Build Survival Model: Cox Proportional Hazards Model

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```r
library(tidyverse)
library(survival)
library(forestplot)
library(glmnet)
library(ggfortify)
library(kableExtra) # include knitr automatically

source("/work/users/y/u/yuukias/BIOS-Material/BIOS992/utils/csv_utils.r")
# * Don't use setwd() for Quarto documents!
# setwd("/work/users/y/u/yuukias/BIOS-Material/BIOS992/data")

adjust_type <- ifelse(exists("params"), params$adjust_type, "minimal") #
↪  options: "minimal", "partial", "full"
```

```r
impute_type <- ifelse(exists("params"), params$impute_type, "unimputed") #
↪  options: "unimputed", "imputed"
include_statin <- ifelse(exists("params"), params$include_statin, "no") #
↪  options: "yes", "no"
```

```r
# string of parameters
adjust_type_str <- switch(adjust_type,
    minimal = "minimal",
    partial = "partial",
    full = "full"
)
print(paste0("Model Adjustment Type: ", adjust_type_str))
```

```
[1] "Model Adjustment Type: minimal"
```

```r
impute_type_str <- switch(impute_type,
    unimputed = "unimputed",
    imputed = "imputed"
)
print(paste0("Data Imputation Type: ", impute_type_str))
```

```
[1] "Data Imputation Type: unimputed"
```

Load Data

```r
if (include_statin == "yes") {
    data_train <-
↪  read.csv(paste0("/work/users/y/u/yuukias/BIOS-Material/BIOS992/data/train_data_",
↪  impute_type_str, "_statin.csv"),
        header = TRUE
    )
} else {
    data_train <-
↪  read.csv(paste0("/work/users/y/u/yuukias/BIOS-Material/BIOS992/data/train_data_",
↪  impute_type_str, ".csv"),
        header = TRUE
    )
```

```r
}

data_train <- data_train[, -1] # the first column is the index generated by
↪  sklearn
(dim(data_train))
```

```
[1] 28127   100
```

```r
data <- select_subset(data_train, type = adjust_type)
(dim(data))
```

```
[1] 28127    48
```

```r
colnames(data)
```

```
 [1] "event"                        "time"
 [3] "HRV_SD1"                      "HRV_SD2"
 [5] "HRV_SD1SD2"                   "HRV_S"
 [7] "HRV_CSI"                      "HRV_CVI"
 [9] "HRV_CSI_Modified"             "HRV_PIP"
[11] "HRV_IALS"                     "HRV_PSS"
[13] "HRV_PAS"                      "HRV_GI"
[15] "HRV_SI"                       "HRV_AI"
[17] "HRV_PI"                       "HRV_C1d"
[19] "HRV_C1a"                      "HRV_SD1d"
[21] "HRV_SD1a"                     "HRV_C2d"
[23] "HRV_C2a"                      "HRV_SD2d"
[25] "HRV_SD2a"                     "HRV_Cd"
[27] "HRV_Ca"                       "HRV_SDNNd"
[29] "HRV_SDNNa"                    "HRV_ApEn"
[31] "HRV_ShanEn"                   "HRV_FuzzyEn"
[33] "HRV_MSEn"                     "HRV_CMSEn"
[35] "HRV_RCMSEn"                   "HRV_CD"
[37] "HRV_HFD"                      "HRV_KFD"
[39] "HRV_LZC"                      "HRV_DFA_alpha1"
[41] "HRV_MFDFA_alpha1_Width"       "HRV_MFDFA_alpha1_Peak"
[43] "HRV_MFDFA_alpha1_Mean"        "HRV_MFDFA_alpha1_Max"
[45] "HRV_MFDFA_alpha1_Delta"       "HRV_MFDFA_alpha1_Asymmetry"
[47] "HRV_MFDFA_alpha1_Fluctuation" "HRV_MFDFA_alpha1_Increment"
```

```r
data <- tibble::as_tibble(data)
```

```r
# * It is very hard to compare the HR as different predictors are on
 ↪  different magnitudes, so we need to normalize them.
time_col <- data$time
event_col <- data$event
data <- data %>%
    select(-c(time, event)) %>%
    mutate(across(where(is.numeric), scale)) %>%
    mutate(
        time = time_col,
        event = event_col
    )
```

Note now the interpretation of HR is different! For example, if HR=1.16 for the predictor in the univariate model fitted using scaled data, it means that each standard deviation increase is associated with 16% higher risk of event.

