Survival_Analysis.R

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```
# loading necessary packages for data manipulation and survival analysis
library(readxl)  # to read Excel files
```

```
## Warning: package 'readxl' was built under R version 4.3.3
```

```
library(dplyr) # for data wrangling and cleaning
```

```
## Warning: package 'dplyr' was built under R version 4.3.3
```

```
##
## Attaching package: 'dplyr'
```

```
## The following objects are masked from 'package:stats':
##
##     filter, lag
```

```
## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
library(survival) # for survival analysis functions
library(survminer) # for plotting survival curves nicely
```

```
## Warning: package 'survminer' was built under R version 4.3.3
```

```
## Loading required package: ggplot2
```

```
## Loading required package: ggpubr
```

```
##
## Attaching package: 'survminer'
```

```
## The following object is masked from 'package:survival':
##
##     myeloma
```

```
library(ggplot2) # load ggplot2 to save plots as PNG

data = read_excel("Clinical_Data_Validation_Cohort.xlsx") # load the clinical dataset from Excel
View(data)  # view the dataset to check its structure

# renaming columns
data <- data %>% rename(
  Event = `Event (death: 1, alive: 0)`,
  Stage = `Stage (TNM 8th edition)`
)

# Convert columns to factors
```

```r
data$Grade <- as.factor(data$Grade)
data$Stage <- as.factor(data$Stage)
data$Sex <- as.factor(data$Sex)
data$Cigarette <- as.factor(data$Cigarette)

data$EGFR <- as.factor(data$EGFR)
data$KRAS <- as.factor(data$KRAS)

data1 <- data %>%
  filter(Type.Adjuvant != "NA") %>%  # remove rows where Type.Adjuvant is "NA"
  droplevels()                       # drop the unused factor level

data$Type.Adjuvant <- as.factor(data$Type.Adjuvant)

View(data1)

summary(data) # quick summary to check data types and missing values
```

```
##   Patient ID        Survival time (days)     Event        Tumor size (cm)
##  Length:95          Min.   :  50.0       Min.   :0.0000   Min.   :1.100
##  Class :character   1st Qu.: 898.5       1st Qu.:0.0000   1st Qu.:2.000
##  Mode  :character   Median :1760.0       Median :0.0000   Median :2.400
##                     Mean   :1471.5       Mean   :0.4105   Mean   :2.855
##                     3rd Qu.:1981.0       3rd Qu.:1.0000   3rd Qu.:3.500
##                     Max.   :2532.0       Max.   :1.0000   Max.   :7.000
##
##  Grade      Stage         Age            Sex       Cigarette  Pack per year
##  1: 6   IB     :21   Min.   :48.00   Female:68   Current:11   Min.   :  0.000
##  2:48   IA2    :20   1st Qu.:60.00   Male  :27   Former :62   1st Qu.:  2.125
##  3:41   IA3    :20   Median :67.00               Never  :22   Median : 25.000
##         IIIA   :13   Mean   :66.59                            Mean   : 29.254
##         IIB    :12   3rd Qu.:72.50                            3rd Qu.: 45.000
##         IIIB   : 3   Max.   :88.00                            Max.   :105.000
##         (Other): 6
##   Type.Adjuvant     batch                          EGFR          KRAS
##  Chemo   :17    Min.   :1.000   Negative             :66   Negative:32
##  Chemorad: 4    1st Qu.:2.000   NA                   : 9   NA      :30
##  NA      : 2    Median :3.000   Exon 19              : 8   G12C    : 9
##  None    :71    Mean   :2.432   Exon 21 (L858R)      : 4   G12V    : 8
##  XRT     : 1    3rd Qu.:3.000   Exon 21              : 3   G12D    : 6
##                 Max.   :3.000   Exon 19 (15bp delete): 2   G12A    : 3
##                                 (Other)              : 3   (Other) : 7
```

```r
summary(data1)  # quick summary to check data types and missing values
```

```
##   Patient ID        Survival time (days)     Event        Tumor size (cm)
##  Length:93          Min.   :  50         Min.   :0.0000   Min.   :1.100
##  Class :character   1st Qu.: 902         1st Qu.:0.0000   1st Qu.:2.000
##  Mode  :character   Median :1810         Median :0.0000   Median :2.400
##                     Mean   :1485         Mean   :0.3978   Mean   :2.832
##                     3rd Qu.:1986         3rd Qu.:1.0000   3rd Qu.:3.500
##                     Max.   :2532         Max.   :1.0000   Max.   :7.000
##
##  Grade      Stage         Age            Sex       Cigarette  Pack per year
```

