Data 621 - Project

Code

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Hide

```
library(dplyr)
library(survival)
library(survminer)
library(KMsurv)
```

Read the dataset

Hide

```
ist<- read.csv("IST_corrected.csv")
```

Creating subsets for the 4 treatment groups:

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```
ist_control<-subset(ist, ist$RXASP=='N' & ist$RXHEP=='N')
ist_aspirin<- subset(ist, ist$RXASP=='Y' & ist$RXHEP=='N')
ist_L_Hep<- subset(ist, ist$RXASP=='N' & ist$RXHEP=='L')
ist_H_Hep<- subset(ist, ist$RXASP=='N' & (ist$RXHEP=='M' | ist$RXHEP=='H'))
```

Creating the Group variable:

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```
ist_control$Group = 'Control'
ist_aspirin$Group = 'Aspirin'
ist_L_Hep$Group = 'L_Hep'
ist_H_Hep$Group = 'H_Hep'
```

Extracting the variables needed:

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```
ist_data <- rbind(ist_control, ist_aspirin, ist_L_Hep, ist_H_Hep)
data <- select(ist_data,'Group', 'DIED', 'TD', 'SEX', 'AGE', 'RSBP', 'RATRIAL', 'RVISINF')
```

Censoring the data at 180 days (6 months):

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```
data$TD[data$TD > 180] = 180
data$DIED[data$TD > 180] = 0
```

factorizing the treatment groups

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```
data$Group = factor(data$Group, levels = c('Control', 'Aspirin', 'L_Hep', 'H_Hep'))
```

Removing the data with no values for RATRIAL variable and factorizing it:

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```
length(data$Group)
```

```
[1] 14573
```

Hide

```
data<-subset(data, data$RATRIAL != '' )
data$RATRIAL = factor(data$RATRIAL, levels = c('N', 'Y'))
length(data$Group)
```

```
[1] 13836
```

Viewing the structure of data:

Hide

```
str(data)
```

```
'data.frame':   13836 obs. of  8 variables:
 $ Group  : Factor w/ 4 levels "Control","Aspirin",..: 1 1 1 1 1 1 1 1 1 1 ...
 $ DIED   : num  1 0 0 0 0 0 1 0 0 0 ...
 $ TD     : num  8 180 180 180 180 180 17 180 180 180 ...
 $ SEX    : Factor w/ 2 levels "F","M": 1 2 2 2 2 2 1 2 2 2 ...
 $ AGE    : int  73 74 80 61 70 62 87 73 71 63 ...
 $ RSBP   : int  120 160 200 180 135 170 170 175 150 180 ...
 $ RATRIAL: Factor w/ 2 levels "N","Y": 1 1 2 1 1 1 1 1 1 2 ...
 $ RVISINF: Factor w/ 2 levels "N","Y": 1 2 2 2 1 1 1 1 1 1 ...
```

Surminer plot:

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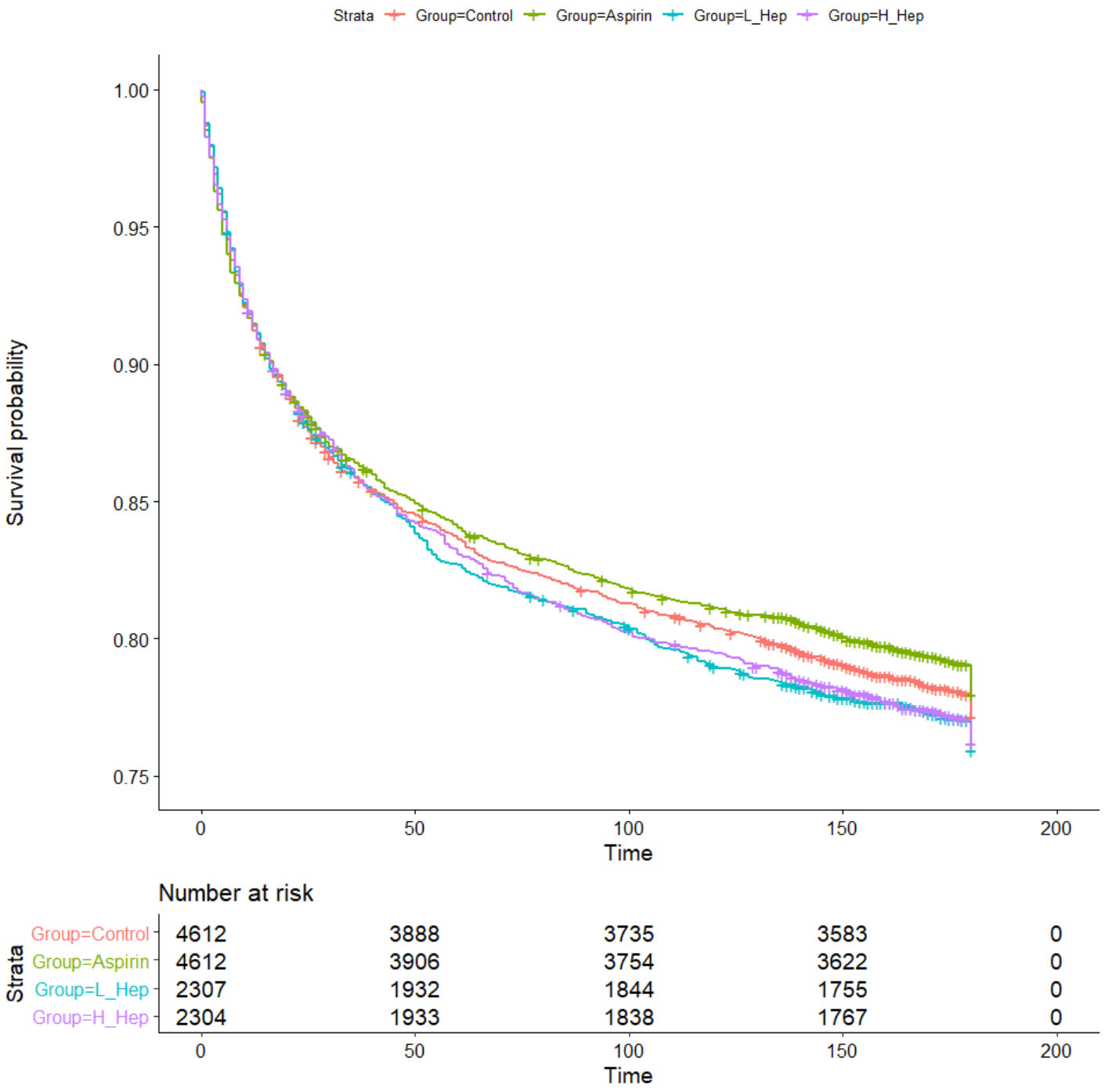
```
thefit <- survfit(Surv(TD,DIED)~Group, data=data)
p1<- survminer::ggsurvplot(thefit,censor=T, size =1, data=data, ylim = c(0.75, 1), risk.table =
TRUE, risk.table.height=.2, fontsize=5)
print(p1)
```



Cox PH model with the treatment groups:

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```
coxph.fit_group<-coxph(Surv(TD,DIED)~Group, data=data, ties ="breslow")
summary(coxph.fit_group)
```

```
Call:
coxph(formula = Surv(TD, DIED) ~ Group, data = data, ties = "breslow")

  n= 13835, number of events= 3130
   (1 observation deleted due to missingness)

                coef exp(coef) se(coef)      z Pr(>|z|)
GroupAspirin -0.04164   0.95922  0.04428 -0.940    0.347
GroupL_Hep    0.05416   1.05565  0.05281  1.026    0.305
GroupH_Hep    0.04497   1.04600  0.05297  0.849    0.396

             exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin    0.9592     1.0425    0.8795     1.046
GroupL_Hep      1.0556     0.9473    0.9519     1.171
GroupH_Hep      1.0460     0.9560    0.9429     1.160

Concordance= 0.51  (se = 0.005 )
Likelihood ratio test= 4.38  on 3 df,   p=0.2
Wald test            = 4.39  on 3 df,   p=0.2
Score (logrank) test = 4.39  on 3 df,   p=0.2
```

Cox PH model with all the variables and interactions:

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```
coxph.fit_full<-coxph(Surv(TD,DIED)~Group*AGE+Group*SEX+Group*RSBP+Group*RATRIAL+Group*RVISINF,
data=data, ties ="breslow")
summary(coxph.fit_full)
```

```
Call:
coxph(formula = Surv(TD, DIED) ~ Group * AGE + Group * SEX +
    Group * RSBP + Group * RATRIAL + Group * RVISINF, data = data,
    ties = "breslow")

  n= 13835, number of events= 3130
   (1 observation deleted due to missingness)

                           coef  exp(coef)   se(coef)      z Pr(>|z|)
GroupAspirin           1.0617124  2.8913179  0.4781447  2.220   0.0264 *
GroupL_Hep            -0.6164711  0.5398462  0.5822698 -1.059   0.2897
GroupH_Hep             0.7543262  2.1261785  0.5820321  1.296   0.1950
AGE                    0.0578124  1.0595162  0.0035951 16.081  < 2e-16 ***
SEXM                   0.0274737  1.0278546  0.0640327  0.429   0.6679
RSBP                  -0.0027022  0.9973014  0.0011423 -2.366   0.0180 *
RATRIALY               0.5617901  1.7538091  0.0695004  8.083 6.31e-16 ***
RVISINFY               0.3681704  1.4450883  0.0633912  5.808 6.33e-09 ***
GroupAspirin:AGE      -0.0102020  0.9898499  0.0050402 -2.024   0.0430 *
GroupL_Hep:AGE         0.0042197  1.0042286  0.0060872  0.693   0.4882
GroupH_Hep:AGE        -0.0063918  0.9936286  0.0061156 -1.045   0.2959
GroupAspirin:SEXM     -0.0812426  0.9219700  0.0917909 -0.885   0.3761
GroupL_Hep:SEXM        0.0604368  1.0623004  0.1081620  0.559   0.5763
GroupH_Hep:SEXM       -0.0088299  0.9912090  0.1094891 -0.081   0.9357
GroupAspirin:RSBP     -0.0019029  0.9980989  0.0016459 -1.156   0.2476
GroupL_Hep:RSBP        0.0021670  1.0021693  0.0019614  1.105   0.2692
GroupH_Hep:RSBP       -0.0009373  0.9990631  0.0019971 -0.469   0.6388
GroupAspirin:RATRIALY  0.0450024  1.0460303  0.0987950  0.456   0.6487
GroupL_Hep:RATRIALY   -0.1557838  0.8557442  0.1199603 -1.299   0.1941
GroupH_Hep:RATRIALY    0.0104762  1.0105312  0.1195221  0.088   0.9302
GroupAspirin:RVISINFY -0.0244460  0.9758504  0.0908992 -0.269   0.7880
GroupL_Hep:RVISINFY   -0.0080491  0.9919832  0.1079002 -0.075   0.9405
GroupH_Hep:RVISINFY   -0.1437281  0.8661232  0.1100764 -1.306   0.1917
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                      exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin             2.8913     0.3459    1.1327    7.3806
GroupL_Hep               0.5398     1.8524    0.1724    1.6900
GroupH_Hep               2.1262     0.4703    0.6795    6.6531
AGE                      1.0595     0.9438    1.0521    1.0670
SEXM                     1.0279     0.9729    0.9066    1.1653
RSBP                     0.9973     1.0027    0.9951    0.9995
RATRIALY                 1.7538     0.5702    1.5305    2.0097
RVISINFY                 1.4451     0.6920    1.2762    1.6363
GroupAspirin:AGE         0.9898     1.0103    0.9801    0.9997
GroupL_Hep:AGE           1.0042     0.9958    0.9923    1.0163
GroupH_Hep:AGE           0.9936     1.0064    0.9818    1.0056
GroupAspirin:SEXM        0.9220     1.0846    0.7702    1.1037
GroupL_Hep:SEXM          1.0623     0.9414    0.8594    1.3132
GroupH_Hep:SEXM          0.9912     1.0089    0.7998    1.2285
GroupAspirin:RSBP        0.9981     1.0019    0.9949    1.0013
GroupL_Hep:RSBP          1.0022     0.9978    0.9983    1.0060
GroupH_Hep:RSBP          0.9991     1.0009    0.9952    1.0030
```

```
GroupAspirin:RATRIALY    1.0460     0.9560    0.8619    1.2695
GroupL_Hep:RATRIALY      0.8557     1.1686    0.6764    1.0826
GroupH_Hep:RATRIALY      1.0105     0.9896    0.7995    1.2773
GroupAspirin:RVISINFY    0.9759     1.0247    0.8166    1.1662
GroupL_Hep:RVISINFY      0.9920     1.0081    0.8029    1.2256
GroupH_Hep:RVISINFY      0.8661     1.1546    0.6980    1.0747

Concordance= 0.684  (se = 0.005 )
Likelihood ratio test= 1378  on 23 df,   p=<2e-16
Wald test            = 1282  on 23 df,   p=<2e-16
Score (logrank) test = 1343  on 23 df,   p=<2e-16
```