```r
data_complete <- na.omit(data)
```

Univariate Cox Proportional Hazards Model

```r
if (!("time" %in% colnames(data) && "event" %in% colnames(data))) {
    stop("time and event columns are required")
}
predictors <- colnames(data)[!colnames(data) %in% c("time", "event")]

results_univariate <- map_dfr(predictors, function(predictor) {
    formula <- as.formula(paste("Surv(time, event) ~", predictor))
    # cox_model_single <- coxph(Surv(time, event) ~ get(predictor), data =
     ↪  data)  # equivalent way
    cox_model_single <- coxph(formula, data = data)

    coef <- coef(cox_model_single) # log hazard ratio
    se <- sqrt(diag(vcov(cox_model_single)))

    hr <- exp(coef)
    lower_ci <- exp(coef - 1.96 * se)
```

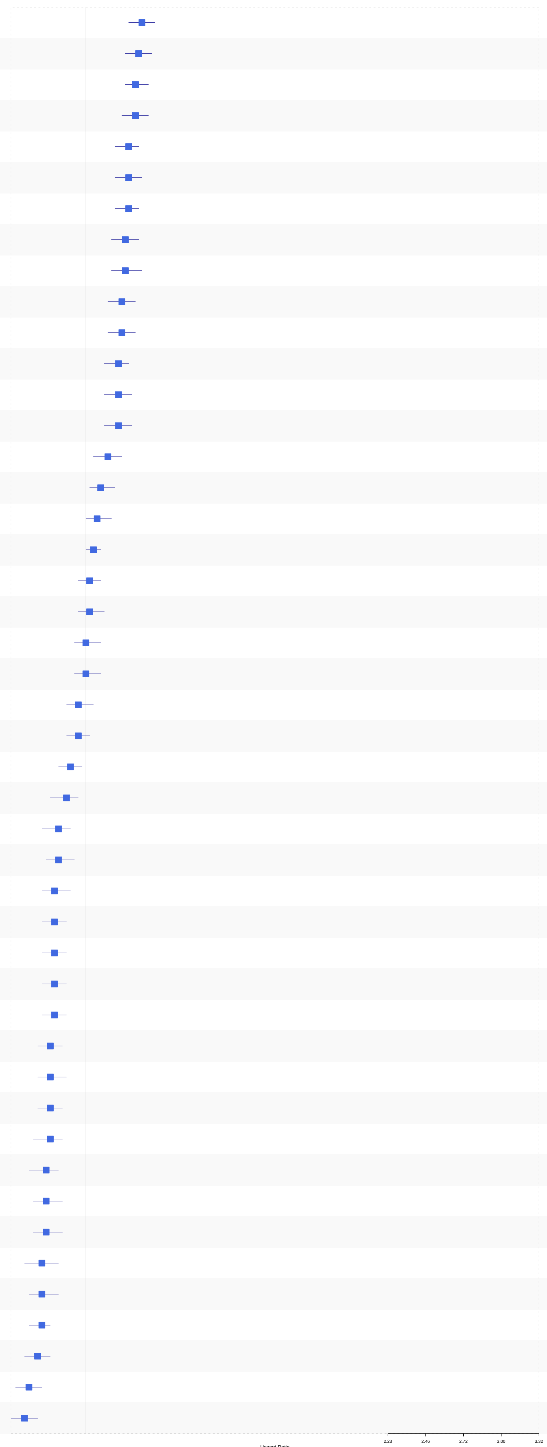
```
    upper_ci <- exp(coef + 1.96 * se)
    p_value <- summary(cox_model_single)$coefficients[5]

    return(
        data.frame(
            predictor = predictor,
            hr = hr,
            lower_ci = lower_ci,
            upper_ci = upper_ci,
            p_value = p_value
        )
    )
})
results_univariate$hr <- round(results_univariate$hr, 2)
results_univariate$lower_ci <- round(results_univariate$lower_ci, 2)
results_univariate$upper_ci <- round(results_univariate$upper_ci, 2)
results_univariate$ci <- paste0("(", results_univariate$lower_ci, ",",
 ↪  results_univariate$upper_ci, ")")
results_univariate$p_value <- round(results_univariate$p_value, 3)
results_univariate <- results_univariate %>% arrange(desc(hr)) # sort
 ↪  descendingly by HR
```

```
# Create forest plot
results_univariate %>%
    forestplot(
        labeltext = c(predictor, hr, ci, p_value),
        mean = hr,
        lower = lower_ci,
        upper = upper_ci,
        xlab = "Hazard Ratio",
        title = "Univariate Cox Models",
        xlog = TRUE, # * Make sure the CI are not symmetric and need to be
         ↪  transformed
        boxsize = 0.2,
        xticks = c(0.8, 0.9, 1.0, 1.1, 1.2),
        clip = c(0.8, 1.2),
        zero = 1
    ) %>%
    fp_set_style(
        box = "royalblue",
        line = "darkblue",
```

