Survival Analysis

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1.1 Copyright Statement

1.1.1 License

1.1.2 Alternative version

Checkout the .txt, the .pdf, and the .html version

1.1.3 Init ORG-MODE

```
;; I need this for org-mode to work well
;; If we have a new org-mode use ob-shell
;; otherwise use ob-sh --- but not both!
(if (require 'ob-shell nil 'noerror)
  (progn
    (org-babel-do-load-languages 'org-babel-load-languages '((shell . t))))
  (progn
    (require 'ob-sh)
    (org-babel-do-load-languages 'org-babel-load-languages '((sh . t)))))
(org-babel-do-load-languages
 'org-babel-load-languages
 '((R . t)))
(org-babel-do-load-languages 'org-babel-load-languages '((C . t)))
(org-babel-do-load-languages 'org-babel-load-languages '((python . t)))
(setq org-src-fontify-natively t)
(setq org-confirm-babel-evaluate nil) ;; danger!
(custom-set-faces
 '(org-block ((t (:inherit shadow :foreground "black"))))
 '(org-code ((t (:inherit shadow :foreground "black")))))
(setq org-startup-with-inline-images t)
(setq org-redisplay-inline-images t)
```

```
(add-hook 'org-babel-after-execute-hook 'org-display-inline-images)
(add-hook 'org-mode-hook 'org-display-inline-images)
```

1.1.4 Org export

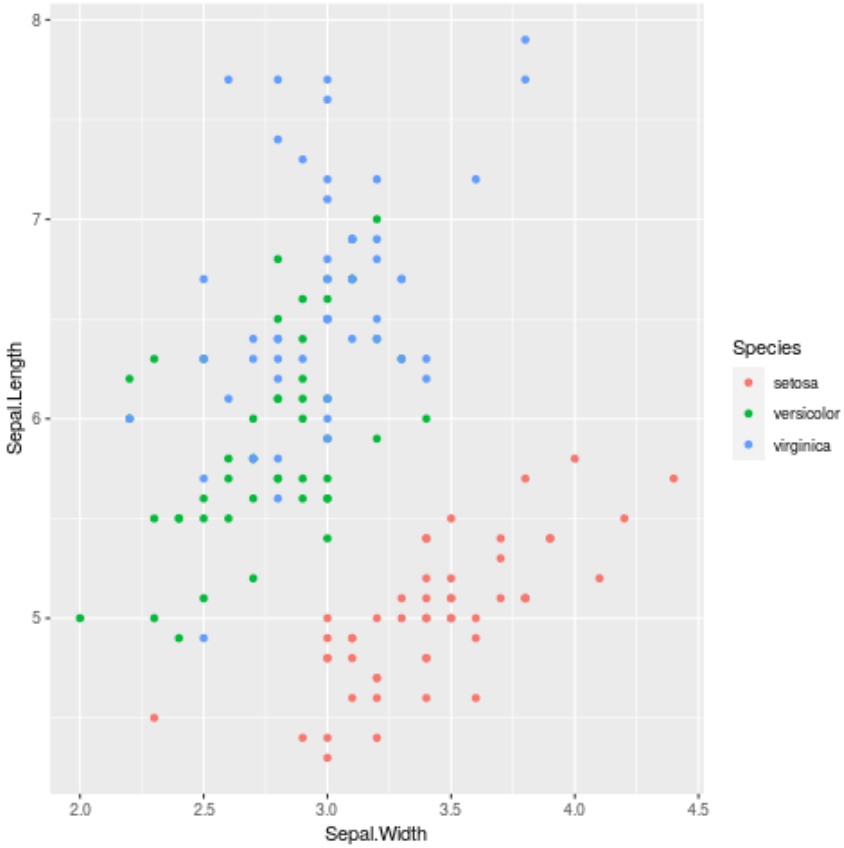
```
(org-html-export-to-html)
(org-latex-export-to-pdf)
(org-ascii-export-to-ascii)
```

1.1.5 Org Template

```
summary(runif(100))
```

```
    Min.  1st Qu.   Median     Mean  3rd Qu.     Max.
0.002381 0.171639 0.526952 0.516076 0.827670 0.986003
```

```
library("ggplot2")
ggplot(iris, aes(x = Sepal.Width, y = Sepal.Length, color = Species)) +
geom_point()
```