Cox PH reduced model: non-significant variables and interactions removed:

Hide

```
coxph.fit_red1<-coxph(Surv(TD,DIED)~Group*AGE+SEX+RSBP+RATRIAL+RVISINF, data=data, ties ="breslo
w")
summary(coxph.fit_red1)
```

```
Call:
coxph(formula = Surv(TD, DIED) ~ Group * AGE + SEX + RSBP + RATRIAL +
    RVISINF, data = data, ties = "breslow")

  n= 13835, number of events= 3130
   (1 observation deleted due to missingness)

                      coef  exp(coef)   se(coef)      z Pr(>|z|)
GroupAspirin      0.6089783  1.8385521  0.3702094  1.645   0.1000 .
GroupL_Hep       -0.1427003  0.8670139  0.4582856 -0.311   0.7555
GroupH_Hep        0.4982035  1.6457621  0.4507673  1.105   0.2691
AGE               0.0576142  1.0593063  0.0034571 16.666  < 2e-16 ***
SEXM              0.0105508  1.0106066  0.0368883  0.286   0.7749
RSBP             -0.0031104  0.9968945  0.0006671 -4.662 3.13e-06 ***
RATRIALY          0.5534807  1.7392964  0.0400931 13.805  < 2e-16 ***
RVISINFY          0.3350698  1.3980380  0.0367414  9.120  < 2e-16 ***
GroupAspirin:AGE -0.0086565  0.9913809  0.0047473 -1.823   0.0682 .
GroupL_Hep:AGE    0.0023883  1.0023912  0.0058446  0.409   0.6828
GroupH_Hep:AGE   -0.0057099  0.9943063  0.0058036 -0.984   0.3252
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                 exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin        1.8386     0.5439    0.8899    3.7984
GroupL_Hep          0.8670     1.1534    0.3531    2.1287
GroupH_Hep          1.6458     0.6076    0.6803    3.9816
AGE                 1.0593     0.9440    1.0522    1.0665
SEXM                1.0106     0.9895    0.9401    1.0864
RSBP                0.9969     1.0031    0.9956    0.9982
RATRIALY            1.7393     0.5749    1.6079    1.8815
RVISINFY            1.3980     0.7153    1.3009    1.5024
GroupAspirin:AGE    0.9914     1.0087    0.9822    1.0006
GroupL_Hep:AGE      1.0024     0.9976    0.9910    1.0139
GroupH_Hep:AGE      0.9943     1.0057    0.9831    1.0057

Concordance= 0.683  (se = 0.005 )
Likelihood ratio test= 1367  on 11 df,   p=<2e-16
Wald test            = 1271  on 11 df,   p=<2e-16
Score (logrank) test = 1332  on 11 df,   p=<2e-16
```

Anova test: lesser model is significant.

Hide

```
anova(coxph.fit_full, coxph.fit_red1)
```

```
Analysis of Deviance Table
 Cox model: response is  Surv(TD, DIED)
 Model 1: ~ Group * AGE + Group * SEX + Group * RSBP + Group * RATRIAL + Group * RVISINF
 Model 2: ~ Group * AGE + SEX + RSBP + RATRIAL + RVISINF
  loglik Chisq Df P(>|Chi|)
1 -28739
2 -28744 11.27 12     0.506
```

Cox PH reduced model: non-significant variables and interactions removed:

Hide

```
coxph.fit_red2<-coxph(Surv(TD,DIED)~Group+AGE+RSBP+RATRIAL+RVISINF, data=data, ties ="breslow")
summary(coxph.fit_red2)
```

```
Call:
coxph(formula = Surv(TD, DIED) ~ Group + AGE + RSBP + RATRIAL +
    RVISINF, data = data, ties = "breslow")

  n= 13835, number of events= 3130
   (1 observation deleted due to missingness)

                   coef  exp(coef)   se(coef)      z Pr(>|z|)
GroupAspirin -0.0614533  0.9403968  0.0442882 -1.388    0.165
GroupL_Hep    0.0440054  1.0449880  0.0528155  0.833    0.405
GroupH_Hep    0.0569237  1.0585750  0.0529764  1.075    0.283
AGE           0.0540766  1.0555655  0.0019960 27.093  < 2e-16 ***
RSBP         -0.0031421  0.9968629  0.0006657 -4.720 2.36e-06 ***
RATRIALY      0.5520140  1.7367474  0.0400641 13.778  < 2e-16 ***
RVISINFY      0.3363346  1.3998074  0.0367172  9.160  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

             exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin    0.9404     1.0634    0.8622    1.0257
GroupL_Hep      1.0450     0.9569    0.9422    1.1590
GroupH_Hep      1.0586     0.9447    0.9542    1.1744
AGE             1.0556     0.9474    1.0514    1.0597
RSBP            0.9969     1.0031    0.9956    0.9982
RATRIALY        1.7367     0.5758    1.6056    1.8786
RVISINFY        1.3998     0.7144    1.3026    1.5043

Concordance= 0.683  (se = 0.005 )
Likelihood ratio test= 1362  on 7 df,   p=<2e-16
Wald test            = 1264  on 7 df,   p=<2e-16
Score (logrank) test = 1325  on 7 df,   p=<2e-16
```

Anova test: lesser model is significant.

Hide

```
anova(coxph.fit_red1, coxph.fit_red2)
```

```
Analysis of Deviance Table
 Cox model: response is  Surv(TD, DIED)
 Model 1: ~ Group * AGE + SEX + RSBP + RATRIAL + RVISINF
 Model 2: ~ Group + AGE + RSBP + RATRIAL + RVISINF
  loglik  Chisq Df P(>|Chi|)
1 -28744
2 -28747 5.3222  4    0.2558
```

Testing assumptions:

1. Testing Proportional Hazards Assumption

Hide

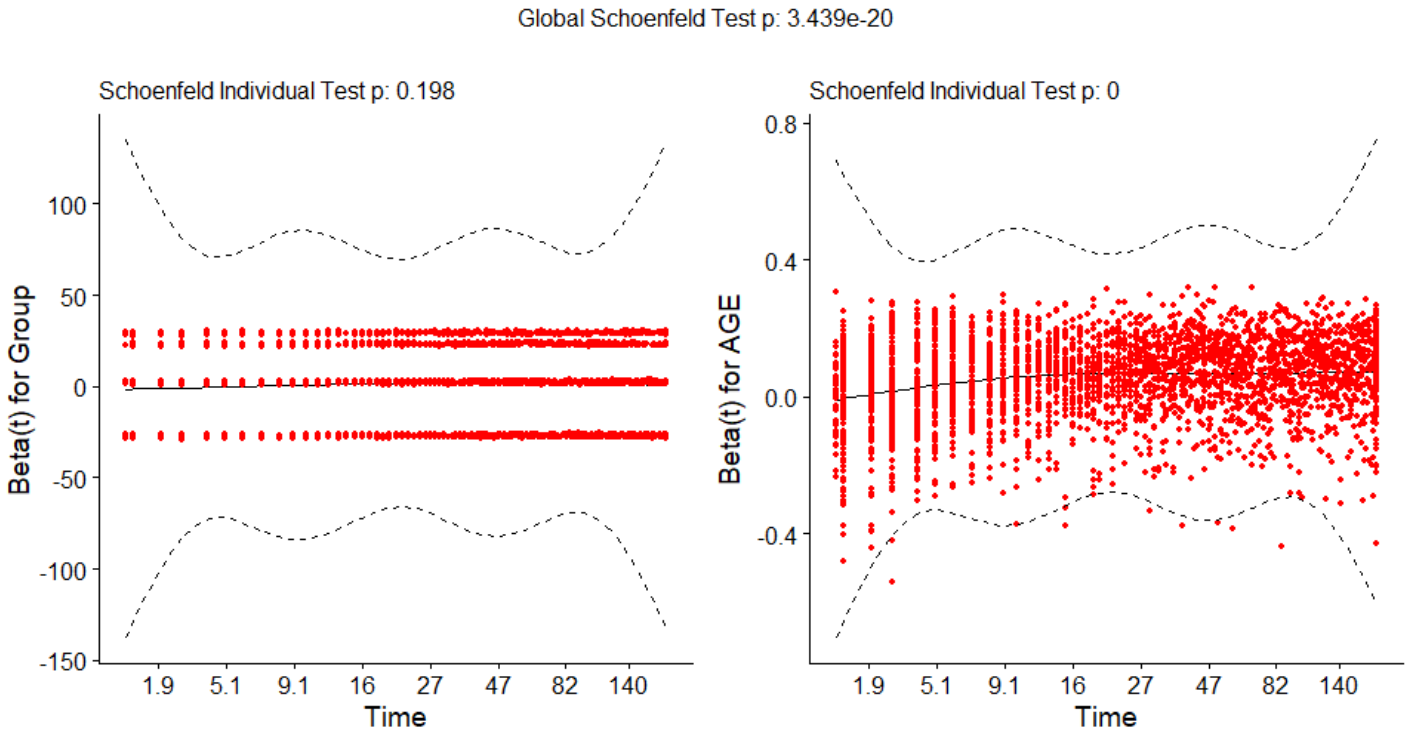
```
test.ph <- cox.zph(coxph.fit_red2)
test.ph
```

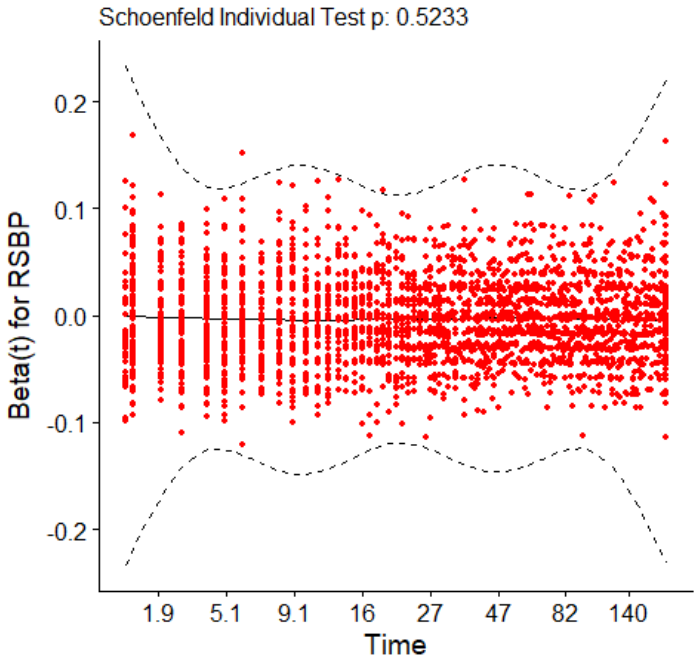
```
          chisq df      p
Group    4.66e+00  3   0.20
AGE      9.45e+01  1 <2e-16
RSBP     4.07e-01  1   0.52
RATRIAL 1.35e-03  1   0.97
RVISINF 3.07e+00  1   0.08
GLOBAL   1.07e+02  7 <2e-16
```

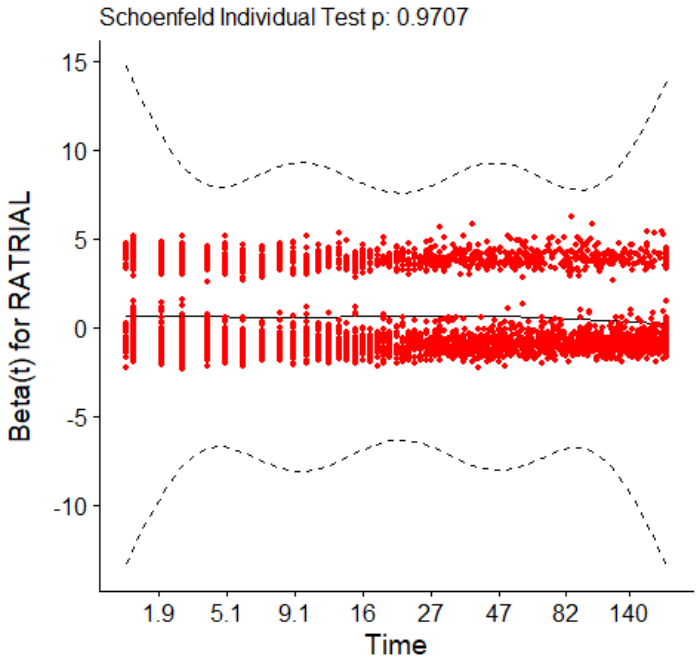
Below is the Schoenfeld Residuals plot for testing PH Assumtion: Both Age and Global test fail, so the PH assumption is not met.