```
##  1: 5   IB     :21   Min.   :48.00   Female:67   Current:10   Min.   :  0.00
##  2:47   IA2    :20   1st Qu.:60.00   Male  :26   Former :62   1st Qu.:  3.00
##  3:41   IA3    :20   Median :67.00               Never  :21   Median : 25.00
##         IIB    :12   Mean   :66.52                            Mean   : 29.56
##         IIIA   :11   3rd Qu.:72.00                            3rd Qu.: 45.00
##         IIIB   : 3   Max.   :88.00                            Max.   :105.00
##         (Other): 6
##  Type.Adjuvant          batch                          EGFR          KRAS
##  Length:93          Min.   :1.000   Negative             :65   Negative:32
##  Class :character   1st Qu.:2.000   NA                   : 9   NA      :29
##  Mode  :character   Median :3.000   Exon 19              : 8   G12C    : 8
##                     Mean   :2.441   Exon 21 (L858R)      : 4   G12V    : 8
##                     3rd Qu.:3.000   Exon 19 (15bp delete): 2   G12D    : 6
##                     Max.   :3.000   Exon 19 (9bp delete) : 2   G12A    : 3
##                                     (Other)              : 3   (Other) : 7
```

```
#### Survival Analysis ######

s = Surv(data$`Survival time (days)`, data$Event) # create a survival object using time and event colum
s # :1 → event (death) happened and # + → censored (alive or lost to follow-up).
```

```
##  [1] 2329  2532+ 2271+ 2193+ 2387+ 2225+ 2240+ 2314+  299  2295+ 2135+ 1956+
## [13] 2278+ 1927   837   453  2238+ 2248+ 1435  1922+ 1300  2318+ 2059+ 1865+
## [25]  978+ 1961+ 2240+ 2186+ 2041  1810  2237   647   874  2021+ 2256+   66
## [37]  855   631   592  1435+ 1760   228+ 1079  2022+ 2059+ 1614+ 1904+  895
## [49] 1986+ 1546+  135+  990+ 1976+  942  1373  1161   354   676  1579  1886+
## [61] 1834+  811  1057  1937+  681   579   208  1860+ 1862+  768+ 1841+  366
## [73] 1349  1834  1054  1353   923   902+ 1868+ 1430+   50+ 1217   335+  403+
## [85] 1945+  819  1881+ 1207+ 1889+ 1033  1919+ 1911+ 1935+ 1760+ 1922+
```

```
sfit = survfit(Surv(`Survival time (days)`, Event) ~ 1, data = data) # baseline hazard
sfit1 = survfit(Surv(`Survival time (days)`, Event) ~ Sex, data = data) # effect of sex
sfit2 = survfit(Surv(`Survival time (days)`, Event) ~ Grade, data = data) # effect of grade
sfit3 = survfit(Surv(`Survival time (days)`, Event) ~ Type.Adjuvant, data = data1) # effect of therapy

# summarize the survival fits
summary(sfit)
```

```
## Call: survfit(formula = Surv(`Survival time (days)`, Event) ~ 1, data = data)
##
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    66     94       1    0.989  0.0106        0.969        1.000
##   208     92       1    0.979  0.0150        0.950        1.000
##   299     90       1    0.968  0.0183        0.932        1.000
##   354     88       1    0.957  0.0212        0.916        0.999
##   366     87       1    0.946  0.0236        0.901        0.993
##   453     85       1    0.935  0.0258        0.885        0.987
##   579     84       1    0.923  0.0278        0.871        0.980
##   592     83       1    0.912  0.0296        0.856        0.972
##   631     82       1    0.901  0.0313        0.842        0.965
##   647     81       1    0.890  0.0328        0.828        0.957
##   676     80       1    0.879  0.0342        0.814        0.949
##   681     79       1    0.868  0.0356        0.801        0.940
##   811     77       1    0.857  0.0368        0.787        0.932
##   819     76       1    0.845  0.0380        0.774        0.923
```

```
##   837     75       1    0.834  0.0392        0.761        0.914
##   855     74       1    0.823  0.0402        0.748        0.906
##   874     73       1    0.812  0.0412        0.735        0.896
##   895     72       1    0.800  0.0422        0.722        0.887
##   923     70       1    0.789  0.0431        0.709        0.878
##   942     69       1    0.777  0.0439        0.696        0.868
##  1033     66       1    0.766  0.0448        0.683        0.859
##  1054     65       1    0.754  0.0457        0.669        0.849
##  1057     64       1    0.742  0.0464        0.656        0.839
##  1079     63       1    0.730  0.0472        0.643        0.829
##  1161     62       1    0.718  0.0479        0.631        0.819
##  1217     60       1    0.707  0.0485        0.617        0.808
##  1300     59       1    0.695  0.0492        0.605        0.798
##  1349     58       1    0.683  0.0498        0.592        0.787
##  1353     57       1    0.671  0.0503        0.579        0.777
##  1373     56       1    0.659  0.0508        0.566        0.766
##  1435     54       1    0.646  0.0513        0.553        0.755
##  1579     51       1    0.634  0.0519        0.540        0.744
##  1760     49       1    0.621  0.0524        0.526        0.732
##  1810     47       1    0.608  0.0529        0.512        0.721
##  1834     46       1    0.594  0.0534        0.498        0.709
##  1927     31       1    0.575  0.0550        0.477        0.694
##  2041     21       1    0.548  0.0588        0.444        0.676
##  2237     14       1    0.509  0.0664        0.394        0.657
##  2329      3       1    0.339  0.1453        0.146        0.786
```