1.2 Survival Analysis

`https://github.com/therneau/survival` `https://cran.r-project.org/web/packages/survival/index.html` `https://cran.r-project.org/web/packages/survival/survival.pdf`

1.2.1 Survival Data

Let's try it out from the R package

Let's look at what is expected from survival data:

```
library(survival)
aml
```

```
   time status             x
1     9      1    Maintained
```

```
2    13      1    Maintained
3    13      0    Maintained
4    18      1    Maintained
5    23      1    Maintained
6    28      0    Maintained
7    31      1    Maintained
8    34      1    Maintained
9    45      0    Maintained
10   48      1    Maintained
11  161      0    Maintained
12    5      1 Nonmaintained
13    5      1 Nonmaintained
14    8      1 Nonmaintained
15    8      1 Nonmaintained
16   12      1 Nonmaintained
17   16      0 Nonmaintained
18   23      1 Nonmaintained
19   27      1 Nonmaintained
20   30      1 Nonmaintained
21   33      1 Nonmaintained
22   43      1 Nonmaintained
23   45      1 Nonmaintained
```

Time is when an event occurs. Status is alive or dead. x is the factor. This is Leukemia survival data.

1.2.2 Surv object

survfit will fit a model to a survival curve. Surv makes such a curve out of 2 variables, time and status.

Status is either censoring or death. 0 for censor often, or 1 for death?

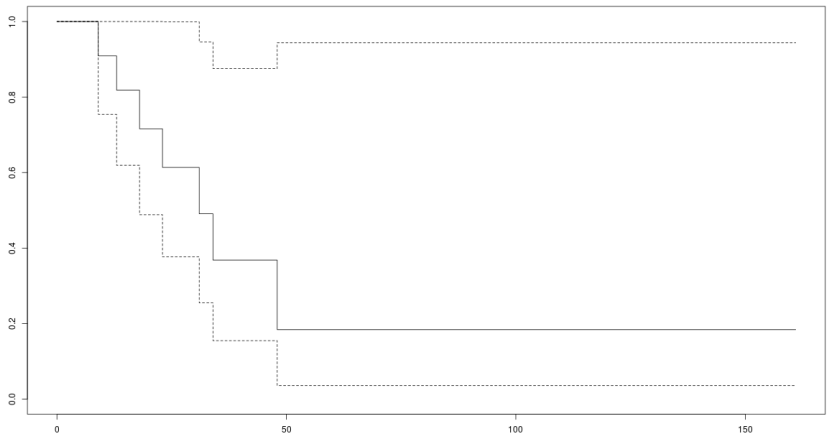
```
maint <- aml[aml$x=="Maintained",]
Surv(maint$time, maint$status)
maint[maint$status==0,]
```

```
 [1]   9   13   13+  18   23   28+  31   34   45+  48  161+
   time status          x
3    13      0 Maintained
6    28      0 Maintained
9    45      0 Maintained
11  161      0 Maintained
```

1.2.3 Plotting Surv object

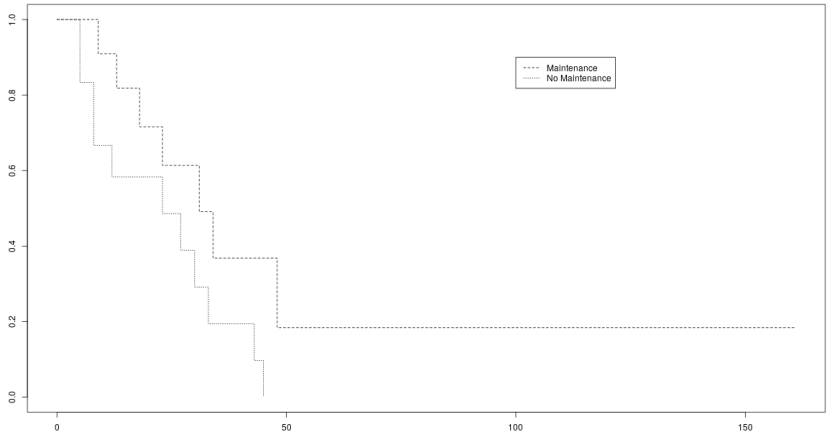
You can plot the curve and the confidence interval

```
maint <- aml[aml$x=="Maintained",]
plot(Surv(maint$time, maint$status))
```



