

Build Survival Model: Cox Proportional Hazards Model

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

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

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

```

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

```

```

# 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: partial"
```

```

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

```

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

```

```
}
```

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

```
[1] 28127    100
```

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

```
[1] 28127    75
```

```
colnames(data)
```

[1] "event"	"time"
[3] "HRV_MeanNN"	"HRV_SDNN"
[5] "HRV_RMSSD"	"HRV_SSD"
[7] "HRV_CVNN"	"HRV_CVSD"
[9] "HRV_MedianNN"	"HRV_MadNN"
[11] "HRV_MCVNN"	"HRV_IQRNN"
[13] "HRV_SDRMSSD"	"HRV_Prc20NN"
[15] "HRV_Prc80NN"	"HRV_pNN50"
[17] "HRV_pNN20"	"HRV_MinNN"
[19] "HRV_MaxNN"	"HRV_HTI"
[21] "HRV_TINN"	"HRV_LF"
[23] "HRV_HF"	"HRV_VHF"
[25] "HRV_TP"	"HRV_LFHF"
[27] "HRV_LFn"	"HRV_HFn"
[29] "HRV_LnHF"	"HRV_SD1"
[31] "HRV_SD2"	"HRV_SD1SD2"
[33] "HRV_S"	"HRV_CSI"
[35] "HRV_CVI"	"HRV_CSI_Modified"
[37] "HRV_PIP"	"HRV_IALS"
[39] "HRV_PSS"	"HRV_PAS"
[41] "HRV_GI"	"HRV_SI"
[43] "HRV_AI"	"HRV_PI"
[45] "HRV_C1d"	"HRV_C1a"
[47] "HRV_SD1d"	"HRV_SD1a"

[49] "HRV_C2d"	"HRV_C2a"
[51] "HRV_SD2d"	"HRV_SD2a"
[53] "HRV_Cd"	"HRV_Ca"
[55] "HRV_SDNNd"	"HRV_SDNNa"
[57] "HRV_ApEn"	"HRV_ShanEn"
[59] "HRV_FuzzyEn"	"HRV_MSEn"
[61] "HRV_CMSEn"	"HRV_RCMSEn"
[63] "HRV_CD"	"HRV_HFD"
[65] "HRV_KFD"	"HRV_LZC"
[67] "HRV_DFA_alpha1"	"HRV_MFDFA_alpha1_Width"
[69] "HRV_MFDFA_alpha1_Peak"	"HRV_MFDFA_alpha1_Mean"
[71] "HRV_MFDFA_alpha1_Max"	"HRV_MFDFA_alpha1_Delta"
[73] "HRV_MFDFA_alpha1_Asymmetry"	"HRV_MFDFA_alpha1_Fluctuation"
[75] "HRV_MFDFA_alpha1_Increment"	

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

```
# * 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.

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

Univariate Cox Proportional Hazards Model

```

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

```

```

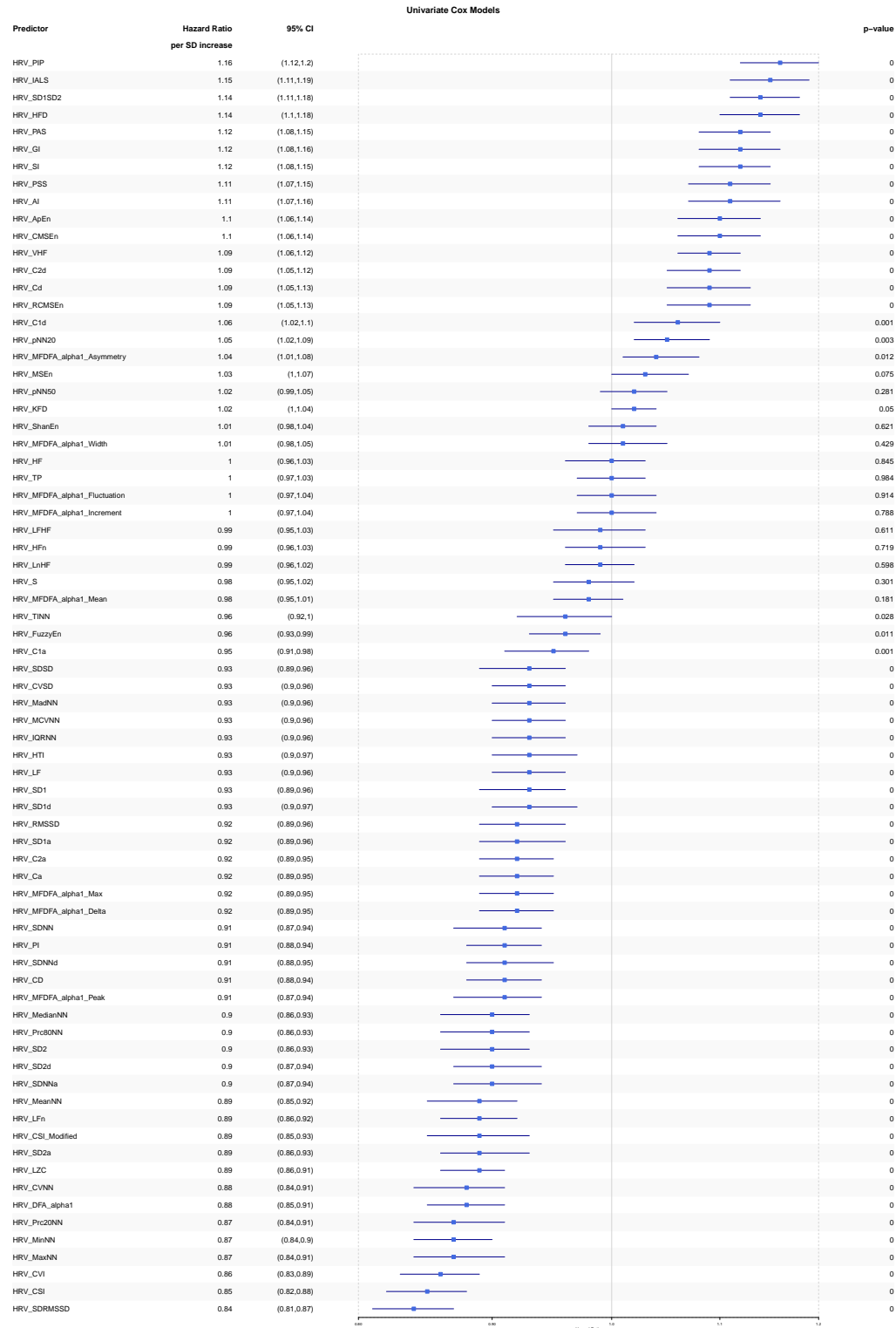
# Create forest plot
results_univariate %>%
  forestplot(

```

```

    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")

```



Multivariate Cox Proportional Hazards Model

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

Call:

```
coxph(formula = Surv(time, event) ~ ., data = data)
```

```
n= 26782, number of events= 3386
(1345 observations deleted due to missingness)
```

	coef	exp(coef)	se(coef)	z	Pr(> z)
HRV_MeanNN	3.147e-01	1.370e+00	5.602e-01	0.562	0.574235
HRV_SDNN	3.476e-01	1.416e+00	1.284e+00	0.271	0.786618
HRV_RMSSD	2.283e+01	8.208e+09	1.222e+01	1.868	0.061703
HRV_SSD	-2.192e+01	3.029e-10	1.191e+01	-1.840	0.065817
HRV_CVNN	-1.601e-01	8.521e-01	3.740e-01	-0.428	0.668581
HRV_CVSD	2.127e-01	1.237e+00	2.921e-01	0.728	0.466575
HRV_MedianNN	-1.061e-01	8.993e-01	1.765e-01	-0.601	0.547740
HRV_MadNN	4.062e-01	1.501e+00	2.034e-01	1.997	0.045861
HRV_MCVNN	-2.747e-01	7.598e-01	9.696e-02	-2.833	0.004606
HRV_IQRNN	1.032e-01	1.109e+00	1.066e-01	0.969	0.332552
HRV_SDRMSSD	1.127e-01	1.119e+00	3.386e-01	0.333	0.739232
HRV_Prc20NN	-1.788e-01	8.363e-01	9.391e-02	-1.904	0.056963
HRV_Prc80NN	-9.794e-02	9.067e-01	1.651e-01	-0.593	0.553129
HRV_pNN50	5.323e-02	1.055e+00	3.386e-02	1.572	0.116010
HRV_pNN20	-2.237e-02	9.779e-01	4.396e-02	-0.509	0.610803
HRV_MinNN	-2.624e-02	9.741e-01	3.499e-02	-0.750	0.453360
HRV_MaxNN	-3.356e-01	7.149e-01	1.582e-01	-2.122	0.033836
HRV_HTI	1.382e-01	1.148e+00	3.375e-02	4.096	4.21e-05
HRV_TINN	5.296e-02	1.054e+00	3.659e-02	1.447	0.147826
HRV_LF	-6.691e-02	9.353e-01	4.589e-02	-1.458	0.144885
HRV_HF	4.940e-03	1.005e+00	4.956e-02	0.100	0.920609
HRV_VHF	1.036e-02	1.010e+00	3.911e-02	0.265	0.791129
HRV_TP	NA	NA	0.000e+00	NA	NA
HRV_LFHF	-1.399e-01	8.694e-01	1.668e-01	-0.839	0.401612
HRV_LFn	1.409e-01	1.151e+00	7.710e-02	1.828	0.067528
HRV_HFn	1.372e-02	1.014e+00	5.882e-02	0.233	0.815594
HRV_LnHF	2.567e-02	1.026e+00	8.534e-02	0.301	0.763546
HRV_SD1	NA	NA	0.000e+00	NA	NA
HRV_SD2	9.793e-01	2.662e+00	1.434e+00	0.683	0.494791

