FRET LCA Classes

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```
load(file = "COIN_Final.Rdata")
```

```
library(survival)

data <- patient_data[patient_data$FRET.cohort==1,]

data$SurvObj.os <- with(data, Surv(ostime, osevent))
data$SurvObj.pfs <- with(data, Surv(pfstime, pfsevent))

col=c("red", "red", "blue", "blue")
lty=c(1,2,1,2)
```

Split FRET by Tertiles, and Rename to use FRET in the paper

```
breaks <- quantile(data$FRET, probs = c(0.0, 0.67, 1.0), na.rm = T)
data$FRETeff <- cut(data$FRET, breaks = breaks, labels = c("low", "high"),
                    include.lowest = T)
data$FRET_raw <- data$FRET
data$FRET <- data$FRETeff
```

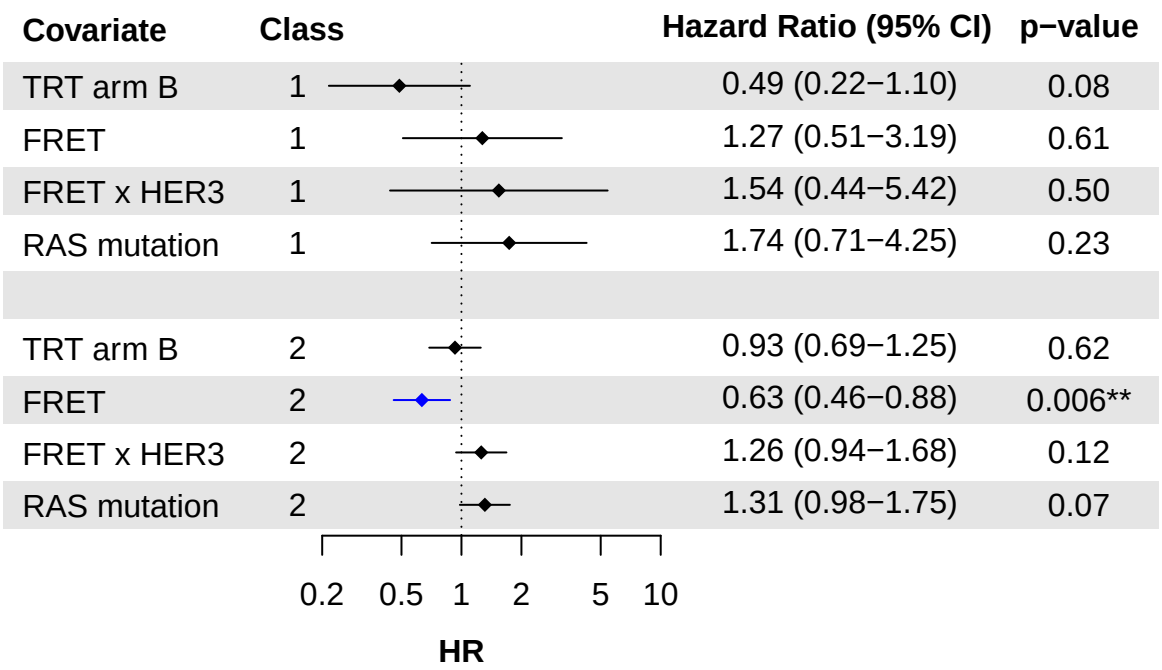
PFS by class

```
library(filesstrings)
```

```
## Loading required package: stringr
```

```
FRET_LCA <- LCA_FRET_PFS_HR

# Change any covarite names
FRET_LCA$Covname[c(1,5)] = "TRT arm B"
FRET_LCA$Covname[c(3,7)] = "FRET x HER3"
FRET_LCA$Covname[c(4,8)] = "RAS mutation"

# insert rows of NA to break the classes up, do lower one first - easier to track row numbers
insert_row <- c(NA,NA,NA,"",NA,"")
FRET_LCA = rbind(FRET_LCA[1:4,], insert_row, FRET_LCA[-(1:4),])

