Introduction to Kaplan-Meier analysis

The Kaplan-Meier estimator is given by the following formula:

$$\hat{S}(t) = \prod_{t_i \leq t} (1 - \hat{q}_i) = \prod_{t_i \leq t} \left(1 - \frac{q_i}{n_i}\right)$$

$\hat{S}(t)$ denoting the survival function at time t. More technical detail found in the book (Applied Survival Analysis Using R)

Dataset

veteran: dataset of 137 observations x 8 variables form a two-treatment randomized trial for lung cancer.

trt: 1=standard 2=test
celltype: 1=squamous, 2=smallcell, 3=adeno, 4=large
time: survival time
status: censoring status
karno: Karnofsky performance score (100=good)
diagtime: months from diagnosis to randomisation
ageA: in years
prior: prior therapy 0=no, 10=yes

```
> head(veteran)
  trt celltype time status karno diagtime age prior
1   1 squamous   72      1    60        7  69     0
2   1 squamous  411      1    70        5  64    10
3   1 squamous  228      1    60        3  38     0
4   1 squamous  126      1    60        9  63    10
5   1 squamous  118      1    70       11  65    10
6   1 squamous   10      1    20        5  49     0
```

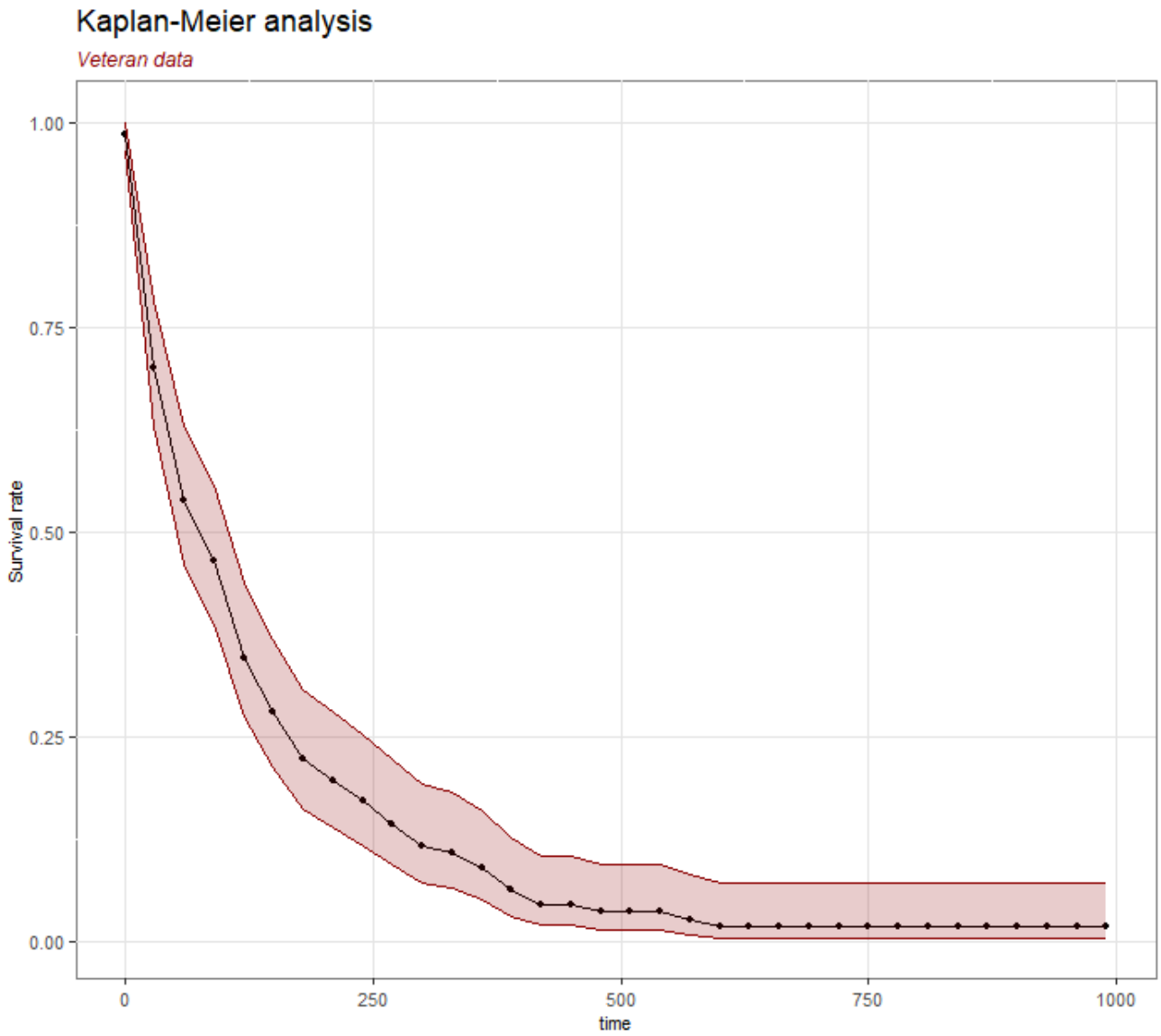
Summary

From this initial summary which has class "summary survfit", we will make a dataframe ready for ploting withing the ggplot2 environment.

```
> survival.30.dataset = summary(kma_1, times = c(1, (1:33)*30))
> survival.30.dataset
Call: survfit(formula = Surv(time, status) ~ 1, data = veteran)

 time n.risk n.event survival std.err lower 95% CI upper 95% CI
    1    137       2    0.985  0.0102       0.96552        1.0000
   30     97      39    0.700  0.0392       0.62774        0.7816
   60     73      22    0.538  0.0427       0.46070        0.6288
   90     62      10    0.464  0.0428       0.38731        0.5560
  120     43      15    0.346  0.0414       0.27345        0.4372
  150     34       8    0.280  0.0395       0.21240        0.3693
  180     27       7    0.222  0.0369       0.16066        0.3079
  210     23       3    0.197  0.0355       0.13814        0.2802
  240     19       3    0.171  0.0338       0.11613        0.2520
  270     16       3    0.144  0.0319       0.09338        0.2223
  300     13       3    0.117  0.0295       0.07147        0.1917
  330     12       1    0.108  0.0285       0.06439        0.1813
  360     10       2    0.090  0.0265       0.05061        0.1602
...
```