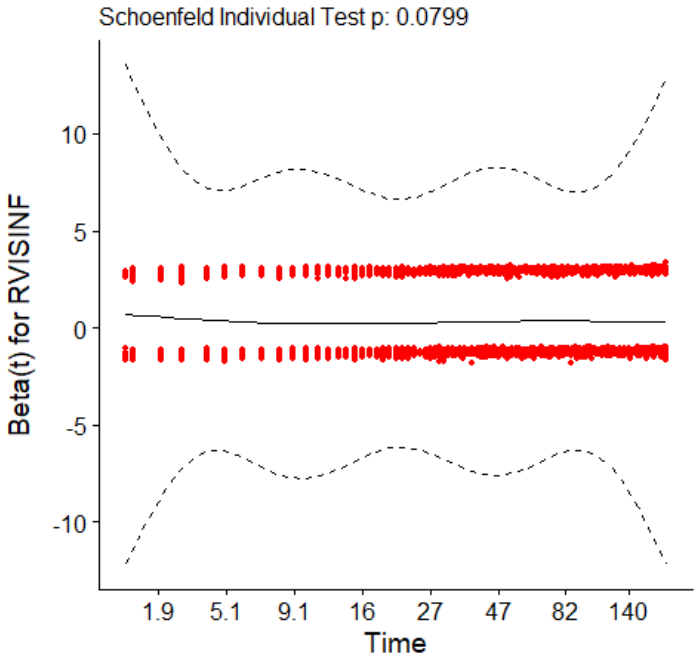
Hide

```
cox.zph.fit = cox.zph(coxph.fit_red2)
zph<-ggcoxzph(cox.zph.fit, font.main = 12, caption = "Schoenfeld Residuals plot")
zph
```









Schoenfeld Residuals plot

Checking the PH assumptions for Age alone:

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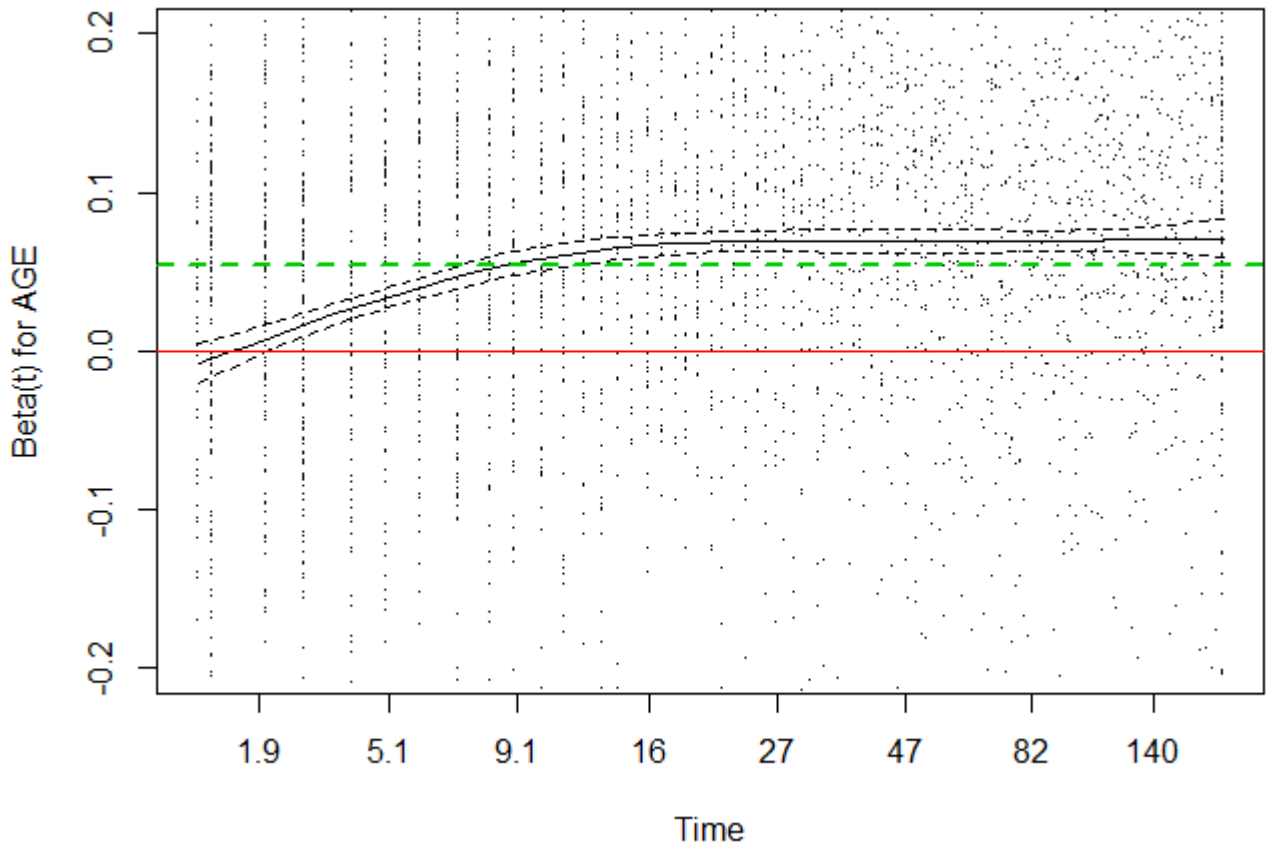
```
par(pch = '.')
plot(test.ph[2], ylim= c(-0.2, 0.2))    # a plot for the 3rd variable in the fit>
chart.plotOptions.line.marker.enabled = FALSE
abline(0,0, col=2)
```

Hide

```
abline(h= coxph.fit_red2$coef[4], col=3, lwd=2, lty=2)
```



To use Survsplit, there should not be any observations are time (TD) = 0.

Hide

```
length(data$Group)
```

```
[1] 13836
```

Hide

```
data <-subset(data, data$TD != 0)
length(data$Group)
```

```
[1] 13795
```

Using survsplit to create 3 stratifications based on the analysis from above plot.

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```
data_tf <- survSplit(Surv(TD, DIED) ~ ., data= data, cut=c(4, 16), start="tstart", zero=0, episo
de= "tgroup", id="id")
head(data_tf)
```

	Group <fctr>	SEX <fctr>	AGE <int>	RSBP <int>	RATRIAL <fctr>	RVISINF <fctr>	id <int>	tstart <dbl>	TD <dbl>
1	Control	F	73	120	N	N	1	0	4
2	Control	F	73	120	N	N	1	4	8
3	Control	M	74	160	N	Y	2	0	4
4	Control	M	74	160	N	Y	2	4	16
5	Control	M	74	160	N	Y	2	16	180
6	Control	M	80	200	Y	Y	3	0	4

6 rows | 1-10 of 11 columns

Structure of the new dataframe

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```
str(data_tf)
```

```
'data.frame':   39528 obs. of  11 variables:
 $ Group  : Factor w/ 4 levels "Control","Aspirin",..: 1 1 1 1 1 1 1 1 1 1 ...
 $ SEX    : Factor w/ 2 levels "F","M": 1 1 2 2 2 2 2 2 2 2 ...
 $ AGE    : int  73 73 74 74 74 80 80 80 61 61 ...
 $ RSBP   : int  120 120 160 160 160 200 200 200 180 180 ...
 $ RATRIAL: Factor w/ 2 levels "N","Y": 1 1 1 1 1 2 2 2 1 1 ...
 $ RVISINF: Factor w/ 2 levels "N","Y": 1 1 2 2 2 2 2 2 2 2 ...
 $ id     : int  1 1 2 2 2 3 3 3 4 4 ...
 $ tstart : num  0 4 0 4 16 0 4 16 0 4 ...
 $ TD     : num  4 8 4 16 180 4 16 180 4 16 ...
 $ DIED   : num  0 1 0 0 0 0 0 0 0 0 ...
 $ tgroup : num  1 2 1 2 3 1 2 3 1 2 ...
```

Final Model:

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```
coxph.fit_FINAL <- coxph(Surv(tstart, TD, DIED) ~ Group+RSBP+RATRIAL+RVISINF + AGE:strata(tgrou
p), data=data_tf, ties ="breslow")
summary(coxph.fit_FINAL)
```

```
Call:
coxph(formula = Surv(tstart, TD, DIED) ~ Group + RSBP + RATRIAL +
    RVISINF + AGE:strata(tgroup), data = data_tf, ties = "breslow")

  n= 39528, number of events= 3090

                               coef exp(coef)  se(coef)      z Pr(>|z|)
GroupAspirin               -0.073757  0.928898  0.044645 -1.652  0.09852 .
GroupL_Hep                  0.051140  1.052471  0.052977  0.965  0.33438
GroupH_Hep                  0.058118  1.059840  0.053268  1.091  0.27525
RSBP                       -0.002975  0.997030  0.000669 -4.446 8.74e-06 ***
RATRIALY                    0.550428  1.733996  0.040332 13.647  < 2e-16 ***
RVISINFY                    0.339934  1.404854  0.036961  9.197  < 2e-16 ***
AGE:strata(tgroup)tgroup=1  0.013189  1.013276  0.004060  3.249  0.00116 **
AGE:strata(tgroup)tgroup=2  0.055798  1.057384  0.003870 14.419  < 2e-16 ***
AGE:strata(tgroup)tgroup=3  0.069314  1.071773  0.002766 25.062  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                           exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin                  0.9289     1.0765    0.8511    1.0138
GroupL_Hep                    1.0525     0.9501    0.9487    1.1676
GroupH_Hep                    1.0598     0.9435    0.9548    1.1765
RSBP                          0.9970     1.0030    0.9957    0.9983
RATRIALY                      1.7340     0.5767    1.6022    1.8766
RVISINFY                      1.4049     0.7118    1.3067    1.5104
AGE:strata(tgroup)tgroup=1    1.0133     0.9869    1.0052    1.0214
AGE:strata(tgroup)tgroup=2    1.0574     0.9457    1.0494    1.0654
AGE:strata(tgroup)tgroup=3    1.0718     0.9330    1.0660    1.0776

