501
##                                                       acvr2a
##                                                  0.000000000
##                                                       acvr2b
##                                                  0.000000000
##                                                       acvrl1
##                                                  0.000000000
```

```
##                                                         akt1
##                                                  0.000000000
##                                                       akt1s1
##                                                  0.000000000
##                                                         akt2
##                                                  0.000000000
##                                                        apaf1
##                                                  0.000000000
##                                                        arl11
##                                                  0.000000000
##                                                          atr
##                                                  0.000000000
##                                                        aurka
##                                                  0.000000000
##                                                          bad
##                                                  0.000000000
##                                                         bcl2
##                                                  0.000000000
##                                                       bcl2l1
##                                                  0.000000000
##                                                        bmp10
##                                                  0.000000000
##                                                        bmp15
##                                                  0.000000000
##                                                         bmp2
##                                                  0.000000000
##                                                         bmp3
##                                                  0.000000000
##                                                         bmp4
##                                                  0.000000000
##                                                         bmp5
##                                                  0.000000000
##                                                         bmp6
##                                                  0.000000000
##                                                         bmp7
##                                                  0.000000000
##                                                       bmpr1a
##                                                  0.000000000
##                                                       bmpr1b
##                                                  0.000000000
##                                                        bmpr2
##                                                  0.000000000
##                                                         braf
##                                                  0.000000000
##                                                       casp10
##                                                  0.000000000
##                                                        casp3
##                                                  0.000000000
##                                                        casp6
##                                                  0.000000000
##                                                        casp7
##                                                 -0.012710693
##                                                        casp8
##                                                  0.000000000
```

```
##                                             casp9
##                                        0.000000000
##                                             chek1
##                                        0.000000000
##                                              csf1
##                                        0.000000000
##                                             csf1r
##                                        0.000000000
##                                             cxcl8
##                                        0.000000000
##                                             cxcr1
##                                        0.000000000
##                                             cxcr2
##                                        0.000000000
##                                              dab2
##                                        0.000000000
##                                            diras3
##                                       -0.078511004
##                                             dlec1
##                                        0.000000000
##                                              dph1
##                                        0.000000000
##                                              egfr
##                                        0.000000000
##                                             eif4e
##                                        0.000000000
##                                           eif4ebp1
##                                        0.129527071
##                                             eif5a2
##                                        0.000000000
##                                             erbb2
##                                        0.000000000
##                                             erbb3
##                                        0.000000000
##                                             erbb4
##                                        0.000000000
##                                               fas
##                                        0.000000000
##                                              fgf1
##                                        0.000000000
##                                             fgfr1
##                                        0.000000000
##                                             folr1
##                                        0.000000000
##                                             folr2
##                                        0.000000000
##                                             folr3
##                                        0.000000000
##                                             foxo1
##                                        0.000000000
##                                             foxo3
##                                        0.000000000
##                                             gdf11
##                                        0.000000000
```

```
##                                                        gdf2
##                                                 0.000000000
##                                                       gsk3b
##                                                 0.239318961
##                                                       hif1a
##                                                 0.000000000
##                                                       hla.g
##                                                 0.000000000
##                                                        hras
##                                                 0.000000000
##                                                        igf1
##                                                -0.015017205
##                                                       igf1r
##                                                 0.000000000
##                                                        inha
##                                                 0.000000000
##                                                       inhba
##                                                 0.000000000
##                                                       inhbc
##                                                 0.000000000
##                                                       itgav
##                                                 0.000000000
##                                                       itgb3
##                                                 0.000000000
##                                                     izumo1r
##                                                 0.000000000
##                                                         kdr
##                                                 0.000000000
##                                                         kit
##                                                 0.000000000
##                                                        kras
##                                                 0.000000000
##                                                      map2k1
##                                                 0.000000000
##                                                      map2k2
##                                                 0.000000000
##                                                      map2k3
##                                                 0.000000000
##                                                      map2k4
##                                                 0.000000000
##                                                      map2k5
##                                                 0.000000000
##                                                      map3k1
##                                                -0.011575291
##                                                      map3k3
##                                                 0.000000000
##                                                      map3k4
##                                                 0.000000000
##                                                      map3k5
##                                                 0.000000000
##                                                       mapk1
##                                                 0.000000000
##                                                      mapk12
##                                                 0.000000000
```

29

```
##                                                                mapk14
##                                                           0.000000000
##                                                                 mapk3
##                                                           0.000000000
##                                                                 mapk4
##                                                           0.000000000
##                                                                 mapk6
##                                                           0.000000000
##                                                                 mapk7
##                                                           0.000000000
##                                                                 mapk8
##                                                           0.000000000
##                                                                 mapk9
##                                                           0.000000000
##                                                                  mdc1
##                                                           0.000000000
##                                                                 mlst8
##                                                           0.000000000
##                                                                  mmp1
##                                                           0.000000000
##                                                                 mmp10
##                                                           0.000000000
##                                                                 mmp11
##                                                           0.000000000
##                                                                 mmp12
##                                                           0.000000000
##                                                                 mmp13
##                                                           0.000000000
##                                                                 mmp14
##                                                           0.000000000
##                                                                 mmp15
##                                                           0.000000000
##                                                                 mmp16
##                                                           0.000000000
##                                                                 mmp17
##                                                           0.000000000
##                                                                 mmp19
##                                                           0.000000000
##                                                                  mmp2
##                                                           0.000000000
##                                                                 mmp21
##                                                           0.000000000
##                                                                mmp23b
##                                                           0.000000000
##                                                                 mmp24
##                                                           0.000000000
##                                                                 mmp25
##                                                          -0.014298532
##                                                                 mmp26
##                                                           0.000000000
##                                                                 mmp27
##                                                           0.000000000
##                                                                 mmp28
##                                                           0.000000000
```

```
##                                                             mmp3
##                                                      0.000000000
##                                                             mmp7
##                                                      0.000000000
##                                                             mmp9
##                                                      0.000000000
##                                                             mtor
##                                                      0.000000000
##                                                            nfkb1
##                                                      0.000000000
##                                                            nfkb2
##                                                      0.000000000
##                                                            opcml
##                                                      0.000000000
##                                                            pdgfa
##                                                      0.000000000
##                                                            pdgfb
##                                                      0.015773806
##                                                            pdgfra
##                                                      0.000000000
##                                                            pdgfrb
##                                                      0.000000000
##                                                            pdpk1
##                                                      0.000000000
##                                                             peg3
##                                                      0.000000000
##                                                            pik3ca
##                                                      0.000000000
##                                                            pik3r1
##                                                      0.000000000
##                                                            pik3r2
##                                                      0.000000000
##                                                            plagl1
##                                                      0.000000000
##                                                             ptk2
##                                                      0.000000000
##                                                            rab25
##                                                      0.000000000
##                                                            rad51
##                                                      0.000000000
##                                                             raf1
##                                                      0.000000000
##                                                            rassf1
##                                                      0.000000000
##                                                             rheb
##                                                      0.000000000
##                                                            rictor
##                                                      0.000000000
##                                                             rps6
##                                                      0.000000000
##                                                           rps6ka1
##                                                      0.000000000
##                                                           rps6ka2
##                                                      0.000000000
```

```
##                                             rps6kb1
##                                          0.000000000
##                                             rps6kb2
##                                          0.000000000
##                                               rptor
##                                          0.000000000
##                                             slc19a1
##                                          0.000000000
##                                               smad1
##                                          0.000000000
##                                               smad2
##                                          0.000000000
##                                               smad3
##                                          0.000000000
##                                               smad4
##                                          0.000000000
##                                               smad5
##                                          0.000000000
##                                               smad6
##                                          0.003035938
##                                               smad7
##                                          0.031579997
##                                               smad9
##                                          0.000000000
##                                              sptbn1
##                                          0.000000000
##                                                terc
##                                          0.000000000
##                                                tert
##                                          0.000000000
##                                               tgfb1
##                                          0.000000000
##                                               tgfb2
##                                          0.000000000
##                                               tgfb3
##                                          0.000000000
##                                              tgfbr1
##                                          0.000000000
##                                              tgfbr2
##                                          0.000000000
##                                              tgfbr3
##                                          0.000000000
##                                                tsc1
##                                          0.000000000
##                                                tsc2
##                                          0.000000000
##                                               vegfa
##                                          0.000000000
##                                               vegfb
##                                          0.000000000
##                                                wfdc2
##                                          0.000000000
##                                                 wwox
##                                          0.000000000
```

```
##                                                        zfyve9
##                                                  0.000000000
##                                                        arid1a
##                                                  0.000000000
##                                                        arid1b
##                                                  0.000000000
##                                                          cbfb
##                                                  0.000000000
##                                                         gata3
##                                                  0.000000000
##                                                         kmt2c
##                                                  0.000000000
##                                                         kmt2d
##                                                  0.000000000
##                                                          myh9
##                                                  0.000000000
##                                                         ncor1
##                                                  0.000000000
##                                                       pde4dip
##                                                  0.000000000
##                                                         ptprd
##                                                  0.000000000
##                                                          ros1
##                                                  0.000000000
##                                                         runx1
##                                                  0.000000000
##                                                          tbx3
##                                                  0.000000000
##                                                         abcb1
##                                                  0.000000000
##                                                        abcb11
##                                                  0.000000000
##                                                         abcc1
##                                                  0.000000000
##                                                        abcc10
##                                                  0.000000000
##                                                          bbc3
##                                                  0.000000000
##                                                           bmf
##                                                  0.000000000
##                                                        cyp2c8
##                                                  0.000000000
##                                                        cyp3a4
##                                                  0.000000000
##                                                          fgf2
##                                                  0.000000000
##                                                           fn1
##                                                  0.000000000
##                                                          map2
##                                                  0.000000000
##                                                          map4
##                                                  0.000000000
##                                                          mapt
##                                                 -0.055817428
```

```
##                                                          nr1i2
##                                               0.000000000
##                                                        slco1b3
##                                               0.000000000
##                                                          tubb1
##                                               0.000000000
##                                                         tubb4a
##                                               0.000000000
##                                                         tubb4b
##                                               0.000000000
##                                                         twist1
##                                               0.000000000
##                                                         adgra2
##                                               0.000000000
##                                                           afdn
##                                               0.000000000
##                                                           aff2
##                                               0.000000000
##                                                           agmo
##                                               0.000000000
##                                                          agtr2
##                                               0.000000000
##                                                          ahnak
##                                               0.000000000
##                                                         ahnak2
##                                               0.000000000
##                                                          akap9
##                                               0.000000000
##                                                            alk
##                                               0.000000000
##                                                            apc
##                                               0.000000000
##                                                          arid2
##                                               0.000000000
##                                                         arid5b
##                                               0.000000000
##                                                          asxl1
##                                               0.000000000
##                                                          asxl2
##                                               0.000000000
##                                                           bap1
##                                               0.000000000
##                                                          bcas3
##                                               0.000000000
##                                                          birc6
##                                               0.000000000
##                                                       cacna2d3
##                                               0.000000000
##                                                           ccnd3
##                                               0.000000000
##                                                            chd1
##                                               0.000000000
##                                                            clk3
##                                               0.000000000
```

```
##                                                                    clrn2
##                                                               0.000000000
##                                                                  col12a1
##                                                               0.000000000
##                                                                  col22a1
##                                                               0.000000000
##                                                                   col6a3
##                                                               0.000000000
##                                                                     ctcf
##                                                               0.000000000
##                                                                   ctnna1
##                                                               0.000000000
##                                                                   ctnna3
##                                                               0.000000000
##                                                                   dnah11
##                                                               0.000000000
##                                                                    dnah2
##                                                               0.000000000
##                                                                    dnah5
##                                                               0.000000000
##                                                                    dtwd2
##                                                               0.000000000
##                                                                   fam20c
##                                                               0.000000000
##                                                                    fanca
##                                                               0.000000000
##                                                                   fancd2
##                                                               0.000000000
##                                                                     flt3
##                                                               0.000000000
##                                                                    foxp1
##                                                               0.000000000
##                                                                    frmd3
##                                                               0.000000000
##                                                                      gh1
##                                                               0.000000000
##                                                                     gldc
##                                                               0.000000000
##                                                                    gpr32
##                                                               0.000000000
##                                                                     gps2
##                                                               0.000000000
##                                                                    hdac9
##                                                               0.000000000
##                                                                    herc2
##                                                               0.000000000
##                                                                 hist1h2bc
##                                                               0.000000000
##                                                                    kdm3a
##                                                               0.000000000
##                                                                    kdm6a
##                                                               0.000000000
##                                                                    klrg1
##                                                               0.000000000
```

```
##                                                 l1cam
##                                            0.000000000
##                                                 lama2
##                                            0.000000000
##                                                 lamb3
##                                            0.000000000
##                                                large1
##                                            0.000000000
##                                               ldlrap1
##                                            0.000000000
##                                                  lifr
##                                            0.000000000
##                                                  lipi
##                                            0.000000000
##                                                magea8
##                                            0.000000000
##                                                map3k10
##                                            0.000000000
##                                                map3k13
##                                            0.000000000
##                                                  men1
##                                            0.006066667
##                                                  mtap
##                                            0.000000000
##                                                 muc16
##                                            0.000000000
##                                                 myo1a
##                                            0.000000000
##                                                 myo3a
##                                            0.000000000
##                                                 ncoa3
##                                            0.000000000
##                                                  nek1
##                                            0.000000000
##                                                   nf2
##                                            0.000000000
##                                                  npnt
##                                            0.000000000
##                                                  nr2f1
##                                            0.000000000
##                                                  nr3c1
##                                            0.000000000
##                                                  nras
##                                            0.000000000
##                                                  nrg3
##                                            0.000000000
##                                                  nt5e
##                                            0.000000000
##                                                  or6a2
##                                            0.000000000
##                                                  palld
##                                            0.000000000
##                                                  pbrm1
##                                            0.000000000
```