```
    summary = "royalblue"
) %>%
fp_add_header(
    predictor = c("Predictor", ""),
    hr = c("Hazard Ratio", "per SD increase"),
    ci = c("95% CI", ""),
    p_value = c("p-value", "")
) %>%
fp_decorate_graph(
    box = gpar(lty = 2, col = "lightgray"),
    graph.pos = 4
) %>% # change the position of forest plot
fp_set_zebra_style("#f9f9f9")
```

Univariate Cox Models

Predictor	Hazard Ratio per SD increase	95% CI	p−value
HRV_PIP	1.16	(1.12,1.2)	0
HRV_IALS	1.15	(1.11,1.19)	0
HRV_SD1SD2	1.14	(1.11,1.18)	0
HRV_HFD	1.14	(1.1,1.18)	0
HRV_PAS	1.12	(1.08,1.15)	0
HRV_GI	1.12	(1.08,1.16)	0
HRV_SI	1.12	(1.08,1.15)	0
HRV_PSS	1.11	(1.07,1.15)	0
HRV_AI	1.11	(1.07,1.16)	0
HRV_ApEn	1.1	(1.06,1.14)	0
HRV_CMSEn	1.1	(1.06,1.14)	0
HRV_C2d	1.09	(1.05,1.12)	0
HRV_Cd	1.09	(1.05,1.13)	0
HRV_RCMSEn	1.09	(1.05,1.13)	0
HRV_C1d	1.06	(1.02,1.1)	0.001
HRV_MFDFA_alpha1_Asymmetry	1.04	(1.01,1.08)	0.012
HRV_MSEn	1.03	(1,1.07)	0.075
HRV_KFD	1.02	(1,1.04)	0.05
HRV_ShanEn	1.01	(0.98,1.04)	0.621
HRV_MFDFA_alpha1_Width	1.01	(0.98,1.05)	0.429
HRV_MFDFA_alpha1_Fluctuation	1	(0.97,1.04)	0.914
HRV_MFDFA_alpha1_Increment	1	(0.97,1.04)	0.788
HRV_S	0.98	(0.95,1.02)	0.301
HRV_MFDFA_alpha1_Mean	0.98	(0.95,1.01)	0.181
HRV_FuzzyEn	0.96	(0.93,0.99)	0.011
HRV_C1a	0.95	(0.91,0.98)	0.001
HRV_SD1	0.93	(0.89,0.96)	0
HRV_SD1d	0.93	(0.9,0.97)	0
HRV_SD1a	0.92	(0.89,0.96)	0
HRV_C2a	0.92	(0.89,0.95)	0
HRV_Ca	0.92	(0.89,0.95)	0
HRV_MFDFA_alpha1_Max	0.92	(0.89,0.95)	0
HRV_MFDFA_alpha1_Delta	0.92	(0.89,0.95)	0
HRV_PI	0.91	(0.88,0.94)	0
HRV_SDNNd	0.91	(0.88,0.95)	0
HRV_CD	0.91	(0.88,0.94)	0
HRV_MFDFA_alpha1_Peak	0.91	(0.87,0.94)	0
HRV_SD2	0.9	(0.86,0.93)	0
HRV_SD2d	0.9	(0.87,0.94)	0
HRV_SDNNa	0.9	(0.87,0.94)	0
HRV_CSI_Modified	0.89	(0.85,0.93)	0
HRV_SD2a	0.89	(0.86,0.93)	0
HRV_LZC	0.89	(0.86,0.91)	0
HRV_DFA_alpha1	0.88	(0.85,0.91)	0
HRV_CVI	0.86	(0.83,0.89)	0
HRV_CSI	0.85	(0.82,0.88)	0



Multivariate Cox Proportional Hazards Model

```r
cox_model_full <- coxph(Surv(time, event) ~ ., data = data)
summary(cox_model_full)
```

```r
cox_model_full_complete <- coxph(Surv(time, event) ~ ., data = data_complete)
summary(cox_model_full_complete)
```

PH Assumption Assessment