```
summary(sfit1)
```

```
## Call: survfit(formula = Surv(`Survival time (days)`, Event) ~ Sex,
##     data = data)
##
##                 Sex=Female
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    66     68       1    0.985  0.0146        0.957        1.000
##   299     65       1    0.970  0.0208        0.930        1.000
##   592     62       1    0.954  0.0257        0.905        1.000
##   631     61       1    0.939  0.0297        0.882        0.999
##   647     60       1    0.923  0.0330        0.861        0.990
##   676     59       1    0.908  0.0360        0.840        0.981
##   681     58       1    0.892  0.0386        0.819        0.971
##   811     56       1    0.876  0.0411        0.799        0.960
##   819     55       1    0.860  0.0433        0.779        0.949
##   837     54       1    0.844  0.0453        0.760        0.938
##   855     53       1    0.828  0.0472        0.741        0.926
##   874     52       1    0.812  0.0489        0.722        0.914
##   895     51       1    0.796  0.0505        0.703        0.902
##   923     49       1    0.780  0.0520        0.685        0.889
##  1033     46       1    0.763  0.0536        0.665        0.876
##  1054     45       1    0.746  0.0550        0.646        0.862
##  1057     44       1    0.729  0.0563        0.627        0.848
##  1079     43       1    0.712  0.0575        0.608        0.834
##  1161     42       1    0.695  0.0586        0.589        0.820
##  1300     40       1    0.678  0.0596        0.571        0.805
##  1349     39       1    0.661  0.0606        0.552        0.791
##  1353     38       1    0.643  0.0614        0.533        0.776
```

```
##  1579     34       1    0.624  0.0625        0.513        0.759
##  1927     23       1    0.597  0.0654        0.482        0.740
##  2041     15       1    0.557  0.0721        0.432        0.718
##
##                Sex=Male
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   208     26       1    0.962  0.0377        0.890        1.000
##   354     25       1    0.923  0.0523        0.826        1.000
##   366     24       1    0.885  0.0627        0.770        1.000
##   453     23       1    0.846  0.0708        0.718        0.997
##   579     22       1    0.808  0.0773        0.670        0.974
##   942     21       1    0.769  0.0826        0.623        0.949
##  1217     20       1    0.731  0.0870        0.579        0.923
##  1373     19       1    0.692  0.0905        0.536        0.895
##  1435     18       1    0.654  0.0933        0.494        0.865
##  1760     17       1    0.615  0.0954        0.454        0.834
##  1810     16       1    0.577  0.0969        0.415        0.802
##  1834     15       1    0.538  0.0978        0.377        0.769
##  2237      4       1    0.404  0.1377        0.207        0.788
##  2329      1       1    0.000     NaN           NA           NA
```

```
summary(sfit2)
```

```
## Call: survfit(formula = Surv(`Survival time (days)`, Event) ~ Grade,
##     data = data)
##
##                Grade=1
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   299      6       1    0.833   0.152        0.583            1
##   895      5       1    0.667   0.192        0.379            1
##
##                Grade=2
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    66     48       1    0.979  0.0206        0.940        1.000
##   453     45       1    0.957  0.0295        0.901        1.000
##   631     44       1    0.936  0.0360        0.868        1.000
##   647     43       1    0.914  0.0412        0.837        0.998
##   819     42       1    0.892  0.0456        0.807        0.986
##   855     41       1    0.870  0.0494        0.779        0.973
##  1079     40       1    0.849  0.0527        0.751        0.959
##  1161     39       1    0.827  0.0557        0.725        0.944
##  1300     38       1    0.805  0.0583        0.699        0.928
##  1353     37       1    0.783  0.0607        0.673        0.912
##  1435     35       1    0.761  0.0629        0.647        0.895
##  1834     31       1    0.736  0.0655        0.619        0.877
##  1927     20       1    0.700  0.0718        0.572        0.856
##  2041     15       1    0.653  0.0808        0.512        0.832
##  2237      9       1    0.580  0.0992        0.415        0.811
##
##                Grade=3
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   208     39       1    0.974  0.0253       0.9260        1.000
##   354     37       1    0.948  0.0358       0.8804        1.000
##   366     36       1    0.922  0.0434       0.8404        1.000
##   579     35       1    0.895  0.0495       0.8034        0.998
```