# Highlight points with colours (account for inserted rows)
colours <- c("black","black","black","black",
             "black",
             "black","blue","black","black")

mydf <- data.frame(
    Covariate = FRET_LCA$Covname,
    Class = FRET_LCA$Class,
```

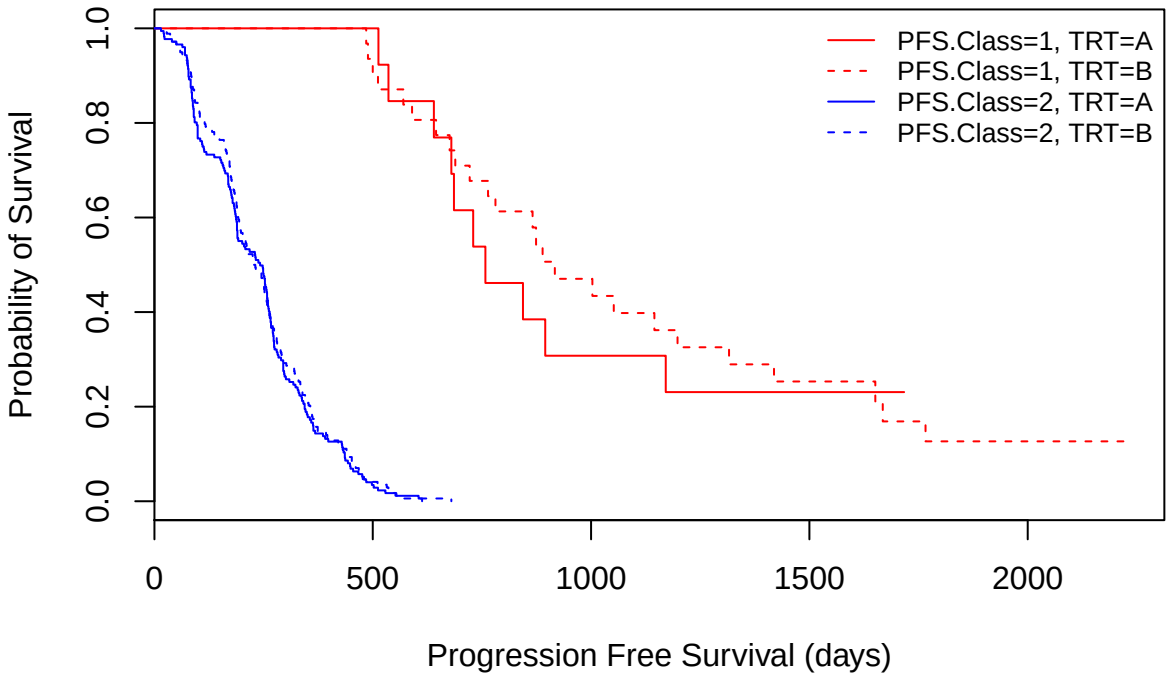
```
    HazardRatio = as.numeric(FRET_LCA$HR),
    HazardLower = first_number(FRET_LCA$X95.CI, decimals=T),
    HazardUpper = nth_number(FRET_LCA$X95.CI, 2, decimals=T),
    Pvalue = sapply(as.numeric(FRET_LCA$p.value), JNCI_pvals),
    stringsAsFactors=FALSE
)

plotHRTable(mydf, useClass = T, useWeight = F, useRank = F, col = colours)
```




```
# rename
data$PFS.Class <- data$Class.FRET.PFS

km <- survfit(SurvObj.pfs ~ PFS.Class, data=data)
print(km)
```

```
## Call: survfit(formula = SurvObj.pfs ~ PFS.Class, data = data)
##
##                n events median 0.95LCL 0.95UCL
## PFS.Class=1   44     35    874     758    1198
## PFS.Class=2 354    352    232     205     254
```

```
km <- survfit(SurvObj.pfs ~ PFS.Class + TRT, data=data)
plot(km, col=col, lty=lty, xlab="Progression Free Survival (days)", ylab="Probability of Survival")
legend("topright", col=col, legend = names(km$strata), lty=lty, bty="n", cex=0.8)
```




```
print(km)
```

```
## Call: survfit(formula = SurvObj.pfs ~ PFS.Class + TRT, data = data)
##
##                       n events median 0.95LCL 0.95UCL
## PFS.Class=1, TRT=A   13     10    758     680      NA
## PFS.Class=1, TRT=B   31     25    917     764    1419
## PFS.Class=2, TRT=A 176    175    242     190     260
## PFS.Class=2, TRT=B 178    177    228     198     258
```

```
survdiff(SurvObj.pfs ~ PFS.Class, data=data)
```

```
## Call:
## survdiff(formula = SurvObj.pfs ~ PFS.Class, data = data)
##
##                N Observed Expected (O-E)^2/E (O-E)^2/V
## PFS.Class=1   44       35      129      68.3       151
## PFS.Class=2 354      352      258      34.1       151
##
##  Chisq= 151  on 1 degrees of freedom, p= <2e-16
```