```r
cox.zph(cox_model_full)
```

```
                              chisq df    p
HRV_SD1                    5.01e-01  1 0.48
HRV_SD2                    3.96e-01  1 0.53
HRV_SD1SD2                 5.07e-01  1 0.48
HRV_S                      1.07e+00  1 0.30
HRV_CSI                    5.14e-01  1 0.47
HRV_CVI                    4.07e-03  1 0.95
HRV_CSI_Modified           3.06e-01  1 0.58
HRV_PIP                    2.45e-02  1 0.88
HRV_IALS                   7.94e-02  1 0.78
HRV_PSS                    5.32e-02  1 0.82
HRV_PAS                    2.08e+00  1 0.15
HRV_GI                     5.67e-02  1 0.81
HRV_SI                     5.29e-03  1 0.94
HRV_AI                     9.58e-02  1 0.76
HRV_PI                     6.22e-01  1 0.43
HRV_C1d                    2.73e-02  1 0.87
HRV_SD1d                   6.07e-01  1 0.44
HRV_SD1a                   4.64e-01  1 0.50
HRV_C2d                    1.41e-02  1 0.91
HRV_SD2d                   3.69e-01  1 0.54
HRV_SD2a                   3.71e-01  1 0.54
HRV_Cd                     1.53e-01  1 0.70
HRV_SDNNd                  5.35e-01  1 0.46
HRV_SDNNa                  4.43e-01  1 0.51
```

```
HRV_ApEn                        1.21e+00  1 0.27
HRV_ShanEn                      1.52e-01  1 0.70
HRV_FuzzyEn                     2.74e-01  1 0.60
HRV_MSEn                        9.20e-02  1 0.76
HRV_CMSEn                       9.87e-01  1 0.32
HRV_RCMSEn                      3.57e-01  1 0.55
HRV_CD                          9.40e-03  1 0.92
HRV_HFD                         1.16e-01  1 0.73
HRV_KFD                         9.12e-01  1 0.34
HRV_LZC                         3.76e-04  1 0.98
HRV_DFA_alpha1                  6.29e-01  1 0.43
HRV_MFDFA_alpha1_Width          4.90e-02  1 0.82
HRV_MFDFA_alpha1_Peak           1.41e-01  1 0.71
HRV_MFDFA_alpha1_Mean           3.71e-02  1 0.85
HRV_MFDFA_alpha1_Max            5.88e-01  1 0.44
HRV_MFDFA_alpha1_Delta          1.75e-01  1 0.68
HRV_MFDFA_alpha1_Asymmetry      5.36e-05  1 0.99
HRV_MFDFA_alpha1_Fluctuation 4.43e-01  1 0.51
HRV_MFDFA_alpha1_Increment      1.79e-01  1 0.67
GLOBAL                          2.95e+01 43 0.94
```

```r
cox.zph(cox_model_full_complete)
```

```
                                   chisq df    p
HRV_SD1                         5.01e-01  1 0.48
HRV_SD2                         3.96e-01  1 0.53
HRV_SD1SD2                      5.07e-01  1 0.48
HRV_S                           1.07e+00  1 0.30
HRV_CSI                         5.14e-01  1 0.47
HRV_CVI                         4.07e-03  1 0.95
HRV_CSI_Modified                3.06e-01  1 0.58
HRV_PIP                         2.45e-02  1 0.88
HRV_IALS                        7.94e-02  1 0.78
HRV_PSS                         5.32e-02  1 0.82
HRV_PAS                         2.08e+00  1 0.15
HRV_GI                          5.67e-02  1 0.81
HRV_SI                          5.29e-03  1 0.94
HRV_AI                          9.58e-02  1 0.76
HRV_PI                          6.22e-01  1 0.43
HRV_C1d                         2.73e-02  1 0.87
HRV_SD1d                        6.07e-01  1 0.44
HRV_SD1a                        4.64e-01  1 0.50
```

```
HRV_C2d                        1.41e-02  1 0.91
HRV_SD2d                       3.69e-01  1 0.54
HRV_SD2a                       3.71e-01  1 0.54
HRV_Cd                         1.53e-01  1 0.70
HRV_SDNNd                      5.35e-01  1 0.46
HRV_SDNNa                      4.43e-01  1 0.51
HRV_ApEn                       1.21e+00  1 0.27
HRV_ShanEn                     1.52e-01  1 0.70
HRV_FuzzyEn                    2.74e-01  1 0.60
HRV_MSEn                       9.20e-02  1 0.76
HRV_CMSEn                      9.87e-01  1 0.32
HRV_RCMSEn                     3.57e-01  1 0.55
HRV_CD                         9.40e-03  1 0.92
HRV_HFD                        1.16e-01  1 0.73
HRV_KFD                        9.12e-01  1 0.34
HRV_LZC                        3.76e-04  1 0.98
HRV_DFA_alpha1                 6.29e-01  1 0.43
HRV_MFDFA_alpha1_Width         4.90e-02  1 0.82
HRV_MFDFA_alpha1_Peak          1.41e-01  1 0.71
HRV_MFDFA_alpha1_Mean          3.71e-02  1 0.85
HRV_MFDFA_alpha1_Max           5.88e-01  1 0.44
HRV_MFDFA_alpha1_Delta         1.75e-01  1 0.68
HRV_MFDFA_alpha1_Asymmetry     5.36e-05  1 0.99
HRV_MFDFA_alpha1_Fluctuation 4.43e-01  1 0.51
HRV_MFDFA_alpha1_Increment     1.79e-01  1 0.67
GLOBAL                         2.95e+01 43 0.94
```

The proportional hazards assumption was tested using Schoenfeld residuals. None of the variables violated the PH assumption (all $p > 0.05$), indicating that the Cox proportional hazards model was appropriate for our analysis.

Variable Selection

LASSO