Kaplan-Meier analysis

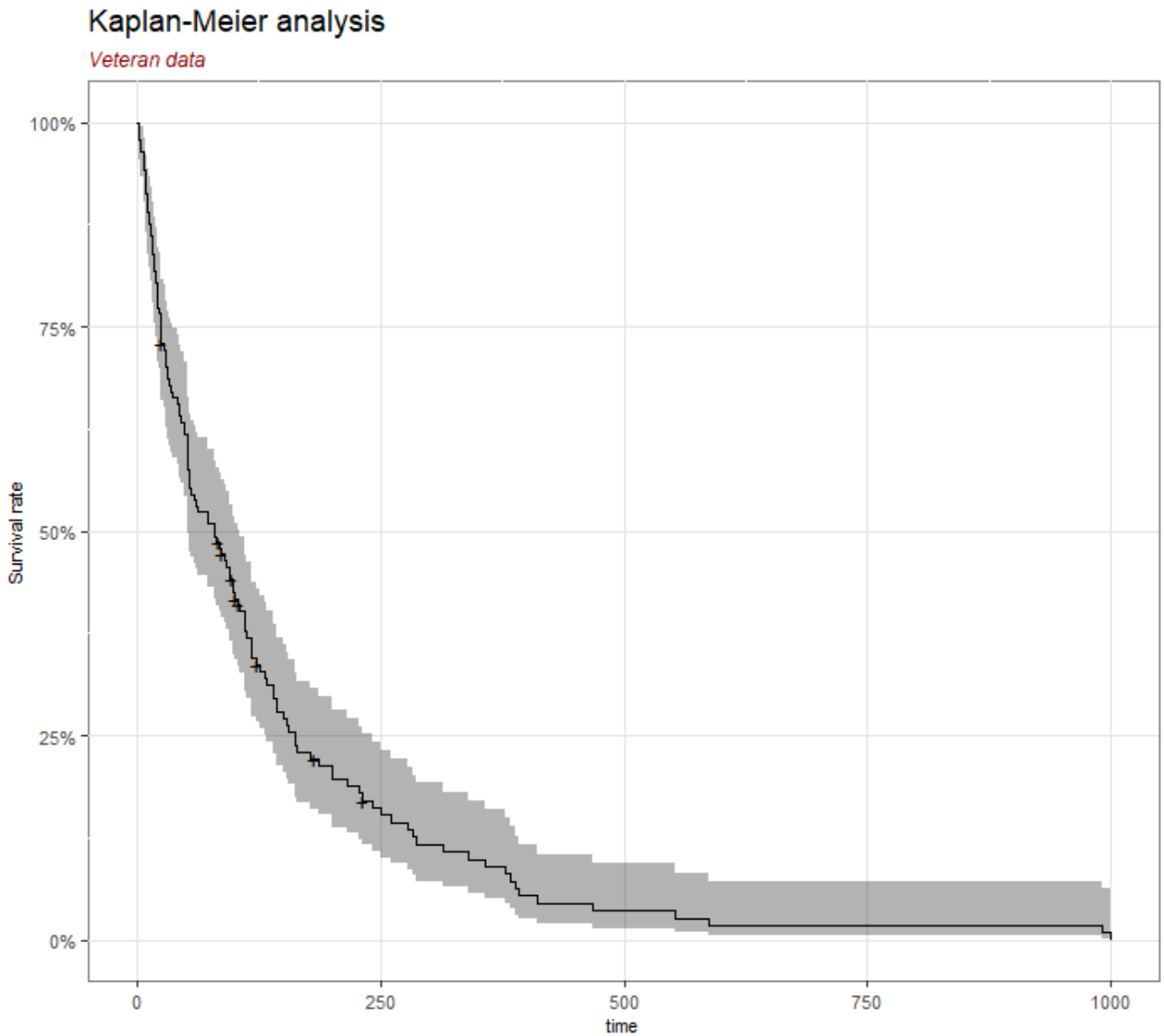


	time	surv
1	1	0.9854
2	30	0.7004
3	60	0.5382
4	90	0.464
5	120	0.3458
6	150	0.2801
7	180	0.2224
8	210	0.1967
9	240	0.1711
10	270	0.1441
11	300	0.1171
12	330	0.1081
13	360	0.09
14	390	0.063
15	420	0.045
16	450	0.045
17	480	0.036
18	510	0.036
19	540	0.036
20	570	0.027

Main observations

- At the first month (after 30 days), the survival rate or probability of survival is about 70%.
- There seems to be some kind of breakup point at 6 months (after 180 days) as the slope gets less steep.
- After on year, the survival rate is lower than 10%. A patient has a 10% or less probability of surving one year.
- Information about censoring (a vertical line on the Kaplan-Maier survival function) is obtained in R using "autoplot()". It is shown in the next slide.

Kaplan-Meier analysis using "autoplot()"