```
##   592     34       1    0.869  0.0546       0.7683        0.983
##   676     33       1    0.843  0.0590       0.7347        0.967
##   681     32       1    0.816  0.0627       0.7022        0.949
##   811     30       1    0.789  0.0663       0.6694        0.930
##   837     29       1    0.762  0.0694       0.6374        0.911
##   874     28       1    0.735  0.0720       0.6063        0.890
##   923     26       1    0.706  0.0746       0.5744        0.869
##   942     25       1    0.678  0.0768       0.5433        0.847
##  1033     22       1    0.647  0.0792       0.5093        0.823
##  1054     21       1    0.617  0.0812       0.4762        0.798
##  1057     20       1    0.586  0.0828       0.4440        0.773
##  1217     18       1    0.553  0.0844       0.4103        0.746
##  1349     17       1    0.521  0.0854       0.3774        0.718
##  1373     16       1    0.488  0.0861       0.3455        0.690
##  1579     15       1    0.456  0.0863       0.3143        0.660
##  1760     14       1    0.423  0.0860       0.2840        0.630
##  1810     13       1    0.390  0.0853       0.2544        0.599
##  2329      2       1    0.195  0.1445       0.0458        0.833
```

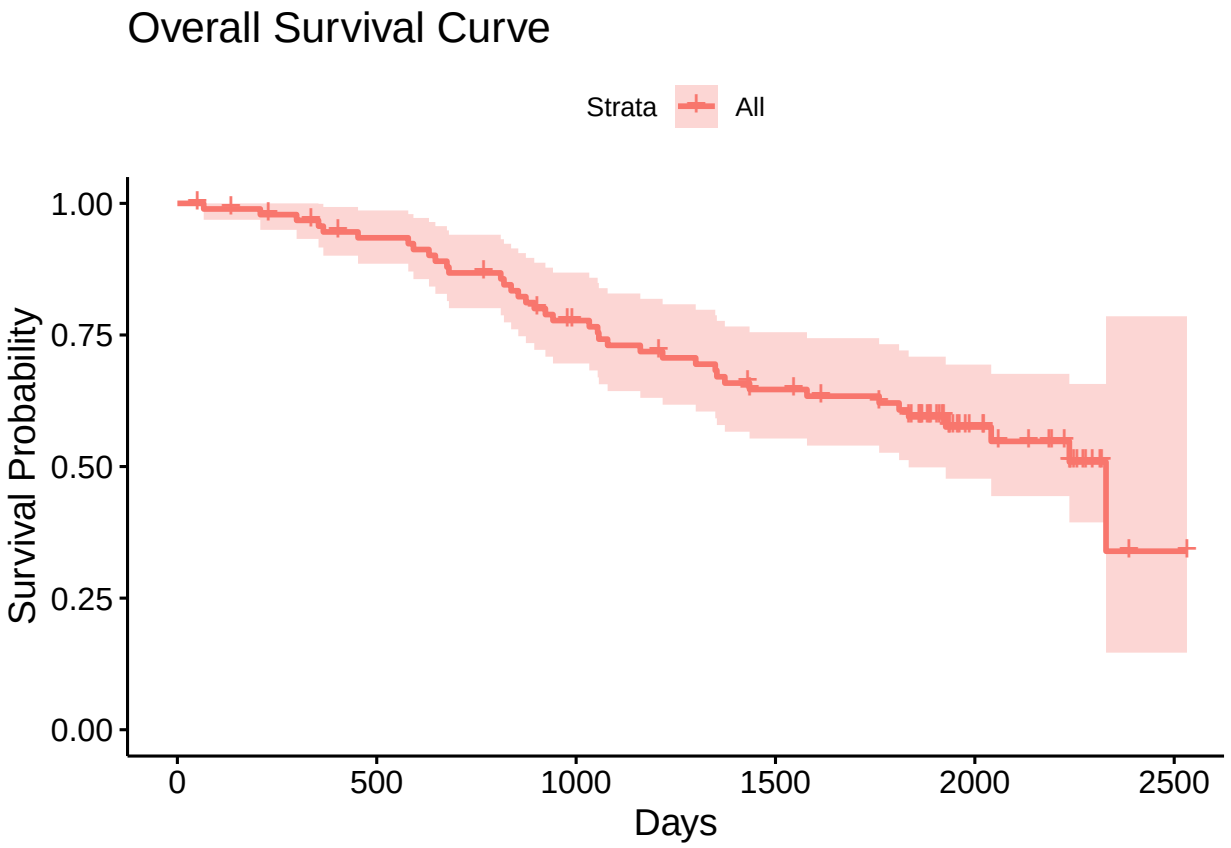
```
summary(sfit3)
```