HRV_SD1SD2	-1.273e-03	9.987e-01	1.039e-01	-0.012	0.990229
HRV_S	-1.826e-01	8.331e-01	3.846e-01	-0.475	0.634995
HRV_CSI	-3.395e-02	9.666e-01	3.624e-01	-0.094	0.925366
HRV_CVI	-3.893e-01	6.776e-01	2.913e-01	-1.336	0.181442
HRV_CSI_Modified	-2.784e-01	7.570e-01	4.832e-01	-0.576	0.564450
HRV_PIP	6.460e-01	1.908e+00	3.166e-01	2.040	0.041302
HRV_IALS	-5.386e-01	5.836e-01	2.972e-01	-1.812	0.070005
HRV_PSS	4.236e-03	1.004e+00	3.692e-02	0.115	0.908671
HRV_PAS	5.749e-03	1.006e+00	2.968e-02	0.194	0.846402
HRV_GI	2.453e-01	1.278e+00	1.897e-01	1.293	0.195844
HRV_SI	-4.342e-02	9.575e-01	7.746e-02	-0.561	0.575095
HRV_AI	-1.028e-01	9.023e-01	2.053e-01	-0.501	0.616413
HRV_PI	-7.616e-02	9.267e-01	3.205e-02	-2.377	0.017473
HRV_C1d	-7.610e-02	9.267e-01	8.358e-02	-0.910	0.362577
HRV_C1a	NA	NA	0.000e+00	NA	NA
HRV_SD1d	2.019e-02	1.020e+00	1.078e+00	0.019	0.985052
HRV_SD1a	-1.164e+00	3.123e-01	1.511e+00	-0.770	0.441346
HRV_C2d	3.550e-02	1.036e+00	7.980e-02	0.445	0.656403
HRV_C2a	NA	NA	0.000e+00	NA	NA
HRV_SD2d	2.966e-01	1.345e+00	1.341e+00	0.221	0.824942
HRV_SD2a	-5.340e-01	5.863e-01	1.584e+00	-0.337	0.735967
HRV_Cd	-4.800e-02	9.531e-01	1.021e-01	-0.470	0.638369
HRV_Ca	NA	NA	0.000e+00	NA	NA
HRV_SDNNd	-6.519e-01	5.211e-01	2.085e+00	-0.313	0.754567
HRV_SDNNa	5.203e-01	1.683e+00	2.689e+00	0.193	0.846575
HRV_ApEn	1.165e-01	1.124e+00	3.524e-02	3.305	0.000949
HRV_ShanEn	-3.011e-03	9.970e-01	4.120e-02	-0.073	0.941729
HRV_FuzzyEn	-5.086e-02	9.504e-01	4.969e-02	-1.024	0.306065
HRV_MSEn	-1.069e-02	9.894e-01	3.015e-02	-0.354	0.722996
HRV_CMSEn	-5.603e-02	9.455e-01	7.241e-02	-0.774	0.439012
HRV_RCMSEn	1.508e-01	1.163e+00	6.759e-02	2.232	0.025638
HRV_CD	-2.574e-01	7.730e-01	3.831e-02	-6.719	1.83e-11
HRV_HFD	2.730e-02	1.028e+00	4.532e-02	0.602	0.546971
HRV_KFD	7.953e-03	1.008e+00	1.061e-02	0.750	0.453513
HRV_LZC	-4.114e-02	9.597e-01	3.008e-02	-1.367	0.171483
HRV_DFA_alpha1	-2.706e-02	9.733e-01	7.796e-02	-0.347	0.728526
HRV_MFDFA_alpha1_Width	-1.548e-01	8.566e-01	1.680e-01	-0.921	0.357000
HRV_MFDFA_alpha1_Peak	-4.803e-02	9.531e-01	4.875e-02	-0.985	0.324504
HRV_MFDFA_alpha1_Mean	1.247e-01	1.133e+00	1.699e-01	0.734	0.462980
HRV_MFDFA_alpha1_Max	-1.133e-01	8.929e-01	1.031e-01	-1.099	0.271850
HRV_MFDFA_alpha1_Delta	6.368e-02	1.066e+00	1.068e-01	0.596	0.551053
HRV_MFDFA_alpha1_Asymmetry	-2.946e-02	9.710e-01	3.235e-02	-0.911	0.362437
HRV_MFDFA_alpha1_Fluctuation	3.577e-02	1.036e+00	1.652e-01	0.216	0.828613

HRV_MFDFA_alpha1_Increment	9.848e-03	1.010e+00	2.126e-01	0.046	0.963050
----------------------------	-----------	-----------	-----------	-------	----------

HRV_MeanNN

HRV_SDNN

HRV_RMSSD

.

HRV_SDS

.

HRV_CVNN

HRV_CVSD

HRV_MedianNN

HRV_MadNN

*

HRV_MCVNN

**

HRV_IQRNN

HRV_SDRMSSD

HRV_Prc20NN

.

HRV_Prc80NN

HRV_pNN50

HRV_pNN20

HRV_MinNN

HRV_MaxNN

*

HRV_HTI

HRV_TINN

HRV_LF

HRV_HF

HRV_VHF

HRV_TP

HRV_LFHF

HRV_LFn

.

HRV_HFn

HRV_LnHF

HRV_SD1

HRV_SD2

HRV_SD1SD2

HRV_S

HRV_CSI

HRV_CVI

HRV_CSI_Modified

HRV_PIP

*

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
---
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

	exp(coef)	exp(-coef)	lower .95	upper .95
HRV_MeanNN	1.370e+00	7.300e-01	4.569e-01	4.107e+00
HRV_SDNN	1.416e+00	7.064e-01	1.143e-01	1.754e+01
HRV_RMSSD	8.208e+09	1.218e-10	3.268e-01	2.062e+20
HRV_SDSD	3.029e-10	3.302e+09	2.188e-20	4.192e+00
HRV_CVNN	8.521e-01	1.174e+00	4.094e-01	1.773e+00
HRV_CVSD	1.237e+00	8.084e-01	6.978e-01	2.193e+00
HRV_MedianNN	8.993e-01	1.112e+00	6.364e-01	1.271e+00