```
##                                                          ppp2cb
##                                                     0.000000000
##                                                          ppp2r2a
##                                                     0.000000000
##                                                           prkacg
##                                                     0.026250727
##                                                            prkce
##                                                     0.000000000
##                                                            prkcq
##                                                     0.000000000
##                                                            prkcz
##                                                     0.000000000
##                                                            prkg1
##                                                     0.199972830
##                                                            prps2
##                                                     0.000000000
##                                                            prr16
##                                                     0.000000000
##                                                           ptpn22
##                                                     0.000000000
##                                                            ptprm
##                                                     0.000000000
##                                                          rasgef1b
##                                                     0.000000000
##                                                             rpgr
##                                                     0.000000000
##                                                             ryr2
##                                                     0.000000000
##                                                            sbno1
##                                                     0.000000000
##                                                           setd1a
##                                                     0.000000000
##                                                            setd2
##                                                     0.000000000
##                                                           setdb1
##                                                     0.000000000
##                                                            sf3b1
##                                                     0.000000000
##                                                             sgcd
##                                                     0.000000000
##                                                           shank2
##                                                     0.000000000
##                                                            siah1
##                                                     0.000000000
##                                                             sik1
##                                                     0.000000000
##                                                             sik2
##                                                     0.000000000
##                                                          smarcb1
##                                                     0.000000000
##                                                          smarcc1
##                                                     0.000000000
##                                                          smarcc2
##                                                     0.000000000
```

```
##                                              smarcd1
##                                         0.000000000
##                                               spaca1
##                                         0.000000000
##                                                stab2
##                                         0.000000000
##                                                stmn2
##                                         0.000000000
##                                                syne1
##                                         0.000000000
##                                                 taf1
##                                         0.000000000
##                                                taf4b
##                                         0.000000000
##                                              tbl1xr1
##                                         0.000000000
##                                                   tg
##                                         0.000000000
##                                                thada
##                                         0.000000000
##                                               thsd7a
##                                         0.000000000
##                                                ttyh1
##                                         0.000000000
##                                                 ubr5
##                                         0.000000000
##                                                ush2a
##                                         0.000000000
##                                                usp9x
##                                         0.000000000
##                                                 utrn
##                                         0.000000000
##                                              zfp36l1
##                                         0.000000000
##                                                ackr3
##                                         0.000000000
##                                               akr1c1
##                                         0.000000000
##                                               akr1c2
##                                         0.000000000
##                                               akr1c3
##                                         0.000000000
##                                               akr1c4
##                                         0.000000000
##                                                 akt3
##                                         0.007516268
##                                                   ar
##                                         0.000000000
##                                                 bche
##                                         0.000000000
##                                                 cdk8
##                                         0.000000000
##                                               cdkn2c
##                                         0.000000000
```

```
##                                                    cyb5a
##                                             0.000000000
##                                                  cyp11a1
##                                             0.000000000
##                                                  cyp11b2
##                                             0.000000000
##                                                  cyp17a1
##                                             0.000000000
##                                                  cyp19a1
##                                             0.000000000
##                                                  cyp21a2
##                                             0.000000000
##                                                  cyp3a43
##                                             0.000000000
##                                                   cyp3a5
##                                             0.000000000
##                                                   cyp3a7
##                                             0.000000000
##                                                      ddc
##                                             0.000000000
##                                                     hes6
##                                             0.000000000
##                                                  hsd17b1
##                                             0.000000000
##                                                 hsd17b10
##                                             0.000000000
##                                                 hsd17b11
##                                             0.000000000
##                                                 hsd17b12
##                                             0.000000000
##                                                 hsd17b13
##                                             0.000000000
##                                                 hsd17b14
##                                             0.000000000
##                                                  hsd17b2
##                                             0.000000000
##                                                  hsd17b3
##                                             0.000000000
##                                                  hsd17b4
##                                             0.000000000
##                                                  hsd17b6
##                                             0.000000000
##                                                  hsd17b7
##                                             0.000000000
##                                                  hsd17b8
##                                             0.000000000
##                                                   hsd3b1
##                                             0.000000000
##                                                   hsd3b2
##                                             0.000000000
##                                                   hsd3b7
##                                             0.000000000
##                                                    mecom
##                                             0.000000000
```

```
##                                 met
##                        0.000000000
##                                ncoa2
##                        0.000000000
##                                nrip1
##                        0.000000000
##                                pik3r3
##                        0.000000000
##                                prkci
##                        0.000000000
##                                prkd1
##                        0.000000000
##                                  ran
##                        0.000000000
##                                 rdh5
##                        0.000000000
##                                 sdc4
##                        0.000000000
##                              serpini1
##                        0.000000000
##                                 shbg
##                        0.000000000
##                               slc29a1
##                        0.000000000
##                                 sox9
##                        0.000000000
##                                 spry2
##                        0.000000000
##                                srd5a1
##                        0.000000000
##                                srd5a2
##                        0.000000000
##                                srd5a3
##                        0.000000000
##                                  st7
##                        0.000000000
##                                 star
##                        0.000000000
##                                 tnk2
##                        0.000000000
##                                tulp4
##                        0.000000000
##                               ugt2b15
##                        0.000000000
##                               ugt2b17
##                       -0.043295059
##                                ugt2b7
##                        0.000000000
##                       brca1:brca1_mut
##                        0.000000000
##                       brca2:brca2_mut
##                        0.000000000
##                       pten:pten_mut
##                        0.000000000
```

```
##                                              tp53:tp53_mut
##                                                -0.121472412
##                                              cdh1:cdh1_mut
##                                                 0.000000000
##                                                 nf1:nf1_mut
##                                                 0.000000000
##                                                 rb1:rb1_mut
##                                                 0.000000000
##                                                jak1:jak1_mut
##                                                 0.000000000
##                                              ep300:ep300_mut
##                                                 0.000000000
##                                              ncor2:ncor2_mut
##                                                 0.000000000
##                                            notch1:notch1_mut
##                                                 0.000000000
##                                                akt1:akt1_mut
##                                                 0.000000000
##                                                 atr:atr_mut
##                                                 0.000000000
##                                                egfr:egfr_mut
##                                                 0.000000000
##                                              erbb2:erbb2_mut
##                                                 0.000000000
##                                              erbb3:erbb3_mut
##                                                 0.000000000
##                                              erbb4:erbb4_mut
##                                                 0.000000000
##                                              foxo3:foxo3_mut
##                                                 0.000000000
##                                            map2k4:map2k4_mut
##                                                 0.000000000
##                                            map3k1:map3k1_mut
##                                                 0.000000000
##                                            pik3ca:pik3ca_mut
##                                                 0.000000000
##                                            pik3r1:pik3r1_mut
##                                                 0.000000000
##                                              smad4:smad4_mut
##                                                 0.000000000
##                                            arid1a:arid1a_mut
##                                                 0.000000000
##                                            arid1b:arid1b_mut
##                                                 0.000000000
##                                                cbfb:cbfb_mut
##                                                 0.000000000
##                                              gata3:gata3_mut
##                                                -0.138823153
##                                              kmt2c:kmt2c_mut
##                                                 0.000000000
##                                              kmt2d:kmt2d_mut
##                                                 0.000000000
##                                                myh9:myh9_mut
##                                                 0.000000000
```

```
##                                    ncor1:ncor1_mut
##                                       0.000000000
##                                  pde4dip:pde4dip_mut
##                                       0.000000000
##                                    ptprd:ptprd_mut
##                                       0.000000000
##                                      ros1:ros1_mut
##                                       0.000000000
##                                    runx1:runx1_mut
##                                       0.000000000
##                                      tbx3:tbx3_mut
##                                      -0.079733374
##                                  adgra2:adgra2_mut
##                                       0.000000000
##                                      afdn:afdn_mut
##                                       0.000000000
##                                      aff2:aff2_mut
##                                       0.000000000
##                                    ahnak:ahnak_mut
##                                       0.000000000
##                                  ahnak2:ahnak2_mut
##                                       0.000000000
##                                    akap9:akap9_mut
##                                       0.000000000
##                                        alk:alk_mut
##                                       0.000000000
##                                        apc:apc_mut
##                                       0.000000000
##                                    arid2:arid2_mut
##                                       0.000000000
##                                  arid5b:arid5b_mut
##                                       0.000000000
##                                    asxl1:asxl1_mut
##                                       0.000000000
##                                    asxl2:asxl2_mut
##                                       0.000000000
##                                      bap1:bap1_mut
##                                       0.000000000
##                                    birc6:birc6_mut
##                                       0.000000000
##                              cacna2d3:cacna2d3_mut
##                                       0.000000000
##                                      chd1:chd1_mut
##                                       0.000000000
##                                  col12a1:col12a1_mut
##                                       0.000000000
##                                  col22a1:col22a1_mut
##                                       0.000000000
##                                    col6a3:col6a3_mut
##                                       0.000000000
##                                      ctcf:ctcf_mut
##                                       0.000000000
##                                    ctnna3:ctnna3_mut
##                                       0.000000000
```

```
##                                dnah11:dnah11_mut
##                                       0.000000000
##                                  dnah2:dnah2_mut
##                                       0.000000000
##                                  dnah5:dnah5_mut
##                                       0.000000000
##                                fam20c:fam20c_mut
##                                       0.000000000
##                                  fanca:fanca_mut
##                                       0.000000000
##                                fancd2:fancd2_mut
##                                       0.000000000
##                                    gldc:gldc_mut
##                                       0.000000000
##                                  herc2:herc2_mut
##                                       0.000000000
##                                  kdm3a:kdm3a_mut
##                                       0.369957710
##                                  kdm6a:kdm6a_mut
##                                       0.000000000
##                                  l1cam:l1cam_mut
##                                       0.000000000
##                                  lama2:lama2_mut
##                                       0.000000000
##                                  lamb3:lamb3_mut
##                                       0.000000000
##                                    lifr:lifr_mut
##                                       0.000000000
##                                  muc16:muc16_mut
##                                       0.000000000
##                                  myo1a:myo1a_mut
##                                       0.000000000
##                                  myo3a:myo3a_mut
##                                       0.000000000
##                                  ncoa3:ncoa3_mut
##                                       0.000000000
##                                  pbrm1:pbrm1_mut
##                                       0.000000000
##                                  ptprm:ptprm_mut
##                                       0.000000000
##                                    ryr2:ryr2_mut
##                                       0.000000000
##                                  sbno1:sbno1_mut
##                                       0.000000000
##                                setd1a:setd1a_mut
##                                       0.000000000
##                                  setd2:setd2_mut
##                                       0.000000000
##                                setdb1:setdb1_mut
##                                       0.000000000
##                                  sf3b1:sf3b1_mut
##                                       0.000000000
##                                shank2:shank2_mut
##                                       0.000000000
```

```
##                                          smarcc2:smarcc2_mut
##                                                    0.000000000
##                                              stab2:stab2_mut
##                                                    0.000000000
##                                              syne1:syne1_mut
##                                                    0.000000000
##                                                taf1:taf1_mut
##                                                    0.000000000
##                                                    tg:tg_mut
##                                                    0.000000000
##                                              thada:thada_mut
##                                                    0.000000000
##                                            thsd7a:thsd7a_mut
##                                                    0.000000000
##                                                ubr5:ubr5_mut
##                                                    0.000000000
##                                              ush2a:ush2a_mut
##                                                    0.000000000
##                                              usp9x:usp9x_mut
##                                                    0.000000000
##                                                utrn:utrn_mut
##                                                    0.000000000
##                                  treatment:age_at_diagnosis
##                                                    0.000000000
##                       treatment:lymph_nodes_examined_positive
##                                                    0.000000000
##                                          treatment:tumor_size
##                                                    0.189831732
##                                      treatment:cellularityHigh
##                                                    0.000000000
##                                       treatment:cellularityLow
##                                                    0.000000000
##                                  treatment:cellularityModerate
##                                                    0.000000000
##           treatment:pam50_._claudin.low_subtypeclaudin-low
##                                                    0.000000000
##                 treatment:pam50_._claudin.low_subtypeHer2
##                                                    0.000000000
##                 treatment:pam50_._claudin.low_subtypeLumA
##                                                    0.000000000
##                 treatment:pam50_._claudin.low_subtypeLumB
##                                                    0.000000000
##               treatment:pam50_._claudin.low_subtypeNormal
##                                                    0.000000000
##                       treatment:neoplasm_histologic_grade2
##                                                    0.000000000
##                       treatment:neoplasm_histologic_grade3
##                                                    0.000000000
##          treatment:tumor_other_histologic_subtypeMedullary
##                                                    0.000000000
## treatment:tumor_other_histologic_subtypeTubular/ cribriform
##                                                    0.000000000
##                           treatment:integrative_cluster10
##                                                    0.000000000
```

```
##                       treatment:integrative_cluster2
##                                            0.000000000
##                       treatment:integrative_cluster3
##                                            0.000000000
##                    treatment:integrative_cluster4ER-
##                                            0.000000000
##                    treatment:integrative_cluster4ER+
##                                            0.000000000
##                       treatment:integrative_cluster5
##                                            0.000000000
##                       treatment:integrative_cluster6
##                                            0.000000000
##                       treatment:integrative_cluster7
##                                            0.000000000
##                       treatment:integrative_cluster8
##                                            0.000000000
##                       treatment:integrative_cluster9
##                                            0.000000000
##          treatment:X3.gene_classifier_subtypeER-/HER2-
##                                            0.000000000
##   treatment:X3.gene_classifier_subtypeER+/HER2- High Prolif
##                                            0.000000000
##   treatment:X3.gene_classifier_subtypeER+/HER2- Low Prolif
##                                            0.000000000
##             treatment:X3.gene_classifier_subtypeHER2+
##                                            0.000000000
##                            treatment:tumor_stage2
##                                            0.000000000
##                            treatment:tumor_stage3
##                                            0.000000000
##                                   treatment:brca1
##                                            0.000000000
##                                   treatment:brca2
##                                            0.000000000
##                                   treatment:palb2
##                                            0.000000000
##                                    treatment:pten
##                                            0.000000000
##                                    treatment:tp53
##                                            0.000000000
##                                     treatment:atm
##                                            0.000000000
##                                    treatment:cdh1
##                                            0.000000000
##                                   treatment:chek2
##                                            0.000000000
##                                     treatment:nbn
##                                            0.000000000
##                                     treatment:nf1
##                                            0.000000000
##                                   treatment:stk11
##                                            0.000000000
##                                   treatment:bard1
##                                            0.000000000
```