So what does it look like with multiple factors?

```
leukemia.surv <- survfit(Surv(time, status) ~ x, data = aml)
plot(leukemia.surv, lty = 2:3)
legend(100, .9, c("Maintenance", "No Maintenance"), lty = 2:3)
```



```
leukemia.surv <- survfit(Surv(time, status) ~ x, data = aml)
summary(leukemia.surv)

Call: survfit(formula = Surv(time, status) ~ x, data = aml)

                x=Maintained
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
    9     11       1    0.909  0.0867       0.7541        1.000
   13     10       1    0.818  0.1163       0.6192        1.000
   18      8       1    0.716  0.1397       0.4884        1.000
   23      7       1    0.614  0.1526       0.3769        0.999
   31      5       1    0.491  0.1642       0.2549        0.946
   34      4       1    0.368  0.1627       0.1549        0.875
   48      2       1    0.184  0.1535       0.0359        0.944

                x=Nonmaintained
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
    5     12       2   0.8333  0.1076       0.6470        1.000
    8     10       2   0.6667  0.1361       0.4468        0.995
   12      8       1   0.5833  0.1423       0.3616        0.941
   23      6       1   0.4861  0.1481       0.2675        0.883
   27      5       1   0.3889  0.1470       0.1854        0.816
   30      4       1   0.2917  0.1387       0.1148        0.741
   33      3       1   0.1944  0.1219       0.0569        0.664
   43      2       1   0.0972  0.0919       0.0153        0.620
   45      1       1   0.0000     NaN           NA           NA
```

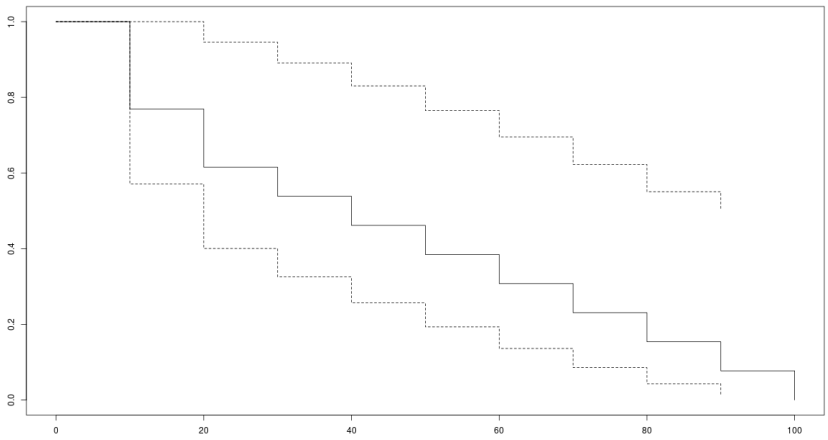
1.2.4 OK but software engineering?

Your times should be time since the start of the intervention or the birth of a bug. If you want to track project lifetime, make it another variable. Your record should be if something has quit or if something has finished.

```
library(survival)
bugs <- c()
# time of bug fix
bugs$time   <- c(10,10,10,20,20,30,40,50,60,70,80,90,100)
# bugs$status <- c( 0, 0, 0, 0, 1, 0, 1, 0, 0, 1, 1, 0,  1)
bugs <- data.frame(bugs)
bugs
```

```
   time
1    10
2    10
3    10
4    20
5    20
6    30
7    40
8    50
9    60
10   70
11   80
12   90
13  100
```

```
plot(Surv(bugs$time))
```