```r
# * LASSO doesn't allow missing values
set.seed(1234)
x <- as.matrix(data_complete %>% select(-c(time, event)))
y <- Surv(data_complete$time, data_complete$event)
cox_model_lasso.cv <- cv.glmnet(
```

```
    x,
    y,
    family = "cox",
    alpha = 1, # 1 for LASSO, 0 for Ridge
    nfolds = 10
)
# plot(cox_model_lasso.cv)  # Plot partial likelihood deviance vs log(lambda)
print(cox_model_lasso.cv$lambda.min)
```

```
[1] 0.0002914579
```

```
print(cox_model_lasso.cv$lambda.1se)
```

```
[1] 0.01592024
```

As mentioned in the paper, we will use the value of hyperparameter `lambda.1se` that gave the most shrunk model but still was within one standard error from the value that gave the lowest error. This is shown to produce consistently better performance than `lambda.min`.

```
cox_model_lasso <- glmnet(
    x,
    y,
    family = "cox",
    alpha = 1,
    lambda = cox_model_lasso.cv$lambda.1se
)
cox_model_lasso.coef <- coef(cox_model_lasso)
print(cox_model_lasso.coef)
```

```
46 x 1 sparse Matrix of class "dgCMatrix"
                                          s0
HRV_SD1                        .
HRV_SD2                        .
HRV_SD1SD2                     .
HRV_S                          .
HRV_CSI                       -0.0009671365
HRV_CVI                       -0.0344744471
HRV_CSI_Modified               .
HRV_PIP                        0.0158238222
```

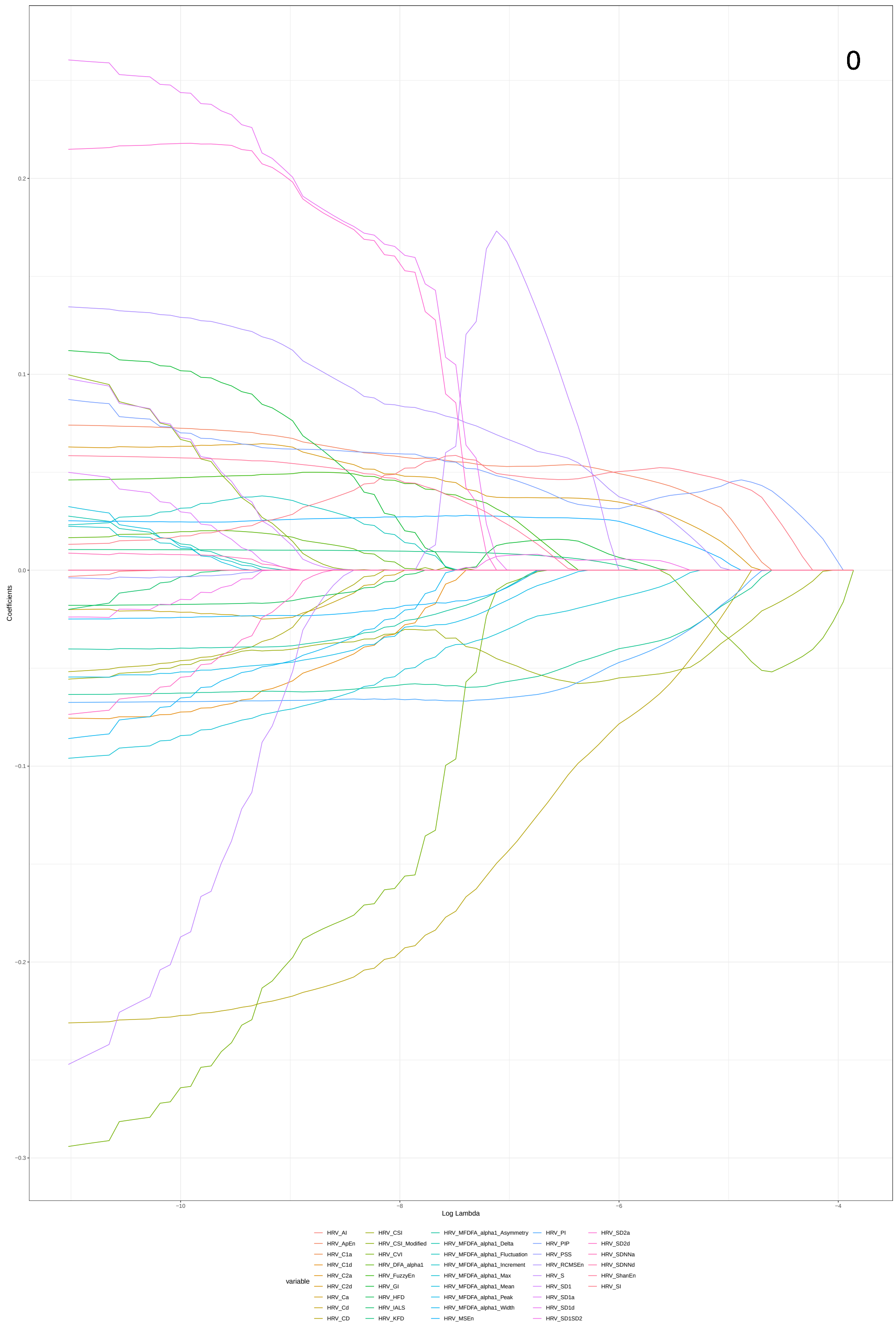
```
HRV_IALS                        .
HRV_PSS                         .
HRV_PAS                         .
HRV_GI                          .
HRV_SI                          .
HRV_AI                          .
HRV_PI                          .
HRV_C1d                         .
HRV_C1a                         .
HRV_SD1d                        .
HRV_SD1a                        .
HRV_C2d                         .
HRV_C2a                         .
HRV_SD2d                        .
HRV_SD2a                        .
HRV_Cd                          .