```
##                                            treatment:mlh1
##                                               0.000000000
##                                            treatment:msh2
##                                               0.000000000
##                                            treatment:msh6
##                                               0.000000000
##                                            treatment:pms2
##                                               0.000000000
##                                           treatment:epcam
##                                               0.000000000
##                                          treatment:rad51c
##                                               0.000000000
##                                          treatment:rad51d
##                                               0.000000000
##                                           treatment:rad50
##                                               0.000000000
##                                             treatment:rb1
##                                               0.000000000
##                                            treatment:rbl1
##                                               0.000000000
##                                            treatment:rbl2
##                                               0.000000000
##                                            treatment:ccna1
##                                               0.000000000
##                                            treatment:ccnb1
##                                               0.000000000
##                                             treatment:cdk1
##                                               0.000000000
##                                            treatment:ccne1
##                                               0.000000000
##                                             treatment:cdk2
##                                               0.000000000
##                                           treatment:cdc25a
##                                               0.000000000
##                                            treatment:ccnd1
##                                               0.000000000
##                                             treatment:cdk4
##                                               0.000000000
##                                             treatment:cdk6
##                                               0.000000000
##                                            treatment:ccnd2
##                                               0.000000000
##                                           treatment:cdkn2a
##                                               0.000000000
##                                           treatment:cdkn2b
##                                               0.000000000
##                                             treatment:myc
##                                               0.000000000
##                                           treatment:cdkn1a
##                                               0.000000000
##                                           treatment:cdkn1b
##                                               0.000000000
##                                             treatment:e2f1
##                                               0.000000000
```

```
##                                treatment:e2f2
##                                   0.000000000
##                                treatment:e2f3
##                                   0.000000000
##                                treatment:e2f4
##                                   0.000000000
##                                treatment:e2f5
##                                   0.000000000
##                                treatment:e2f6
##                                   0.000000000
##                                treatment:e2f7
##                                   0.040005288
##                                treatment:e2f8
##                                   0.219624668
##                                 treatment:src
##                                   0.000000000
##                                treatment:jak1
##                                   0.000000000
##                                treatment:jak2
##                                   0.000000000
##                               treatment:stat1
##                                   0.000000000
##                               treatment:stat2
##                                   0.000000000
##                               treatment:stat3
##                                   0.000000000
##                              treatment:stat5a
##                                   0.000000000
##                              treatment:stat5b
##                                   0.000000000
##                                treatment:mdm2
##                                   0.000000000
##                              treatment:tp53bp1
##                                   0.000000000
##                              treatment:adam10
##                                   0.000000000
##                              treatment:adam17
##                                   0.000000000
##                               treatment:aph1a
##                                   0.000000000
##                               treatment:aph1b
##                                   0.000000000
##                              treatment:arrdc1
##                                   0.000000000
##                                treatment:cir1
##                                   0.000000000
##                               treatment:ctbp1
##                                   0.000000000
##                               treatment:ctbp2
##                                   0.000000000
##                                treatment:cul1
##                                  -0.145590316
##                                treatment:dll1
##                                   0.000000000
```

```
##                                              treatment:dll3
##                                                 0.000000000
##                                              treatment:dll4
##                                                 0.000000000
##                                              treatment:dtx1
##                                                 0.000000000
##                                              treatment:dtx2
##                                                 0.000000000
##                                              treatment:dtx3
##                                                 0.000000000
##                                              treatment:dtx4
##                                                 0.000000000
##                                              treatment:ep300
##                                                 0.000000000
##                                              treatment:fbxw7
##                                                 0.000000000
##                                              treatment:hdac1
##                                                 0.000000000
##                                              treatment:hdac2
##                                                 0.000000000
##                                              treatment:hes1
##                                                 0.000000000
##                                              treatment:hes5
##                                                 0.000000000
##                                              treatment:heyl
##                                                 0.000000000
##                                              treatment:itch
##                                                 0.000000000
##                                              treatment:jag1
##                                                 0.000000000
##                                              treatment:jag2
##                                                 0.000000000
##                                              treatment:kdm5a
##                                                 0.000000000
##                                              treatment:lfng
##                                                 0.000000000
##                                              treatment:maml1
##                                                 0.000000000
##                                              treatment:maml2
##                                                 0.000000000
##                                              treatment:maml3
##                                                 0.000000000
##                                              treatment:ncor2
##                                                 0.000000000
##                                              treatment:ncstn
##                                                 0.000000000
##                                              treatment:notch1
##                                                 0.000000000
##                                              treatment:notch2
##                                                 0.000000000
##                                              treatment:notch3
##                                                 0.000000000
##                                              treatment:nrarp
##                                                 0.031220094
```

```
##                                                treatment:numb
##                                                   0.000000000
##                                               treatment:numbl
##                                                   0.000000000
##                                               treatment:psen1
##                                                   0.000000000
##                                               treatment:psen2
##                                                   0.000000000
##                                              treatment:psenen
##                                                   0.000000000
##                                                treatment:rbpj
##                                                   0.000000000
##                                               treatment:rbpjl
##                                                   0.000000000
##                                                treatment:rfng
##                                                   0.000000000
##                                                treatment:snw1
##                                                   0.000000000
##                                                treatment:spen
##                                                   0.000000000
##                                                treatment:hes2
##                                                   0.000000000
##                                                treatment:hes4
##                                                   0.000000000
##                                                treatment:hes7
##                                                   0.000000000
##                                                treatment:hey1
##                                                   0.000000000
##                                                treatment:hey2
##                                                   0.000000000
##                                                treatment:acvr1
##                                                   0.000000000
##                                              treatment:acvr1b
##                                                   0.000000000
##                                              treatment:acvr1c
##                                                  -0.014745488
##                                              treatment:acvr2a
##                                                   0.000000000
##                                              treatment:acvr2b
##                                                   0.000000000
##                                              treatment:acvrl1
##                                                   0.000000000
##                                                treatment:akt1
##                                                   0.000000000
##                                              treatment:akt1s1
##                                                   0.000000000
##                                                treatment:akt2
##                                                   0.000000000
##                                               treatment:apaf1
##                                                   0.000000000
##                                               treatment:arl11
##                                                   0.000000000
##                                                 treatment:atr
##                                                   0.000000000
```

```
##                                         treatment:aurka
##                                            0.000000000
##                                           treatment:bad
##                                            0.000000000
##                                          treatment:bcl2
##                                            0.000000000
##                                        treatment:bcl2l1
##                                            0.000000000
##                                         treatment:bmp10
##                                            0.000000000
##                                         treatment:bmp15
##                                            0.000000000
##                                          treatment:bmp2
##                                            0.000000000
##                                          treatment:bmp3
##                                            0.000000000
##                                          treatment:bmp4
##                                            0.000000000
##                                          treatment:bmp5
##                                            0.000000000
##                                          treatment:bmp6
##                                            0.000000000
##                                          treatment:bmp7
##                                            0.000000000
##                                        treatment:bmpr1a
##                                            0.000000000
##                                        treatment:bmpr1b
##                                            0.000000000
##                                         treatment:bmpr2
##                                            0.000000000
##                                          treatment:braf
##                                            0.000000000
##                                        treatment:casp10
##                                            0.000000000
##                                         treatment:casp3
##                                            0.000000000
##                                         treatment:casp6
##                                            0.000000000
##                                         treatment:casp7
##                                            0.000000000
##                                         treatment:casp8
##                                            0.000000000
##                                         treatment:casp9
##                                            0.000000000
##                                         treatment:chek1
##                                            0.000000000
##                                          treatment:csf1
##                                            0.000000000
##                                         treatment:csf1r
##                                            0.000000000
##                                         treatment:cxcl8
##                                            0.000000000
##                                         treatment:cxcr1
##                                            0.000000000
```

```
##                            treatment:cxcr2
##                               0.000000000
##                             treatment:dab2
##                               0.000000000
##                           treatment:diras3
##                               0.000000000
##                            treatment:dlec1
##                               0.000000000
##                             treatment:dph1
##                               0.000000000
##                             treatment:egfr
##                               0.000000000
##                            treatment:eif4e
##                               0.000000000
##                         treatment:eif4ebp1
##                               0.000000000
##                           treatment:eif5a2
##                               0.000000000
##                            treatment:erbb2
##                               0.000000000
##                            treatment:erbb3
##                               0.000000000
##                            treatment:erbb4
##                               0.000000000
##                              treatment:fas
##                               0.000000000
##                             treatment:fgf1
##                               0.000000000
##                            treatment:fgfr1
##                               0.000000000
##                            treatment:folr1
##                               0.000000000
##                            treatment:folr2
##                               0.000000000
##                            treatment:folr3
##                               0.000000000
##                            treatment:foxo1
##                               0.000000000
##                            treatment:foxo3
##                               0.000000000
##                            treatment:gdf11
##                               0.000000000
##                             treatment:gdf2
##                               0.000000000
##                            treatment:gsk3b
##                               0.000000000
##                            treatment:hif1a
##                               0.000000000
##                            treatment:hla.g
##                               0.000000000
##                             treatment:hras
##                               0.000000000
##                             treatment:igf1
##                               0.000000000
```

```
##                             treatment:igf1r
##                                 0.000000000
##                              treatment:inha
##                                -0.052234841
##                             treatment:inhba
##                                 0.000000000
##                             treatment:inhbc
##                                 0.000000000
##                             treatment:itgav
##                                 0.000000000
##                             treatment:itgb3
##                                 0.000000000
##                           treatment:izumo1r
##                                 0.000000000
##                              treatment:kdr
##                                 0.000000000
##                              treatment:kit
##                                 0.000000000
##                             treatment:kras
##                                 0.000000000
##                            treatment:map2k1
##                                 0.000000000
##                            treatment:map2k2
##                                 0.000000000
##                            treatment:map2k3
##                                 0.000000000
##                            treatment:map2k4
##                                 0.000000000
##                            treatment:map2k5
##                                 0.000000000
##                            treatment:map3k1
##                                 0.000000000
##                            treatment:map3k3
##                                 0.000000000
##                            treatment:map3k4
##                                 0.000000000
##                            treatment:map3k5
##                                 0.000000000
##                             treatment:mapk1
##                                 0.000000000
##                            treatment:mapk12
##                                 0.000000000
##                            treatment:mapk14
##                                 0.000000000
##                             treatment:mapk3
##                                 0.000000000
##                             treatment:mapk4
##                                 0.000000000
##                             treatment:mapk6
##                                 0.000000000
##                             treatment:mapk7
##                                 0.000000000
##                             treatment:mapk8
##                                 0.000000000
```

```
##                                    treatment:mapk9
##                                       0.000000000
##                                     treatment:mdc1
##                                       0.000000000
##                                    treatment:mlst8
##                                       0.000000000
##                                     treatment:mmp1
##                                       0.000000000
##                                    treatment:mmp10
##                                       0.000000000
##                                    treatment:mmp11
##                                       0.000000000
##                                    treatment:mmp12
##                                       0.000000000
##                                    treatment:mmp13
##                                       0.000000000
##                                    treatment:mmp14
##                                       0.000000000
##                                    treatment:mmp15
##                                       0.000000000
##                                    treatment:mmp16
##                                       0.000000000
##                                    treatment:mmp17
##                                       0.000000000
##                                    treatment:mmp19
##                                       0.000000000
##                                     treatment:mmp2
##                                       0.000000000
##                                    treatment:mmp21
##                                       0.000000000
##                                   treatment:mmp23b
##                                       0.000000000
##                                    treatment:mmp24
##                                       0.000000000
##                                    treatment:mmp25
##                                       0.000000000
##                                    treatment:mmp26
##                                       0.000000000
##                                    treatment:mmp27
##                                       0.000000000
##                                    treatment:mmp28
##                                       0.000000000
##                                     treatment:mmp3
##                                       0.000000000
##                                     treatment:mmp7
##                                       0.000000000
##                                     treatment:mmp9
##                                       0.000000000
##                                     treatment:mtor
##                                       0.000000000
##                                    treatment:nfkb1
##                                       0.000000000
##                                    treatment:nfkb2
##                                       0.000000000
```

```
##                                             treatment:opcml
##                                               0.000000000
##                                             treatment:pdgfa
##                                               0.000000000
##                                             treatment:pdgfb
##                                               0.000000000
##                                            treatment:pdgfra
##                                               0.000000000
##                                            treatment:pdgfrb
##                                               0.000000000
##                                             treatment:pdpk1
##                                               0.000000000
##                                              treatment:peg3
##                                               0.000000000
##                                            treatment:pik3ca
##                                               0.000000000
##                                            treatment:pik3r1
##                                               0.000000000
##                                            treatment:pik3r2
##                                               0.000000000
##                                            treatment:plagl1
##                                               0.000000000
##                                              treatment:ptk2
##                                               0.000000000
##                                             treatment:rab25
##                                               0.000000000
##                                             treatment:rad51
##                                               0.000000000
##                                              treatment:raf1
##                                               0.000000000
##                                            treatment:rassf1
##                                               0.000000000
##                                              treatment:rheb
##                                               0.000000000
##                                            treatment:rictor
##                                               0.000000000
##                                              treatment:rps6
##                                               0.000000000
##                                            treatment:rps6ka1
##                                               0.000000000
##                                            treatment:rps6ka2
##                                               0.000000000
##                                            treatment:rps6kb1
##                                               0.000000000
##                                            treatment:rps6kb2
##                                               0.000000000
##                                             treatment:rptor
##                                               0.000000000
##                                            treatment:slc19a1
##                                               0.000000000
##                                             treatment:smad1
##                                               0.000000000
##                                             treatment:smad2
##                                               0.000000000
```