```
survdiff(SurvObj.pfs[PFS.Class==1] ~ TRT[PFS.Class==1], data=data)
```

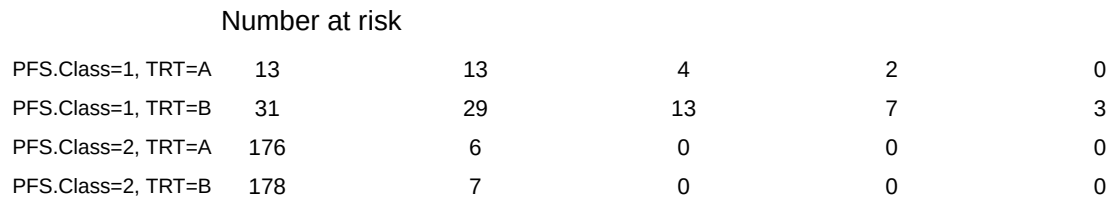
```
## Call:
## survdiff(formula = SurvObj.pfs[PFS.Class == 1] ~ TRT[PFS.Class ==
##     1], data = data)
##
##                        N Observed Expected (O-E)^2/E (O-E)^2/V
```

```
## TRT[PFS.Class == 1]=A 13       10     8.92    0.1295     0.177
## TRT[PFS.Class == 1]=B 31       25    26.08    0.0443     0.177
##
##  Chisq= 0.2  on 1 degrees of freedom, p= 0.7
```

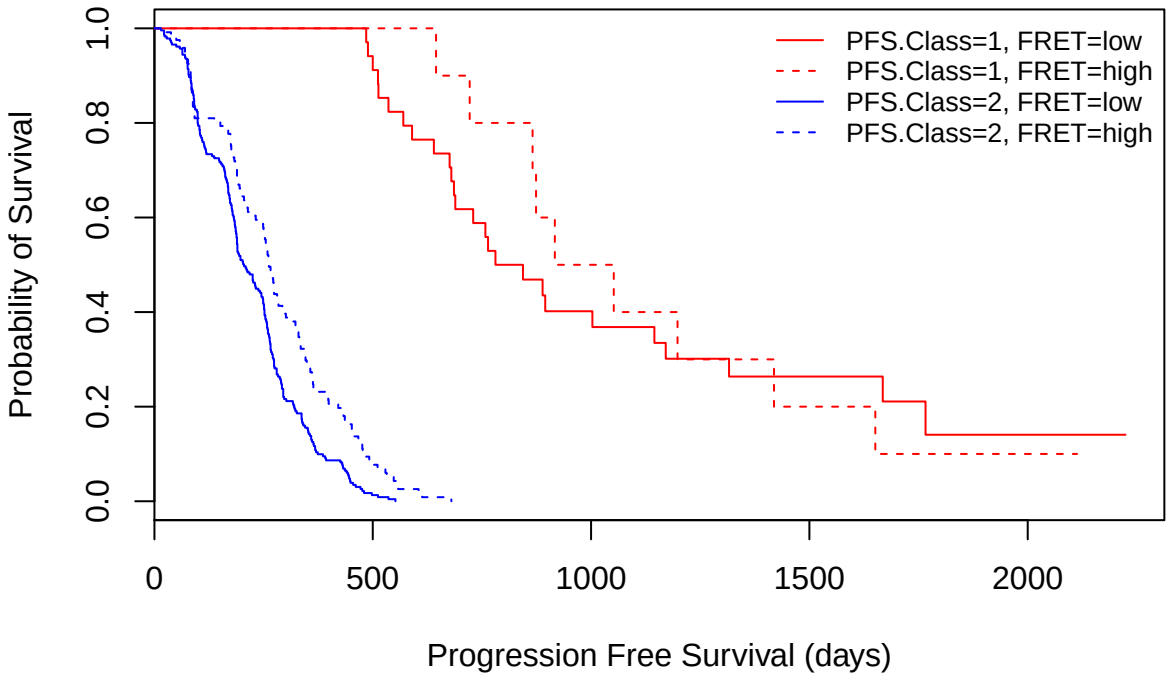
```
survdiff(SurvObj.pfs[PFS.Class==2] ~ TRT[PFS.Class==2], data=data)
```