```
## Call: survfit(formula = Surv(`Survival time (days)`, Event) ~ Type.Adjuvant,
##     data = data1)
##
##                 Type.Adjuvant=Chemo
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    66     17       1    0.941  0.0571        0.836        1.000
##   354     16       1    0.882  0.0781        0.742        1.000
##   453     15       1    0.824  0.0925        0.661        1.000
##   647     14       1    0.765  0.1029        0.587        0.995
##  1300     13       1    0.706  0.1105        0.519        0.959
##  1349     12       1    0.647  0.1159        0.455        0.919
##  1373     11       1    0.588  0.1194        0.395        0.876
##
##                 Type.Adjuvant=Chemorad
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   676      4       1     0.75   0.217       0.4259            1
##   811      3       1     0.50   0.250       0.1877            1
##   942      2       1     0.25   0.217       0.0458            1
##  1054      1       1     0.00     NaN           NA           NA
##
##                 Type.Adjuvant=None
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   208     69       1    0.986  0.0144        0.958        1.000
##   366     66       1    0.971  0.0205        0.931        1.000
##   579     64       1    0.955  0.0252        0.907        1.000
##   592     63       1    0.940  0.0290        0.885        0.999
##   631     62       1    0.925  0.0322        0.864        0.990
##   819     60       1    0.910  0.0352        0.843        0.981
##   837     59       1    0.894  0.0378        0.823        0.972
##   855     58       1    0.879  0.0402        0.803        0.961
##   874     57       1    0.863  0.0423        0.784        0.951
##   895     56       1    0.848  0.0443        0.765        0.939
##   923     54       1    0.832  0.0462        0.747        0.928
##  1033     51       1    0.816  0.0481        0.727        0.916
```

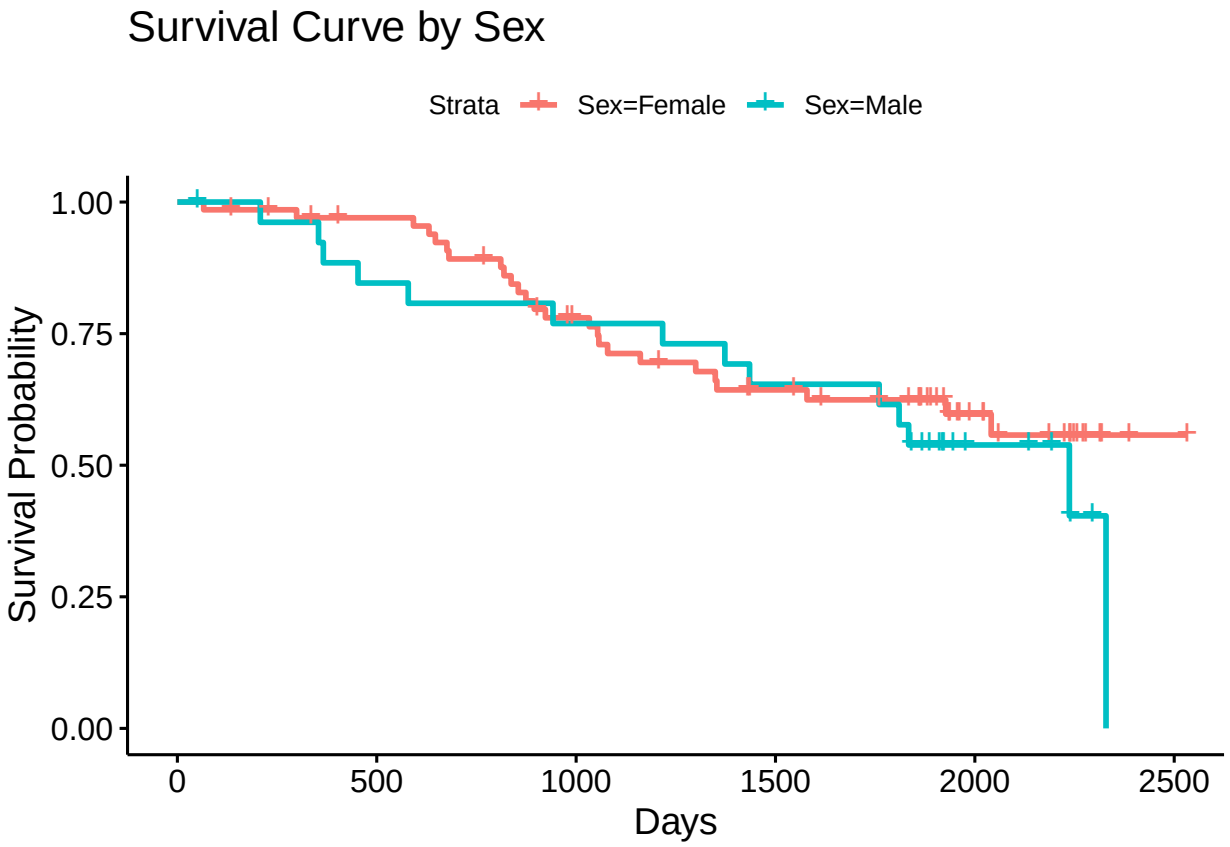
```
##  1057     50       1    0.800  0.0498        0.708        0.903
##  1079     49       1    0.783  0.0514        0.689        0.891
##  1161     48       1    0.767  0.0529        0.670        0.878
##  1217     46       1    0.750  0.0543        0.651        0.865
##  1353     45       1    0.734  0.0556        0.632        0.851
##  1579     42       1    0.716  0.0569        0.613        0.837
##  1760     40       1    0.698  0.0582        0.593        0.822
##  1810     38       1    0.680  0.0595        0.573        0.807
##  1834     37       1    0.662  0.0607        0.553        0.792
##  1927     24       1    0.634  0.0641        0.520        0.773
##  2041     18       1    0.599  0.0696        0.477        0.752
##  2237     12       1    0.549  0.0797        0.413        0.730
##  2329      3       1    0.366  0.1585        0.157        0.855
##
##                 Type.Adjuvant=XRT
##         time       n.risk      n.event     survival      std.err lower 95% CI
##          681            1            1            0          NaN           NA
## upper 95% CI
##           NA
```