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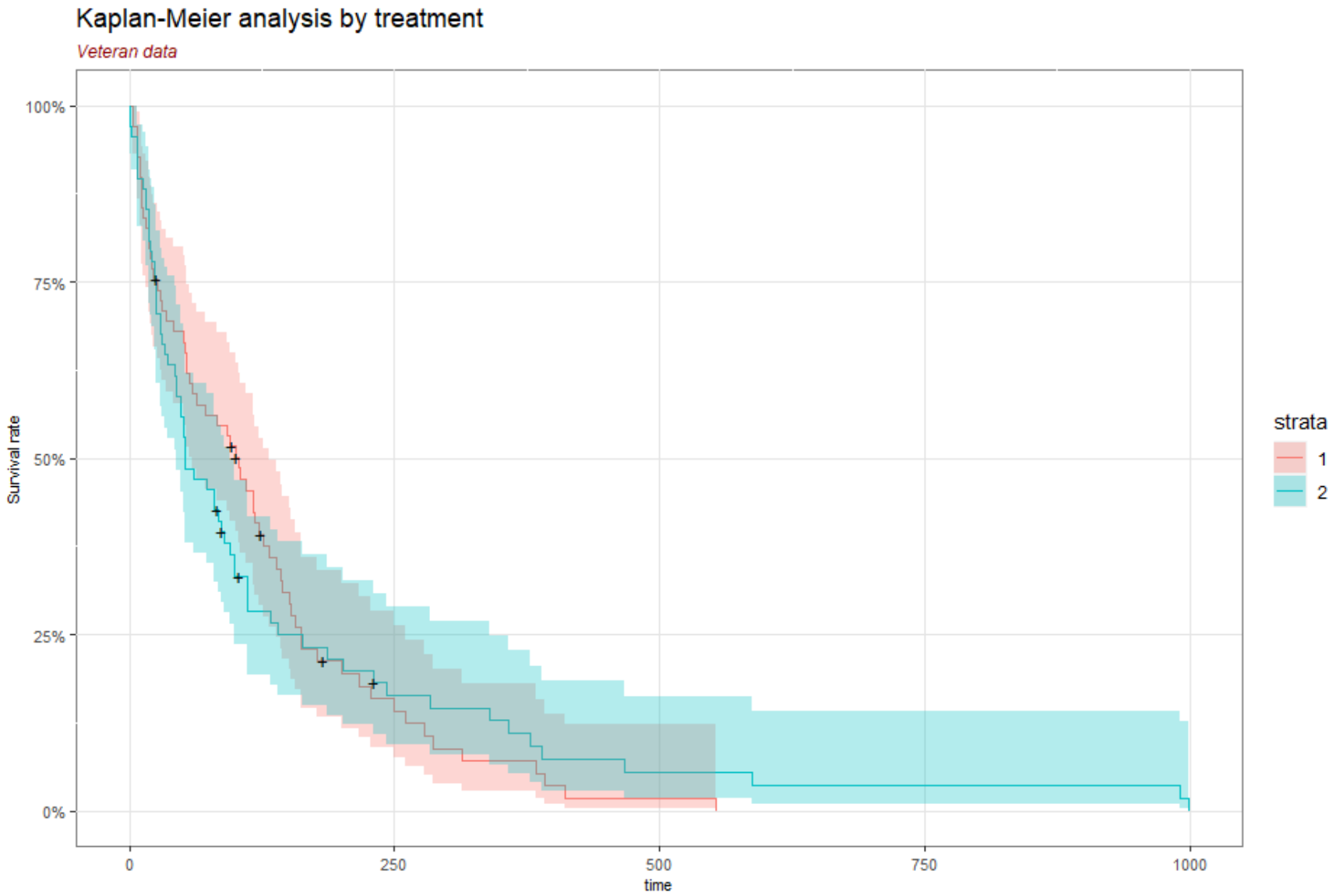