HRV_MadNN	1.501e+00	6.662e-01	1.007e+00	2.236e+00
HRV_MCVNN	7.598e-01	1.316e+00	6.283e-01	9.188e-01
HRV_IQRNN	1.109e+00	9.019e-01	8.998e-01	1.366e+00
HRV_SDRMSSD	1.119e+00	8.934e-01	5.764e-01	2.174e+00
HRV_Prc20NN	8.363e-01	1.196e+00	6.957e-01	1.005e+00
HRV_Prc80NN	9.067e-01	1.103e+00	6.560e-01	1.253e+00
HRV_pNN50	1.055e+00	9.482e-01	9.869e-01	1.127e+00
HRV_pNN20	9.779e-01	1.023e+00	8.972e-01	1.066e+00
HRV_MinNN	9.741e-01	1.027e+00	9.095e-01	1.043e+00
HRV_MaxNN	7.149e-01	1.399e+00	5.243e-01	9.747e-01
HRV_HTI	1.148e+00	8.709e-01	1.075e+00	1.227e+00
HRV_TINN	1.054e+00	9.484e-01	9.814e-01	1.133e+00
HRV_LF	9.353e-01	1.069e+00	8.548e-01	1.023e+00
HRV_HF	1.005e+00	9.951e-01	9.119e-01	1.107e+00
HRV_VHF	1.010e+00	9.897e-01	9.359e-01	1.091e+00
HRV_TP	NA	NA	NA	NA
HRV_LFHF	8.694e-01	1.150e+00	6.270e-01	1.206e+00
HRV_LFn	1.151e+00	8.685e-01	9.899e-01	1.339e+00
HRV_HFn	1.014e+00	9.864e-01	9.034e-01	1.138e+00
HRV_LnHF	1.026e+00	9.747e-01	8.680e-01	1.213e+00
HRV_SD1	NA	NA	NA	NA
HRV_SD2	2.662e+00	3.756e-01	1.601e-01	4.428e+01
HRV_SD1SD2	9.987e-01	1.001e+00	8.147e-01	1.224e+00
HRV_S	8.331e-01	1.200e+00	3.920e-01	1.771e+00
HRV_CSI	9.666e-01	1.035e+00	4.751e-01	1.967e+00
HRV_CVI	6.776e-01	1.476e+00	3.828e-01	1.199e+00
HRV_CSI_Modified	7.570e-01	1.321e+00	2.936e-01	1.951e+00
HRV_PIP	1.908e+00	5.241e-01	1.026e+00	3.549e+00
HRV_IALS	5.836e-01	1.714e+00	3.259e-01	1.045e+00
HRV_PSS	1.004e+00	9.958e-01	9.341e-01	1.080e+00
HRV_PAS	1.006e+00	9.943e-01	9.489e-01	1.066e+00
HRV_GI	1.278e+00	7.825e-01	8.813e-01	1.853e+00
HRV_SI	9.575e-01	1.044e+00	8.226e-01	1.114e+00
HRV_AI	9.023e-01	1.108e+00	6.034e-01	1.349e+00
HRV_PI	9.267e-01	1.079e+00	8.703e-01	9.867e-01
HRV_C1d	9.267e-01	1.079e+00	7.867e-01	1.092e+00
HRV_C1a	NA	NA	NA	NA
HRV_SD1d	1.020e+00	9.800e-01	1.235e-01	8.432e+00
HRV_SD1a	3.123e-01	3.202e+00	1.615e-02	6.042e+00
HRV_C2d	1.036e+00	9.651e-01	8.861e-01	1.212e+00
HRV_C2a	NA	NA	NA	NA
HRV_SD2d	1.345e+00	7.433e-01	9.713e-02	1.863e+01
HRV_SD2a	5.863e-01	1.706e+00	2.631e-02	1.306e+01

HRV_Cd	9.531e-01	1.049e+00	7.802e-01	1.164e+00
HRV_Ca	NA	NA	NA	NA
HRV_SDNNd	5.211e-01	1.919e+00	8.750e-03	3.103e+01
HRV_SDNNa	1.683e+00	5.943e-01	8.650e-03	3.273e+02
HRV_ApEn	1.124e+00	8.901e-01	1.049e+00	1.204e+00
HRV_ShanEn	9.970e-01	1.003e+00	9.197e-01	1.081e+00
HRV_FuzzyEn	9.504e-01	1.052e+00	8.622e-01	1.048e+00
HRV_MSEn	9.894e-01	1.011e+00	9.326e-01	1.050e+00
HRV_CMSEn	9.455e-01	1.058e+00	8.204e-01	1.090e+00
HRV_RCMSEn	1.163e+00	8.600e-01	1.019e+00	1.327e+00
HRV_CD	7.730e-01	1.294e+00	7.171e-01	8.333e-01
HRV_HFD	1.028e+00	9.731e-01	9.403e-01	1.123e+00
HRV_KFD	1.008e+00	9.921e-01	9.872e-01	1.029e+00
HRV_LZC	9.597e-01	1.042e+00	9.047e-01	1.018e+00
HRV_DFA_alpha1	9.733e-01	1.027e+00	8.354e-01	1.134e+00
HRV_MFDFA_alpha1_Width	8.566e-01	1.167e+00	6.162e-01	1.191e+00
HRV_MFDFA_alpha1_Peak	9.531e-01	1.049e+00	8.662e-01	1.049e+00
HRV_MFDFA_alpha1_Mean	1.133e+00	8.827e-01	8.119e-01	1.581e+00
HRV_MFDFA_alpha1_Max	8.929e-01	1.120e+00	7.295e-01	1.093e+00
HRV_MFDFA_alpha1_Delta	1.066e+00	9.383e-01	8.644e-01	1.314e+00
HRV_MFDFA_alpha1_Asymmetry	9.710e-01	1.030e+00	9.113e-01	1.035e+00
HRV_MFDFA_alpha1_Fluctuation	1.036e+00	9.649e-01	7.497e-01	1.433e+00
HRV_MFDFA_alpha1_Increment	1.010e+00	9.902e-01	6.658e-01	1.532e+00

Concordance= 0.59 (se = 0.005)

Likelihood ratio test= 338.6 on 68 df, p=<2e-16

Wald test = 323.5 on 68 df, p=<2e-16

Score (logrank) test = 327.3 on 68 df, p=<2e-16

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

Call:

```
coxph(formula = Surv(time, event) ~ ., data = data_complete)
```

n= 26782, number of events= 3386

	coef	exp(coef)	se(coef)	z	Pr(> z)
HRV_MeanNN	3.147e-01	1.370e+00	5.602e-01	0.562	0.574235
HRV_SDNN	3.476e-01	1.416e+00	1.284e+00	0.271	0.786618
HRV_RMSSD	2.283e+01	8.208e+09	1.222e+01	1.868	0.061703
HRV_SDSD	-2.192e+01	3.029e-10	1.191e+01	-1.840	0.065817

HRV_CVNN	-1.601e-01	8.521e-01	3.740e-01	-0.428	0.668581
HRV_CVSD	2.127e-01	1.237e+00	2.921e-01	0.728	0.466575
HRV_MedianNN	-1.061e-01	8.993e-01	1.765e-01	-0.601	0.547740
HRV_MadNN	4.062e-01	1.501e+00	2.034e-01	1.997	0.045861
HRV_MCVNN	-2.747e-01	7.598e-01	9.696e-02	-2.833	0.004606
HRV_IQRNN	1.032e-01	1.109e+00	1.066e-01	0.969	0.332552
HRV_SDRMSSD	1.127e-01	1.119e+00	3.386e-01	0.333	0.739232
HRV_Prc20NN	-1.788e-01	8.363e-01	9.391e-02	-1.904	0.056963
HRV_Prc80NN	-9.794e-02	9.067e-01	1.651e-01	-0.593	0.553129
HRV_pNN50	5.323e-02	1.055e+00	3.386e-02	1.572	0.116010
HRV_pNN20	-2.237e-02	9.779e-01	4.396e-02	-0.509	0.610803
HRV_MinNN	-2.624e-02	9.741e-01	3.499e-02	-0.750	0.453360
HRV_MaxNN	-3.356e-01	7.149e-01	1.582e-01	-2.122	0.033836
HRV_HTI	1.382e-01	1.148e+00	3.375e-02	4.096	4.21e-05
HRV_TINN	5.296e-02	1.054e+00	3.659e-02	1.447	0.147826
HRV_LF	-6.691e-02	9.353e-01	4.589e-02	-1.458	0.144885
HRV_HF	4.940e-03	1.005e+00	4.956e-02	0.100	0.920609
HRV_VHF	1.036e-02	1.010e+00	3.911e-02	0.265	0.791129
HRV_TP	NA	NA	0.000e+00	NA	NA
HRV_LFHF	-1.399e-01	8.694e-01	1.668e-01	-0.839	0.401612
HRV_LFn	1.409e-01	1.151e+00	7.710e-02	1.828	0.067528
HRV_HFn	1.372e-02	1.014e+00	5.882e-02	0.233	0.815594
HRV_LnHF	2.567e-02	1.026e+00	8.534e-02	0.301	0.763546
HRV_SD1	NA	NA	0.000e+00	NA	NA
HRV_SD2	9.793e-01	2.662e+00	1.434e+00	0.683	0.494791
HRV_SD1SD2	-1.273e-03	9.987e-01	1.039e-01	-0.012	0.990229
HRV_S	-1.826e-01	8.331e-01	3.846e-01	-0.475	0.634995
HRV_CSI	-3.395e-02	9.666e-01	3.624e-01	-0.094	0.925366
HRV_CVI	-3.893e-01	6.776e-01	2.913e-01	-1.336	0.181442
HRV_CSI_Modified	-2.784e-01	7.570e-01	4.832e-01	-0.576	0.564450
HRV_PIP	6.460e-01	1.908e+00	3.166e-01	2.040	0.041302
HRV_IALS	-5.386e-01	5.836e-01	2.972e-01	-1.812	0.070005
HRV_PSS	4.236e-03	1.004e+00	3.692e-02	0.115	0.908671
HRV_PAS	5.749e-03	1.006e+00	2.968e-02	0.194	0.846402
HRV_GI	2.453e-01	1.278e+00	1.897e-01	1.293	0.195844
HRV_SI	-4.342e-02	9.575e-01	7.746e-02	-0.561	0.575095
HRV_AI	-1.028e-01	9.023e-01	2.053e-01	-0.501	0.616413
HRV_PI	-7.616e-02	9.267e-01	3.205e-02	-2.377	0.017473
HRV_C1d	-7.610e-02	9.267e-01	8.358e-02	-0.910	0.362577
HRV_C1a	NA	NA	0.000e+00	NA	NA
HRV_SD1d	2.019e-02	1.020e+00	1.078e+00	0.019	0.985052
HRV_SD1a	-1.164e+00	3.123e-01	1.511e+00	-0.770	0.441346
HRV_C2d	3.550e-02	1.036e+00	7.980e-02	0.445	0.656403