```r
# plot Kaplan-Meier curves using ggsurvplot

p = ggsurvplot(
  sfit,
  data = data,
  xlab = "Days",
  ylab = "Survival Probability",
  title = "Overall Survival Curve"
)

p1 = ggsurvplot(
  sfit1,
  data = data,
  xlab = "Days",
  ylab = "Survival Probability",
  title = "Survival Curve by Sex"
)

p2 = ggsurvplot(
  sfit2,
  data = data,
  xlab = "Days",
  ylab = "Survival Probability",
  title = "Survival Curve by Grade"
)

p3 = ggsurvplot(
  sfit3,
  data = data1,
  xlab = "Days",
  ylab = "Survival Probability",
  title = "Survival Curve by Therapy"
)
```

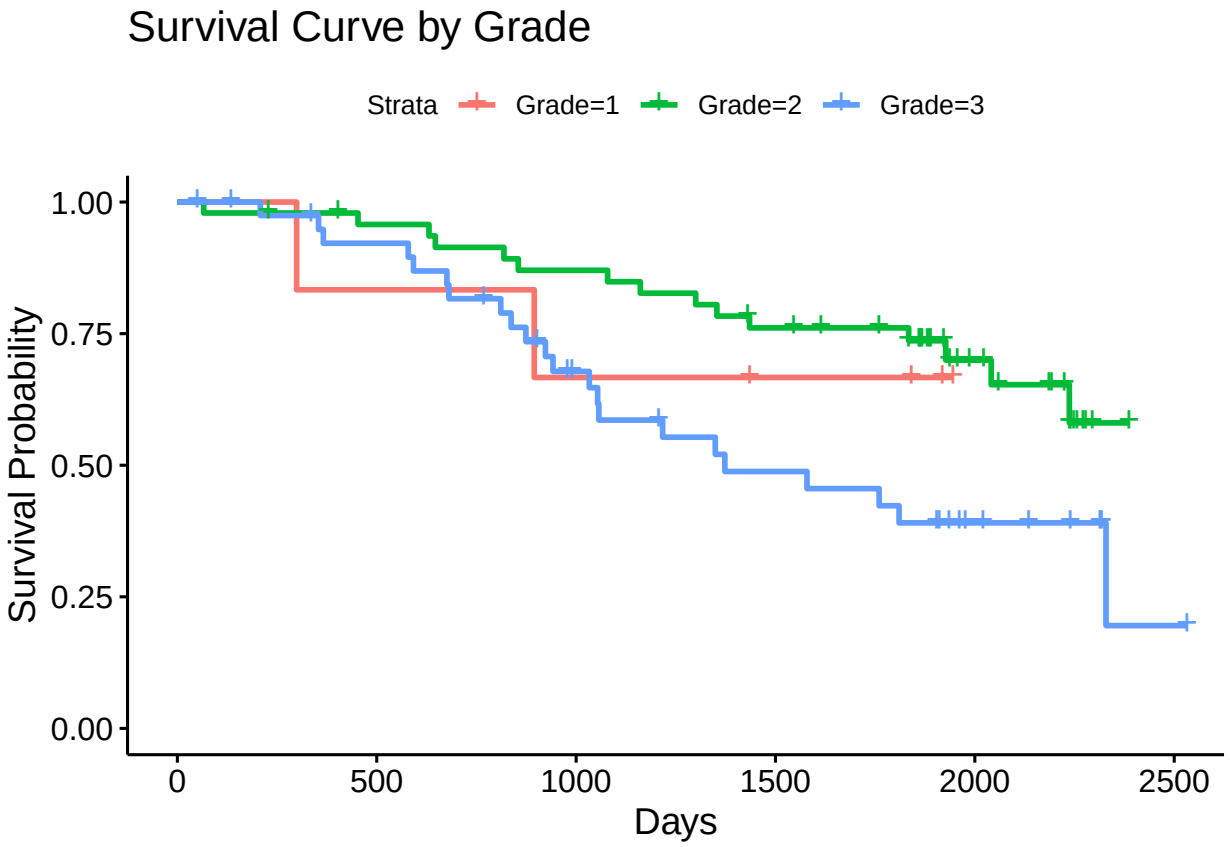
```
p
```


Overall Survival Curve
Strata
All
1.00
0.75
0.50
0.25
0.00
Survival Probability
0
500
1000
1500
2000
2500
Days

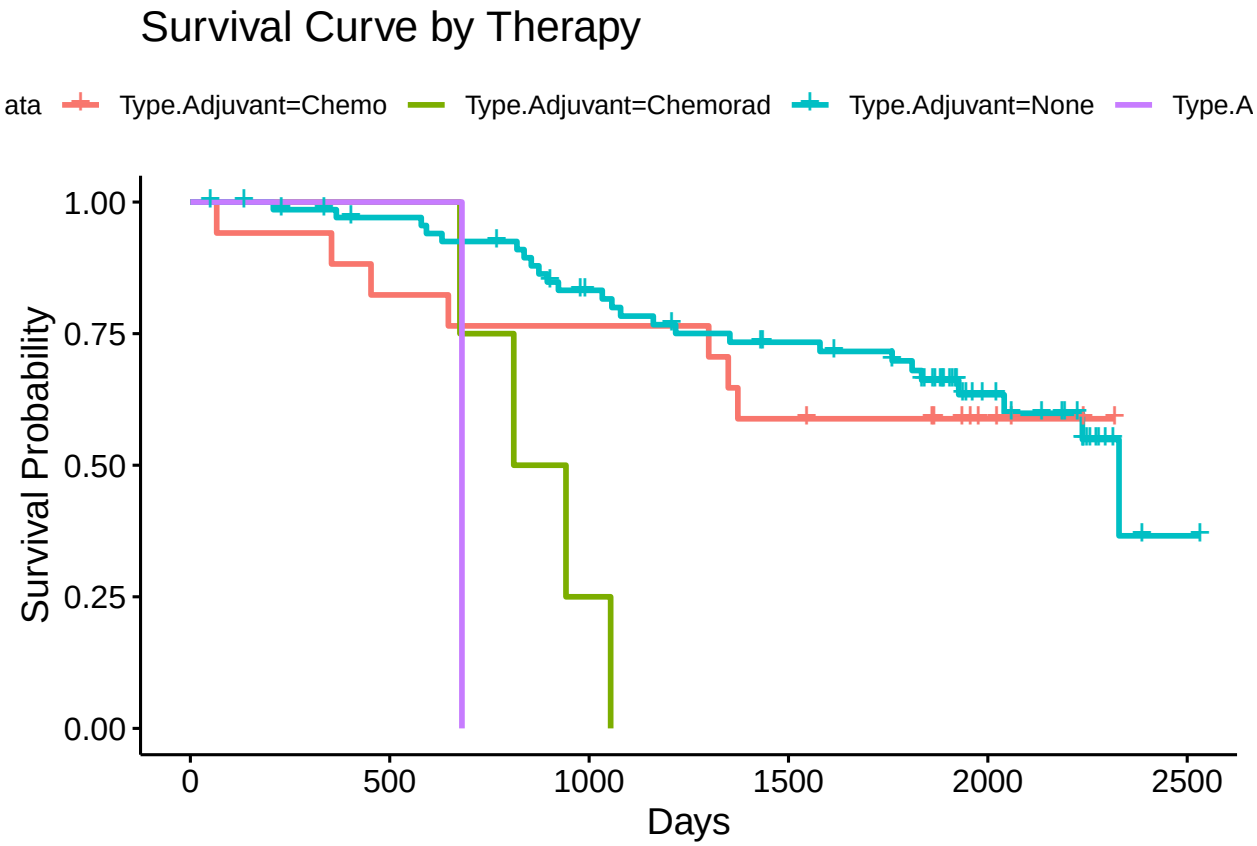
```
p1
```


Survival Curve by Sex
Strata
Sex=Female
Sex=Male
Survival Probability
1.00
0.75
0.50
0.25
0.00
0
500
1000
1500
2000
2500
Days