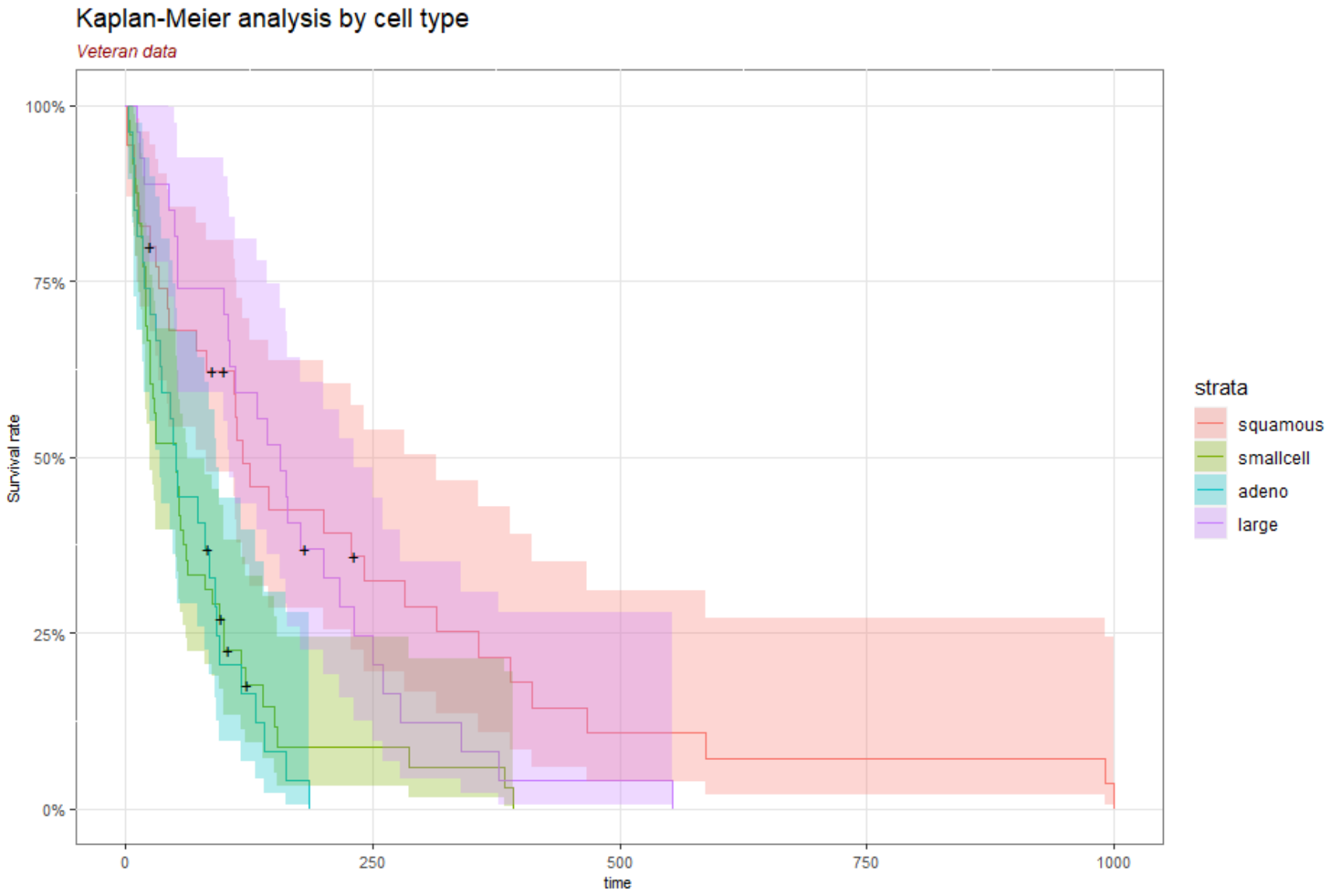
Kaplan-Meier analysis by treatment