```
## Call:
## survdiff(formula = SurvObj.pfs[PFS.Class == 2] ~ TRT[PFS.Class ==
##     2], data = data)
##
##                          N Observed Expected (O-E)^2/E (O-E)^2/V
## TRT[PFS.Class == 2]=A 176      175      170     0.136     0.267
## TRT[PFS.Class == 2]=B 178      177      182     0.127     0.267
##
##  Chisq= 0.3  on 1 degrees of freedom, p= 0.6
```

```
ggrisktable(km, data=data) + theme_cleantable()
```




```
km <- survfit(SurvObj.pfs ~ PFS.Class + FRET, data=data)
plot(km, col=col, lty=lty, xlab="Progression Free Survival (days)", ylab="Probability of Survival")
legend("topright", col=col, legend = names(km$strata), lty=lty, bty="n", cex=0.8)
```




```
print(km)
```

```
## Call: survfit(formula = SurvObj.pfs ~ PFS.Class + FRET, data = data)
##
##                           n events median 0.95LCL 0.95UCL
## PFS.Class=1, FRET=low    34     26    812     689    1316
## PFS.Class=1, FRET=high   10      9    984     866      NA
## PFS.Class=2, FRET=low   233    232    205     188     248
## PFS.Class=2, FRET=high  121    120    262     249     298
```

```
survdiff(SurvObj.pfs ~ PFS.Class, data=data)
```

```
## Call:
## survdiff(formula = SurvObj.pfs ~ PFS.Class, data = data)
##
##                N Observed Expected (O-E)^2/E (O-E)^2/V
## PFS.Class=1   44       35      129      68.3       151
## PFS.Class=2 354      352      258      34.1       151
##
##  Chisq= 151  on 1 degrees of freedom, p= <2e-16
```

```
survdiff(SurvObj.pfs[PFS.Class==1] ~ FRET[PFS.Class==1], data=data)
```

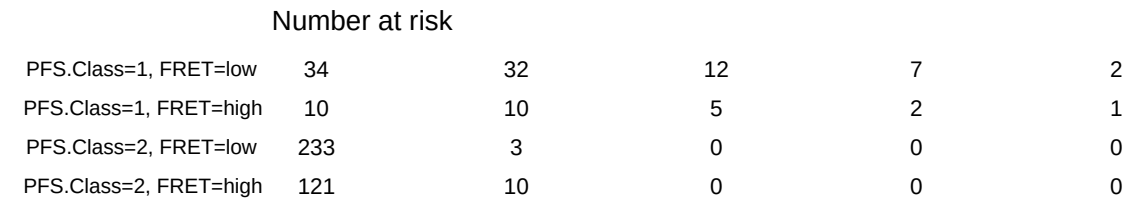
```
## Call:
## survdiff(formula = SurvObj.pfs[PFS.Class == 1] ~ FRET[PFS.Class ==
##     1], data = data)
##
##                             N Observed Expected (O-E)^2/E (O-E)^2/V
```

```
## FRET[PFS.Class == 1]=low  34       26    25.21    0.0247    0.0889
## FRET[PFS.Class == 1]=high 10        9     9.79    0.0637    0.0889
##
##  Chisq= 0.1  on 1 degrees of freedom, p= 0.8
```