```
##                                                  treatment:smad3
##                                                   0.000000000
##                                                  treatment:smad4
##                                                   0.000000000
##                                                  treatment:smad5
##                                                   0.000000000
##                                                  treatment:smad6
##                                                   0.000000000
##                                                  treatment:smad7
##                                                   0.000000000
##                                                  treatment:smad9
##                                                   0.000000000
##                                                 treatment:sptbn1
##                                                   0.000000000
##                                                   treatment:terc
##                                                   0.000000000
##                                                   treatment:tert
##                                                   0.000000000
##                                                  treatment:tgfb1
##                                                   0.000000000
##                                                  treatment:tgfb2
##                                                   0.000000000
##                                                  treatment:tgfb3
##                                                   0.000000000
##                                                 treatment:tgfbr1
##                                                   0.000000000
##                                                 treatment:tgfbr2
##                                                   0.000000000
##                                                 treatment:tgfbr3
##                                                   0.000000000
##                                                   treatment:tsc1
##                                                   0.000000000
##                                                   treatment:tsc2
##                                                   0.000000000
##                                                  treatment:vegfa
##                                                   0.000000000
##                                                  treatment:vegfb
##                                                   0.000000000
##                                                  treatment:wfdc2
##                                                   0.000000000
##                                                   treatment:wwox
##                                                   0.000000000
##                                                 treatment:zfyve9
##                                                   0.084331358
##                                                 treatment:arid1a
##                                                   0.000000000
##                                                 treatment:arid1b
##                                                   0.000000000
##                                                   treatment:cbfb
##                                                   0.000000000
##                                                  treatment:gata3
##                                                   0.000000000
##                                                  treatment:kmt2c
##                                                   0.000000000
```

```
##                                treatment:kmt2d
##                                   0.000000000
##                                 treatment:myh9
##                                   0.000000000
##                                 treatment:ncor1
##                                   0.000000000
##                               treatment:pde4dip
##                                   0.000000000
##                                 treatment:ptprd
##                                   0.000000000
##                                  treatment:ros1
##                                   0.000000000
##                                 treatment:runx1
##                                   0.000000000
##                                  treatment:tbx3
##                                   0.000000000
##                                 treatment:abcb1
##                                   0.000000000
##                                treatment:abcb11
##                                   0.000000000
##                                 treatment:abcc1
##                                   0.000000000
##                                treatment:abcc10
##                                   0.000000000
##                                  treatment:bbc3
##                                   0.000000000
##                                   treatment:bmf
##                                   0.000000000
##                                treatment:cyp2c8
##                                   0.000000000
##                                treatment:cyp3a4
##                                   0.000000000
##                                  treatment:fgf2
##                                   0.000000000
##                                   treatment:fn1
##                                   0.000000000
##                                  treatment:map2
##                                   0.000000000
##                                  treatment:map4
##                                   0.000000000
##                                  treatment:mapt
##                                  -0.317144317
##                                 treatment:nr1i2
##                                   0.000000000
##                               treatment:slco1b3
##                                   0.000000000
##                                 treatment:tubb1
##                                   0.000000000
##                                treatment:tubb4a
##                                   0.000000000
##                                treatment:tubb4b
##                                   0.000000000
##                                treatment:twist1
##                                   0.000000000
```

```
##                                treatment:adgra2
##                                     0.000000000
##                                  treatment:afdn
##                                     0.000000000
##                                  treatment:aff2
##                                     0.000000000
##                                  treatment:agmo
##                                     0.000000000
##                                 treatment:agtr2
##                                     0.000000000
##                                 treatment:ahnak
##                                     0.000000000
##                                treatment:ahnak2
##                                     0.000000000
##                                 treatment:akap9
##                                     0.000000000
##                                   treatment:alk
##                                     0.000000000
##                                   treatment:apc
##                                     0.000000000
##                                 treatment:arid2
##                                     0.000000000
##                                treatment:arid5b
##                                     0.000000000
##                                 treatment:asxl1
##                                     0.000000000
##                                 treatment:asxl2
##                                     0.000000000
##                                  treatment:bap1
##                                     0.000000000
##                                 treatment:bcas3
##                                     0.000000000
##                                 treatment:birc6
##                                     0.000000000
##                              treatment:cacna2d3
##                                     0.000000000
##                                 treatment:ccnd3
##                                     0.000000000
##                                  treatment:chd1
##                                     0.000000000
##                                  treatment:clk3
##                                     0.000000000
##                                 treatment:clrn2
##                                     0.000000000
##                               treatment:col12a1
##                                     0.000000000
##                               treatment:col22a1
##                                     0.000000000
##                                treatment:col6a3
##                                     0.000000000
##                                  treatment:ctcf
##                                     0.000000000
##                                treatment:ctnna1
##                                     0.000000000
```

```
##                                              treatment:ctnna3
##                                                  0.000000000
##                                              treatment:dnah11
##                                                  0.000000000
##                                               treatment:dnah2
##                                                  0.000000000
##                                               treatment:dnah5
##                                                  0.000000000
##                                               treatment:dtwd2
##                                                  0.000000000
##                                               treatment:fam20c
##                                                  0.000000000
##                                               treatment:fanca
##                                                  0.000000000
##                                              treatment:fancd2
##                                                  0.000000000
##                                                treatment:flt3
##                                                  0.000000000
##                                               treatment:foxp1
##                                                  0.000000000
##                                               treatment:frmd3
##                                                  0.000000000
##                                                 treatment:gh1
##                                                  0.000000000
##                                                treatment:gldc
##                                                  0.000000000
##                                               treatment:gpr32
##                                                  0.000000000
##                                                treatment:gps2
##                                                  0.000000000
##                                               treatment:hdac9
##                                                  0.000000000
##                                               treatment:herc2
##                                                  0.000000000
##                                            treatment:hist1h2bc
##                                                  0.000000000
##                                               treatment:kdm3a
##                                                  0.000000000
##                                               treatment:kdm6a
##                                                  0.000000000
##                                               treatment:klrg1
##                                                  0.000000000
##                                               treatment:l1cam
##                                                  0.000000000
##                                               treatment:lama2
##                                                  0.000000000
##                                               treatment:lamb3
##                                                  0.000000000
##                                              treatment:large1
##                                                  0.000000000
##                                              treatment:ldlrap1
##                                                  0.000000000
##                                                treatment:lifr
##                                                  0.000000000
```

```
##                                 treatment:lipi
##                                  0.000000000
##                                treatment:magea8
##                                  0.000000000
##                               treatment:map3k10
##                                  0.000000000
##                               treatment:map3k13
##                                  0.000000000
##                                 treatment:men1
##                                  0.000000000
##                                 treatment:mtap
##                                  0.000000000
##                                treatment:muc16
##                                  0.000000000
##                                treatment:myo1a
##                                  0.000000000
##                                treatment:myo3a
##                                  0.000000000
##                                treatment:ncoa3
##                                  0.000000000
##                                 treatment:nek1
##                                  0.000000000
##                                 treatment:nf2
##                                  0.000000000
##                                 treatment:npnt
##                                  0.000000000
##                                treatment:nr2f1
##                                  0.000000000
##                                treatment:nr3c1
##                                  0.000000000
##                                 treatment:nras
##                                  0.000000000
##                                 treatment:nrg3
##                                 -0.008037592
##                                 treatment:nt5e
##                                  0.000000000
##                                 treatment:or6a2
##                                  0.000000000
##                                 treatment:palld
##                                  0.000000000
##                                 treatment:pbrm1
##                                  0.000000000
##                                treatment:ppp2cb
##                                  0.000000000
##                                treatment:ppp2r2a
##                                  0.000000000
##                                treatment:prkacg
##                                  0.000000000
##                                 treatment:prkce
##                                  0.000000000
##                                 treatment:prkcq
##                                  0.000000000
##                                 treatment:prkcz
##                                  0.000000000
```

```
##                                   treatment:prkg1
##                                      0.000000000
##                                   treatment:prps2
##                                      0.000000000
##                                   treatment:prr16
##                                      0.000000000
##                                  treatment:ptpn22
##                                      0.000000000
##                                   treatment:ptprm
##                                      0.000000000
##                                treatment:rasgef1b
##                                      0.000000000
##                                    treatment:rpgr
##                                     -0.031102534
##                                    treatment:ryr2
##                                      0.000000000
##                                   treatment:sbno1
##                                      0.000000000
##                                  treatment:setd1a
##                                      0.000000000
##                                   treatment:setd2
##                                      0.000000000
##                                  treatment:setdb1
##                                      0.000000000
##                                   treatment:sf3b1
##                                      0.000000000
##                                    treatment:sgcd
##                                      0.000000000
##                                  treatment:shank2
##                                      0.000000000
##                                   treatment:siah1
##                                      0.000000000
##                                    treatment:sik1
##                                      0.000000000
##                                    treatment:sik2
##                                      0.000000000
##                                 treatment:smarcb1
##                                      0.000000000
##                                 treatment:smarcc1
##                                      0.000000000
##                                 treatment:smarcc2
##                                      0.000000000
##                                 treatment:smarcd1
##                                      0.000000000
##                                  treatment:spaca1
##                                      0.000000000
##                                   treatment:stab2
##                                      0.000000000
##                                   treatment:stmn2
##                                      0.000000000
##                                   treatment:syne1
##                                      0.000000000
##                                    treatment:taf1
##                                      0.000000000
```

```
##                                                     treatment:taf4b
##                                                          0.000000000
##                                                    treatment:tbl1xr1
##                                                          0.000000000
##                                                        treatment:tg
##                                                          0.000000000
##                                                     treatment:thada
##                                                          0.000000000
##                                                    treatment:thsd7a
##                                                          0.000000000
##                                                     treatment:ttyh1
##                                                          0.000000000
##                                                      treatment:ubr5
##                                                          0.000000000
##                                                     treatment:ush2a
##                                                          0.013131015
##                                                     treatment:usp9x
##                                                          0.000000000
##                                                      treatment:utrn
##                                                          0.000000000
##                                                    treatment:zfp36l1
##                                                          0.000000000
##                                                     treatment:ackr3
##                                                          0.000000000
##                                                    treatment:akr1c1
##                                                          0.000000000
##                                                    treatment:akr1c2
##                                                          0.000000000
##                                                    treatment:akr1c3
##                                                          0.000000000
##                                                    treatment:akr1c4
##                                                          0.000000000
##                                                      treatment:akt3
##                                                          0.000000000
##                                                        treatment:ar
##                                                          0.000000000
##                                                      treatment:bche
##                                                          0.000000000
##                                                      treatment:cdk8
##                                                          0.000000000
##                                                    treatment:cdkn2c
##                                                          0.000000000
##                                                     treatment:cyb5a
##                                                          0.000000000
##                                                    treatment:cyp11a1
##                                                         -0.154061815
##                                                    treatment:cyp11b2
##                                                          0.000000000
##                                                    treatment:cyp17a1
##                                                          0.000000000
##                                                    treatment:cyp19a1
##                                                          0.000000000
##                                                    treatment:cyp21a2
##                                                          0.000000000
```

```
##                         treatment:cyp3a43
##                            0.000000000
##                          treatment:cyp3a5
##                            0.000000000
##                          treatment:cyp3a7
##                            0.000000000
##                            treatment:ddc
##                            0.000000000
##                           treatment:hes6
##                            0.000000000
##                         treatment:hsd17b1
##                            0.000000000
##                        treatment:hsd17b10
##                            0.000000000
##                        treatment:hsd17b11
##                            0.000000000
##                        treatment:hsd17b12
##                            0.000000000
##                        treatment:hsd17b13
##                            0.000000000
##                        treatment:hsd17b14
##                            0.000000000
##                         treatment:hsd17b2
##                            0.000000000
##                         treatment:hsd17b3
##                            0.000000000
##                         treatment:hsd17b4
##                            0.000000000
##                         treatment:hsd17b6
##                            0.000000000
##                         treatment:hsd17b7
##                           -0.003366814
##                         treatment:hsd17b8
##                            0.000000000
##                          treatment:hsd3b1
##                            0.000000000
##                          treatment:hsd3b2
##                            0.000000000
##                          treatment:hsd3b7
##                            0.000000000
##                           treatment:mecom
##                            0.000000000
##                            treatment:met
##                            0.000000000
##                           treatment:ncoa2
##                            0.000000000
##                           treatment:nrip1
##                            0.000000000
##                          treatment:pik3r3
##                            0.000000000
##                           treatment:prkci
##                            0.000000000
##                           treatment:prkd1
##                            0.000000000
```

```
##                                    treatment:ran
##                                      0.000000000
##                                   treatment:rdh5
##                                      0.000000000
##                                   treatment:sdc4
##                                      0.000000000
##                                treatment:serpini1
##                                      0.000000000
##                                   treatment:shbg
##                                      0.000000000
##                                treatment:slc29a1
##                                      0.000000000
##                                   treatment:sox9
##                                      0.000000000
##                                  treatment:spry2
##                                      0.000000000
##                                 treatment:srd5a1
##                                      0.000000000
##                                 treatment:srd5a2
##                                      0.000000000
##                                 treatment:srd5a3
##                                     -0.002806890
##                                    treatment:st7
##                                      0.000000000
##                                   treatment:star
##                                      0.000000000
##                                   treatment:tnk2
##                                      0.000000000
##                                  treatment:tulp4
##                                      0.000000000
##                                treatment:ugt2b15
##                                      0.000000000
##                                treatment:ugt2b17
##                                     -0.041345522
##                                 treatment:ugt2b7
##                                      0.000000000
##                       treatment:brca1:brca1_mut
##                                      0.000000000
##                       treatment:brca2:brca2_mut
##                                      0.000000000
##                         treatment:pten:pten_mut
##                                      0.000000000
##                         treatment:tp53:tp53_mut
##                                      0.000000000
##                         treatment:cdh1:cdh1_mut
##                                      0.000000000
##                           treatment:nf1:nf1_mut
##                                      0.000000000
##                           treatment:rb1:rb1_mut
##                                      0.000000000
##                         treatment:jak1:jak1_mut
##                                      0.000000000
##                       treatment:ep300:ep300_mut
##                                      0.000000000
```