Concordance= 0.689  (se = 0.005 )
Likelihood ratio test= 1484  on 9 df,   p=<2e-16
Wald test            = 1341  on 9 df,   p=<2e-16
Score (logrank) test = 1407  on 9 df,   p=<2e-16
```

Testing Assumptions:

1. Testing Proportional Hazards Assumption

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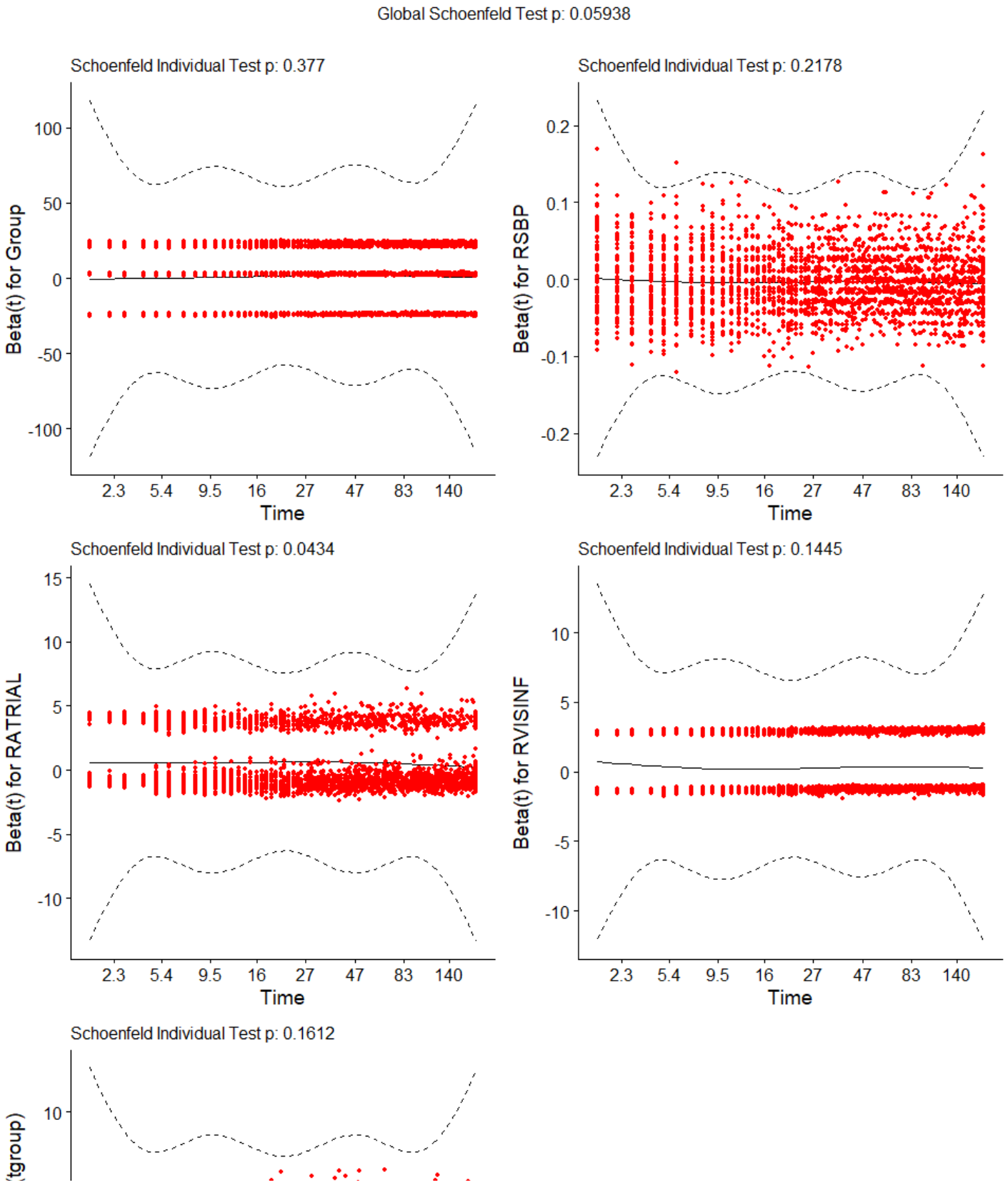
```
test.ph <- cox.zph(coxph.fit_FINAL)
test.ph
```

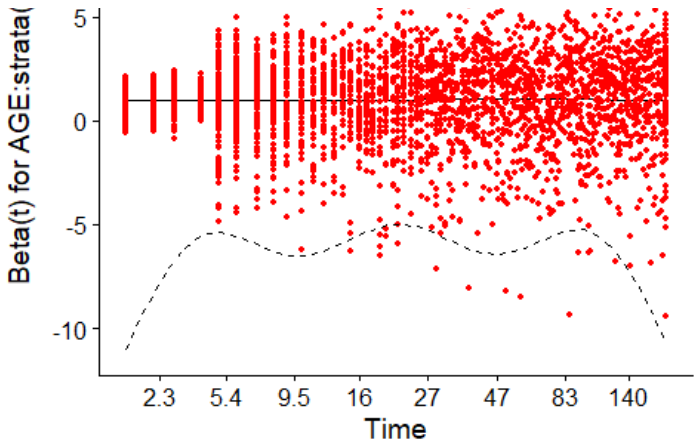
```
                   chisq df     p
Group               3.10  3 0.377
RSBP                1.52  1 0.218
RATRIAL             4.08  1 0.043
RVISINF             2.13  1 0.144
AGE:strata(tgroup)  5.15  3 0.161
GLOBAL             16.38  9 0.059
```

Below is the Schoenfeld Residuals plot for testing PH Assumtion: All variables and global test pass the PH assumtion. RATRIAL variable p-values is 0.042 but it is close to 0.05.

Hide

```
cox.zph.fit = cox.zph(coxph.fit_FINAL)
zph<-ggcoxzph(cox.zph.fit, font.main = 12, caption = "Schoenfeld Residuals plot")
zph
```



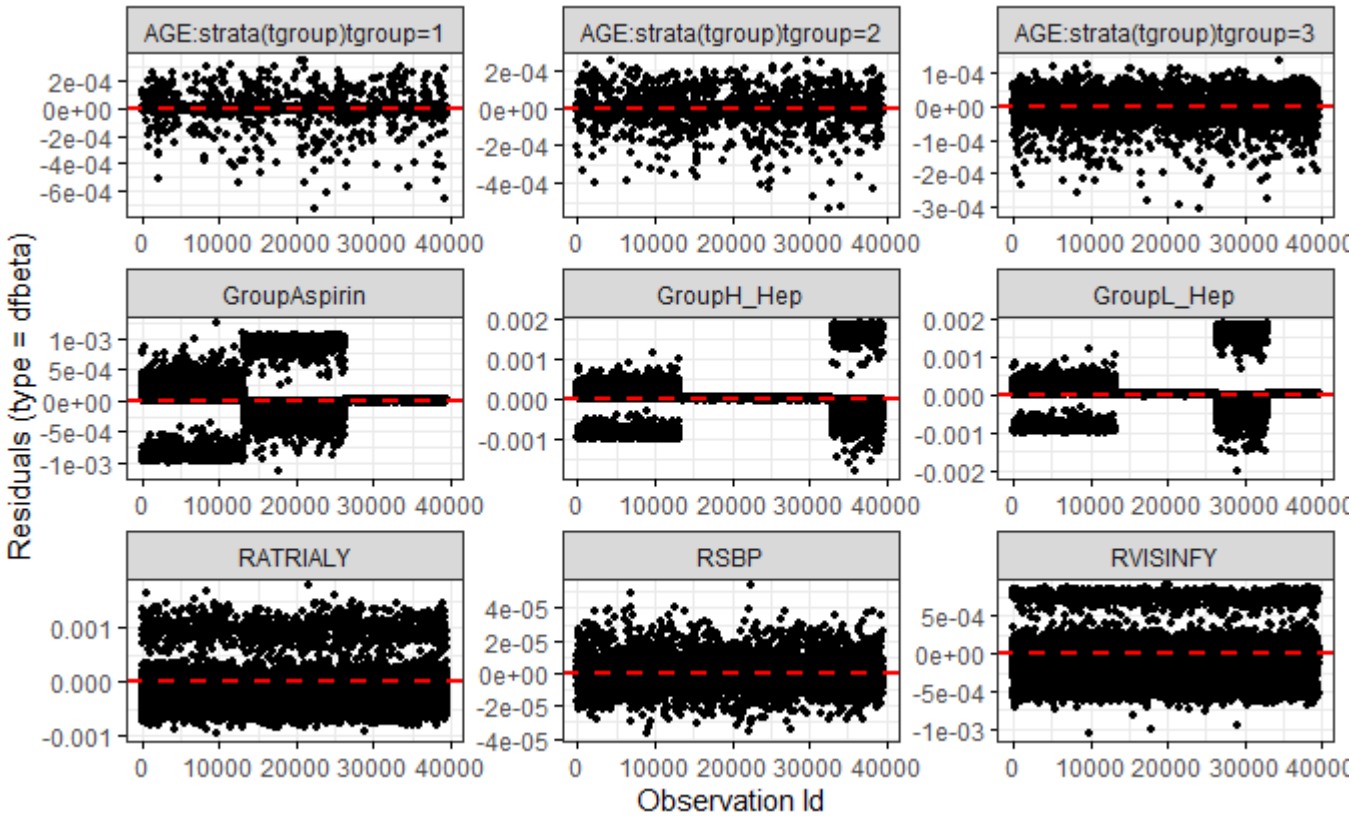


Schoenfeld Residuals plot

2. Testing influential observations

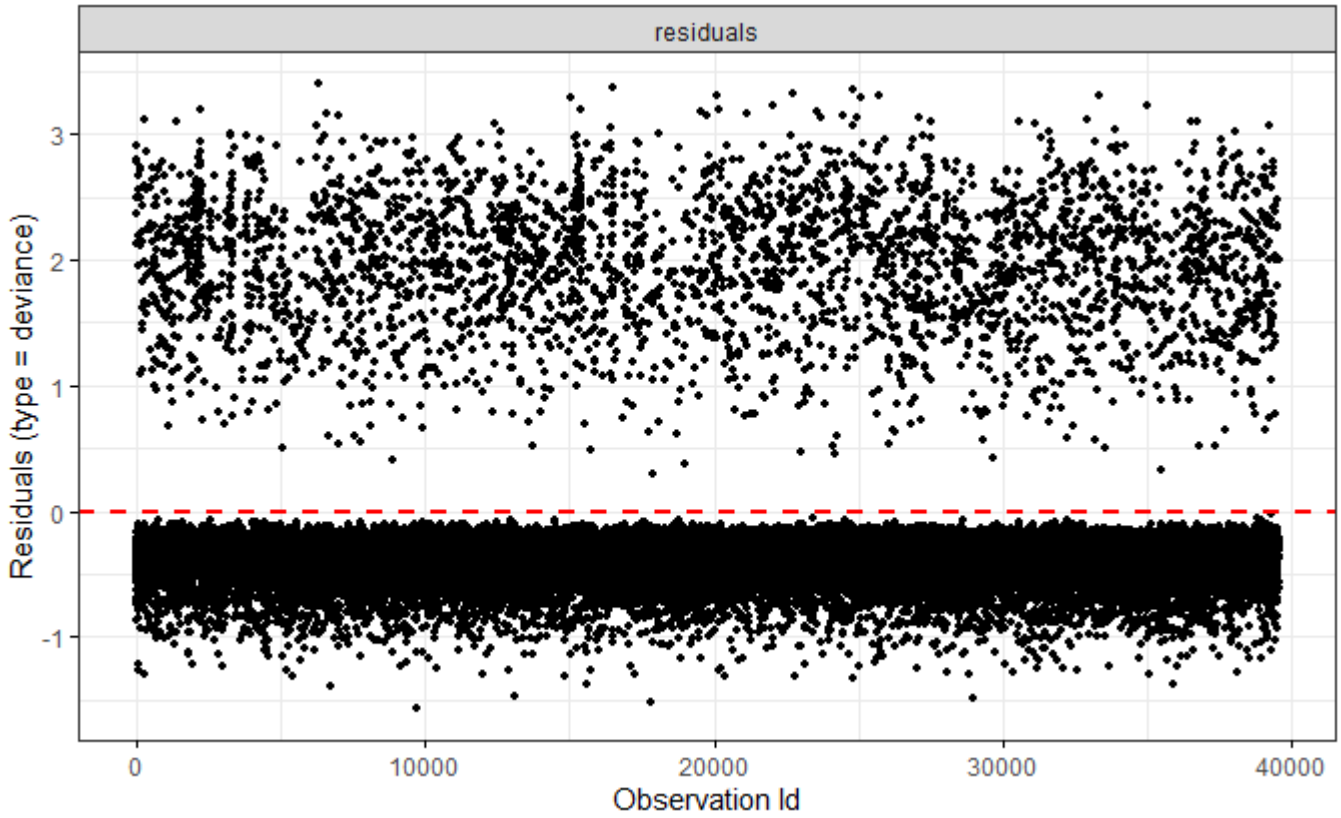
Hide

```
ggcoxdiagnostics(coxph.fit_FINAL, type = "dfbeta", linear.predictions = FALSE)
```



Hide