```
p2
```


Survival Curve by Grade
Strata
Grade=1
Grade=2
Grade=3
Survival Probability
1.00
0.75
0.50
0.25
0.00
0
500
1000
1500
2000
2500
Days

```
p3
```




```
# Save p
ggsave("Overall_Survival.png", plot = p$plot, width = 7, height = 5, dpi = 300)

# Save p1
ggsave("Survival_by_Sex.png", plot = p1$plot, width = 7, height = 5, dpi = 300)

# Save p2
ggsave("Survival_by_Grade.png", plot = p2$plot, width = 7, height = 5, dpi = 300)

# Save p3
ggsave("Survival_by_Therapy.png", plot = p3$plot, width = 7, height = 5, dpi = 300)

# fit Cox proportional hazards models to estimate risk (hazard ratios)

sfit_none = coxph(Surv(`Survival time (days)`, Event) ~ 1, data = data)
summary(sfit_none)
```

```
## Call:  coxph(formula = Surv(`Survival time (days)`, Event) ~ 1, data = data)
##
## Null model
##   log likelihood= -158.5004
##   n= 95
```

```
sfit1_sex = coxph(Surv(`Survival time (days)`, Event) ~ Sex, data = data)
summary(sfit1_sex)
```

```
## Call:
```

```
## coxph(formula = Surv(`Survival time (days)`, Event) ~ Sex, data = data)
##
##   n= 95, number of events= 39
##
##           coef exp(coef) se(coef)     z Pr(>|z|)
## SexMale 0.2828    1.3268   0.3345 0.845    0.398
##
##         exp(coef) exp(-coef) lower .95 upper .95
## SexMale     1.327     0.7537    0.6888     2.556
##
## Concordance= 0.518  (se = 0.04 )
## Likelihood ratio test= 0.69  on 1 df,   p=0.4
## Wald test            = 0.71  on 1 df,   p=0.4
## Score (logrank) test = 0.72  on 1 df,   p=0.4
```

```
sfit2_grade = coxph(Surv(`Survival time (days)`, Event) ~ Grade, data = data)
summary(sfit2_grade)
```

```
## Call:
## coxph(formula = Surv(`Survival time (days)`, Event) ~ Grade,
##     data = data)
##
##   n= 95, number of events= 39
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## Grade2 -0.2907    0.7477   0.7546 -0.385    0.700
## Grade3  0.5908    1.8054   0.7412  0.797    0.425
##
##        exp(coef) exp(-coef) lower .95 upper .95
## Grade2    0.7477     1.3374    0.1704     3.281
## Grade3    1.8054     0.5539    0.4223     7.718
##
## Concordance= 0.617  (se = 0.041 )
## Likelihood ratio test= 6.98  on 2 df,   p=0.03
## Wald test            = 6.89  on 2 df,   p=0.03
## Score (logrank) test = 7.3  on 2 df,   p=0.03
```

```
sfit3_adjuvant = coxph(Surv(`Survival time (days)`, Event) ~ Type.Adjuvant, data = data1)
summary(sfit3_adjuvant)
```

```
## Call:
## coxph(formula = Surv(`Survival time (days)`, Event) ~ Type.Adjuvant,
##     data = data1)
##
##   n= 93, number of events= 37
##
##                           coef exp(coef) se(coef)      z Pr(>|z|)
## Type.AdjuvantChemorad  1.7277    5.6276   0.6564  2.632  0.00849 **
## Type.AdjuvantNone     -0.2077    0.8125   0.4301 -0.483  0.62924
## Type.AdjuvantXRT       2.1821    8.8646   1.1102  1.965  0.04937 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                       exp(coef) exp(-coef) lower .95 upper .95
## Type.AdjuvantChemorad    5.6276     0.1777    1.5545    20.373
```

```
## Type.AdjuvantNone        0.8125     1.2308    0.3497     1.888
## Type.AdjuvantXRT         8.8646     0.1128    1.0060    78.110
##
## Concordance= 0.589  (se = 0.041 )
## Likelihood ratio test= 10.25  on 3 df,   p=0.02
## Wald test            = 14.65  on 3 df,   p=0.002
## Score (logrank) test = 20.24  on 3 df,   p=2e-04
```