```
##                            treatment:ncor2:ncor2_mut
##                                          0.000000000
##                          treatment:notch1:notch1_mut
##                                          0.000000000
##                              treatment:akt1:akt1_mut
##                                          0.000000000
##                                treatment:atr:atr_mut
##                                          0.000000000
##                              treatment:egfr:egfr_mut
##                                          0.000000000
##                            treatment:erbb2:erbb2_mut
##                                         -0.030886788
##                            treatment:erbb3:erbb3_mut
##                                          0.000000000
##                            treatment:erbb4:erbb4_mut
##                                          0.000000000
##                            treatment:foxo3:foxo3_mut
##                                          0.000000000
##                          treatment:map2k4:map2k4_mut
##                                          0.000000000
##                          treatment:map3k1:map3k1_mut
##                                          0.000000000
##                          treatment:pik3ca:pik3ca_mut
##                                          0.000000000
##                          treatment:pik3r1:pik3r1_mut
##                                          0.000000000
##                            treatment:smad4:smad4_mut
##                                          0.000000000
##                          treatment:arid1a:arid1a_mut
##                                          0.000000000
##                          treatment:arid1b:arid1b_mut
##                                          0.000000000
##                              treatment:cbfb:cbfb_mut
##                                          0.000000000
##                            treatment:gata3:gata3_mut
##                                          0.000000000
##                            treatment:kmt2c:kmt2c_mut
##                                          0.000000000
##                            treatment:kmt2d:kmt2d_mut
##                                          0.000000000
##                              treatment:myh9:myh9_mut
##                                          0.000000000
##                            treatment:ncor1:ncor1_mut
##                                          0.000000000
##                        treatment:pde4dip:pde4dip_mut
##                                          0.000000000
##                            treatment:ptprd:ptprd_mut
##                                          0.000000000
##                              treatment:ros1:ros1_mut
##                                          0.000000000
##                            treatment:runx1:runx1_mut
##                                          0.000000000
##                              treatment:tbx3:tbx3_mut
##                                          0.000000000
```

```
##                             treatment:adgra2:adgra2_mut
##                                        0.000000000
##                                 treatment:afdn:afdn_mut
##                                        0.000000000
##                                 treatment:aff2:aff2_mut
##                                        0.000000000
##                               treatment:ahnak:ahnak_mut
##                                        0.000000000
##                             treatment:ahnak2:ahnak2_mut
##                                        0.000000000
##                               treatment:akap9:akap9_mut
##                                        0.000000000
##                                   treatment:alk:alk_mut
##                                        0.000000000
##                                   treatment:apc:apc_mut
##                                        0.000000000
##                               treatment:arid2:arid2_mut
##                                        0.000000000
##                             treatment:arid5b:arid5b_mut
##                                        0.000000000
##                               treatment:asxl1:asxl1_mut
##                                        0.000000000
##                               treatment:asxl2:asxl2_mut
##                                        0.000000000
##                                 treatment:bap1:bap1_mut
##                                        0.000000000
##                               treatment:birc6:birc6_mut
##                                        0.000000000
##                         treatment:cacna2d3:cacna2d3_mut
##                                        0.000000000
##                                 treatment:chd1:chd1_mut
##                                       -0.059168382
##                             treatment:col12a1:col12a1_mut
##                                        0.000000000
##                             treatment:col22a1:col22a1_mut
##                                        0.000000000
##                               treatment:col6a3:col6a3_mut
##                                        0.000000000
##                                 treatment:ctcf:ctcf_mut
##                                        0.000000000
##                             treatment:ctnna3:ctnna3_mut
##                                        0.000000000
##                             treatment:dnah11:dnah11_mut
##                                        0.000000000
##                               treatment:dnah2:dnah2_mut
##                                        0.000000000
##                               treatment:dnah5:dnah5_mut
##                                        0.000000000
##                             treatment:fam20c:fam20c_mut
##                                        0.000000000
##                               treatment:fanca:fanca_mut
##                                        0.000000000
##                             treatment:fancd2:fancd2_mut
##                                        0.000000000
```

```
##                          treatment:gldc:gldc_mut
##                                        0.000000000
##                          treatment:herc2:herc2_mut
##                                        0.000000000
##                          treatment:kdm3a:kdm3a_mut
##                                        0.000000000
##                          treatment:kdm6a:kdm6a_mut
##                                        0.000000000
##                          treatment:l1cam:l1cam_mut
##                                        0.000000000
##                          treatment:lama2:lama2_mut
##                                        0.000000000
##                          treatment:lamb3:lamb3_mut
##                                        0.000000000
##                            treatment:lifr:lifr_mut
##                                        0.000000000
##                          treatment:muc16:muc16_mut
##                                        0.000000000
##                          treatment:myo1a:myo1a_mut
##                                        0.000000000
##                          treatment:myo3a:myo3a_mut
##                                        0.000000000
##                          treatment:ncoa3:ncoa3_mut
##                                        0.000000000
##                          treatment:pbrm1:pbrm1_mut
##                                        0.000000000
##                          treatment:ptprm:ptprm_mut
##                                        0.000000000
##                            treatment:ryr2:ryr2_mut
##                                        0.000000000
##                          treatment:sbno1:sbno1_mut
##                                        0.000000000
##                        treatment:setd1a:setd1a_mut
##                                        0.000000000
##                          treatment:setd2:setd2_mut
##                                        0.000000000
##                        treatment:setdb1:setdb1_mut
##                                        0.000000000
##                          treatment:sf3b1:sf3b1_mut
##                                        0.000000000
##                        treatment:shank2:shank2_mut
##                                        0.000000000
##                      treatment:smarcc2:smarcc2_mut
##                                        0.000000000
##                          treatment:stab2:stab2_mut
##                                        0.000000000
##                          treatment:syne1:syne1_mut
##                                        0.000000000
##                            treatment:taf1:taf1_mut
##                                        0.000000000
##                                treatment:tg:tg_mut
##                                        0.000000000
##                          treatment:thada:thada_mut
##                                        0.000000000
```

```
##                        treatment:thsd7a:thsd7a_mut
##                                         0.000000000
##                              treatment:ubr5:ubr5_mut
##                                         0.000000000
##                            treatment:ush2a:ush2a_mut
##                                         0.000000000
##                            treatment:usp9x:usp9x_mut
##                                         0.000000000
##                              treatment:utrn:utrn_mut
##                                         0.000000000
```

cox.en.beta.nonzero

```
##      lymph_nodes_examined_positive                      kdm3a:kdm3a_mut
##                        0.429991335                          0.369957710
##                          treatment                integrative_cluster5
##                        0.347782309                          0.261403318
##                              gsk3b                         treatment:e2f8
##                        0.239318961                          0.219624668
##                               prkg1                   treatment:tumor_size
##                        0.199972830                          0.189831732
##                            eif4ebp1                     treatment:zfyve9
##                        0.129527071                          0.084331358
##                                e2f7                                  dll3
##                        0.060377905                          0.054955479
##                         treatment:e2f7                            tumor_size
##                        0.040005288                          0.039285186
##                               smad7                       treatment:nrarp
##                        0.031579997                          0.031220094
##                              prkacg                                 pdgfb
##                        0.026250727                          0.015773806
##                       treatment:ush2a                                  akt3
##                        0.013131015                          0.007516268
##                                men1                                 smad6
##                        0.006066667                          0.003035938
##                       treatment:srd5a3                   treatment:hsd17b7
##                       -0.002806890                         -0.003366814
##                        treatment:nrg3                               map3k1
##                       -0.008037592                         -0.011575291
##                                casp7                                 mmp25
##                       -0.012710693                         -0.014298532
##                       treatment:acvr1c                                 igf1
##                       -0.014745488                         -0.015017205
##           treatment:erbb2:erbb2_mut                         treatment:rpgr
##                       -0.030886788                         -0.031102534
##                integrative_cluster3                     treatment:ugt2b17
##                       -0.036916691                         -0.041345522
##                                brca2                               ugt2b17
##                       -0.042959447                         -0.043295059
##                       treatment:inha                                  mapt
##                       -0.052234841                         -0.055817428
##                                e2f1                 treatment:chd1:chd1_mut
##                       -0.057084879                         -0.059168382
##                              diras3                       tbx3:tbx3_mut
##                       -0.078511004                         -0.079733374
```

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```
##                      acvr1c                              cul1
##                -0.105162501                      -0.106889044
##                      stat5a                      tp53:tp53_mut
##                -0.111515329                      -0.121472412
##             gata3:gata3_mut                    treatment:cul1
##                -0.138823153                      -0.145590316
## pam50_._claudin.low_subtypeLumA              treatment:cyp11a1
##                -0.152032481                      -0.154061815
##               treatment:mapt
##                -0.317144317
```

```
cox.en.beta_2 = cox.fit_2$beta[,1]
cox.en.beta.nonzero_2 = cox.fit_2$beta[,1][abs(cox.fit_2$beta[,1]) > 1e-10][order(cox.fit_2$beta[,1][abs

cox.en.beta_3 = cox.fit_3$beta[,1]
cox.en.beta.nonzero_3 = cox.fit_3$beta[,1][abs(cox.fit_3$beta[,1]) > 1e-10][order(cox.fit_3$beta[,1][abs

cox.en.beta_2 = cox.fit_2$beta[,1]
cox.en.beta.nonzero_2 = cox.fit_2$beta[,1][abs(cox.fit_2$beta[,1]) > 1e-10][order(cox.fit_2$beta[,1][abs

cox.en.beta.nonzero_2
```

```
##    lymph_nodes_examined_positive                     treatment
##                   0.3962247677                  0.3643216028
##                kdm3a:kdm3a_mut          integrative_cluster5
##                   0.3415824700                  0.2874316842
##                          gsk3b          treatment:tumor_size
##                   0.2434052539                  0.2022740288
##                 treatment:e2f8                          prkg1
##                   0.1786587844                  0.1395393081
##                       eif4ebp1                   tumor_stage3
##                   0.1299748576                  0.1213385278
##               treatment:zfyve9               treatment:nrarp
##                   0.1081327068                  0.0703986734
##                treatment:prkcz                   tumor_stage2
##                   0.0565429854                  0.0500720413
##                     tumor_size                 treatment:e2f7
##                   0.0357496013                  0.0321913606
##                           e2f7                           dll3
##                   0.0280666054                  0.0266294111
##                treatment:ush2a                treatment:cxcl8
##                   0.0240795448                  0.0103307838
##                          pdgfb             treatment:eif4ebp1
##                   0.0094421874                  0.0080216058
##                           men1                 treatment:terc
##                   0.0077136094                  0.0076179627
##                          smad7              shank2:shank2_mut
##                   0.0025447624                 -0.0001583666
##                treatment:pbrm1                           nr3c1
##                  -0.0011144275                 -0.0034206502
##                birc6:birc6_mut               treatment:srd5a3
##                  -0.0042340371                 -0.0080621912
##                          casp7               treatment:acvr1c
##                  -0.0114110918                 -0.0166340409
##                           igf1          integrative_cluster3
```

```
##                         -0.0196002170                      -0.0197492308
##                                  brca2                               e2f1
##                         -0.0318839150                      -0.0329041489
##                                 map3k1                               mapt
##                         -0.0350371329                      -0.0382757821
##                         treatment:nrg3                      gata3:gata3_mut
##                         -0.0468981186                      -0.0539752577
##                         treatment:inha                             ugt2b17
##                         -0.0581064544                      -0.0653846921
##                       treatment:hsd17b7             treatment:chd1:chd1_mut
##                         -0.0665996709                      -0.0768081300
##                                  diras3                      tp53:tp53_mut
##                         -0.0804763607                      -0.0813106049
##                       treatment:cyp11a1                         atr:atr_mut
##                         -0.0860935572                      -0.0878894843
##                                   cul1                              acvr1c
##                         -0.0944239601                      -0.0997078098
##                         tbx3:tbx3_mut                       treatment:cul1
##                         -0.1021060807                      -0.1254065359
##                                 stat5a  pam50_._claudin.low_subtypeLumA
##                         -0.1442501922                      -0.1679222503
##                         treatment:mapt
##                         -0.3331440694
```