```
ggcoxdiagnostics(coxph.fit_FINAL, type = "deviance",
                 linear.predictions = FALSE, ggtheme = theme_bw())
```

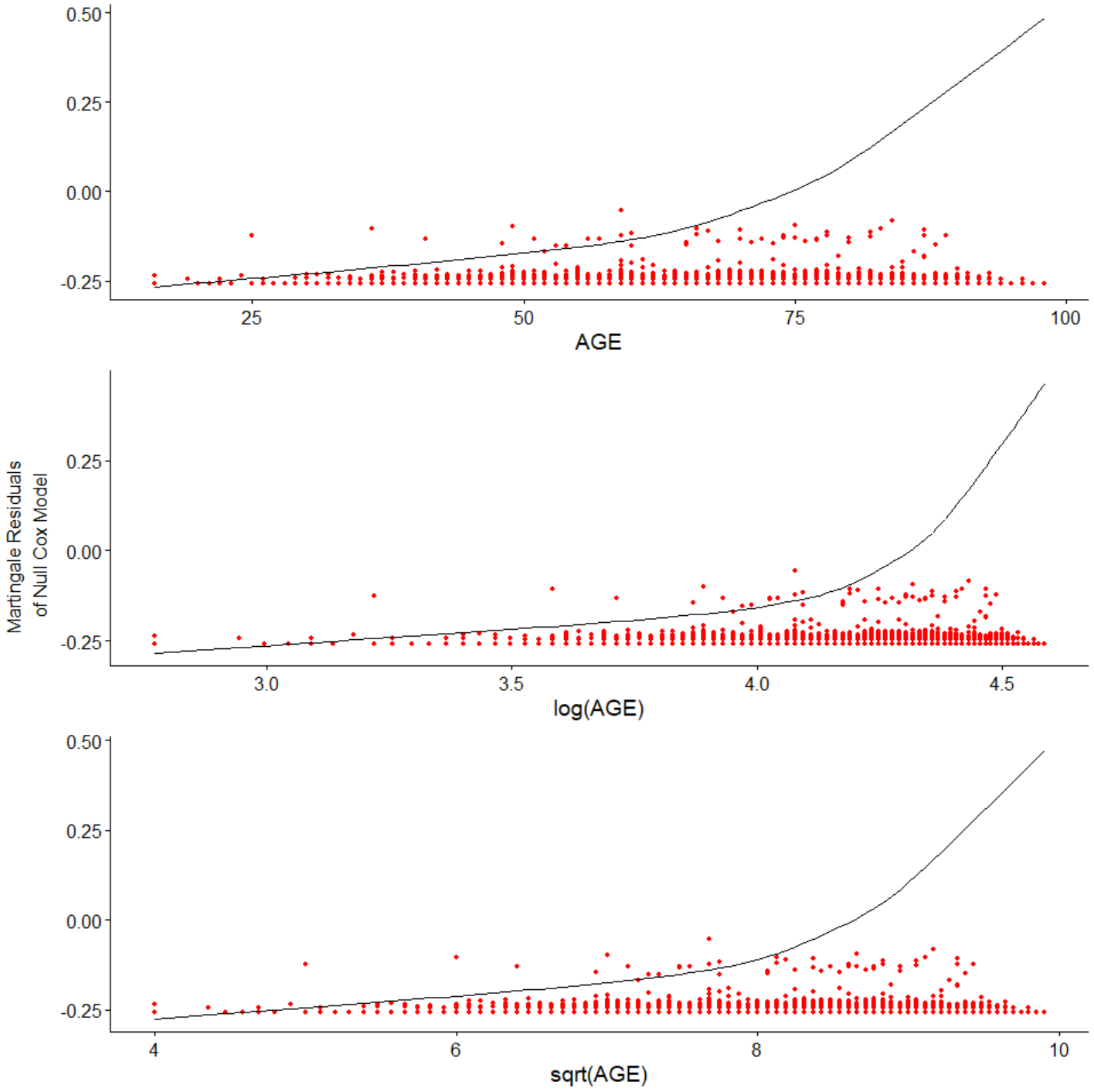


3. Non Linearity Assumption:

Hide

```
ggcoxfunctional(Surv(TD, DIED) ~ AGE + log(AGE) + sqrt(AGE) , data = data)
```

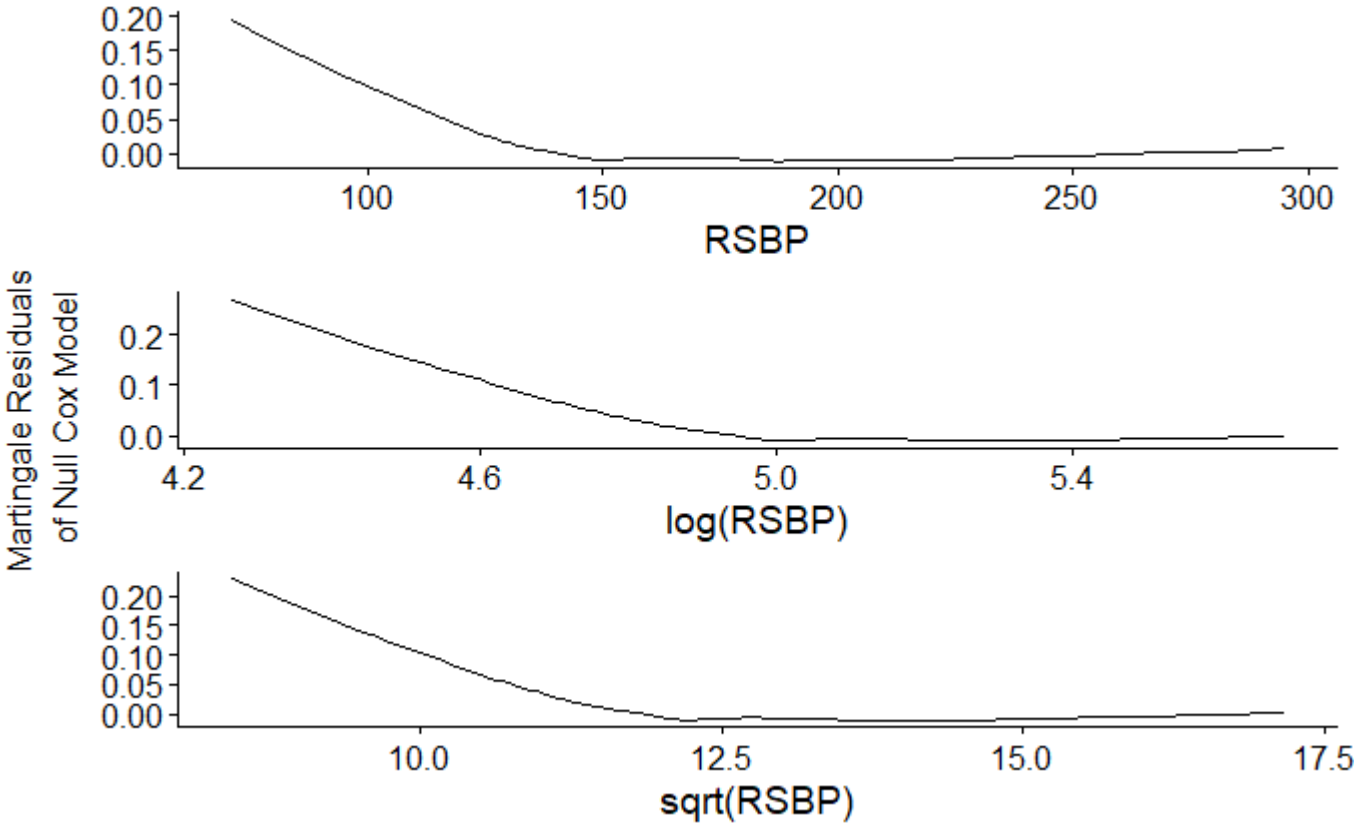
```
arguments formula is deprecated; will be removed in the next version; please use fit instead.
```



Hide

```
ggcoxfunctional(Surv(TD, DIED) ~ RSBP + log(RSBP) + sqrt(RSBP), data = data)
```

```
arguments formula is deprecated; will be removed in the next version; please use fit instead.
```



APPENDIX# 1: Model with higher order terms based on non-linearity assumption check.

Hide

```
coxph.fit_HIGH1 <- coxph(Surv(tstart, TD, DIED) ~ Group+RSBP+ I(RSBP^2)+ I(RSBP^3)+ I(AGE^2) +RA
TRIAL+RVISINF + AGE, data=data_tf, ties ="breslow")
```

```
Ran out of iterations and did not converge
```

Hide

```
summary(coxph.fit_HIGH1)
```

```
Call:
coxph(formula = Surv(tstart, TD, DIED) ~ Group + RSBP + I(RSBP^2) +
    I(RSBP^3) + I(AGE^2) + RATRIAL + RVISINF + AGE, data = data_tf,
    ties = "breslow")

  n= 39528, number of events= 3090

             coef exp(coef) se(coef)  z Pr(>|z|)
GroupAspirin   NA        NA        0 NA       NA
GroupL_Hep     NA        NA        0 NA       NA
GroupH_Hep     NA        NA        0 NA       NA
RSBP           NA        NA        0 NA       NA
I(RSBP^2)      NA        NA        0 NA       NA
I(RSBP^3)      NA        NA        0 NA       NA
I(AGE^2)       NA        NA        0 NA       NA
RATRIALY       NA        NA        0 NA       NA
RVISINFY       NA        NA        0 NA       NA
AGE            NA        NA        0 NA       NA

             exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin        NA         NA        NA        NA
GroupL_Hep          NA         NA        NA        NA
GroupH_Hep          NA         NA        NA        NA
RSBP                NA         NA        NA        NA
I(RSBP^2)           NA         NA        NA        NA
I(RSBP^3)           NA         NA        NA        NA
I(AGE^2)            NA         NA        NA        NA
RATRIALY            NA         NA        NA        NA
RVISINFY            NA         NA        NA        NA
AGE                 NA         NA        NA        NA

Concordance= 0.447  (se = 0.005 )
Likelihood ratio test= NaN  on 0 df,   p=NA
Wald test            = NA  on 0 df,   p=NA
Score (logrank) test = -1741397  on 0 df,   p=1
```

Hide

```
coxph.fit_HIGH2 <- coxph(Surv(tstart, TD, DIED) ~ Group+RSBP+ I(RSBP^2)+ I(AGE^2) +RATRIAL+RVISI
NF + AGE, data=data_tf, ties ="breslow")
summary(coxph.fit_HIGH2)
```

```
Call:
coxph(formula = Surv(tstart, TD, DIED) ~ Group + RSBP + I(RSBP^2) +
    I(AGE^2) + RATRIAL + RVISINF + AGE, data = data_tf, ties = "breslow")

  n= 39528, number of events= 3090

                   coef  exp(coef)   se(coef)      z Pr(>|z|)
GroupAspirin -7.219e-02  9.304e-01  4.465e-02 -1.617   0.1059
GroupL_Hep    5.392e-02  1.055e+00  5.298e-02  1.018   0.3088
GroupH_Hep    6.123e-02  1.063e+00  5.328e-02  1.149   0.2505
RSBP         -2.357e-02  9.767e-01  5.022e-03 -4.694 2.68e-06 ***
I(RSBP^2)     6.270e-05  1.000e+00  1.506e-05  4.164 3.12e-05 ***
I(AGE^2)      2.207e-04  1.000e+00  1.283e-04  1.720   0.0853 .
RATRIALY      5.475e-01  1.729e+00  4.040e-02 13.553  < 2e-16 ***
RVISINFY      3.385e-01  1.403e+00  3.696e-02  9.159  < 2e-16 ***
AGE           2.223e-02  1.022e+00  1.888e-02  1.178   0.2389
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

             exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin    0.9304     1.0749    0.8524    1.0154
GroupL_Hep      1.0554     0.9475    0.9513    1.1709
GroupH_Hep      1.0631     0.9406    0.9577    1.1802
RSBP            0.9767     1.0239    0.9671    0.9864
I(RSBP^2)       1.0001     0.9999    1.0000    1.0001
I(AGE^2)        1.0002     0.9998    1.0000    1.0005
RATRIALY        1.7290     0.5784    1.5974    1.8714
RVISINFY        1.4029     0.7128    1.3049    1.5083
AGE             1.0225     0.9780    0.9853    1.0610

Concordance= 0.686  (se = 0.005 )
Likelihood ratio test= 1380  on 9 df,   p=<2e-16
Wald test            = 1325  on 9 df,   p=<2e-16
Score (logrank) test = 1492  on 9 df,   p=<2e-16
```

Hide

```
coxph.fit_HIGH3 <- coxph(Surv(tstart, TD, DIED) ~ Group+RSBP+ I(RSBP^2) +RATRIAL+RVISINF + AGE:s
trata(tgroup), data=data_tf, ties ="breslow")
summary(coxph.fit_HIGH3)
```

```
Call:
coxph(formula = Surv(tstart, TD, DIED) ~ Group + RSBP + I(RSBP^2) +
    RATRIAL + RVISINF + AGE:strata(tgroup), data = data_tf, ties = "breslow")

  n= 39528, number of events= 3090

                                 coef  exp(coef)   se(coef)      z Pr(>|z|)
GroupAspirin                -7.323e-02  9.294e-01  4.465e-02 -1.640  0.10094
GroupL_Hep                   5.419e-02  1.056e+00  5.298e-02  1.023  0.30642
GroupH_Hep                   6.118e-02  1.063e+00  5.328e-02  1.148  0.25081
RSBP                        -2.367e-02  9.766e-01  5.009e-03 -4.725 2.30e-06 ***
I(RSBP^2)                    6.286e-05  1.000e+00  1.502e-05  4.184 2.87e-05 ***
RATRIALY                     5.526e-01  1.738e+00  4.034e-02 13.698  < 2e-16 ***
RVISINFY                     3.404e-01  1.405e+00  3.696e-02  9.209  < 2e-16 ***
AGE:strata(tgroup)tgroup=1   1.329e-02  1.013e+00  4.045e-03  3.284  0.00102 **
AGE:strata(tgroup)tgroup=2   5.566e-02  1.057e+00  3.858e-03 14.426  < 2e-16 ***
AGE:strata(tgroup)tgroup=3   6.905e-02  1.071e+00  2.757e-03 25.046  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