```
survdiff(SurvObj.pfs[PFS.Class==2] ~ FRET[PFS.Class==2], data=data)
```

```
## Call:
## survdiff(formula = SurvObj.pfs[PFS.Class == 2] ~ FRET[PFS.Class ==
##     2], data = data)
##
##                               N Observed Expected (O-E)^2/E (O-E)^2/V
## FRET[PFS.Class == 2]=low  233      232      195      7.08        17
## FRET[PFS.Class == 2]=high 121      120      157      8.78        17
##
##  Chisq= 17  on 1 degrees of freedom, p= 4e-05
```

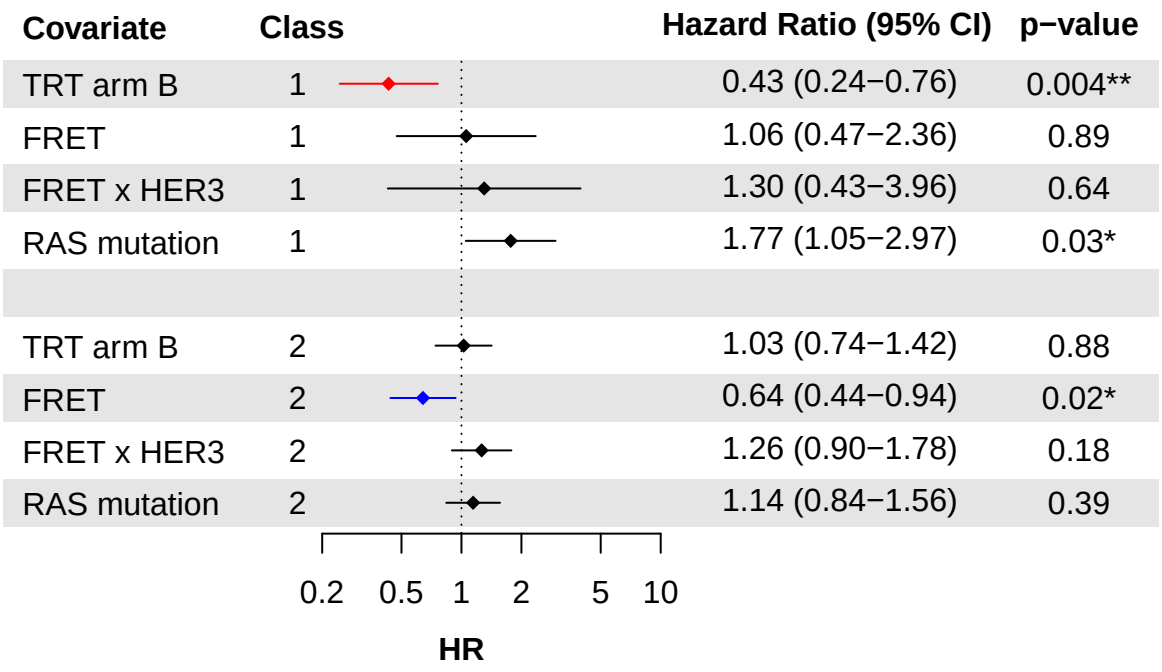
```
ggrisktable(km, data=data) + theme_cleantable()
```



OS by class

```
library(filesstrings)

FRET_LCA <- LCA_FRET_OS_HR

# Change any covarite names
FRET_LCA$Covname[c(1,5)] = "TRT arm B"
FRET_LCA$Covname[c(3,7)] = "FRET x HER3"
FRET_LCA$Covname[c(4,8)] = "RAS mutation"

# insert rows of NA to break the classes up, do lower one first - easier to track row numbers
insert_row <- c(NA,NA,NA,"",NA,"")
FRET_LCA = rbind(FRET_LCA[1:4,], insert_row, FRET_LCA[-(1:4),])

# Highlight points with colours (account for inserted rows)
colours <- c("red","black","black","black",
             "black",
             "black","blue","black","black")

mydf <- data.frame(
    Covariate = FRET_LCA$Covname,
    Class = FRET_LCA$Class,
    HazardRatio = as.numeric(FRET_LCA$HR),
    HazardLower = first_number(FRET_LCA$X95.CI, decimals=T),
    HazardUpper = nth_number(FRET_LCA$X95.CI, 2, decimals=T),
    Pvalue = sapply(as.numeric(FRET_LCA$p.value), JNCI_pvals),
```

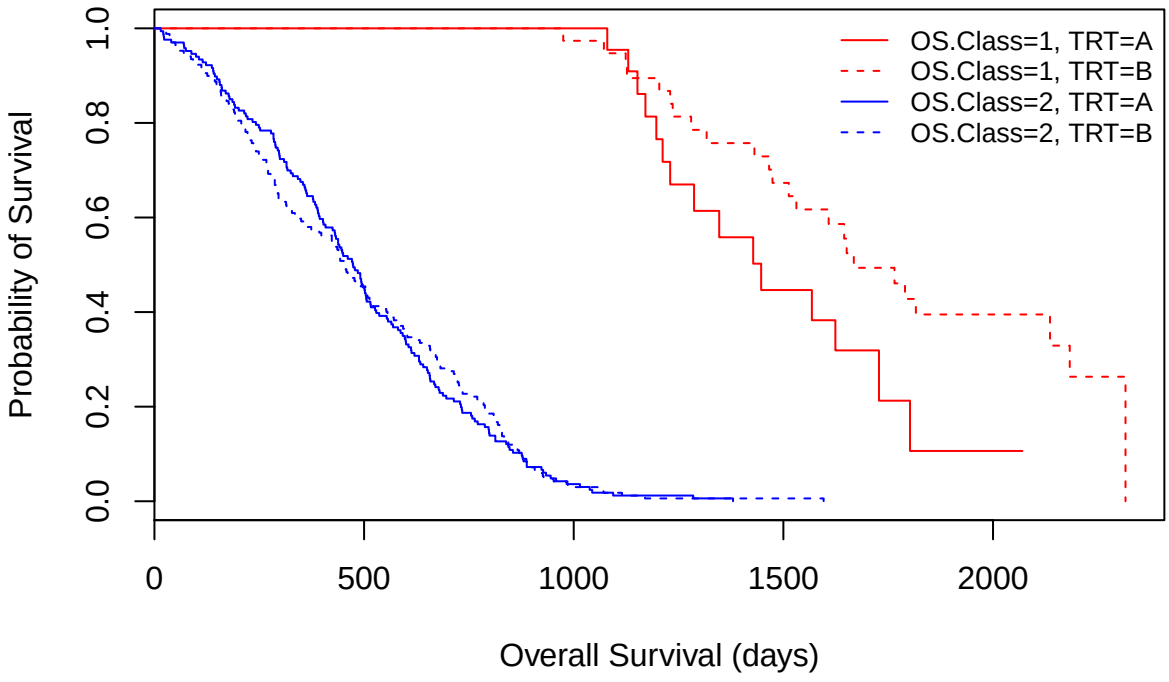
```
    stringsAsFactors=FALSE
)