HRV_Ca                          .
HRV_SDNNd                       .
HRV_SDNNa                       .
HRV_ApEn                        .
HRV_ShanEn                      .
HRV_FuzzyEn                     .
HRV_MSEn                        .
HRV_CMSEn                       .
HRV_RCMSEn                      .
HRV_CD                          .
HRV_HFD                         .
HRV_KFD                         .
HRV_LZC                         .
HRV_DFA_alpha1                  .
HRV_MFDFA_alpha1_Width          .
HRV_MFDFA_alpha1_Peak           .
HRV_MFDFA_alpha1_Mean           .
HRV_MFDFA_alpha1_Max            .
HRV_MFDFA_alpha1_Delta          .
HRV_MFDFA_alpha1_Asymmetry      .
HRV_MFDFA_alpha1_Fluctuation    .
HRV_MFDFA_alpha1_Increment      .
```

```
selected_vars <- rownames(cox_model_lasso.coef)[which(cox_model_lasso.coef !=
↪  0)]
print(selected_vars)
```

```
[1] "HRV_CSI" "HRV_CVI" "HRV_PIP"
```

```
# * To visualize the LASSO path, we should not supply lambda
cox_model_lasso_fullpath <- glmnet(
    x,
    y,
    family = "cox",
    alpha = 1
)
```

```
# plot(cox_model_lasso_fullpath, xvar = "lambda", label = TRUE)
autoplot(cox_model_lasso_fullpath, xvar = "lambda", label = TRUE, label.size
 ↪  = 15) +
    theme_bw() +
    theme(legend.position = "bottom") # better way of visualizing the LASSO
     ↪  path
```


0
Coefficients
0.2
0.1
0.0
−0.1
−0.2
−0.3
−10
−8
−6
−4
Log Lambda
variable
HRV_AI
HRV_ApEn
HRV_C1a
HRV_C1d
HRV_C2a
HRV_C2d
HRV_Ca
HRV_Cd
HRV_CD
HRV_CMSEn
HRV_CSI
HRV_CSI_Modified
HRV_CVI
HRV_DFA_alpha1
HRV_FuzzyEn
HRV_GI
HRV_HFD
HRV_IALS
HRV_KFD
HRV_LZC
HRV_MFDFA_alpha1_Asymmetry
HRV_MFDFA_alpha1_Delta
HRV_MFDFA_alpha1_Fluctuation
HRV_MFDFA_alpha1_Increment
HRV_MFDFA_alpha1_Max
HRV_MFDFA_alpha1_Mean
HRV_MFDFA_alpha1_Peak
HRV_MFDFA_alpha1_Width
HRV_MSEn
HRV_PAS
HRV_PI
HRV_PIP
HRV_PSS
HRV_RCMSEn
HRV_S
HRV_SD1
HRV_SD1a
HRV_SD1d
HRV_SD1SD2
HRV_SD2
HRV_SD2a
HRV_SD2d
HRV_SDNNa
HRV_SDNNd
HRV_ShanEn
HRV_SI

Stepwise Selection based on BIC