                            exp(coef) exp(-coef) lower .95 upper .95
GroupAspirin                   0.9294     1.0760    0.8515    1.0144
GroupL_Hep                     1.0557     0.9473    0.9516    1.1712
GroupH_Hep                     1.0631     0.9407    0.9577    1.1801
RSBP                           0.9766     1.0240    0.9671    0.9862
I(RSBP^2)                      1.0001     0.9999    1.0000    1.0001
RATRIALY                       1.7378     0.5755    1.6057    1.8807
RVISINFY                       1.4055     0.7115    1.3073    1.5111
AGE:strata(tgroup)tgroup=1     1.0134     0.9868    1.0054    1.0214
AGE:strata(tgroup)tgroup=2     1.0572     0.9459    1.0493    1.0653
AGE:strata(tgroup)tgroup=3     1.0715     0.9333    1.0657    1.0773

Concordance= 0.691  (se = 0.005 )
Likelihood ratio test= 1500  on 10 df,   p=<2e-16
Wald test            = 1365  on 10 df,   p=<2e-16
Score (logrank) test = 1435  on 10 df,   p=<2e-16
```

APPENDIX# 2:To obtain the survival probability, using the summary of survfit.

Hide

```
options(max.print=999999)
thefit <- survfit(Surv(TD,DIED)~Group, data=data)
summary(thefit)
```

```
Call: survfit(formula = Surv(TD, DIED) ~ Group, data = data)