plotHRTable(mydf, useClass = T, useWeight = F, useRank = F, col = colours)
```




```
# rename
data$OS.Class <- data$Class.FRET.OS

km <- survfit(SurvObj.os ~ OS.Class, data=data)
print(km)
```

```
## Call: survfit(formula = SurvObj.os ~ OS.Class, data = data)
##
##               n events median 0.95LCL 0.95UCL
## OS.Class=1  62     39   1624    1466    1816
## OS.Class=2 336    334    461     431     504
```

```
km <- survfit(SurvObj.os ~ OS.Class + TRT, data=data)
plot(km, col=col, lty=lty, xlab="Overall Survival (days)", ylab="Probability of Survival")
legend("topright", col=col, legend = names(km$strata), lty=lty, bty="n", cex=0.8)
```




```
print(km)
```

```
## Call: survfit(formula = SurvObj.os ~ OS.Class + TRT, data = data)
##
##                       n events median 0.95LCL 0.95UCL
## OS.Class=1, TRT=A  22     15   1447    1230      NA
## OS.Class=1, TRT=B  40     24   1668    1531      NA
## OS.Class=2, TRT=A 167    166    474     430     515
## OS.Class=2, TRT=B 169    168    455     393     521
```

```
survdiff(SurvObj.os ~ OS.Class, data=data)
```

```
## Call:
## survdiff(formula = SurvObj.os ~ OS.Class, data = data)
##
##              N Observed Expected (O-E)^2/E (O-E)^2/V
## OS.Class=1  62       39      151      83.5       197
## OS.Class=2 336      334      222      57.1       197
##
##  Chisq= 197  on 1 degrees of freedom, p= <2e-16
```

```
survdiff(SurvObj.os[OS.Class==1] ~ TRT[OS.Class==1], data=data)
```

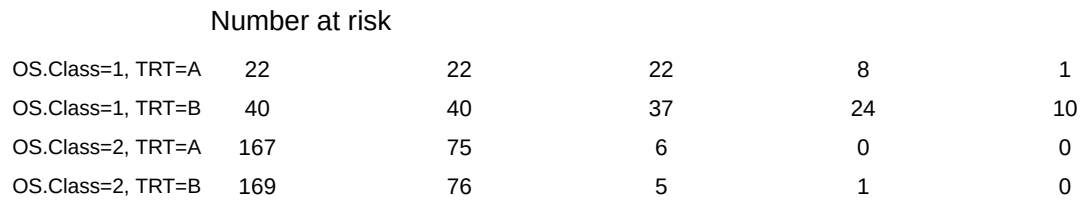
```
## Call:
## survdiff(formula = SurvObj.os[OS.Class == 1] ~ TRT[OS.Class ==
##     1], data = data)
##
##                       N Observed Expected (O-E)^2/E (O-E)^2/V
```