```r
# * Stepwise selection doesn't allow missing values
cox_model_step <- MASS::stepAIC(cox_model_full_complete,
    direction = "both",
    k = log(nrow(data)), # Use BIC instead of AIC
    trace = FALSE
)
```

```r
summary(cox_model_step)
```

```
Call:
coxph(formula = Surv(time, event) ~ HRV_SD1 + HRV_CVI + HRV_PIP +
    HRV_PI + HRV_RCMSEn + HRV_CD, data = data_complete)

  n= 27198, number of events= 3435

               coef exp(coef) se(coef)      z Pr(>|z|)
HRV_SD1     0.37451   1.45428  0.06154  6.086 1.16e-09 ***
HRV_CVI    -0.26757   0.76524  0.04621 -5.791 7.02e-09 ***
HRV_PIP     0.09227   1.09666  0.02344  3.936 8.28e-05 ***
HRV_PI     -0.12237   0.88482  0.02044 -5.986 2.15e-09 ***
HRV_RCMSEn  0.13889   1.14900  0.02187  6.350 2.15e-10 ***
HRV_CD     -0.16319   0.84943  0.02434 -6.704 2.03e-11 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

           exp(coef) exp(-coef) lower .95 upper .95
HRV_SD1       1.4543     0.6876    1.2890    1.6407
HRV_CVI       0.7652     1.3068    0.6990    0.8378
HRV_PIP       1.0967     0.9119    1.0474    1.1482
HRV_PI        0.8848     1.1302    0.8501    0.9210
HRV_RCMSEn    1.1490     0.8703    1.1008    1.1993
HRV_CD        0.8494     1.1773    0.8099    0.8909

Concordance= 0.574  (se = 0.005 )
Likelihood ratio test= 209.3  on 6 df,   p=<2e-16
Wald test            = 195.1  on 6 df,   p=<2e-16
Score (logrank) test = 195.8  on 6 df,   p=<2e-16
```

Summary of Variable Selection

We will compare the selection of variables from all models we have built.

```
# Obtain the selected variables from all models
variable_names_all <- colnames(data) %>%
    setdiff(c("time", "event"))

variable_names_univariate <- results_univariate %>%
    filter(p_value < 0.05) %>%
    pull(predictor)

variable_names_multivariate <- summary(cox_model_full_complete)$coefficients
 ↪  %>%
    as.data.frame() %>%
    rownames_to_column(var = "predictor") %>% # transpose, "predictor" will
     ↪  now be the column name
    filter(`Pr(>|z|)` < 0.05) %>%
    pull(predictor)

variable_names_lasso <-
 ↪  rownames(cox_model_lasso.coef)[which(cox_model_lasso.coef != 0)]

variable_names_step <- cox_model_step$coefficients %>%
    names()
```

```
variable_selection_matrix <- matrix(
    0,
    nrow = length(variable_names_all),
    ncol = 4 # univariate, multivariate, lasso, stepwise
)
colnames(variable_selection_matrix) <- c("univariate", "multivariate",
 ↪  "lasso", "stepwise")
rownames(variable_selection_matrix) <- variable_names_all

for (variable in variable_names_all) {
    if (variable %in% variable_names_univariate) {
        variable_selection_matrix[variable, "univariate"] <- 1
    }
    if (variable %in% variable_names_multivariate) {
        variable_selection_matrix[variable, "multivariate"] <- 1
    }
```

```
    if (variable %in% variable_names_lasso) {
        variable_selection_matrix[variable, "lasso"] <- 1
    }
    if (variable %in% variable_names_step) {
        variable_selection_matrix[variable, "stepwise"] <- 1
    }
}
```