               Group=Control
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
    1   4601      50    0.989 0.00153        0.986        0.992
    2   4551      35    0.982 0.00199        0.978        0.985
    3   4516      46    0.972 0.00245        0.967        0.976
    4   4470      34    0.964 0.00274        0.959        0.970
    5   4436      30    0.958 0.00297        0.952        0.963
    6   4406      45    0.948 0.00328        0.941        0.954
    7   4361      36    0.940 0.00350        0.933        0.947
    8   4325      25    0.935 0.00365        0.927        0.942
    9   4300      30    0.928 0.00381        0.921        0.936
   10   4270      24    0.923 0.00393        0.915        0.931
   11   4246      18    0.919 0.00402        0.911        0.927
   12   4228      21    0.914 0.00413        0.906        0.922
   13   4207      13    0.912 0.00419        0.903        0.920
   14   4194      13    0.909 0.00425        0.900        0.917
   15   4180      13    0.906 0.00430        0.897        0.914
   16   4167      11    0.903 0.00435        0.895        0.912
   17   4156      14    0.900 0.00441        0.892        0.909
   18   4142      11    0.898 0.00446        0.889        0.907
   19   4129      12    0.895 0.00451        0.887        0.904
   20   4117      15    0.892 0.00457        0.883        0.901
   21   4102      11    0.890 0.00462        0.881        0.899
   22   4090      18    0.886 0.00469        0.877        0.895
   23   4072      18    0.882 0.00476        0.873        0.891
   24   4053      12    0.879 0.00480        0.870        0.889
   25   4041       8    0.878 0.00483        0.868        0.887
   26   4033      10    0.875 0.00487        0.866        0.885
   27   4022       8    0.874 0.00490        0.864        0.883
   28   4012       8    0.872 0.00493        0.862        0.882
   29   4004       7    0.870 0.00495        0.861        0.880
   30   3996      11    0.868 0.00499        0.858        0.878
   31   3984      10    0.866 0.00503        0.856        0.876
   32   3974       8    0.864 0.00505        0.854        0.874
   33   3966       4    0.863 0.00507        0.853        0.873
   34   3961       3    0.863 0.00508        0.853        0.873
   35   3958       4    0.862 0.00509        0.852        0.872
   36   3954       4    0.861 0.00510        0.851        0.871
   37   3950       7    0.859 0.00513        0.849        0.869
   38   3942       6    0.858 0.00515        0.848        0.868
   39   3936       5    0.857 0.00516        0.847        0.867
   40   3931       3    0.856 0.00517        0.846        0.866
   41   3927       5    0.855 0.00519        0.845        0.865
   42   3922       3    0.855 0.00520        0.844        0.865
   43   3919       6    0.853 0.00522        0.843        0.864
   44   3913       4    0.852 0.00523        0.842        0.863
   45   3909       5    0.851 0.00525        0.841        0.862
   46   3904       7    0.850 0.00527        0.839        0.860
   47   3897       6    0.848 0.00529        0.838        0.859
   48   3891       3    0.848 0.00530        0.837        0.858
   50   3888       3    0.847 0.00531        0.837        0.858
```

51	3885	4	0.846	0.00532	0.836	0.857
52	3881	6	0.845	0.00534	0.835	0.855
53	3874	4	0.844	0.00535	0.834	0.855
54	3870	2	0.844	0.00536	0.833	0.854
55	3868	4	0.843	0.00537	0.832	0.853
56	3864	6	0.841	0.00539	0.831	0.852
57	3858	3	0.841	0.00540	0.830	0.851
58	3855	3	0.840	0.00541	0.830	0.851
59	3852	4	0.839	0.00542	0.829	0.850
60	3848	5	0.838	0.00543	0.828	0.849
61	3843	5	0.837	0.00545	0.826	0.848
62	3838	8	0.835	0.00547	0.825	0.846
63	3830	3	0.835	0.00548	0.824	0.845
64	3827	7	0.833	0.00550	0.822	0.844
65	3820	5	0.832	0.00551	0.821	0.843
66	3815	3	0.831	0.00552	0.821	0.842
67	3812	4	0.831	0.00553	0.820	0.841
68	3808	3	0.830	0.00554	0.819	0.841
69	3805	1	0.830	0.00555	0.819	0.841
70	3804	1	0.829	0.00555	0.819	0.840
71	3803	3	0.829	0.00556	0.818	0.840
72	3800	3	0.828	0.00556	0.817	0.839
73	3797	1	0.828	0.00557	0.817	0.839
74	3796	3	0.827	0.00558	0.816	0.838
75	3793	3	0.827	0.00558	0.816	0.838
76	3790	1	0.826	0.00559	0.816	0.837
77	3789	2	0.826	0.00559	0.815	0.837
78	3787	1	0.826	0.00560	0.815	0.837
79	3786	3	0.825	0.00560	0.814	0.836
80	3783	3	0.824	0.00561	0.813	0.835
81	3780	1	0.824	0.00561	0.813	0.835
82	3779	4	0.823	0.00563	0.812	0.834
83	3775	3	0.823	0.00563	0.812	0.834
84	3772	3	0.822	0.00564	0.811	0.833
85	3769	1	0.822	0.00564	0.811	0.833
86	3768	4	0.821	0.00566	0.810	0.832
87	3764	3	0.820	0.00566	0.809	0.831
88	3761	2	0.820	0.00567	0.809	0.831
89	3759	1	0.820	0.00567	0.809	0.831
90	3757	1	0.819	0.00567	0.808	0.831
91	3756	1	0.819	0.00568	0.808	0.830
93	3755	4	0.818	0.00569	0.807	0.830
94	3751	5	0.817	0.00570	0.806	0.828
95	3746	4	0.816	0.00571	0.805	0.828
96	3742	2	0.816	0.00572	0.805	0.827
97	3740	3	0.815	0.00573	0.804	0.827
98	3737	2	0.815	0.00573	0.804	0.826
100	3735	1	0.815	0.00573	0.803	0.826
101	3734	2	0.814	0.00574	0.803	0.825
102	3732	4	0.813	0.00575	0.802	0.825
103	3728	2	0.813	0.00575	0.802	0.824
104	3726	4	0.812	0.00576	0.801	0.823
105	3721	1	0.812	0.00577	0.801	0.823
106	3720	2	0.811	0.00577	0.800	0.823

107	3718	3	0.811	0.00578	0.799	0.822
108	3715	1	0.810	0.00578	0.799	0.822
109	3714	1	0.810	0.00578	0.799	0.822
110	3713	1	0.810	0.00579	0.799	0.821
112	3711	2	0.810	0.00579	0.798	0.821
113	3707	6	0.808	0.00581	0.797	0.820
115	3701	1	0.808	0.00581	0.797	0.820
116	3700	5	0.807	0.00582	0.796	0.818
119	3694	3	0.806	0.00583	0.795	0.818
120	3691	3	0.806	0.00584	0.794	0.817
121	3688	1	0.805	0.00584	0.794	0.817
122	3687	1	0.805	0.00584	0.794	0.817
123	3686	3	0.805	0.00585	0.793	0.816
124	3683	2	0.804	0.00586	0.793	0.816
126	3680	1	0.804	0.00586	0.793	0.815
127	3679	3	0.803	0.00587	0.792	0.815
128	3676	2	0.803	0.00587	0.791	0.814
129	3674	1	0.803	0.00587	0.791	0.814
130	3673	2	0.802	0.00588	0.791	0.814
131	3671	3	0.802	0.00588	0.790	0.813
132	3667	3	0.801	0.00589	0.789	0.812
133	3663	3	0.800	0.00590	0.789	0.812
134	3658	1	0.800	0.00590	0.788	0.812
135	3655	1	0.800	0.00590	0.788	0.811
136	3654	1	0.800	0.00591	0.788	0.811
137	3651	2	0.799	0.00591	0.788	0.811
138	3648	4	0.798	0.00592	0.787	0.810
139	3643	3	0.798	0.00593	0.786	0.809
140	3639	3	0.797	0.00594	0.785	0.809
141	3632	4	0.796	0.00595	0.784	0.808
142	3627	1	0.796	0.00595	0.784	0.808
143	3622	2	0.795	0.00595	0.784	0.807
145	3617	3	0.795	0.00596	0.783	0.806
146	3612	3	0.794	0.00597	0.782	0.806
147	3606	2	0.794	0.00597	0.782	0.805
148	3598	2	0.793	0.00598	0.782	0.805
149	3589	1	0.793	0.00598	0.781	0.805
150	3583	2	0.793	0.00598	0.781	0.804
151	3577	3	0.792	0.00599	0.780	0.804
152	3572	2	0.791	0.00600	0.780	0.803
153	3563	3	0.791	0.00600	0.779	0.803
154	3550	2	0.790	0.00601	0.779	0.802
155	3540	2	0.790	0.00601	0.778	0.802
156	3533	2	0.789	0.00602	0.778	0.801
157	3527	2	0.789	0.00602	0.777	0.801
158	3521	2	0.789	0.00603	0.777	0.800
161	3485	1	0.788	0.00603	0.777	0.800
162	3475	4	0.787	0.00604	0.776	0.799
163	3463	1	0.787	0.00604	0.775	0.799
166	3422	1	0.787	0.00605	0.775	0.799
167	3403	2	0.786	0.00605	0.775	0.798
168	3389	3	0.786	0.00606	0.774	0.798
169	3370	4	0.785	0.00607	0.773	0.797
170	3349	2	0.784	0.00608	0.773	0.796

171	3327	1	0.784	0.00608	0.772	0.796
172	3305	1	0.784	0.00608	0.772	0.796
175	3189	3	0.783	0.00609	0.771	0.795
176	3130	2	0.783	0.00610	0.771	0.795
178	3011	2	0.782	0.00610	0.770	0.794
179	2957	2	0.782	0.00611	0.770	0.794
180	2895	30	0.773	0.00622	0.761	0.786

Group=Aspirin

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1	4591	48	0.990	0.00150	0.987	0.992
2	4543	46	0.980	0.00209	0.975	0.984
3	4497	56	0.967	0.00262	0.962	0.972
4	4441	32	0.960	0.00288	0.955	0.966
5	4409	39	0.952	0.00316	0.946	0.958
6	4370	35	0.944	0.00339	0.938	0.951
7	4335	30	0.938	0.00357	0.931	0.945
8	4305	18	0.934	0.00367	0.927	0.941
9	4287	22	0.929	0.00379	0.922	0.936
10	4265	15	0.926	0.00387	0.918	0.933
11	4250	21	0.921	0.00398	0.913	0.929
12	4229	11	0.919	0.00403	0.911	0.927
13	4218	17	0.915	0.00411	0.907	0.923
14	4201	15	0.912	0.00419	0.904	0.920
15	4186	18	0.908	0.00427	0.900	0.916
16	4167	11	0.905	0.00432	0.897	0.914
17	4156	16	0.902	0.00439	0.893	0.911
18	4139	12	0.899	0.00444	0.891	0.908
19	4127	11	0.897	0.00449	0.888	0.906
20	4115	14	0.894	0.00454	0.885	0.903
21	4101	9	0.892	0.00458	0.883	0.901
22	4092	7	0.890	0.00461	0.881	0.900
23	4084	9	0.888	0.00465	0.879	0.898
24	4075	7	0.887	0.00467	0.878	0.896
25	4067	9	0.885	0.00471	0.876	0.894
26	4057	11	0.883	0.00475	0.873	0.892
27	4044	8	0.881	0.00478	0.872	0.890
28	4035	14	0.878	0.00483	0.868	0.887
29	4020	11	0.875	0.00488	0.866	0.885
30	4009	6	0.874	0.00490	0.865	0.884
31	4003	3	0.873	0.00491	0.864	0.883
32	4000	2	0.873	0.00492	0.863	0.883
33	3996	10	0.871	0.00495	0.861	0.881
34	3986	6	0.869	0.00497	0.860	0.879
35	3979	2	0.869	0.00498	0.859	0.879
36	3977	6	0.868	0.00500	0.858	0.878
37	3971	4	0.867	0.00502	0.857	0.877
38	3967	4	0.866	0.00503	0.856	0.876
39	3962	3	0.865	0.00504	0.856	0.875
40	3957	8	0.864	0.00507	0.854	0.874
41	3949	9	0.862	0.00510	0.852	0.872
42	3940	4	0.861	0.00511	0.851	0.871
43	3936	9	0.859	0.00514	0.849	0.869
44	3927	4	0.858	0.00516	0.848	0.868

45	3923	3	0.857	0.00517	0.847	0.867
46	3920	4	0.856	0.00518	0.846	0.867
47	3916	2	0.856	0.00518	0.846	0.866
48	3914	4	0.855	0.00520	0.845	0.865
49	3910	4	0.854	0.00521	0.844	0.864
50	3906	6	0.853	0.00523	0.843	0.863
51	3900	2	0.852	0.00524	0.842	0.863
52	3898	6	0.851	0.00526	0.841	0.861
53	3891	4	0.850	0.00527	0.840	0.861
54	3887	2	0.850	0.00528	0.840	0.860
55	3885	4	0.849	0.00529	0.839	0.859
56	3881	4	0.848	0.00530	0.838	0.859
57	3877	4	0.847	0.00531	0.837	0.858
58	3873	3	0.847	0.00532	0.836	0.857
59	3870	5	0.845	0.00534	0.835	0.856
60	3865	5	0.844	0.00535	0.834	0.855
61	3860	6	0.843	0.00537	0.833	0.854
62	3854	7	0.841	0.00539	0.831	0.852
63	3847	1	0.841	0.00540	0.831	0.852
64	3845	1	0.841	0.00540	0.831	0.852
66	3843	3	0.840	0.00541	0.830	0.851
67	3840	4	0.840	0.00542	0.829	0.850
68	3836	3	0.839	0.00543	0.828	0.850
69	3833	3	0.838	0.00544	0.828	0.849
71	3830	6	0.837	0.00546	0.826	0.848
72	3824	2	0.836	0.00546	0.826	0.847
73	3822	2	0.836	0.00547	0.825	0.847
74	3820	5	0.835	0.00548	0.824	0.846
75	3815	2	0.834	0.00549	0.824	0.845
76	3813	2	0.834	0.00549	0.823	0.845
77	3811	4	0.833	0.00551	0.822	0.844
78	3806	1	0.833	0.00551	0.822	0.844
79	3805	1	0.833	0.00551	0.822	0.844
80	3803	1	0.833	0.00551	0.822	0.843
81	3802	2	0.832	0.00552	0.821	0.843
82	3800	2	0.832	0.00553	0.821	0.843
83	3798	3	0.831	0.00554	0.820	0.842
84	3795	1	0.831	0.00554	0.820	0.842
85	3794	3	0.830	0.00555	0.819	0.841
86	3791	5	0.829	0.00556	0.818	0.840
87	3786	5	0.828	0.00557	0.817	0.839
88	3781	2	0.827	0.00558	0.817	0.838
89	3779	1	0.827	0.00558	0.816	0.838
90	3778	1	0.827	0.00559	0.816	0.838
91	3777	2	0.827	0.00559	0.816	0.838
92	3775	4	0.826	0.00560	0.815	0.837
93	3771	1	0.826	0.00561	0.815	0.837
94	3770	2	0.825	0.00561	0.814	0.836
95	3767	4	0.824	0.00562	0.813	0.835
96	3763	1	0.824	0.00563	0.813	0.835
97	3762	3	0.823	0.00563	0.812	0.834
98	3759	3	0.823	0.00564	0.812	0.834
99	3756	2	0.822	0.00565	0.811	0.833
100	3754	3	0.822	0.00566	0.811	0.833

101	3751	3	0.821	0.00566	0.810	0.832
102	3747	2	0.820	0.00567	0.809	0.832
103	3745	1	0.820	0.00567	0.809	0.831
104	3744	1	0.820	0.00567	0.809	0.831
105	3743	3	0.819	0.00568	0.808	0.831
106	3740	1	0.819	0.00569	0.808	0.830
108	3739	3	0.818	0.00569	0.807	0.830
109	3735	2	0.818	0.00570	0.807	0.829
110	3733	1	0.818	0.00570	0.807	0.829
111	3732	1	0.818	0.00570	0.807	0.829
112	3731	2	0.817	0.00571	0.806	0.828
113	3729	1	0.817	0.00571	0.806	0.828
114	3728	1	0.817	0.00571	0.806	0.828
116	3727	1	0.817	0.00572	0.805	0.828
117	3726	3	0.816	0.00573	0.805	0.827
119	3723	3	0.815	0.00573	0.804	0.827
120	3719	2	0.815	0.00574	0.804	0.826
121	3717	1	0.815	0.00574	0.803	0.826
122	3716	1	0.814	0.00574	0.803	0.826
123	3715	3	0.814	0.00575	0.802	0.825
124	3711	2	0.813	0.00576	0.802	0.825
125	3709	1	0.813	0.00576	0.802	0.824
126	3708	1	0.813	0.00576	0.802	0.824
127	3706	2	0.812	0.00577	0.801	0.824
131	3703	1	0.812	0.00577	0.801	0.824
132	3702	1	0.812	0.00577	0.801	0.823
134	3698	2	0.811	0.00578	0.800	0.823
137	3693	1	0.811	0.00578	0.800	0.823
138	3690	1	0.811	0.00578	0.800	0.822
139	3688	4	0.810	0.00579	0.799	0.822
140	3679	3	0.810	0.00580	0.798	0.821
141	3672	4	0.809	0.00581	0.797	0.820
142	3664	2	0.808	0.00582	0.797	0.820
144	3660	2	0.808	0.00582	0.796	0.819
145	3655	3	0.807	0.00583	0.796	0.819
146	3648	3	0.806	0.00584	0.795	0.818
147	3641	2	0.806	0.00584	0.795	0.818
148	3636	3	0.805	0.00585	0.794	0.817
150	3622	4	0.804	0.00586	0.793	0.816
151	3615	5	0.803	0.00587	0.792	0.815
152	3604	1	0.803	0.00588	0.792	0.815
153	3593	1	0.803	0.00588	0.791	0.814