```
## TRT[OS.Class == 1]=A 22       15     9.77     2.794      3.97
## TRT[OS.Class == 1]=B 40       24    29.23     0.934      3.97
##
##  Chisq= 4  on 1 degrees of freedom, p= 0.05
```

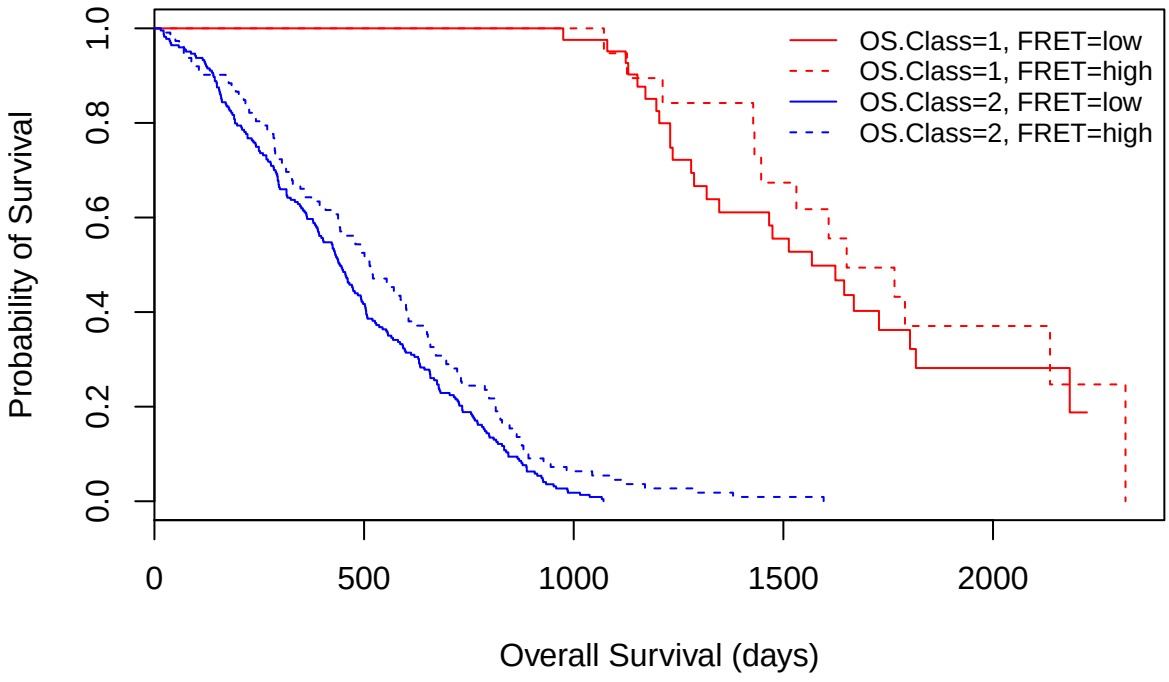
```
survdiff(SurvObj.os[OS.Class==2] ~ TRT[OS.Class==2], data=data)
```

```
## Call:
## survdiff(formula = SurvObj.os[OS.Class == 2] ~ TRT[OS.Class ==
##     2], data = data)
##
##                          N Observed Expected (O-E)^2/E (O-E)^2/V
## TRT[OS.Class == 2]=A 167      166      164    0.0168    0.0335
## TRT[OS.Class == 2]=B 169      168      170    0.0163    0.0335
##
##  Chisq= 0  on 1 degrees of freedom, p= 0.9
```

```
ggrisktable(km, data=data) + theme_cleantable()
```




```
km <- survfit(SurvObj.os ~ OS.Class + FRET, data=data)
plot(km, col=col, lty=lty, xlab="Overall Survival (days)", ylab="Probability of Survival")
legend("topright", col=col, legend = names(km$strata), lty=lty, bty="n", cex=0.8)
```




```
print(km)
```

```
## Call: survfit(formula = SurvObj.os ~ OS.Class + FRET, data = data)
##
##                          n events median 0.95LCL 0.95UCL
## OS.Class=1, FRET=low    43     26   1568    1347    1816
## OS.Class=1, FRET=high   19     13   1651    1447      NA
## OS.Class=2, FRET=low   224    223    442     393     493
## OS.Class=2, FRET=high  112    111    513     441     603
```