HRV_C2a	NA	NA	0.000e+00	NA	NA
HRV_SD2d	2.966e-01	1.345e+00	1.341e+00	0.221	0.824942
HRV_SD2a	-5.340e-01	5.863e-01	1.584e+00	-0.337	0.735967
HRV_Cd	-4.800e-02	9.531e-01	1.021e-01	-0.470	0.638369
HRV_Ca	NA	NA	0.000e+00	NA	NA
HRV_SDNNd	-6.519e-01	5.211e-01	2.085e+00	-0.313	0.754567
HRV_SDNNa	5.203e-01	1.683e+00	2.689e+00	0.193	0.846575
HRV_ApEn	1.165e-01	1.124e+00	3.524e-02	3.305	0.000949
HRV_ShanEn	-3.011e-03	9.970e-01	4.120e-02	-0.073	0.941729
HRV_FuzzyEn	-5.086e-02	9.504e-01	4.969e-02	-1.024	0.306065
HRV_MSEn	-1.069e-02	9.894e-01	3.015e-02	-0.354	0.722996
HRV_CMSEn	-5.603e-02	9.455e-01	7.241e-02	-0.774	0.439012
HRV_RCMSEn	1.508e-01	1.163e+00	6.759e-02	2.232	0.025638
HRV_CD	-2.574e-01	7.730e-01	3.831e-02	-6.719	1.83e-11
HRV_HFD	2.730e-02	1.028e+00	4.532e-02	0.602	0.546971
HRV_KFD	7.953e-03	1.008e+00	1.061e-02	0.750	0.453513
HRV_LZC	-4.114e-02	9.597e-01	3.008e-02	-1.367	0.171483
HRV_DFA_alpha1	-2.706e-02	9.733e-01	7.796e-02	-0.347	0.728526
HRV_MFDFA_alpha1_Width	-1.548e-01	8.566e-01	1.680e-01	-0.921	0.357000
HRV_MFDFA_alpha1_Peak	-4.803e-02	9.531e-01	4.875e-02	-0.985	0.324504
HRV_MFDFA_alpha1_Mean	1.247e-01	1.133e+00	1.699e-01	0.734	0.462980
HRV_MFDFA_alpha1_Max	-1.133e-01	8.929e-01	1.031e-01	-1.099	0.271850
HRV_MFDFA_alpha1_Delta	6.368e-02	1.066e+00	1.068e-01	0.596	0.551053
HRV_MFDFA_alpha1_Asymmetry	-2.946e-02	9.710e-01	3.235e-02	-0.911	0.362437
HRV_MFDFA_alpha1_Fluctuation	3.577e-02	1.036e+00	1.652e-01	0.216	0.828613
HRV_MFDFA_alpha1_Increment	9.848e-03	1.010e+00	2.126e-01	0.046	0.963050
HRV_MeanNN					
HRV_SDNN					
HRV_RMSSD	.				
HRV_SSD	.				
HRV_CVNN					
HRV_CVSD					
HRV_MedianNN					
HRV_MadNN	*				
HRV_MCVNN	**				
HRV_IQRNN					
HRV_SDRMSSD					
HRV_Prc20NN	.				
HRV_Prc80NN					
HRV_pNN50					
HRV_pNN20					
HRV_MinNN					

HRV_MaxNN	*
HRV_HTI	***
HRV_TINN	
HRV_LF	
HRV_HF	
HRV_VHF	
HRV_TP	
HRV_LFHF	
HRV_LFn	.
HRV_HFn	
HRV_LnHF	
HRV_SD1	
HRV_SD2	
HRV_SD1SD2	
HRV_S	
HRV_CSI	
HRV_CVI	
HRV_CSI_Modified	
HRV_PIP	*
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	


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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
---
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

	exp(coef)	exp(-coef)	lower .95	upper .95
HRV_MeanNN	1.370e+00	7.300e-01	4.569e-01	4.107e+00
HRV_SDNN	1.416e+00	7.064e-01	1.143e-01	1.754e+01
HRV_RMSSD	8.208e+09	1.218e-10	3.268e-01	2.062e+20
HRV_SDSD	3.029e-10	3.302e+09	2.188e-20	4.192e+00
HRV_CVNN	8.521e-01	1.174e+00	4.094e-01	1.773e+00
HRV_CVSD	1.237e+00	8.084e-01	6.978e-01	2.193e+00
HRV_MedianNN	8.993e-01	1.112e+00	6.364e-01	1.271e+00
HRV_MadNN	1.501e+00	6.662e-01	1.007e+00	2.236e+00
HRV_MCVNN	7.598e-01	1.316e+00	6.283e-01	9.188e-01
HRV_IQRNN	1.109e+00	9.019e-01	8.998e-01	1.366e+00
HRV_SDRMSSD	1.119e+00	8.934e-01	5.764e-01	2.174e+00
HRV_Prc20NN	8.363e-01	1.196e+00	6.957e-01	1.005e+00
HRV_Prc80NN	9.067e-01	1.103e+00	6.560e-01	1.253e+00
HRV_pNN50	1.055e+00	9.482e-01	9.869e-01	1.127e+00
HRV_pNN20	9.779e-01	1.023e+00	8.972e-01	1.066e+00
HRV_MinNN	9.741e-01	1.027e+00	9.095e-01	1.043e+00
HRV_MaxNN	7.149e-01	1.399e+00	5.243e-01	9.747e-01
HRV_HTI	1.148e+00	8.709e-01	1.075e+00	1.227e+00
HRV_TINN	1.054e+00	9.484e-01	9.814e-01	1.133e+00
HRV_LF	9.353e-01	1.069e+00	8.548e-01	1.023e+00
HRV_HF	1.005e+00	9.951e-01	9.119e-01	1.107e+00
HRV_VHF	1.010e+00	9.897e-01	9.359e-01	1.091e+00
HRV_TP	NA	NA	NA	NA
HRV_LFHF	8.694e-01	1.150e+00	6.270e-01	1.206e+00
HRV_LFn	1.151e+00	8.685e-01	9.899e-01	1.339e+00