cox.en.beta.nonzero_3

```
##    lymph_nodes_examined_positive                           treatment
##                          0.3841860734                       0.3476927998
##              integrative_cluster5                               gsk3b
##                          0.2384409930                       0.2284688367
##                       tumor_stage3                        treatment:e2f8
##                          0.2141502347                       0.1785825332
##               treatment:tumor_size                            eif4ebp1
##                          0.1514550933                       0.1186634378
##                                 prkg1                               e2f7
##                          0.1026237250                       0.0375293907
##                                 aurka                               dll3
##                          0.0241813119                       0.0221239338
##                     treatment:zfyve9                       treatment:e2f7
##                          0.0100678051                       0.0090238419
##                                 smad7                              pdgfb
##                          0.0069072699                       0.0009589283
##                                 brca2                       treatment:rpgr
##                         -0.0016476231                      -0.0058930115
##                                  e2f1                               mapt
##                         -0.0065817850                      -0.0207472337
##                               ugt2b17                      tp53:tp53_mut
##                         -0.0228313861                      -0.0299565115
##                       gata3:gata3_mut                             map3k1
##                         -0.0303628989                      -0.0335650384
##                                   cul1             treatment:hsd17b7
##                         -0.0352237413                      -0.0394587768
##                                  diras3                             acvr1c
##                         -0.0605019989                      -0.0774130175
##                                 stat5a                   treatment:cyp11a1
```

```
##                      -0.1088171940                          -0.1148574350
##                 treatment:cul1 pam50_._claudin.low_subtypeLumA
##                      -0.1158318310                          -0.1289206891
##                  treatment:mapt
##                      -0.2602185733
```

```
nonzero_2 = as.numeric(which(abs(cox.fit_2$beta[,1]) > 1e-10))
nonzero_3 = as.numeric(which(abs(cox.fit_3$beta[,1]) > 1e-10))
nonzero_4 = as.numeric(which(abs(cox.fit_4$beta[,1]) > 1e-10))
nonzero_5 = as.numeric(which(abs(cox.fit_5$beta[,1]) > 1e-10))
```

```
common = intersect(nonzero_2, intersect(nonzero_3, intersect(nonzero_4, nonzero_5)))
```

```
cox.fit_2$beta[common,1]
```

```
##                          treatment    lymph_nodes_examined_positive
##                        0.364321603                      0.396224768
## pam50_._claudin.low_subtypeLumA            integrative_cluster5
##                       -0.167922250                      0.287431684
##                              e2f7                            stat5a
##                        0.028066605                     -0.144250192
##                              cul1                            acvr1c
##                       -0.094423960                     -0.099707810
##                             diras3                          eif4ebp1
##                       -0.080476361                      0.129974858
##                              gsk3b                            map3k1
##                        0.243405254                     -0.035037133
##                              pdgfb                              mapt
##                        0.009442187                     -0.038275782
##                              prkg1                           ugt2b17
##                        0.139539308                     -0.065384692
##                        tp53:tp53_mut                   gata3:gata3_mut
##                       -0.081310605                     -0.053975258
##                 treatment:tumor_size                    treatment:e2f8
##                        0.202274029                      0.178658784
##                     treatment:cul1                 treatment:zfyve9
##                       -0.125406536                      0.108132707
##                     treatment:mapt                 treatment:cyp11a1
##                       -0.333144069                     -0.086093557
##                  treatment:hsd17b7
##                       -0.066599671
```

```
cox.fit_2$beta[common]
```

```
##  [1]   0.364321603   0.396224768  -0.167922250   0.287431684   0.028066605
##  [6]  -0.144250192  -0.094423960  -0.099707810  -0.080476361   0.129974858
## [11]   0.243405254  -0.035037133   0.009442187  -0.038275782   0.139539308
## [16]  -0.065384692  -0.081310605  -0.053975258   0.202274029   0.178658784
## [21]  -0.125406536   0.108132707  -0.333144069  -0.086093557  -0.066599671
```

```
cox.fit_3$beta[common]
```

```
##  [1]   0.3476927998   0.3841860734  -0.1289206891   0.2384409930   0.0375293907
##  [6]  -0.1088171940  -0.0352237413  -0.0774130175  -0.0605019989   0.1186634378
## [11]   0.2284688367  -0.0335650384   0.0009589283  -0.0207472337   0.1026237250
## [16]  -0.0228313861  -0.0299565115  -0.0303628989   0.1514550933   0.1785825332
```

```
## [21] -0.1158318310  0.0100678051 -0.2602185733 -0.1148574350 -0.0394587768
```

```
cox.fit_4$beta[common]
```

```
##  [1]   0.34996087   0.37844573  -0.13994924   0.31536490   0.05016256  -0.10684454
##  [7]  -0.05271470  -0.07773049  -0.07644247   0.10434735   0.20454000  -0.03935772
## [13]   0.01722024  -0.03311242   0.12420754  -0.02813309  -0.07297772  -0.03921558
## [19]   0.23477622   0.17115736  -0.13667896   0.08778544  -0.25136692  -0.11628356
## [25]  -0.02933571
```

```
cox.fit_5$beta[common]
```

```
##  [1]   0.331994022   0.396280534  -0.144294892   0.240822534   0.029789071
##  [6]  -0.132510561  -0.100009043  -0.102728346  -0.078702380   0.122959331
## [11]   0.243855479  -0.022577776   0.001276889  -0.033054844   0.146136591
## [16]  -0.070581607  -0.061837565  -0.093933651   0.122027642   0.196330185
## [21]  -0.148044856   0.100526881  -0.309994398  -0.165852232  -0.058253673
```

```
sum((cox.fit$beta[common] > 0 & cox.fit_2$beta[common] <= 0) | (cox.fit$beta[common] <= 0 & cox.fit_2$b
```

```
## [1] 0
```

```
sum((cox.fit_2$beta[common] > 0 & cox.fit_3$beta[common] <= 0) | (cox.fit_2$beta[common] <= 0 & cox.fit
```

```
## [1] 0
```

```
sum((cox.fit_2$beta[common] > 0 & cox.fit_4$beta[common] <= 0) | (cox.fit_2$beta[common] <= 0 & cox.fit
```

```
## [1] 0
```

```
sum((cox.fit_2$beta[common] > 0 & cox.fit_5$beta[common] <= 0) | (cox.fit_2$beta[common] <= 0 & cox.fit
```

```
## [1] 0
```

```
get.race.unpenalized = function(x, model, weights)
{
  n = nrow(x)
  ind = which(names(x) == 'treatment')
  x0 = x
  x1 = x
  x0[,ind] = 0
  x1[,ind] = 1

  scurve0 = survfit(model, newdata = x0, weights = W.vec)
  scurve1 = survfit(model, newdata = x1, weights = W.vec)

  AUC0 = sum(rowMeans(scurve0$surv) * c(scurve0$time[1], diff(scurve0$time)))
  AUC1 = sum(rowMeans(scurve1$surv) * c(scurve1$time[1], diff(scurve1$time)))

  RACE = AUC1 - AUC0
  return(RACE)

}
```

Fitting the Cox model with selected variables

```
data_matrix = data.frame(model_matrix)
```

```
coxmodel <- coxph(y ~ kdm3a.kdm3a_mut  + lymph_nodes_examined_positive +
                      treatment       +     as.factor(integrative_cluster5) +
```

```
                  as.factor(integrative_cluster3) +
                      gsk3b       +        treatment.tumor_size +
                      prkg1       +            treatment.e2f8 +
                    eif4ebp1      +          treatment.zfyve9 +
              treatment.ush2a        +                    dll3 +
              treatment.nrarp         +            tumor_size +
             treatment.e2f7           +                  e2f7 +
                      smad7          +                  men1 +
                    prkacg            +      treatment.notch1 +
                      pdgfb            +        as.factor(tumor_stage2) +
                      mmp25             +    treatment.acvr1c +
             treatment.srd5a3           +    treatment.hsd17b7 +
                      mlh1              +                 casp7 +
                      brca2             +        treatment.rpgr +
            treatment.ugt2b17           +                  igf1 +
              treatment.nrg3            +               map3k1 +
                      mapt              +                  e2f1 +
                  ugt2b17 +
              treatment.inha            +                diras3 +
              tp53.tp53_mut             +           atr.atr_mut +
             gata3.gata3_mut            +                acvr1c +
                      cul1              +                stat5a +
          treatment.cul1 + as.factor(pam50_._claudin.low_subtypeLumA) +
             birc6.birc6_mut           +      treatment.cyp11a1 +
               tbx3.tbx3_mut              +         treatment.mapt, weights = c(W.vec), data = data_matri
```

```
summary(coxmodel)
```

```
## Call:
## coxph(formula = y ~ kdm3a.kdm3a_mut + lymph_nodes_examined_positive +
##     treatment + as.factor(integrative_cluster5) + as.factor(integrative_cluster3) +
##     gsk3b + treatment.tumor_size + prkg1 + treatment.e2f8 + eif4ebp1 +
##     treatment.zfyve9 + treatment.ush2a + dll3 + treatment.nrarp +
##     tumor_size + treatment.e2f7 + e2f7 + smad7 + men1 + prkacg +
##     treatment.notch1 + pdgfb + as.factor(tumor_stage2) + mmp25 +
##     treatment.acvr1c + treatment.srd5a3 + treatment.hsd17b7 +
##     mlh1 + casp7 + brca2 + treatment.rpgr + treatment.ugt2b17 +
##     igf1 + treatment.nrg3 + map3k1 + mapt + e2f1 + ugt2b17 +
##     treatment.inha + diras3 + tp53.tp53_mut + atr.atr_mut + gata3.gata3_mut +
##     acvr1c + cul1 + stat5a + treatment.cul1 + as.factor(pam50_._claudin.low_subtypeLumA) +
##     birc6.birc6_mut + treatment.cyp11a1 + tbx3.tbx3_mut + treatment.mapt,
##     data = data_matrix, weights = c(W.vec))
##
##   n= 879, number of events= 303
##
##
##                                      coef exp(coef) se(coef)
## kdm3a.kdm3a_mut                   3.43128  30.91621  0.87534
## lymph_nodes_examined_positive     0.72412   2.06292  0.07472
## treatment                         0.26090   1.29810  0.11607
## as.factor(integrative_cluster5)1  0.40535   1.49983  0.13883
## as.factor(integrative_cluster3)1 -0.32163   0.72497  0.21011
## gsk3b                             0.15196   1.16411  0.11760
## treatment.tumor_size              0.71672   2.04770  0.26737
## prkg1                             0.56714   1.76322  0.09176
```

```
## treatment.e2f8                                      0.34472   1.41159  0.13453
## eif4ebp1                                            0.16990   1.18518  0.10304
## treatment.zfyve9                                    0.16526   1.17970  0.12904
## treatment.ush2a                                     0.46345   1.58955  0.15592
## dll3                                                0.14217   1.15278  0.09442
## treatment.nrarp                                     0.32735   1.38729  0.13669
## tumor_size                                         -0.20912   0.81129  0.24517
## treatment.e2f7                                     -0.05427   0.94718  0.18771
## e2f7                                                0.09505   1.09971  0.14381
## smad7                                               0.18508   1.20331  0.10507
## men1                                                0.14010   1.15039  0.10113
## prkacg                                              0.28760   1.33322  0.09446
## treatment.notch1                                    0.22936   1.25780  0.16225
## pdgfb                                               0.07733   1.08040  0.10269
## as.factor(tumor_stage2)1                            0.22849   1.25670  0.10079
## mmp25                                              -0.26227   0.76930  0.10686
## treatment.acvr1c                                   -0.09333   0.91089  0.20565
## treatment.srd5a3                                   -0.28892   0.74907  0.12379
## treatment.hsd17b7                                   0.07064   1.07319  0.15018
## mlh1                                               -0.16297   0.84962  0.10250
## casp7                                              -0.21199   0.80898  0.10512
## brca2                                              -0.27453   0.75993  0.09850
## treatment.rpgr                                     -0.06215   0.93974  0.15395
## treatment.ugt2b17                                   0.10298   1.10847  0.28363
## igf1                                               -0.11583   0.89063  0.13754
## treatment.nrg3                                     -0.52297   0.59276  0.18325
## map3k1                                              0.07408   1.07690  0.11572
## mapt                                               -0.10249   0.90258  0.16762
## e2f1                                               -0.27502   0.75956  0.09713
## ugt2b17                                            -0.73711   0.47849  0.21794
## treatment.inha                                     -0.41856   0.65799  0.13396
## diras3                                             -0.31422   0.73036  0.13913
## tp53.tp53_mut                                      -0.44054   0.64369  0.10476
## atr.atr_mut                                        -0.80931   0.44517  0.51444
## gata3.gata3_mut                                    -0.93305   0.39335  0.37258
## acvr1c                                             -0.36373   0.69508  0.14311
## cul1                                               -0.51979   0.59465  0.15983
## stat5a                                             -0.20024   0.81854  0.10493
## treatment.cul1                                     -0.07283   0.92976  0.19944
## as.factor(pam50_._claudin.low_subtypeLumA)1 -0.21972   0.80274  0.13744
## birc6.birc6_mut                                    -0.75198   0.47143  0.49710
## treatment.cyp11a1                                  -0.46299   0.62940  0.15905
## tbx3.tbx3_mut                                      -1.80113   0.16511  0.49935
## treatment.mapt                                     -0.64863   0.52276  0.23365
##                                                  robust se       z Pr(>|z|)
## kdm3a.kdm3a_mut                                     0.87844   3.906 9.38e-05 ***
## lymph_nodes_examined_positive                       0.09717   7.452 9.21e-14 ***
## treatment                                           0.15719   1.660  0.09695 .
## as.factor(integrative_cluster5)1                    0.18966   2.137  0.03257 *
## as.factor(integrative_cluster3)1                    0.25933  -1.240  0.21488
## gsk3b                                               0.16454   0.923  0.35575
## treatment.tumor_size                                0.39037   1.836  0.06636 .
## prkg1                                               0.12583   4.507 6.56e-06 ***
## treatment.e2f8                                      0.19751   1.745  0.08093 .
```