Kaplan-Meier analysis by cell type



Main observations

- Treatment stratum 2 has the overall better survival rate with a better suvival curve (overall less steep)
- Cell type "squamous" has the overall better survival rate compared to small cell, adeno and lage.

R code (1/5) - Load libraries and dataset

```
> #load libraries
> library(survival)
> library(ggplot2)
> library(gridExtra)

> # load data and head of the dataset
> data(veteran)
> head(veteran)
  trt celltype time status karno diagtime age prior
1   1 squamous   72      1    60        7  69     0
2   1 squamous  411      1    70        5  64    10
3   1 squamous  228      1    60        3  38     0
4   1 squamous  126      1    60        9  63    10
5   1 squamous  118      1    70       11  65    10
6   1 squamous   10      1    20        5  49     0
```

R code (2/6) - Dataset with censoring

```
> km = with(veteran, Surv(time, status))
> head(km, 100)
  [1]  72  411  228  126  118   10   82  110  314  100+  42    8  144   25+  11
        30  384    4   54   13  123+
 [22]  97+ 153   59  117   16  151   22   56   21   18  139   20   31   52  287
        18   51  122   27   54    7
 [43]  63  392   10    8   92   35  117  132   12  162    3   95  177  162  216
       553  278   12  260  200  156
 [64] 182+ 143  105  103  250  100  999  112   87+ 231+ 242  991  111    1  587
       389   33   25  357  467  201
 [85]   1   30   44  283   15   25  103+  21   13   87    2   20    7   24   99
         8
```

R code (3/6) - Kaplan-Meier analysis

```
 1 > # Kaplan-Meier estimates of the probability of survival over time
 2 > kma_1 = survfit(Surv(time, status) ~ 1, data=veteran)
 3 > # max time: 999 days (about 33 months (30 days))
 4 > survival.30.dataset = summary(kma_1, times = c(1, (1:33)*30))
 5 > # convert summary to data.frame for plotting
 6 > cols = lapply(1:15 , function(x) survival.30.dataset[x])
 7 > df = do.call(data.frame, cols)
 8 >
 9 > # table to be displayed next to the graph as a second graph
10 > df2 = df[1:20, c(2,6)]
11 > df2$surv = round(df2$surv, 4)
```

R code (4/6) - plotting with ggplot2

```
# KM plot (ggplot2)
p1 = ggplot(df, aes(x = time, y = surv)) +
  geom_line(color = 'black') +
  geom_point(size = 1.2) +
  geom_ribbon(aes(ymin = lower, ymax = upper), alpha=0.2, fill= 'darkred', col =
      'darkred') +

  labs(title = 'Kaplan-Meier analysis',
       subtitle = 'Veteran data',
       y="Survival rate", x="time") +
  theme(axis.text=element_text(size=8),
        axis.title=element_text(size=8),
        plot.subtitle=element_text(size=9, face="italic", color="darkred"),
        panel.background = element_rect(fill = "white", colour = "grey50"),
        panel.grid.major = element_line(colour = "grey90"))

p2 = tableGrob(df2)

grid.arrange(p1, p2, ncol = 2, nrow = 1, widths = c(6, 2))
```

R code (5/6) - autoplot

```
# or, more quickly (and with information about censoring)
p3 = autoplot(kma_1) +
  labs(title = 'Kaplan-Meier analysis',
       subtitle = 'Veteran data',
       y="Survival rate", x="time") +
  theme(axis.text=element_text(size=8),
        axis.title=element_text(size=8),
        plot.subtitle=element_text(size=9, face="italic", color="darkred"),
        panel.background = element_rect(fill = "white", colour = "grey50"),
        panel.grid.major = element_line(colour = "grey90"))

p4 = tableGrob(df2) # to have a table with time and survival rate
grid.arrange(p3, p4, ncol = 2, nrow = 1, widths = c(6, 2))
```

R code (6/6) - Analysis by treatment

```r
# Analysis by treatment

# Kaplan-Meier estimates of the probability of survival over time
kma_3 = survfit(Surv(time, status) ~ trt, data=veteran)
# max time: 999 days (about 33 months (30 days))
survival.30.dataset.celltype = summary(kma_3, times = c(1, (1:33)*30))

# plotting
autoplot(kma_3) +
  labs(title = 'Kaplan-Meier analysis by celltype',
       subtitle = 'Veteran data',
       y="Survival rate", x="time") +
  theme(axis.text=element_text(size=8),
        axis.title=element_text(size=8),
        plot.subtitle=element_text(size=9, face="italic", color="darkred"),
        panel.background = element_rect(fill = "white", colour = "grey50"),
        panel.grid.major = element_line(colour = "grey90"))
```

References

Survival Analysis with R, by Joseph Rickert, 2017-09-25, link to the article on R-views:
https://rviews.rstudio.com/2017/09/25/survival-analysis-with-r/

Applied Survival Analysis Using R, Dirk F. Moore, 2016, Springer, ISBN 978-3-319-31245-3 (e-book)