HRV_HFn	1.014e+00	9.864e-01	9.034e-01	1.138e+00
HRV_LnHF	1.026e+00	9.747e-01	8.680e-01	1.213e+00
HRV_SD1	NA	NA	NA	NA
HRV_SD2	2.662e+00	3.756e-01	1.601e-01	4.428e+01
HRV_SD1SD2	9.987e-01	1.001e+00	8.147e-01	1.224e+00
HRV_S	8.331e-01	1.200e+00	3.920e-01	1.771e+00
HRV_CSI	9.666e-01	1.035e+00	4.751e-01	1.967e+00
HRV_CVI	6.776e-01	1.476e+00	3.828e-01	1.199e+00
HRV_CSI_Modified	7.570e-01	1.321e+00	2.936e-01	1.951e+00
HRV_PIP	1.908e+00	5.241e-01	1.026e+00	3.549e+00
HRV_IALS	5.836e-01	1.714e+00	3.259e-01	1.045e+00
HRV_PSS	1.004e+00	9.958e-01	9.341e-01	1.080e+00
HRV_PAS	1.006e+00	9.943e-01	9.489e-01	1.066e+00
HRV_GI	1.278e+00	7.825e-01	8.813e-01	1.853e+00
HRV_SI	9.575e-01	1.044e+00	8.226e-01	1.114e+00
HRV_AI	9.023e-01	1.108e+00	6.034e-01	1.349e+00
HRV_PI	9.267e-01	1.079e+00	8.703e-01	9.867e-01
HRV_C1d	9.267e-01	1.079e+00	7.867e-01	1.092e+00
HRV_C1a	NA	NA	NA	NA
HRV_SD1d	1.020e+00	9.800e-01	1.235e-01	8.432e+00
HRV_SD1a	3.123e-01	3.202e+00	1.615e-02	6.042e+00
HRV_C2d	1.036e+00	9.651e-01	8.861e-01	1.212e+00
HRV_C2a	NA	NA	NA	NA
HRV_SD2d	1.345e+00	7.433e-01	9.713e-02	1.863e+01
HRV_SD2a	5.863e-01	1.706e+00	2.631e-02	1.306e+01
HRV_Cd	9.531e-01	1.049e+00	7.802e-01	1.164e+00
HRV_Ca	NA	NA	NA	NA
HRV_SDNNd	5.211e-01	1.919e+00	8.750e-03	3.103e+01
HRV_SDNNa	1.683e+00	5.943e-01	8.650e-03	3.273e+02
HRV_ApEn	1.124e+00	8.901e-01	1.049e+00	1.204e+00
HRV_ShanEn	9.970e-01	1.003e+00	9.197e-01	1.081e+00
HRV_FuzzyEn	9.504e-01	1.052e+00	8.622e-01	1.048e+00
HRV_MSEn	9.894e-01	1.011e+00	9.326e-01	1.050e+00
HRV_CMSEn	9.455e-01	1.058e+00	8.204e-01	1.090e+00
HRV_RCMSEn	1.163e+00	8.600e-01	1.019e+00	1.327e+00
HRV_CD	7.730e-01	1.294e+00	7.171e-01	8.333e-01
HRV_HFD	1.028e+00	9.731e-01	9.403e-01	1.123e+00
HRV_KFD	1.008e+00	9.921e-01	9.872e-01	1.029e+00
HRV_LZC	9.597e-01	1.042e+00	9.047e-01	1.018e+00
HRV_DFA_alpha1	9.733e-01	1.027e+00	8.354e-01	1.134e+00
HRV_MFDFA_alpha1_Width	8.566e-01	1.167e+00	6.162e-01	1.191e+00
HRV_MFDFA_alpha1_Peak	9.531e-01	1.049e+00	8.662e-01	1.049e+00
HRV_MFDFA_alpha1_Mean	1.133e+00	8.827e-01	8.119e-01	1.581e+00

HRV_MFDFA_alpha1_Max	8.929e-01	1.120e+00	7.295e-01	1.093e+00
HRV_MFDFA_alpha1_Delta	1.066e+00	9.383e-01	8.644e-01	1.314e+00
HRV_MFDFA_alpha1_Asymmetry	9.710e-01	1.030e+00	9.113e-01	1.035e+00
HRV_MFDFA_alpha1_Fluctuation	1.036e+00	9.649e-01	7.497e-01	1.433e+00
HRV_MFDFA_alpha1_Increment	1.010e+00	9.902e-01	6.658e-01	1.532e+00

Concordance= 0.59 (se = 0.005)

Likelihood ratio test= 338.6 on 68 df, p=<2e-16

Wald test = 323.5 on 68 df, p=<2e-16

Score (logrank) test = 327.3 on 68 df, p=<2e-16

PH Assumption Assessment

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

	chisq	df	p
HRV_MeanNN	1.10e+00	1	0.29
HRV_SDNN	7.94e-01	1	0.37
HRV_RMSSD	8.20e-01	1	0.37
HRV_SSD	8.32e-01	1	0.36
HRV_CVNN	3.02e-02	1	0.86
HRV_CVSD	1.03e-01	1	0.75
HRV_MedianNN	1.79e+00	1	0.18
HRV_MadNN	3.93e-01	1	0.53
HRV_MCVNN	6.12e-01	1	0.43
HRV_IQRNN	7.95e-01	1	0.37
HRV_SDRMSSD	2.28e-01	1	0.63
HRV_Prc20NN	2.64e-01	1	0.61
HRV_Prc80NN	1.55e+00	1	0.21
HRV_pNN50	8.50e-01	1	0.36
HRV_pNN20	1.17e+00	1	0.28
HRV_MinNN	1.49e-02	1	0.90
HRV_MaxNN	4.55e-01	1	0.50
HRV_HTI	9.39e-02	1	0.76
HRV_TINN	5.92e-01	1	0.44
HRV_LF	5.05e-01	1	0.48
HRV_HF	2.94e-01	1	0.59
HRV_VHF	1.67e+00	1	0.20
HRV_LFHF	6.86e-01	1	0.41

HRV_LFn	2.09e-02	1	0.88
HRV_HFn	1.73e-01	1	0.68
HRV_LnHF	9.73e-02	1	0.76
HRV_SD2	6.66e-01	1	0.41
HRV_SD1SD2	7.02e-01	1	0.40
HRV_S	1.50e+00	1	0.22
HRV_CSI	5.09e-01	1	0.48
HRV_CVI	3.17e-02	1	0.86
HRV_CSI_Modified	5.10e-01	1	0.48
HRV_PIP	5.48e-02	1	0.81
HRV_IALS	1.16e-01	1	0.73
HRV_PSS	8.10e-02	1	0.78
HRV_PAS	2.00e+00	1	0.16
HRV_GI	5.72e-01	1	0.45
HRV_SI	7.15e-02	1	0.79
HRV_AI	6.37e-01	1	0.42
HRV_PI	7.35e-01	1	0.39
HRV_C1d	3.06e-01	1	0.58
HRV_SD1d	7.57e-01	1	0.38
HRV_SD1a	8.99e-01	1	0.34
HRV_C2d	2.00e-01	1	0.65
HRV_SD2d	4.67e-01	1	0.49
HRV_SD2a	7.42e-01	1	0.39
HRV_Cd	6.00e-01	1	0.44
HRV_SDNNd	6.66e-01	1	0.41
HRV_SDNNa	8.69e-01	1	0.35
HRV_ApEn	9.19e-01	1	0.34
HRV_ShanEn	3.02e-01	1	0.58
HRV_FuzzyEn	2.47e-01	1	0.62
HRV_MSEn	7.32e-02	1	0.79
HRV_CMSEn	9.87e-01	1	0.32
HRV_RCMSEn	3.56e-01	1	0.55
HRV_CD	3.82e-02	1	0.85
HRV_HFD	1.19e-01	1	0.73
HRV_KFD	9.54e-01	1	0.33
HRV_LZC	3.03e-02	1	0.86
HRV_DFA_alpha1	5.27e-01	1	0.47
HRV_MFDFA_alpha1_Width	3.60e-02	1	0.85
HRV_MFDFA_alpha1_Peak	8.66e-02	1	0.77
HRV_MFDFA_alpha1_Mean	4.83e-02	1	0.83
HRV_MFDFA_alpha1_Max	4.88e-01	1	0.48
HRV_MFDFA_alpha1_Delta	1.16e-01	1	0.73
HRV_MFDFA_alpha1_Asymmetry	1.03e-05	1	1.00

HRV_MFDFA_alpha1_Fluctuation	4.80e-01	1	0.49
HRV_MFDFA_alpha1_Increment	2.00e-01	1	0.66
GLOBAL	5.46e+01	68	0.88