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```
## eif4ebp1                                     0.14410  1.179  0.23839
## treatment.zfyve9                             0.17868  0.925  0.35503
## treatment.ush2a                              0.21685  2.137  0.03258 *
## dll3                                         0.13962  1.018  0.30854
## treatment.nrarp                              0.17981  1.820  0.06868 .
## tumor_size                                   0.36376 -0.575  0.56537
## treatment.e2f7                               0.25431 -0.213  0.83103
## e2f7                                         0.19582  0.485  0.62741
## smad7                                        0.16864  1.097  0.27244
## men1                                         0.14157  0.990  0.32236
## prkacg                                       0.12491  2.302  0.02131 *
## treatment.notch1                             0.23105  0.993  0.32085
## pdgfb                                        0.15567  0.497  0.61934
## as.factor(tumor_stage2)1                     0.13628  1.677  0.09363 .
## mmp25                                        0.14638 -1.792  0.07317 .
## treatment.acvr1c                             0.28847 -0.324  0.74628
## treatment.srd5a3                             0.16516 -1.749  0.08023 .
## treatment.hsd17b7                            0.19819  0.356  0.72154
## mlh1                                         0.15217 -1.071  0.28417
## casp7                                        0.13960 -1.519  0.12887
## brca2                                        0.13500 -2.033  0.04200 *
## treatment.rpgr                               0.20772 -0.299  0.76477
## treatment.ugt2b17                            0.41469  0.248  0.80387
## igf1                                         0.18137 -0.639  0.52307
## treatment.nrg3                               0.28169 -1.857  0.06338 .
## map3k1                                       0.15638  0.474  0.63569
## mapt                                         0.23227 -0.441  0.65902
## e2f1                                         0.13588 -2.024  0.04298 *
## ugt2b17                                      0.32051 -2.300  0.02146 *
## treatment.inha                               0.15524 -2.696  0.00701 **
## diras3                                       0.18277 -1.719  0.08558 .
## tp53.tp53_mut                                0.16012 -2.751  0.00594 **
## atr.atr_mut                                  0.46068 -1.757  0.07896 .
## gata3.gata3_mut                              0.42745 -2.183  0.02905 *
## acvr1c                                       0.21455 -1.695  0.09001 .
## cul1                                         0.25120 -2.069  0.03853 *
## stat5a                                       0.16514 -1.213  0.22530
## treatment.cul1                               0.28862 -0.252  0.80078
## as.factor(pam50_._claudin.low_subtypeLumA)1  0.18119 -1.213  0.22525
## birc6.birc6_mut                              0.76160 -0.987  0.32346
## treatment.cyp11a1                            0.19968 -2.319  0.02042 *
## tbx3.tbx3_mut                                0.80544 -2.236  0.02534 *
## treatment.mapt                               0.32369 -2.004  0.04508 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                                     exp(coef) exp(-coef) lower .95
## kdm3a.kdm3a_mut                       30.9162    0.03235   5.52654
## lymph_nodes_examined_positive          2.0629    0.48475   1.70517
## treatment                              1.2981    0.77036   0.95392
## as.factor(integrative_cluster5)1       1.4998    0.66674   1.03420
## as.factor(integrative_cluster3)1       0.7250    1.37938   0.43609
## gsk3b                                  1.1641    0.85903   0.84321
## treatment.tumor_size                   2.0477    0.48835   0.95275
```

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```
## prkg1                                              1.7632    0.56714   1.37786
## treatment.e2f8                                      1.4116    0.70842   0.95849
## eif4ebp1                                            1.1852    0.84375   0.89357
## treatment.zfyve9                                    1.1797    0.84767   0.83115
## treatment.ush2a                                     1.5895    0.62911   1.03918
## dll3                                                1.1528    0.86747   0.87680
## treatment.nrarp                                     1.3873    0.72083   0.97523
## tumor_size                                          0.8113    1.23260   0.39769
## treatment.e2f7                                      0.9472    1.05576   0.57539
## e2f7                                                1.0997    0.90933   0.74919
## smad7                                               1.2033    0.83104   0.86463
## men1                                                1.1504    0.86927   0.87164
## prkacg                                              1.3332    0.75006   1.04370
## treatment.notch1                                    1.2578    0.79504   0.79973
## pdgfb                                               1.0804    0.92558   0.79631
## as.factor(tumor_stage2)1                            1.2567    0.79574   0.96211
## mmp25                                               0.7693    1.29988   0.57743
## treatment.acvr1c                                    0.9109    1.09783   0.51752
## treatment.srd5a3                                    0.7491    1.33499   0.54192
## treatment.hsd17b7                                   1.0732    0.93180   0.72774
## mlh1                                                0.8496    1.17700   0.63052
## casp7                                               0.8090    1.23613   0.61534
## brca2                                               0.7599    1.31591   0.58326
## treatment.rpgr                                      0.9397    1.06413   0.62545
## treatment.ugt2b17                                   1.1085    0.90214   0.49174
## igf1                                                0.8906    1.12280   0.62419
## treatment.nrg3                                      0.5928    1.68703   0.34127
## map3k1                                              1.0769    0.92859   0.79261
## mapt                                                0.9026    1.10793   0.57250
## e2f1                                                0.7596    1.31655   0.58197
## ugt2b17                                             0.4785    2.08989   0.25531
## treatment.inha                                      0.6580    1.51977   0.48538
## diras3                                              0.7304    1.36919   0.51046
## tp53.tp53_mut                                       0.6437    1.55355   0.47031
## atr.atr_mut                                         0.4452    2.24636   0.18046
## gata3.gata3_mut                                     0.3934    2.54225   0.17019
## acvr1c                                              0.6951    1.43869   0.45647
## cul1                                                0.5946    1.68167   0.36344
## stat5a                                              0.8185    1.22169   0.59221
## treatment.cul1                                      0.9298    1.07555   0.52808
## as.factor(pam50_._claudin.low_subtypeLumA)1         0.8027    1.24573   0.56279
## birc6.birc6_mut                                     0.4714    2.12120   0.10596
## treatment.cyp11a1                                   0.6294    1.58882   0.42556
## tbx3.tbx3_mut                                       0.1651    6.05646   0.03406
## treatment.mapt                                      0.5228    1.91293   0.27719
##                                              upper .95
## kdm3a.kdm3a_mut                               172.9494
## lymph_nodes_examined_positive                   2.4957
## treatment                                       1.7665
## as.factor(integrative_cluster5)1                2.1751
## as.factor(integrative_cluster3)1                1.2052
## gsk3b                                           1.6071
## treatment.tumor_size                            4.4010
## prkg1                                           2.2564
```

```
## treatment.e2f8                                        2.0789
## eif4ebp1                                              1.5720
## treatment.zfyve9                                      1.6744
## treatment.ush2a                                       2.4314
## dll3                                                  1.5156
## treatment.nrarp                                       1.9734
## tumor_size                                            1.6551
## treatment.e2f7                                        1.5592
## e2f7                                                  1.6142
## smad7                                                 1.6747
## men1                                                  1.5183
## prkacg                                                1.7030
## treatment.notch1                                      1.9782
## pdgfb                                                 1.4658
## as.factor(tumor_stage2)1                              1.6415
## mmp25                                                 1.0249
## treatment.acvr1c                                      1.6033
## treatment.srd5a3                                      1.0354
## treatment.hsd17b7                                     1.5826
## mlh1                                                  1.1448
## casp7                                                 1.0636
## brca2                                                 0.9901
## treatment.rpgr                                        1.4119
## treatment.ugt2b17                                     2.4987
## igf1                                                  1.2708
## treatment.nrg3                                        1.0296
## map3k1                                                1.4631
## mapt                                                  1.4230
## e2f1                                                  0.9913
## ugt2b17                                               0.8968
## treatment.inha                                        0.8920
## diras3                                                1.0450
## tp53.tp53_mut                                         0.8810
## atr.atr_mut                                           1.0981
## gata3.gata3_mut                                       0.9091
## acvr1c                                                1.0584
## cul1                                                  0.9729
## stat5a                                                1.1314
## treatment.cul1                                        1.6370
## as.factor(pam50_._claudin.low_subtypeLumA)1   1.1450
## birc6.birc6_mut                                       2.0975
## treatment.cyp11a1                                     0.9309
## tbx3.tbx3_mut                                         0.8005
## treatment.mapt                                        0.9859
##
## Concordance= 0.808   (se = 0.013 )
## Likelihood ratio test= 694.6  on 52 df,   p=<2e-16
## Wald test            = 502.7  on 52 df,   p=<2e-16
## Score (logrank) test = 834.7  on 52 df,   p=<2e-16,   Robust = 214.2  p=<2e-16
##
##   (Note: the likelihood ratio and score tests assume independence of
##       observations within a cluster, the Wald and robust score tests do not).
```

```
mod = coxmodel
sum.cox = summary(coxmodel)

sum.cox$coefficients
```

```
##                                                     coef   exp(coef)   se(coef)
## kdm3a.kdm3a_mut                                  3.43128063 30.9162096 0.87533658
## lymph_nodes_examined_positive                    0.72412208  2.0629192 0.07471657
## treatment                                        0.26090224  1.2981008 0.11606538
## as.factor(integrative_cluster5)1                 0.40535206  1.4998304 0.13883499
## as.factor(integrative_cluster3)1                -0.32163112  0.7249656 0.21011256
## gsk3b                                            0.15195506  1.1641079 0.11760331
## treatment.tumor_size                             0.71671626  2.0476980 0.26737407
## prkg1                                            0.56714275  1.7632219 0.09176190
## treatment.e2f8                                   0.34471991  1.4115945 0.13452821
## eif4ebp1                                         0.16989771  1.1851836 0.10304041
## treatment.zfyve9                                 0.16525917  1.1796988 0.12904053
## treatment.ush2a                                  0.46344797  1.5895453 0.15591579
## dll3                                             0.14217304  1.1527761 0.09442464
## treatment.nrarp                                  0.32735148  1.3872890 0.13669412
## tumor_size                                      -0.20912356  0.8112950 0.24516521
## treatment.e2f7                                  -0.05426543  0.9471807 0.18770652
## e2f7                                             0.09504816  1.0997118 0.14380892
## smad7                                            0.18507795  1.2033122 0.10506580
## men1                                             0.14010413  1.1503936 0.10112524
## prkacg                                           0.28759578  1.3332183 0.09446375
## treatment.notch1                                 0.22936329  1.2577989 0.16225380
## pdgfb                                            0.07733314  1.0804019 0.10268740
## as.factor(tumor_stage2)1                         0.22848613  1.2566961 0.10079390
## mmp25                                           -0.26226930  0.7693038 0.10686085
## treatment.acvr1c                                -0.09333213  0.9108909 0.20564650
## treatment.srd5a3                                -0.28892172  0.7490708 0.12379355
## treatment.hsd17b7                                0.07063676  1.0731913 0.15017965
## mlh1                                            -0.16297151  0.8496154 0.10250335
## casp7                                           -0.21198567  0.8089763 0.10511610
## brca2                                           -0.27452524  0.7599328 0.09850426
## treatment.rpgr                                  -0.06215372  0.9397384 0.15394690
## treatment.ugt2b17                                0.10298370  1.1084733 0.28363251
## igf1                                            -0.11582710  0.8906292 0.13753803
## treatment.nrg3                                  -0.52297085  0.5927569 0.18324556
## map3k1                                           0.07408287  1.0768960 0.11571953
## mapt                                            -0.10249324  0.9025842 0.16761950
## e2f1                                            -0.27501543  0.7595604 0.09712506
## ugt2b17                                         -0.73710986  0.4784948 0.21794217
## treatment.inha                                  -0.41856185  0.6579924 0.13396076
## diras3                                          -0.31421748  0.7303602 0.13912730
## tp53.tp53_mut                                   -0.44053949  0.6436891 0.10475601
## atr.atr_mut                                     -0.80931011  0.4451651 0.51443996
## gata3.gata3_mut                                 -0.93305056  0.3933519 0.37257845
## acvr1c                                          -0.36373322  0.6950766 0.14311082
## cul1                                            -0.51978521  0.5946483 0.15982677
## stat5a                                          -0.20023811  0.8185358 0.10493288
## treatment.cul1                                  -0.07282955  0.9297593 0.19943786
## as.factor(pam50_._claudin.low_subtypeLumA)1     -0.21972172  0.8027422 0.13744390
```

```
## birc6.birc6_mut                                     -0.75198266   0.4714309 0.49710438
## treatment.cyp11a1                                    -0.46298904   0.6293995 0.15905476
## tbx3.tbx3_mut                                        -1.80112564   0.1651129 0.49934880
## treatment.mapt                                       -0.64863482   0.5227589 0.23364665
##                                                        robust se         z     Pr(>|z|)
## kdm3a.kdm3a_mut                                       0.87844389   3.9060897 9.380171e-05
## lymph_nodes_examined_positive                         0.09717444   7.4517750 9.209268e-14
## treatment                                             0.15718601   1.6598312 9.694842e-02
## as.factor(integrative_cluster5)1                      0.18965755   2.1372841 3.257489e-02
## as.factor(integrative_cluster3)1                      0.25932535  -1.2402610 2.148789e-01
## gsk3b                                                 0.16454298   0.9234977 3.557479e-01
## treatment.tumor_size                                  0.39037447   1.8359711 6.636193e-02
## prkg1                                                 0.12582532   4.5073818 6.563246e-06
## treatment.e2f8                                        0.19751076   1.7453222 8.092880e-02
## eif4ebp1                                              0.14409919   1.1790330 2.383850e-01
## treatment.zfyve9                                      0.17868104   0.9248836 3.550264e-01
## treatment.ush2a                                       0.21684668   2.1372150 3.258051e-02
## dll3                                                  0.13961913   1.0182920 3.085392e-01
## treatment.nrarp                                       0.17981464   1.8204940 6.868381e-02
## tumor_size                                            0.36376281  -0.5748899 5.653658e-01
## treatment.e2f7                                        0.25431345  -0.2133801 8.310305e-01
## e2f7                                                  0.19582417   0.4853750 6.274103e-01
## smad7                                                 0.16864305   1.0974538 2.724431e-01
## men1                                                  0.14157371   0.9896197 3.223601e-01
## prkacg                                                0.12491001   2.3024237 2.131129e-02
## treatment.notch1                                      0.23104541   0.9927195 3.208466e-01
## pdgfb                                                 0.15566633   0.4967878 6.193387e-01
## as.factor(tumor_stage2)1                              0.13628255   1.6765619 9.362819e-02
## mmp25                                                 0.14637605  -1.7917501 7.317300e-02
## treatment.acvr1c                                      0.28846578  -0.3235466 7.462813e-01
## treatment.srd5a3                                      0.16516027  -1.7493415 8.023200e-02
## treatment.hsd17b7                                     0.19819419   0.3564018 7.215397e-01
## mlh1                                                  0.15216652  -1.0710076 2.841660e-01
## casp7                                                 0.13959532  -1.5185730 1.288700e-01
## brca2                                                 0.13500276  -2.0334786 4.200419e-02
## treatment.rpgr                                        0.20772003  -0.2992187 7.647732e-01
## treatment.ugt2b17                                     0.41469452   0.2483363 8.038742e-01
## igf1                                                  0.18137107  -0.6386195 5.230705e-01
## treatment.nrg3                                        0.28169400  -1.8565211 6.337933e-02
## map3k1                                                0.15638240   0.4737290 6.356932e-01
## mapt                                                  0.23227235  -0.4412632 6.590225e-01
## e2f1                                                  0.13588075  -2.0239470 4.297560e-02
## ugt2b17                                               0.32050869  -2.2998124 2.145885e-02
## treatment.inha                                        0.15523830  -2.6962538 7.012422e-03
## diras3                                                0.18277159  -1.7191812 8.558139e-02
## tp53.tp53_mut                                         0.16012105  -2.7512903 5.936102e-03
## atr.atr_mut                                           0.46068497  -1.7567539 7.895976e-02
## gata3.gata3_mut                                       0.42744665  -2.1828468 2.904709e-02
## acvr1c                                                0.21454785  -1.6953478 9.000947e-02
## cul1                                                  0.25120008  -2.0692080 3.852658e-02
## stat5a                                                0.16513718  -1.2125562 2.252995e-01
## treatment.cul1                                        0.28861813  -0.2523388 8.007792e-01
## as.factor(pam50_._claudin.low_subtypeLumA)1 0.18118632  -1.2126838 2.252507e-01
## birc6.birc6_mut                                       0.76160103  -0.9873709 3.234609e-01
```

```
## treatment.cyp11a1                              0.19968264 -2.3186244 2.041541e-02
## tbx3.tbx3_mut                                  0.80544247 -2.2361940 2.533906e-02
## treatment.mapt                                 0.32369130 -2.0038686 4.508414e-02
```

```r
coefs = tibble(coef = rownames(sum.cox$coefficients), estimate = unname(sum.cox$coefficients[,1]), exp_
           robust_se = unname(sum.cox$coefficients[,4]), pval = unname(sum.cox$coefficients[,6]))

xtable(coefs, caption = "...", digits = 3, display = c('g','g', 'g', 'g', 'g', 'g'))
```

```
## % latex table generated in R 4.1.3 by xtable 1.8-4 package
## % Wed Apr 26 17:00:18 2023
## \begin{table}[ht]
## \centering
## \begin{tabular}{rlrrrr}
##   \hline
##  & coef & estimate & exp\_estimate & robust\_se & pval \\
##   \hline
## 1 & kdm3a.kdm3a\_mut & 3.43 & 30.9 & 0.878 & 9.38e-05 \\
##   2 & lymph\_nodes\_examined\_positive & 0.724 & 2.06 & 0.0972 & 9.21e-14 \\
##   3 & treatment & 0.261 &  1.3 & 0.157 & 0.0969 \\
##   4 & as.factor(integrative\_cluster5)1 & 0.405 &  1.5 & 0.19 & 0.0326 \\
##   5 & as.factor(integrative\_cluster3)1 & -0.322 & 0.725 & 0.259 & 0.215 \\
##   6 & gsk3b & 0.152 & 1.16 & 0.165 & 0.356 \\
##   7 & treatment.tumor\_size & 0.717 & 2.05 & 0.39 & 0.0664 \\
##   8 & prkg1 & 0.567 & 1.76 & 0.126 & 6.56e-06 \\
##   9 & treatment.e2f8 & 0.345 & 1.41 & 0.198 & 0.0809 \\
##   10 & eif4ebp1 & 0.17 & 1.19 & 0.144 & 0.238 \\
##   11 & treatment.zfyve9 & 0.165 & 1.18 & 0.179 & 0.355 \\
##   12 & treatment.ush2a & 0.463 & 1.59 & 0.217 & 0.0326 \\
##   13 & dll3 & 0.142 & 1.15 & 0.14 & 0.309 \\
##   14 & treatment.nrarp & 0.327 & 1.39 & 0.18 & 0.0687 \\
##   15 & tumor\_size & -0.209 & 0.811 & 0.364 & 0.565 \\
##   16 & treatment.e2f7 & -0.0543 & 0.947 & 0.254 & 0.831 \\
##   17 & e2f7 & 0.095 &  1.1 & 0.196 & 0.627 \\
##   18 & smad7 & 0.185 &  1.2 & 0.169 & 0.272 \\
##   19 & men1 & 0.14 & 1.15 & 0.142 & 0.322 \\
##   20 & prkacg & 0.288 & 1.33 & 0.125 & 0.0213 \\
##   21 & treatment.notch1 & 0.229 & 1.26 & 0.231 & 0.321 \\
##   22 & pdgfb & 0.0773 & 1.08 & 0.156 & 0.619 \\
##   23 & as.factor(tumor\_stage2)1 & 0.228 & 1.26 & 0.136 & 0.0936 \\
##   24 & mmp25 & -0.262 & 0.769 & 0.146 & 0.0732 \\
##   25 & treatment.acvr1c & -0.0933 & 0.911 & 0.288 & 0.746 \\
##   26 & treatment.srd5a3 & -0.289 & 0.749 & 0.165 & 0.0802 \\
##   27 & treatment.hsd17b7 & 0.0706 & 1.07 & 0.198 & 0.722 \\
##   28 & mlh1 & -0.163 & 0.85 & 0.152 & 0.284 \\
##   29 & casp7 & -0.212 & 0.809 & 0.14 & 0.129 \\
##   30 & brca2 & -0.275 & 0.76 & 0.135 & 0.042 \\
##   31 & treatment.rpgr & -0.0622 & 0.94 & 0.208 & 0.765 \\
##   32 & treatment.ugt2b17 & 0.103 & 1.11 & 0.415 & 0.804 \\
##   33 & igf1 & -0.116 & 0.891 & 0.181 & 0.523 \\
##   34 & treatment.nrg3 & -0.523 & 0.593 & 0.282 & 0.0634 \\
##   35 & map3k1 & 0.0741 & 1.08 & 0.156 & 0.636 \\
##   36 & mapt & -0.102 & 0.903 & 0.232 & 0.659 \\
##   37 & e2f1 & -0.275 & 0.76 & 0.136 & 0.043 \\
##   38 & ugt2b17 & -0.737 & 0.478 & 0.321 & 0.0215 \\
```

```
##    39 & treatment.inha & -0.419 & 0.658 & 0.155 & 0.00701 \\
##    40 & diras3 & -0.314 & 0.73 & 0.183 & 0.0856 \\
##    41 & tp53.tp53\_mut & -0.441 & 0.644 & 0.16 & 0.00594 \\
##    42 & atr.atr\_mut & -0.809 & 0.445 & 0.461 & 0.079 \\
##    43 & gata3.gata3\_mut & -0.933 & 0.393 & 0.427 & 0.029 \\
##    44 & acvr1c & -0.364 & 0.695 & 0.215 & 0.09 \\
##    45 & cul1 & -0.52 & 0.595 & 0.251 & 0.0385 \\
##    46 & stat5a & -0.2 & 0.819 & 0.165 & 0.225 \\
##    47 & treatment.cul1 & -0.0728 & 0.93 & 0.289 & 0.801 \\
##    48 & as.factor(pam50\_.\_claudin.low\_subtypeLumA)1 & -0.22 & 0.803 & 0.181 & 0.225 \\
##    49 & birc6.birc6\_mut & -0.752 & 0.471 & 0.762 & 0.323 \\
##    50 & treatment.cyp11a1 & -0.463 & 0.629 &  0.2 & 0.0204 \\
##    51 & tbx3.tbx3\_mut & -1.8 & 0.165 & 0.805 & 0.0253 \\
##    52 & treatment.mapt & -0.649 & 0.523 & 0.324 & 0.0451 \\
##     \hline
## \end{tabular}
## \caption{...}
## \end{table}
```

```
#coefs
```

```
#survfit(formula = coxmodel, newdata = data_matrix)
```

```
get.race.unpenalized(data_matrix, coxmodel, W.vec)
```

```
## [1] -15.73215
```