154	3587	1	0.803	0.00588	0.791	0.814
155	3577	1	0.802	0.00588	0.791	0.814
157	3566	4	0.802	0.00590	0.790	0.813
158	3554	2	0.801	0.00590	0.790	0.813
161	3511	1	0.801	0.00590	0.789	0.812
162	3498	4	0.800	0.00591	0.788	0.812
163	3485	2	0.799	0.00592	0.788	0.811
164	3464	2	0.799	0.00593	0.787	0.811
166	3444	2	0.799	0.00593	0.787	0.810
167	3423	1	0.798	0.00593	0.787	0.810
168	3409	2	0.798	0.00594	0.786	0.810
169	3388	1	0.798	0.00594	0.786	0.809

170	3367	2	0.797	0.00595	0.786	0.809
172	3319	2	0.797	0.00595	0.785	0.808
173	3285	1	0.796	0.00596	0.785	0.808
174	3245	3	0.796	0.00597	0.784	0.807
175	3194	1	0.795	0.00597	0.784	0.807
176	3138	2	0.795	0.00598	0.783	0.807
177	3068	2	0.794	0.00599	0.783	0.806
179	2949	1	0.794	0.00599	0.782	0.806
180	2902	39	0.783	0.00615	0.771	0.796

Group=L_Hep

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1	2305	26	0.989	0.00220	0.984	0.993
2	2279	19	0.980	0.00288	0.975	0.986
3	2260	18	0.973	0.00340	0.966	0.979
4	2242	18	0.965	0.00384	0.957	0.972
5	2224	19	0.957	0.00424	0.948	0.965
6	2205	18	0.949	0.00459	0.940	0.958
7	2186	14	0.943	0.00484	0.933	0.952
8	2172	19	0.934	0.00515	0.924	0.945
9	2153	12	0.929	0.00534	0.919	0.940
10	2141	14	0.923	0.00555	0.912	0.934
11	2127	10	0.919	0.00569	0.908	0.930
12	2117	10	0.915	0.00582	0.903	0.926
13	2107	6	0.912	0.00590	0.900	0.924
14	2101	13	0.906	0.00607	0.894	0.918
15	2088	8	0.903	0.00617	0.891	0.915
16	2080	9	0.899	0.00628	0.887	0.911
17	2071	5	0.897	0.00634	0.884	0.909
18	2066	6	0.894	0.00641	0.882	0.907
19	2060	5	0.892	0.00647	0.879	0.905
20	2055	6	0.889	0.00653	0.877	0.902
21	2049	2	0.888	0.00656	0.876	0.901
22	2047	6	0.886	0.00662	0.873	0.899
23	2041	6	0.883	0.00669	0.870	0.896
24	2034	8	0.880	0.00677	0.867	0.893
25	2025	6	0.877	0.00684	0.864	0.891
26	2019	5	0.875	0.00689	0.862	0.889
27	2014	3	0.874	0.00692	0.860	0.887
28	2008	4	0.872	0.00696	0.858	0.886
29	2004	4	0.870	0.00700	0.857	0.884
30	2000	4	0.868	0.00704	0.855	0.882
31	1996	3	0.867	0.00707	0.853	0.881
32	1993	4	0.865	0.00711	0.852	0.879
33	1989	4	0.864	0.00715	0.850	0.878
34	1984	3	0.862	0.00718	0.848	0.877
35	1981	2	0.862	0.00720	0.848	0.876
36	1978	5	0.859	0.00724	0.845	0.874
37	1973	2	0.858	0.00726	0.844	0.873
38	1971	4	0.857	0.00730	0.843	0.871
39	1967	2	0.856	0.00732	0.842	0.870
40	1965	6	0.853	0.00737	0.839	0.868
41	1959	1	0.853	0.00738	0.838	0.867
42	1958	4	0.851	0.00742	0.837	0.866

43	1954	2	0.850	0.00744	0.836	0.865
44	1952	2	0.849	0.00745	0.835	0.864
45	1950	3	0.848	0.00748	0.833	0.863
46	1947	6	0.845	0.00753	0.831	0.860
47	1941	2	0.845	0.00755	0.830	0.859
48	1939	3	0.843	0.00758	0.829	0.858
49	1936	4	0.841	0.00761	0.827	0.857
50	1932	6	0.839	0.00766	0.824	0.854
51	1926	4	0.837	0.00770	0.822	0.852
52	1922	2	0.836	0.00771	0.821	0.852
53	1920	7	0.833	0.00777	0.818	0.849
54	1913	4	0.831	0.00780	0.816	0.847
55	1909	4	0.830	0.00783	0.815	0.845
56	1905	2	0.829	0.00785	0.814	0.844
57	1903	1	0.828	0.00786	0.813	0.844
58	1902	1	0.828	0.00787	0.813	0.844
60	1901	1	0.828	0.00787	0.812	0.843
61	1900	3	0.826	0.00790	0.811	0.842
62	1897	3	0.825	0.00792	0.810	0.841
63	1894	2	0.824	0.00794	0.809	0.840
64	1892	1	0.824	0.00794	0.808	0.839
65	1891	2	0.823	0.00796	0.807	0.839
66	1889	3	0.821	0.00798	0.806	0.837
67	1886	2	0.821	0.00800	0.805	0.836
68	1884	1	0.820	0.00801	0.805	0.836
69	1883	1	0.820	0.00801	0.804	0.836
70	1882	1	0.819	0.00802	0.804	0.835
72	1881	2	0.818	0.00804	0.803	0.834
73	1879	1	0.818	0.00804	0.802	0.834
74	1878	1	0.818	0.00805	0.802	0.833
75	1877	1	0.817	0.00806	0.801	0.833
76	1876	1	0.817	0.00807	0.801	0.833
77	1875	1	0.816	0.00807	0.801	0.832
78	1873	1	0.816	0.00808	0.800	0.832
79	1872	2	0.815	0.00810	0.799	0.831
81	1869	2	0.814	0.00811	0.798	0.830
82	1867	1	0.814	0.00812	0.798	0.830
83	1866	1	0.813	0.00813	0.797	0.829
84	1865	1	0.813	0.00813	0.797	0.829
85	1864	1	0.812	0.00814	0.797	0.828
86	1863	1	0.812	0.00815	0.796	0.828
87	1862	1	0.811	0.00815	0.796	0.828
90	1860	4	0.810	0.00818	0.794	0.826
91	1856	1	0.809	0.00819	0.793	0.825
92	1855	2	0.808	0.00820	0.792	0.825
94	1853	2	0.808	0.00822	0.792	0.824
95	1851	1	0.807	0.00823	0.791	0.823
96	1850	2	0.806	0.00824	0.790	0.823
98	1848	1	0.806	0.00825	0.790	0.822
99	1847	1	0.805	0.00825	0.789	0.822
100	1844	2	0.804	0.00827	0.788	0.821
102	1841	4	0.803	0.00830	0.787	0.819
103	1837	1	0.802	0.00830	0.786	0.819
104	1836	4	0.801	0.00833	0.784	0.817

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 105   1832       2    0.800 0.00835        0.783        0.816
 106   1830       3    0.798 0.00837        0.782        0.815
 107   1827       2    0.797 0.00838        0.781        0.814
 108   1825       1    0.797 0.00839        0.781        0.814
 110   1824       1    0.797 0.00839        0.780        0.813
 112   1823       2    0.796 0.00841        0.779        0.812
 113   1821       1    0.795 0.00841        0.779        0.812
 114   1820       2    0.794 0.00843        0.778        0.811
 115   1817       1    0.794 0.00843        0.778        0.811
 116   1816       4    0.792 0.00846        0.776        0.809
 118   1812       1    0.792 0.00847        0.775        0.809
 119   1811       1    0.791 0.00847        0.775        0.808
 120   1809       2    0.790 0.00849        0.774        0.807
 121   1806       1    0.790 0.00849        0.774        0.807
 124   1805       1    0.790 0.00850        0.773        0.806
 125   1804       1    0.789 0.00851        0.773        0.806
 126   1803       2    0.788 0.00852        0.772        0.805
 127   1800       1    0.788 0.00853        0.771        0.805
 128   1798       3    0.787 0.00855        0.770        0.803
 129   1795       1    0.786 0.00855        0.770        0.803
 133   1794       1    0.786 0.00856        0.769        0.803
 134   1793       1    0.785 0.00856        0.769        0.802
 135   1792       1    0.785 0.00857        0.768        0.802
 136   1791       1    0.784 0.00858        0.768        0.801
 137   1788       1    0.784 0.00858        0.767        0.801
 139   1785       1    0.783 0.00859        0.767        0.800
 140   1783       1    0.783 0.00860        0.766        0.800
 142   1780       2    0.782 0.00861        0.765        0.799
 143   1778       1    0.782 0.00862        0.765        0.799
 144   1776       1    0.781 0.00862        0.765        0.798
 145   1773       2    0.780 0.00864        0.764        0.797
 146   1768       1    0.780 0.00864        0.763        0.797
 149   1762       2    0.779 0.00865        0.762        0.796
 153   1743       2    0.778 0.00867        0.761        0.795
 154   1738       1    0.778 0.00867        0.761        0.795
 156   1727       1    0.777 0.00868        0.760        0.794
 164   1686       2    0.776 0.00869        0.759        0.794
 166   1675       1    0.776 0.00870        0.759        0.793
 167   1665       2    0.775 0.00872        0.758        0.792
 169   1646       1    0.774 0.00872        0.758        0.792
 170   1636       2    0.774 0.00874        0.757        0.791
 171   1622       1    0.773 0.00875        0.756        0.790
 173   1599       2    0.772 0.00876        0.755        0.789
 175   1552       1    0.772 0.00877        0.755        0.789
 178   1473       1    0.771 0.00878        0.754        0.788
 180   1411      20    0.760 0.00899        0.743        0.778

               Group=H_Hep
time n.risk n.event survival std.err lower 95% CI upper 95% CI
   1   2298      34    0.985 0.00252        0.980        0.990
   2   2264      16    0.978 0.00304        0.972        0.984
   3   2248      24    0.968 0.00368        0.961        0.975
   4   2224      16    0.961 0.00405        0.953        0.969
   5   2208      13    0.955 0.00432        0.947        0.964
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6	2195	13	0.950	0.00457	0.941	0.959
7	2182	13	0.944	0.00480	0.934	0.953
8	2169	14	0.938	0.00504	0.928	0.948
9	2155	14	0.932	0.00526	0.921	0.942
10	2141	13	0.926	0.00546	0.915	0.937
11	2128	10	0.922	0.00560	0.911	0.933
12	2117	13	0.916	0.00579	0.905	0.927
13	2104	11	0.911	0.00593	0.900	0.923
14	2093	5	0.909	0.00600	0.897	0.921
15	2088	6	0.906	0.00608	0.895	0.918
16	2082	9	0.903	0.00619	0.890	0.915
17	2073	5	0.900	0.00625	0.888	0.913
18	2066	6	0.898	0.00632	0.885	0.910
19	2060	5	0.896	0.00638	0.883	0.908
20	2055	8	0.892	0.00647	0.879	0.905
21	2045	7	0.889	0.00655	0.876	0.902
22	2038	2	0.888	0.00658	0.875	0.901
23	2036	6	0.886	0.00664	0.873	0.899
24	2029	4	0.884	0.00669	0.871	0.897
25	2024	5	0.882	0.00674	0.868	0.895
26	2019	4	0.880	0.00678	0.867	0.893
27	2015	3	0.879	0.00682	0.865	0.892
28	2012	3	0.877	0.00685	0.864	0.891
29	2008	3	0.876	0.00688	0.863	0.889
30	2005	3	0.875	0.00691	0.861	0.888
31	2002	7	0.872	0.00698	0.858	0.885
32	1994	5	0.869	0.00703	0.856	0.883
33	1989	5	0.867	0.00708	0.853	0.881
34	1984	5	0.865	0.00713	0.851	0.879
35	1979	2	0.864	0.00715	0.850	0.878
36	1977	8	0.861	0.00723	0.847	0.875
37	1969	2	0.860	0.00725	0.846	0.874
38	1967	5	0.858	0.00730	0.843	0.872
39	1962	2	0.857	0.00731	0.842	0.871
40	1960	3	0.855	0.00734	0.841	0.870
41	1957	3	0.854	0.00737	0.840	0.869
43	1954	3	0.853	0.00740	0.838	0.867
44	1951	3	0.851	0.00742	0.837	0.866
45	1948	4	0.850	0.00746	0.835	0.864
46	1944	5	0.848	0.00750	0.833	0.862
47	1939	1	0.847	0.00751	0.832	0.862
48	1938	4	0.845	0.00755	0.831	0.860
49	1934	1	0.845	0.00756	0.830	0.860
50	1933	2	0.844	0.00757	0.829	0.859
51	1931	2	0.843	0.00759	0.828	0.858
52	1929	1	0.843	0.00760	0.828	0.858
53	1928	1	0.842	0.00761	0.827	0.857
54	1927	1	0.842	0.00762	0.827	0.857
55	1926	2	0.841	0.00764	0.826	0.856
56	1924	2	0.840	0.00765	0.825	0.855
57	1922	8	0.837	0.00772	0.822	0.852
58	1914	3	0.835	0.00774	0.820	0.851
59	1911	1	0.835	0.00775	0.820	0.850
60	1910	5	0.833	0.00779	0.818	0.848

61	1905	2	0.832	0.00781	0.817	0.847
63	1903	2	0.831	0.00783	0.816	0.846
64	1901	2	0.830	0.00784	0.815	0.846
65	1899	1	0.830	0.00785	0.814	0.845
66	1898	4	0.828	0.00788	0.813	0.843
67	1894	4	0.826	0.00791	0.811	0.842
68	1889	2	0.825	0.00793	0.810	0.841
70	1887	1	0.825	0.00794	0.809	0.840
71	1886	4	0.823	0.00797	0.808	0.839
72	1882	2	0.822	0.00798	0.807	0.838
73	1880	4	0.820	0.00802	0.805	0.836
74	1876	3	0.819	0.00804	0.803	0.835
75	1873	1	0.819	0.00805	0.803	0.835
77	1872	2	0.818	0.00806	0.802	0.834
78	1870	3	0.816	0.00808	0.801	0.832
79	1867	1	0.816	0.00809	0.800	0.832
81	1866	1	0.816	0.00810	0.800	0.832
83	1865	2	0.815	0.00811	0.799	0.831
84	1863	1	0.814	0.00812	0.799	0.830
85	1861	3	0.813	0.00814	0.797	0.829
86	1858	1	0.813	0.00815	0.797	0.829
87	1857	1	0.812	0.00816	0.796	0.828
88	1856	2	0.811	0.00817	0.795	0.827
89	1854	2	0.810	0.00819	0.794	0.827
90	1852	1	0.810	0.00819	0.794	0.826
91	1851	1	0.809	0.00820	0.794	0.826
92	1850	1	0.809	0.00821	0.793	0.825
94	1849	2	0.808	0.00822	0.792	0.824
95	1847	2	0.807	0.00824	0.791	0.824
96	1845	3	0.806	0.00826	0.790	0.822
97	1842	1	0.806	0.00827	0.789	0.822
98	1841	2	0.805	0.00828	0.789	0.821
99	1839	1	0.804	0.00829	0.788	0.821
101	1838	3	0.803	0.00831	0.787	0.819
102	1835	1	0.802	0.00832	0.786	0.819
105	1834	1	0.802	0.00832	0.786	0.819
106	1833	3	0.801	0.00834	0.785	0.817
109	1830	1	0.800	0.00835	0.784	0.817
110	1829	1	0.800	0.00836	0.784	0.816
112	1827	2	0.799	0.00837	0.783	0.816
114	1825	1	0.799	0.00838	0.782	0.815
116	1824	2	0.798	0.00839	0.781	0.814
119	1822	1	0.797	0.00840	0.781	0.814
120	1821	1	0.797	0.00840	0.780	0.813
122	1820	1	0.796	0.00841	0.780	0.813
123	1819	2	0.795	0.00842	0.779	0.812
124	1817	1	0.795	0.00843	0.779	0.812
126	1816	2	0.794	0.00845	0.778	0.811
127	1814	3	0.793	0.00847	0.776	0.810
129	1811	2	0.792	0.00848	0.776	0.809
133	1807	2	0.791	0.00849	0.775	0.808
135	1805	2	0.790	0.00850	0.774	0.807
136	1802	1	0.790	0.00851	0.773	0.807
137	1800	1	0.789	0.00852	0.773	0.806

138	1797	3	0.788	0.00854	0.771	0.805
139	1792	2	0.787	0.00855	0.771	0.804
141	1789	1	0.787	0.00856	0.770	0.804
142	1785	1	0.786	0.00856	0.770	0.803
143	1782	1	0.786	0.00857	0.769	0.803
144	1781	1	0.785	0.00858	0.769	0.802
145	1779	1	0.785	0.00858	0.768	0.802
146	1777	1	0.784	0.00859	0.768	0.802
148	1772	1	0.784	0.00860	0.767	0.801
149	1771	1	0.784	0.00860	0.767	0.801
151	1763	1	0.783	0.00861	0.766	0.800
152	1758	2	0.782	0.00862	0.766	0.799
153	1752	1	0.782	0.00863	0.765	0.799
156	1735	1	0.781	0.00864	0.765	0.798
157	1729	2	0.780	0.00865	0.764	0.798
159	1719	3	0.779	0.00867	0.762	0.796
161	1710	1	0.779	0.00868	0.762	0.796
163	1695	2	0.778	0.00869	0.761	0.795
164	1684	2	0.777	0.00871	0.760	0.794
167	1662	1	0.776	0.00871	0.759	0.794
170	1642	1	0.776	0.00872	0.759	0.793
172	1623	1	0.775	0.00873	0.758	0.793
173	1609	1	0.775	0.00874	0.758	0.792
174	1593	2	0.774	0.00875	0.757	0.791
176	1552	1	0.773	0.00876	0.756	0.791
178	1504	1	0.773	0.00877	0.756	0.790
180	1439	17	0.764	0.00894	0.746	0.782