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

	chisq	df	p
HRV_MeanNN	1.10e+00	1	0.29
HRV_SDNN	7.94e-01	1	0.37
HRV_RMSSD	8.20e-01	1	0.37
HRV_SSD	8.32e-01	1	0.36
HRV_CVNN	3.02e-02	1	0.86
HRV_CVSD	1.03e-01	1	0.75
HRV_MedianNN	1.79e+00	1	0.18
HRV_MadNN	3.93e-01	1	0.53
HRV_MCVNN	6.12e-01	1	0.43
HRV_IQRNN	7.95e-01	1	0.37
HRV_SDRMSSD	2.28e-01	1	0.63
HRV_Prc20NN	2.64e-01	1	0.61
HRV_Prc80NN	1.55e+00	1	0.21
HRV_pNN50	8.50e-01	1	0.36
HRV_pNN20	1.17e+00	1	0.28
HRV_MinNN	1.49e-02	1	0.90
HRV_MaxNN	4.55e-01	1	0.50
HRV_HTI	9.39e-02	1	0.76
HRV_TINN	5.92e-01	1	0.44
HRV_LF	5.05e-01	1	0.48
HRV_HF	2.94e-01	1	0.59
HRV_VHF	1.67e+00	1	0.20
HRV_LFHF	6.86e-01	1	0.41
HRV_LF _n	2.09e-02	1	0.88
HRV_HF _n	1.73e-01	1	0.68
HRV_LnHF	9.73e-02	1	0.76
HRV_SD2	6.66e-01	1	0.41
HRV_SD1SD2	7.02e-01	1	0.40
HRV_S	1.50e+00	1	0.22
HRV_CSI	5.09e-01	1	0.48
HRV_CVI	3.17e-02	1	0.86
HRV_CSI_Modified	5.10e-01	1	0.48
HRV_PIP	5.48e-02	1	0.81
HRV_IALS	1.16e-01	1	0.73
HRV_PSS	8.10e-02	1	0.78

HRV_PAS	2.00e+00	1	0.16
HRV_GI	5.72e-01	1	0.45
HRV_SI	7.15e-02	1	0.79
HRV_AI	6.37e-01	1	0.42
HRV_PI	7.35e-01	1	0.39
HRV_C1d	3.06e-01	1	0.58
HRV_SD1d	7.57e-01	1	0.38
HRV_SD1a	8.99e-01	1	0.34
HRV_C2d	2.00e-01	1	0.65
HRV_SD2d	4.67e-01	1	0.49
HRV_SD2a	7.42e-01	1	0.39
HRV_Cd	6.00e-01	1	0.44
HRV_SDNNd	6.66e-01	1	0.41
HRV_SDNNa	8.69e-01	1	0.35
HRV_ApEn	9.19e-01	1	0.34
HRV_ShanEn	3.02e-01	1	0.58
HRV_FuzzyEn	2.47e-01	1	0.62
HRV_MSEn	7.32e-02	1	0.79
HRV_CMSEn	9.87e-01	1	0.32
HRV_RCMSEn	3.56e-01	1	0.55
HRV_CD	3.82e-02	1	0.85
HRV_HFD	1.19e-01	1	0.73
HRV_KFD	9.54e-01	1	0.33
HRV_LZC	3.03e-02	1	0.86
HRV_DFA_alpha1	5.27e-01	1	0.47
HRV_MFDFA_alpha1_Width	3.60e-02	1	0.85
HRV_MFDFA_alpha1_Peak	8.66e-02	1	0.77
HRV_MFDFA_alpha1_Mean	4.83e-02	1	0.83
HRV_MFDFA_alpha1_Max	4.88e-01	1	0.48
HRV_MFDFA_alpha1_Delta	1.16e-01	1	0.73
HRV_MFDFA_alpha1_Asymmetry	1.03e-05	1	1.00
HRV_MFDFA_alpha1_Fluctuation	4.80e-01	1	0.49
HRV_MFDFA_alpha1_Increment	2.00e-01	1	0.66
GLOBAL	5.46e+01	68	0.88

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

```
# * 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)

# * We choose the range based on plot(cox_model_lasso.cv) for previous run
#   ↪ when not providing lambda_seq
lambda_seq <- exp(seq(-8, -6, length.out = 100))
cox_model_lasso.cv <- cv.glmnet(
  x,
  y,
  family = "cox",
  alpha = 1, # 1 for LASSO, 0 for Ridge
  nfolds = 10,
  lambda = lambda_seq
)
print(cox_model_lasso.cv$lambda.min)
```

```
[1] 0.0007083833
```

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

```
[1] 0.002478752
```

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)

```

```

73 x 1 sparse Matrix of class "dgCMatrix"
                                s0
HRV_MeanNN                      .
HRV_SDNN                        .
HRV_RMSSD                       .
HRV_SDSD                        .
HRV_CVNN                        .
HRV_CVSD                        .
HRV_MedianNN                    .
HRV_MadNN                       .
HRV_MCVNN                       .
HRV_IQRNN                       0.0095959298
HRV_SDRMSSD                     -0.0239984153
HRV_Prc20NN                     -0.0425670353
HRV_Prc80NN                     .
HRV_pNN50                       .
HRV_pNN20                       .
HRV_MinNN                       -0.0631234047
HRV_MaxNN                       .
HRV_HTI                         0.0343782769
HRV_TINN                        .
HRV_LF                          .
HRV_HF                          .
HRV_VHF                         .
HRV_TP                          .
HRV_LFHF                        .
HRV_LFn                         .
HRV_HFn                         .
HRV_LnHF                        .
HRV_SD1                         .
HRV_SD2                         .

```


HRV_SD1SD2	0.0413992298
HRV_S	.
HRV_CSI	-0.0005100190
HRV_CVI	.
HRV_CSI_Modified	.
HRV_PIP	0.0229910474
HRV_IALS	.
HRV_PSS	.
HRV_PAS	0.0169771089
HRV_GI	0.0123172955
HRV_SI	0.0341293966
HRV_AI	.
HRV_PI	-0.0547899196
HRV_C1d	.
HRV_C1a	.
HRV_SD1d	.
HRV_SD1a	.
HRV_C2d	0.0205952215
HRV_C2a	-0.0019200457
HRV_SD2d	.
HRV_SD2a	.
HRV_Cd	.
HRV_Ca	.
HRV_SDNNd	.
HRV_SDNNa	.
HRV_ApEn	0.0513880197
HRV_ShanEn	.
HRV_FuzzyEn	.
HRV_MSEn	.
HRV_CMSEn	.
HRV_RCMSEn	0.0214151199
HRV_CD	-0.1150440780
HRV_HFD	.
HRV_KFD	0.0003577586
HRV_LZC	-0.0241285491
HRV_DFA_alpha1	.
HRV_MFDFA_alpha1_Width	.
HRV_MFDFA_alpha1_Peak	.
HRV_MFDFA_alpha1_Mean	.
HRV_MFDFA_alpha1_Max	-0.0102270849
HRV_MFDFA_alpha1_Delta	.
HRV_MFDFA_alpha1_Asymmetry	.
HRV_MFDFA_alpha1_Fluctuation	.

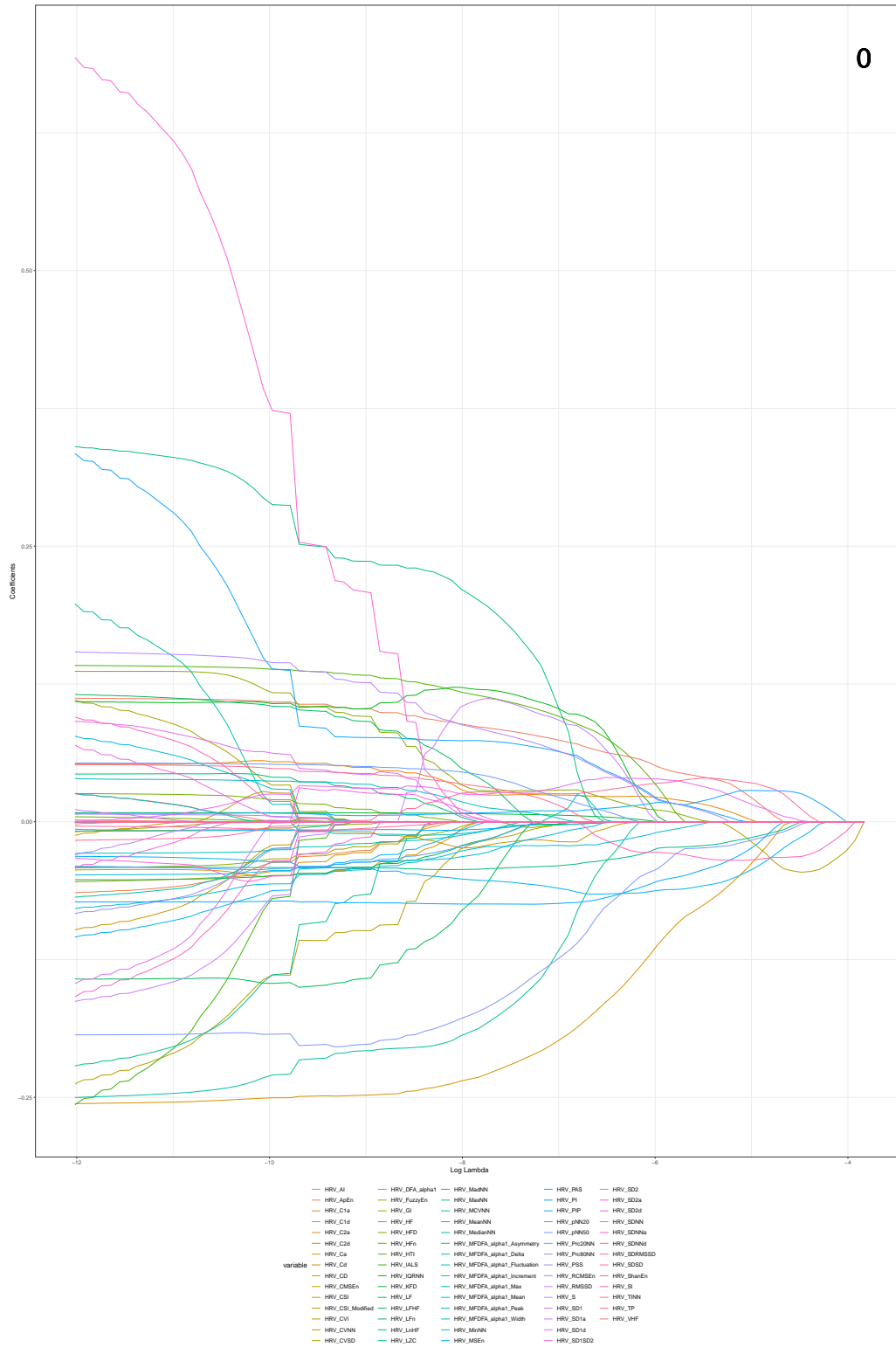
```
HRV_MFDFA_alpha1_Increment      .
```

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