Sensitivity Analysis - Propensity Scores

```
coxmodel_overlap <- coxph(y[e.vec > 0.35 & e.vec < 0.8] ~ kdm3a.kdm3a_mut  + lymph_nodes_examined_posit:
                   treatment     +      as.factor(integrative_cluster5) +
                as.factor(integrative_cluster3) +
                      gsk3b      +       treatment.tumor_size +
                      prkg1      +          treatment.e2f8 +
                    eif4ebp1     +        treatment.zfyve9 +
              treatment.ush2a      +                dll3 +
              treatment.nrarp        +          tumor_size +
               treatment.e2f7         +              e2f7 +
                    smad7          +                men1 +
                    prkacg          +       treatment.notch1 +
                    pdgfb              +        as.factor(tumor_stage2) +
                    mmp25              +     treatment.acvr1c +
              treatment.srd5a3         +     treatment.hsd17b7 +
                     mlh1             +              casp7 +
                    brca2             +       treatment.rpgr +
             treatment.ugt2b17        +                igf1 +
               treatment.nrg3         +              map3k1 +
                     mapt             +               e2f1 +
                 ugt2b17 +
              treatment.inha              +             diras3 +
                tp53.tp53_mut            +      atr.atr_mut +
                gata3.gata3_mut          +              acvr1c +
                     cul1             +              stat5a +
             treatment.cul1 + as.factor(pam50_._claudin.low_subtypeLumA) +
              birc6.birc6_mut              +    treatment.cyp11a1 +
```

```
                    tbx3.tbx3_mut              +        treatment.mapt, weights = W.vec[e.vec > 0.35 & e.vec
```

```
get.race.unpenalized(data_matrix[e.vec > 0.35 & e.vec < 0.8,], coxmodel_overlap, W.vec[e.vec > 0.35 & e
```

```
## [1] -20.6392
```

```r
# BOOTSTARP
n = nrow(data_matrix)
S = 1000
boot.RACE.unpenalized = vector(length = S)
ind_matrix = array(rep(NA, n*S), c(S,n))

# set.seed(4)
# for (i in 1:S)
# {
#   cat('Progress: ', i/S, '\n')
#   boot_ind = sample(1:n, size = n, replace = TRUE)
#   data_matrix_boot = x[boot_ind,]
#   y_boot = y[boot_ind,]
#   W_boot = W.vec[boot_ind]
#
#   ind_matrix[i,] = boot_ind
#
#   coxmodel.boot <- coxph(y_boot ~ kdm3a.kdm3a_mut  + lymph_nodes_examined_positive +
#                   treatment      +     as.factor(integrative_cluster5) +
#                 as.factor(integrative_cluster3) +
#                      gsk3b      +       treatment.tumor_size +
#                      prkg1      +          treatment.e2f8 +
#                    eif4ebp1     +       treatment.zfyve9 +
#             treatment.ush2a        +               dll3 +
#             treatment.nrarp         +          tumor_size +
#            treatment.e2f7           +             e2f7 +
#                    smad7          +            men1 +
#                   prkacg          +     treatment.notch1 +
#                   pdgfb            +      as.factor(tumor_stage2) +
#                   mmp25            +    treatment.acvr1c +
#            treatment.srd5a3           +    treatment.hsd17b7 +
#                    mlh1            +             casp7 +
#                   brca2            +     treatment.rpgr +
#           treatment.ugt2b17          +             igf1 +
#             treatment.nrg3            +            map3k1 +
#                   mapt            +             e2f1 +
#                 ugt2b17 +
#           treatment.inha              +          diras3 +
#            tp53.tp53_mut             +       atr.atr_mut +
#           gata3.gata3_mut            +          acvr1c +
#                   cul1             +           stat5a +
#           treatment.cul1 + as.factor(pam50_._claudin.low_subtypeLumA) +
#           birc6.birc6_mut               +     treatment.cyp11a1 +
#              tbx3.tbx3_mut            +        treatment.mapt, weights = W_boot, data = data_matri
#
#
#   boot.RACE.unpenalized[i] = get.race.unpenalized(data_matrix_boot, coxmodel.boot, W_boot)
# }
```

```r
#saveRDS(boot.RACE.unpenalized, file = 'boot_RACE_unpenalized.RDS')

boot.RACE.unpenalized = readRDS(file = 'boot_RACE_unpenalized.RDS')

#boot.RACE.unpenalized

#boot.RACE.unpenalized
quantile(boot.RACE.unpenalized, c(0.025, 0.975))
```

```
##      2.5%      97.5%
## -35.055441   3.424606
```

Diagnostics

Cox-Snell Residuals

```r
source("http://myweb.uiowa.edu/pbreheny/7210/f18/notes/fun.R")
sfit <- survfit(coxmodel)
H0 <- -log(sfit$surv)
H <- approxfun(c(0, sfit$time), c(0, H0), method='constant')
e1 <- H(coxmodel$y[,1])*exp(coxmodel$linear.predictors)
e2 <- coxmodel$y[,2]-residuals(coxmodel)
head(e1)
```

```
## [1] 2.342085e-01 4.409510e-02 8.648566e-02 2.494864e-02 8.578785e-05
## [6] 2.084147e-01
```

```r
head(e2)
```

```
##            1            2            3            7           12           13
## 2.342085e-01 4.409510e-02 8.648566e-02 2.494864e-02 8.578785e-05 2.084147e-01
```

```r
efit <- survfit(Surv(e1, coxmodel$y[,2])~1)
lim <- c(0,5)
pdf("plots/cox_snell_resid.pdf", height = 3.5, width = 6)
plot(efit, fun='cumhaz', mark.time=FALSE, bty='n', conf.int=FALSE, lwd=1, las=1,
     xlab='Residual', ylab='Cumulative hazard', xlim=lim, ylim=lim)
ciband(efit, fun=function(x) -log(x))
lines(lim, lim, col='red', lwd=1)
dev.off()
```

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