```
survdiff(SurvObj.os ~ OS.Class, data=data)
```

```
## Call:
## survdiff(formula = SurvObj.os ~ OS.Class, data = data)
##
##              N Observed Expected (O-E)^2/E (O-E)^2/V
## OS.Class=1  62       39      151      83.5       197
## OS.Class=2 336      334      222      57.1       197
##
##  Chisq= 197  on 1 degrees of freedom, p= <2e-16
```

```
survdiff(SurvObj.os[OS.Class==1] ~ FRET[OS.Class==1], data=data)
```

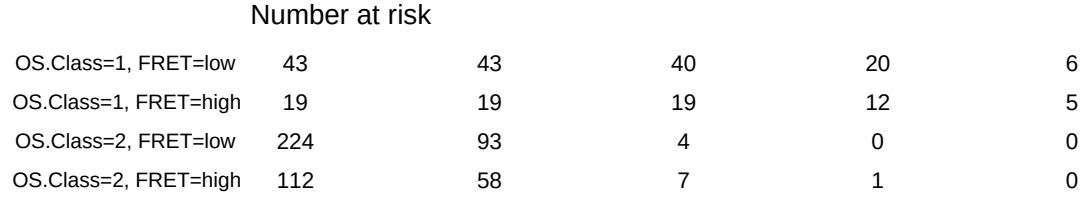
```
## Call:
## survdiff(formula = SurvObj.os[OS.Class == 1] ~ FRET[OS.Class ==
##     1], data = data)
##
##                           N Observed Expected (O-E)^2/E (O-E)^2/V
```

```
## FRET[OS.Class == 1]=low  43       26     23.9     0.187     0.508
## FRET[OS.Class == 1]=high 19       13     15.1     0.295     0.508
##
##  Chisq= 0.5  on 1 degrees of freedom, p= 0.5
```

```
survdiff(SurvObj.os[OS.Class==2] ~ FRET[OS.Class==2], data=data)
```

```
## Call:
## survdiff(formula = SurvObj.os[OS.Class == 2] ~ FRET[OS.Class ==
##     2], data = data)
##
##                              N Observed Expected (O-E)^2/E (O-E)^2/V
## FRET[OS.Class == 2]=low  224      223      202      2.11       5.6
## FRET[OS.Class == 2]=high 112      111      132      3.24       5.6
##
##  Chisq= 5.6  on 1 degrees of freedom, p= 0.02
```

```
ggrisktable(km, data=data) + theme_cleantable()
```



Session Information

```
sessionInfo()
```

```
## R version 3.5.1 (2018-07-02)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 10 x64 (build 16299)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=English_United Kingdom.1252
## [2] LC_CTYPE=English_United Kingdom.1252
## [3] LC_MONETARY=English_United Kingdom.1252
## [4] LC_NUMERIC=C
## [5] LC_TIME=English_United Kingdom.1252
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
## [1] filesstrings_3.0.0 stringr_1.3.1      survival_2.42-3
## [4] survminer_0.4.6    ggpubr_0.2         magrittr_1.5
## [7] ggplot2_3.1.1
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_1.0.1         pillar_1.4.1       compiler_3.5.1
##  [4] plyr_1.8.4         tools_3.5.1        zeallot_0.1.0
```

```
##  [7] digest_0.6.18      checkmate_1.9.3    lifecycle_0.1.0
## [10] evaluate_0.12      tibble_2.1.1       gtable_0.2.0
## [13] nlme_3.1-137       lattice_0.20-35    pkgconfig_2.0.2
## [16] rlang_0.4.0        strex_1.0.1        Matrix_1.2-14
## [19] yaml_2.2.0         gridExtra_2.3      withr_2.1.2
## [22] dplyr_0.8.3        knitr_1.20         survMisc_0.5.5
## [25] vctrs_0.2.0        generics_0.0.2     rprojroot_1.3-2
## [28] grid_3.5.1         tidyselect_0.2.5   data.table_1.12.2
## [31] glue_1.3.0         KMsurv_0.1-5       R6_2.3.0
## [34] km.ci_0.5-2        rmarkdown_1.10     purrr_0.2.5
## [37] tidyr_1.0.0        matrixStats_0.54.0 splines_3.5.1
## [40] backports_1.1.2    scales_1.0.0       htmltools_0.3.6
## [43] assertthat_0.2.0   xtable_1.8-4       colorspace_1.3-2
## [46] labeling_0.3       stringi_1.2.4      lazyeval_0.2.1
## [49] munsell_0.5.0      broom_0.5.2        crayon_1.3.4
## [52] zoo_1.8-4
```