```
[1] "HRV_IQRNN"           "HRV_SDRMSSD"           "HRV_Prc20NN"  
[4] "HRV_MinNN"           "HRV_HTI"               "HRV_SD1SD2"  
[7] "HRV_CSI"             "HRV_PIP"               "HRV_PAS"  
[10] "HRV_GI"              "HRV_SI"                "HRV_PI"  
[13] "HRV_C2d"             "HRV_C2a"               "HRV_ApEn"  
[16] "HRV_RCMSEn"          "HRV_CD"                "HRV_KFD"  
[19] "HRV_LZC"             "HRV_MFDFA_alpha1_Max"
```

```
# * 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
```



Stepwise Selection based on BIC

```
# * 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
)
```

```
summary(cox_model_step)
```

Call:

```
coxph(formula = Surv(time, event) ~ HRV_MeanNN + HRV_SDNN + HRV_RMSSD +
  HRV_SDSO + HRV_CVNN + HRV_CVSD + HRV_MedianNN + HRV_MadNN +
  HRV_MCVNN + HRV_IQRNN + HRV_SDRMSSD + HRV_Prc20NN + HRV_Prc80NN +
  HRV_pNN50 + HRV_pNN20 + HRV_MinNN + HRV_MaxNN + HRV_HTI +
  HRV_TINN + HRV_LF + HRV_HF + HRV_VHF + HRV_TP + HRV_LFHF +
  HRV_LFn + HRV_HFn + HRV_LnHF + HRV_SD1 + HRV_SD2 + HRV_SD1SD2 +
  HRV_S + HRV_CSI + HRV_CVI + HRV_CSI_Modified + HRV_PIP +
  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_RCMSEn + HRV_CD +
  HRV_HFD, data = data_complete)
```

n= 26782, number of events= 3386

	coef	exp(coef)	se(coef)	z	Pr(> z)
HRV_MeanNN	7.564e-02	1.079e+00	5.484e-01	0.138	0.89030
HRV_SDNN	5.576e-01	1.747e+00	1.253e+00	0.445	0.65624
HRV_RMSSD	2.189e+01	3.201e+09	1.185e+01	1.847	0.06470 .
HRV_SDSO	-2.120e+01	6.180e-10	1.148e+01	-1.847	0.06472 .
HRV_CVNN	-2.283e-01	7.959e-01	3.701e-01	-0.617	0.53740
HRV_CVSD	2.681e-01	1.308e+00	2.849e-01	0.941	0.34663
HRV_MedianNN	-1.269e-01	8.808e-01	1.753e-01	-0.724	0.46908
HRV_MadNN	4.480e-01	1.565e+00	2.019e-01	2.219	0.02650 *
HRV_MCVNN	-3.035e-01	7.382e-01	9.590e-02	-3.165	0.00155 **
HRV_IQRNN	9.520e-02	1.100e+00	1.063e-01	0.895	0.37068
HRV_SDRMSSD	1.530e-01	1.165e+00	3.365e-01	0.455	0.64930
HRV_Prc20NN	-1.625e-01	8.500e-01	9.311e-02	-1.745	0.08100 .
HRV_Prc80NN	-9.657e-02	9.079e-01	1.658e-01	-0.582	0.56032

HRV_pNN50	5.276e-02	1.054e+00	3.140e-02	1.680	0.09294	.
HRV_pNN20	-3.467e-02	9.659e-01	4.062e-02	-0.854	0.39333	
HRV_MinNN	-1.644e-02	9.837e-01	3.407e-02	-0.483	0.62935	
HRV_MaxNN	-3.078e-01	7.351e-01	1.544e-01	-1.994	0.04617	*
HRV_HTI	1.329e-01	1.142e+00	3.081e-02	4.313	1.61e-05	***
HRV_TINN	5.595e-02	1.058e+00	3.656e-02	1.530	0.12593	
HRV_LF	-1.127e+00	3.239e-01	5.124e+02	-0.002	0.99824	
HRV_HF	-2.680e+00	6.859e-02	1.300e+03	-0.002	0.99836	
HRV_VHF	-1.001e+00	3.674e-01	4.914e+02	-0.002	0.99837	
HRV_TP	3.706e+00	4.067e+01	1.800e+03	0.002	0.99836	
HRV_LFHF	-1.430e-01	8.667e-01	1.627e-01	-0.879	0.37943	
HRV_LFn	1.495e-01	1.161e+00	7.499e-02	1.994	0.04614	*
HRV_HFn	1.191e-02	1.012e+00	5.815e-02	0.205	0.83770	
HRV_LnHF	3.399e-02	1.035e+00	8.430e-02	0.403	0.68681	
HRV_SD1	NA	NA	0.000e+00	NA	NA	
HRV_SD2	9.298e-01	2.534e+00	1.402e+00	0.663	0.50715	
HRV_SD1SD2	3.317e-02	1.034e+00	9.595e-02	0.346	0.72953	
HRV_S	-2.282e-01	7.960e-01	3.775e-01	-0.605	0.54551	
HRV_CSI	-3.304e-02	9.675e-01	3.586e-01	-0.092	0.92659	
HRV_CVI	-4.225e-01	6.554e-01	2.866e-01	-1.474	0.14051	
HRV_CSI_Modified	-2.870e-01	7.505e-01	3.126e-01	-0.918	0.35856	
HRV_PIP	6.060e-01	1.833e+00	3.116e-01	1.945	0.05180	.
HRV_IALS	-4.686e-01	6.259e-01	2.917e-01	-1.607	0.10814	
HRV_PSS	-7.486e-03	9.925e-01	3.631e-02	-0.206	0.83667	
HRV_PAS	-6.844e-04	9.993e-01	2.947e-02	-0.023	0.98147	
HRV_GI	2.707e-01	1.311e+00	1.866e-01	1.451	0.14683	
HRV_SI	-5.510e-02	9.464e-01	7.586e-02	-0.726	0.46760	
HRV_AI	-1.271e-01	8.807e-01	2.029e-01	-0.626	0.53110	
HRV_PI	-8.850e-02	9.153e-01	3.162e-02	-2.799	0.00513	**
HRV_C1d	-5.642e-02	9.451e-01	7.689e-02	-0.734	0.46309	
HRV_C1a	NA	NA	0.000e+00	NA	NA	
HRV_SD1d	-1.615e-01	8.509e-01	7.370e-01	-0.219	0.82659	
HRV_SD1a	-8.564e-01	4.247e-01	1.019e+00	-0.840	0.40073	
HRV_C2d	6.128e-02	1.063e+00	6.087e-02	1.007	0.31403	
HRV_C2a	NA	NA	0.000e+00	NA	NA	
HRV_SD2d	-6.930e-02	9.331e-01	5.377e-01	-0.129	0.89746	
HRV_SD2a	-1.531e-01	8.581e-01	5.569e-01	-0.275	0.78343	
HRV_Cd	-7.895e-02	9.241e-01	8.777e-02	-0.900	0.36835	
HRV_RCMSEn	1.190e-01	1.126e+00	3.009e-02	3.954	7.68e-05	***
HRV_CD	-2.598e-01	7.712e-01	3.173e-02	-8.186	2.69e-16	***
HRV_HFD	4.636e-02	1.047e+00	4.188e-02	1.107	0.26834	

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

	exp(coef)	exp(-coef)	lower .95	upper .95
HRV_MeanNN	1.079e+00	9.271e-01	3.682e-01	3.160e+00
HRV_SDNN	1.747e+00	5.726e-01	1.499e-01	2.035e+01