```
symbol_selected <- "*"

selection_table <- data.frame(
    Variable = variable_names_all,
    Univariate = ifelse(variable_selection_matrix[, "univariate"] == 1,
     ↪  symbol_selected, ""),
    Multivariate = ifelse(variable_selection_matrix[, "multivariate"] == 1,
     ↪  symbol_selected, ""),
    LASSO = ifelse(variable_selection_matrix[, "lasso"] == 1,
     ↪  symbol_selected, ""),
    Stepwise = ifelse(variable_selection_matrix[, "stepwise"] == 1,
     ↪  symbol_selected, "")
) %>%
    mutate(Num_Selected = rowSums(variable_selection_matrix)) %>%
    arrange(desc(Num_Selected), Variable) %>%
    as.data.frame() %>%
    remove_rownames()

variable_categories <- sapply(variable_names_all, determine_category)
category_colors <- c(
    "covariate" = "#FFB6C1", #
    "time"      = "#1E90FF", #
    "frequency" = "#32CD32", #
    "poincare"  = "#FF4500", #
    "entropy"   = "#FF8C00", #
    "fractal"   = "#FFD700", #
    "unknown"   = "#000000" #
)
category_colors_names <- c(
    "covariate"  = "pink",      #
    "time"       = "blue",      #
    "frequency"  = "green",     #
    "poincare"   = "red",       #
```

```r
    "entropy"    = "orange",    #
    "fractal"    = "gold"       #
)
category_legend <- sapply(names(category_colors_names), function(cat) {
    sprintf("%s: %s",
            tools::toTitleCase(cat),
            tools::toTitleCase(category_colors_names[cat]))
}) %>%
    paste(collapse = "; ")


selection_table %>%
    kbl(
        caption = "Variable Selection by Different Models",
        align = c("|l", "c", "c", "c", "c", "c|"),
        col.names = c("Variable", "Univariate", "Multivariate", "LASSO",
         ↪  "Stepwise", "Selected Times"),
        longtable = TRUE
    ) %>%
    kable_styling(
        bootstrap_options = c("striped", "hover", "condensed", "responsive"),
        position = "center",
        font_size = 9,
        latex_options = c("repeat_header", "striped", "HOLD_position")
    ) %>%
    # Add color for different categories of variables
    column_spec(1,
        color =
         ↪  category_colors[variable_categories[selection_table$Variable]],
        bold = TRUE
    ) %>%
    # Add a header colname for four columns: Univariate, Multivariate, LASSO,
     ↪  Stepwise
    add_header_above(c(
        " " = 1,
        "Selection Methods" = 4,
        " " = 1
    )) %>%
    footnote(
        general = sprintf("%s", category_legend),
        general_title = "Note:"
    )
```

Table 1: Variable Selection by Different Models

Variable	Selection Methods				Selected Times
	Univariate	Multivariate	LASSO	Stepwise	
HRV__CVI	*	*	*	*	4
HRV__CD	*	*		*	3
HRV__PI	*	*		*	3
HRV__PIP	*		*	*	3
HRV__RCMSEn	*	*		*	3
HRV__ApEn	*	*			2
HRV__CSI	*		*		2
HRV__LZC	*	*			2
HRV__SD1	*			*	2
HRV__AI	*				1
HRV__C1a	*				1
HRV__C1d	*				1
HRV__C2a	*				1
HRV__C2d	*				1
HRV__CMSEn	*				1
HRV__CSI__Modified	*				1
HRV__Ca	*				1
HRV__Cd	*				1
HRV__DFA__alpha1	*				1
HRV__FuzzyEn	*				1
HRV__GI	*				1
HRV__HFD	*				1
HRV__IALS	*				1
HRV__MFDFA__alpha1__Asymmetry	*				1
HRV__MFDFA__alpha1__Delta	*				1
HRV__MFDFA__alpha1__Max	*				1
HRV__MFDFA__alpha1__Peak	*				1
HRV__PAS	*				1
HRV__PSS	*				1
HRV__S		*			1
HRV__SD1SD2	*				1
HRV__SD1a	*				1
HRV__SD1d	*				1
HRV__SD2	*				1
HRV__SD2a	*				1
HRV__SD2d	*				1
HRV__SDNNa	*				1
HRV__SDNNd	*				1
HRV__SI	*				1
HRV__KFD					0
HRV__MFDFA__alpha1__Fluctuation					0
HRV__MFDFA__alpha1__Increment					0
HRV__MFDFA__alpha1__Mean					0
HRV__MFDFA__alpha1__Width					0
HRV__MSEn					0
HRV__ShanEn					0

Note:

Table 1: Variable Selection by Different Models *(continued)*

Variable	Univariate	Multivariate	LASSO	Stepwise	Selected Times

Covariate: Pink; Time: Blue; Frequency: Green; Poincare: Red; Entropy: Orange; Fractal: Gold