HRV_RMSSD	3.201e+09	3.124e-10	2.634e-01	3.891e+19
HRV_SDSD	6.180e-10	1.618e+09	1.046e-19	3.651e+00
HRV_CVNN	7.959e-01	1.256e+00	3.853e-01	1.644e+00
HRV_CVSD	1.308e+00	7.648e-01	7.481e-01	2.285e+00
HRV_MedianNN	8.808e-01	1.135e+00	6.247e-01	1.242e+00
HRV_MadNN	1.565e+00	6.389e-01	1.054e+00	2.325e+00
HRV_MCVNN	7.382e-01	1.355e+00	6.117e-01	8.908e-01
HRV_IQRNN	1.100e+00	9.092e-01	8.929e-01	1.355e+00
HRV_SDRMSSD	1.165e+00	8.581e-01	6.026e-01	2.253e+00
HRV_Prc20NN	8.500e-01	1.176e+00	7.083e-01	1.020e+00
HRV_Prc80NN	9.079e-01	1.101e+00	6.560e-01	1.257e+00
HRV_pNN50	1.054e+00	9.486e-01	9.912e-01	1.121e+00
HRV_pNN20	9.659e-01	1.035e+00	8.920e-01	1.046e+00
HRV_MinNN	9.837e-01	1.017e+00	9.202e-01	1.052e+00
HRV_MaxNN	7.351e-01	1.360e+00	5.432e-01	9.948e-01
HRV_HTI	1.142e+00	8.756e-01	1.075e+00	1.213e+00
HRV_TINN	1.058e+00	9.456e-01	9.844e-01	1.136e+00
HRV_LF	3.239e-01	3.087e+00	0.000e+00	Inf
HRV_HF	6.859e-02	1.458e+01	0.000e+00	Inf
HRV_VHF	3.674e-01	2.722e+00	0.000e+00	Inf
HRV_TP	4.067e+01	2.459e-02	0.000e+00	Inf
HRV_LFHF	8.667e-01	1.154e+00	6.301e-01	1.192e+00
HRV_LF _n	1.161e+00	8.611e-01	1.003e+00	1.345e+00
HRV_HF _n	1.012e+00	9.882e-01	9.030e-01	1.134e+00
HRV_LnHF	1.035e+00	9.666e-01	8.770e-01	1.220e+00
HRV_SD1	NA	NA	NA	NA
HRV_SD2	2.534e+00	3.946e-01	1.624e-01	3.954e+01
HRV_SD1SD2	1.034e+00	9.674e-01	8.565e-01	1.248e+00
HRV_S	7.960e-01	1.256e+00	3.798e-01	1.668e+00
HRV_CSI	9.675e-01	1.034e+00	4.790e-01	1.954e+00
HRV_CVI	6.554e-01	1.526e+00	3.737e-01	1.149e+00
HRV_CSI_Modified	7.505e-01	1.332e+00	4.067e-01	1.385e+00
HRV_PIP	1.833e+00	5.455e-01	9.953e-01	3.376e+00
HRV_IALS	6.259e-01	1.598e+00	3.534e-01	1.109e+00
HRV_PSS	9.925e-01	1.008e+00	9.244e-01	1.066e+00
HRV_PAS	9.993e-01	1.001e+00	9.432e-01	1.059e+00
HRV_GI	1.311e+00	7.628e-01	9.094e-01	1.890e+00
HRV_SI	9.464e-01	1.057e+00	8.156e-01	1.098e+00
HRV_AI	8.807e-01	1.135e+00	5.918e-01	1.311e+00

HRV_PI	9.153e-01	1.093e+00	8.603e-01	9.738e-01
HRV_C1d	9.451e-01	1.058e+00	8.129e-01	1.099e+00
HRV_C1a	NA	NA	NA	NA
HRV_SD1d	8.509e-01	1.175e+00	2.007e-01	3.608e+00
HRV_SD1a	4.247e-01	2.355e+00	5.762e-02	3.130e+00
HRV_C2d	1.063e+00	9.406e-01	9.436e-01	1.198e+00
HRV_C2a	NA	NA	NA	NA
HRV_SD2d	9.331e-01	1.072e+00	3.252e-01	2.677e+00
HRV_SD2a	8.581e-01	1.165e+00	2.880e-01	2.556e+00
HRV_Cd	9.241e-01	1.082e+00	7.780e-01	1.098e+00
HRV_RCMSEn	1.126e+00	8.878e-01	1.062e+00	1.195e+00
HRV_CD	7.712e-01	1.297e+00	7.247e-01	8.207e-01
HRV_HFD	1.047e+00	9.547e-01	9.649e-01	1.137e+00

Concordance= 0.587 (se = 0.005)

Likelihood ratio test= 320.9 on 51 df, p=<2e-16

Wald test = 306.5 on 51 df, p=<2e-16

Score (logrank) test = 309.9 on 51 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",       #
  "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_CD	*	*	*	*	4
HRV_HTI	*	*	*	*	4
HRV_PI	*	*	*	*	4
HRV_PIP	*	*	*	*	4
HRV_RCMSEn	*	*	*	*	4
HRV_ApEn	*	*	*		3
HRV_C2a	*		*	*	3
HRV_C2d	*		*	*	3
HRV_CSI	*		*	*	3
HRV_GI	*		*	*	3
HRV_IQRNN	*		*	*	3
HRV_MCVNN	*	*		*	3
HRV_MadNN	*	*		*	3
HRV_MaxNN	*	*		*	3
HRV_MinNN	*		*	*	3
HRV_PAS	*		*	*	3
HRV_Prc20NN	*		*	*	3
HRV_SD1SD2	*		*	*	3
HRV_SDRMSSD	*		*	*	3
HRV_SI	*		*	*	3

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

Variable	Univariate	Multivariate	LASSO	Stepwise	Selected Times
HRV_AI	*			*	2
HRV_C1a	*			*	2
HRV_C1d	*			*	2
HRV_CSI_Modified	*			*	2
HRV_CVI	*			*	2
HRV_CVNN	*			*	2
HRV_CVSD	*			*	2
HRV_Cd	*			*	2
HRV_HFD	*			*	2
HRV_IALS	*			*	2
HRV_LF	*			*	2
HRV_LFn	*			*	2
HRV_LZC	*		*		2
HRV_MFDFA_alpha1_Max	*		*		2
HRV_MeanNN	*			*	2
HRV_MedianNN	*			*	2
HRV_PSS	*			*	2
HRV_Prc80NN	*			*	2
HRV_RMSSD	*			*	2
HRV_SD1	*			*	2
HRV_SD1a	*			*	2
HRV_SD1d	*			*	2
HRV_SD2	*			*	2
HRV_SD2a	*			*	2
HRV_SD2d	*			*	2
HRV_SDNN	*			*	2
HRV_SDS	*			*	2
HRV_TINN	*			*	2
HRV_VHF	*			*	2
HRV_pNN20	*			*	2
HRV_CMSEn	*				1
HRV_Ca	*				1
HRV_DFA_alpha1	*				1
HRV_FuzzyEn	*				1
HRV_HF				*	1
HRV_HFn				*	1
HRV_KFD			*		1
HRV_LFHF				*	1
HRV_LnHF				*	1
HRV_MFDFA_alpha1_Asymmetry	*				1
HRV_MFDFA_alpha1_Delta	*				1
HRV_MFDFA_alpha1_Peak	*				1
HRV_S				*	1
HRV_SDNNa	*				1
HRV_SDNND	*				1
HRV_TP				*	1
HRV_pNN50				*	1
HRV_MFDFA_alpha1_Fluctuation					0

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

Variable	Univariate	Multivariate	LASSO	Stepwise	Selected Times
HRV_MFDFA_alpha1_Increment					0
HRV_MFDFA_alpha1_Mean					0
HRV_MFDFA_alpha1_Width					0
HRV_MSEn					0
HRV_ShanEn					0

Note:

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