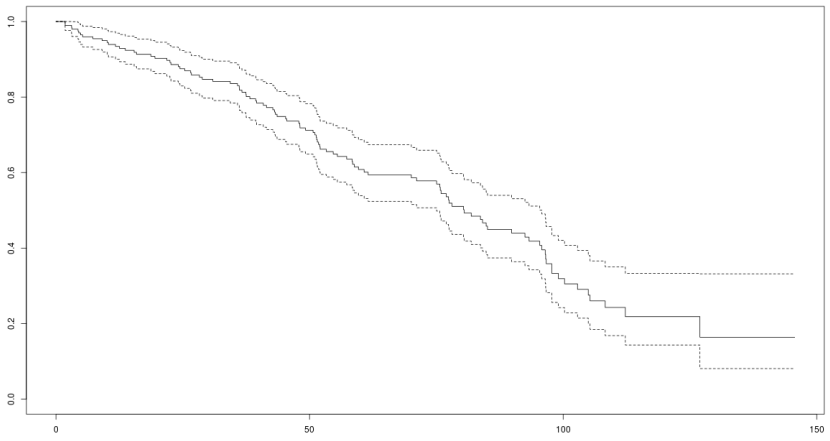


1.2.5 What about for a lot more bugs?

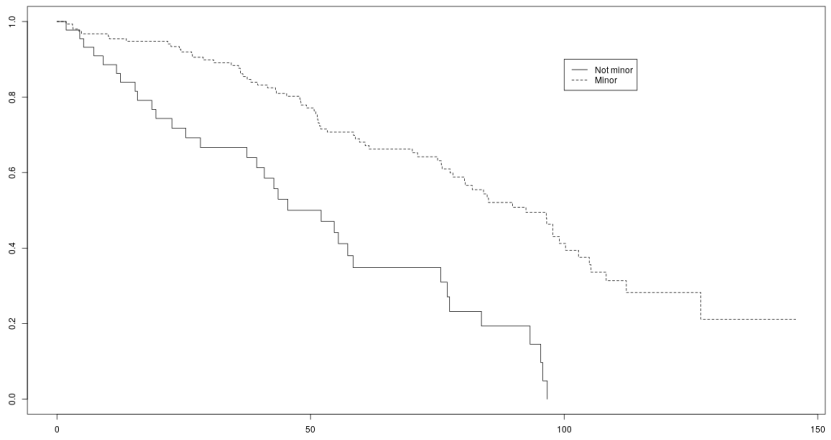
We're going to invent a dataset where minor revision bugs last longer. They are fixed later. Which means they survive longer.

```
bugs <- c()
# bug survival
bugs$time   <- sort(runif(100)*100)
# longer surviving bugs at the end
```

```
bugs$time   <- c(bugs$time,sort(bugs$time + runif(100)*50))
# the first half are half minor revisions
# the second half are mostly minor revision bugs and they last a long time
bugs$minor  <- c(sample(c(0,1),100,replace=TRUE),sample(c(1),100,replace=TRUE))
# this is just noise to show what happens with uncorrelated results
bugs$noise  <- sample(c(0,1),200,replace=TRUE)
# minor are censored more
bugs$status <- c(sample(c(1,1,1,0),100,replace=TRUE),sample(c(1,0,0),100,replace=TRUE))
bugs <- data.frame(bugs)
# plot(bugs$time[bugs$status==1])
# plot(bugs$time[bugs$status==0])
plot(Surv(bugs$time,bugs$status))
```




```
plot(survfit(Surv(time,status) ~ factor(minor), data = bugs),lty=c(1:2))
legend(100, .9, c("Not minor", "Minor"), lty = 1:2)
```




```
summary(survfit(Surv(time,status) ~ factor(minor), data = bugs))

Call: survfit(formula = Surv(time, status) ~ factor(minor), data = bugs)

                factor(minor)=0
  time n.risk n.event survival std.err lower 95% CI upper 95% CI
  1.81     44       1   0.9773  0.0225      0.93421        1.000
  4.50     43       1   0.9545  0.0314      0.89494        1.000
  5.26     42       1   0.9318  0.0380      0.86024        1.000
  7.28     41       1   0.9091  0.0433      0.82800        0.998
  9.10     39       1   0.8858  0.0481      0.79637        0.985
 11.74     38       1   0.8625  0.0522      0.76605        0.971
 12.52     37       1   0.8392  0.0557      0.73675        0.956
 15.41     35       1   0.8152  0.0591      0.70726        0.940
 15.88     34       1   0.7912  0.0620      0.67856        0.923
 18.71     33       1   0.7672  0.0646      0.65053        0.905
 19.51     32       1   0.7433  0.0669      0.62309        0.887
 22.66     29       1   0.7176  0.0693      0.59387        0.867
 25.41     28       1   0.6920  0.0714      0.56528        0.847
 28.29     27       1   0.6664  0.0732      0.53725        0.827
 37.46     25       1   0.6397  0.0750      0.50840        0.805
 39.38     24       1   0.6131  0.0765      0.48012        0.783
 40.89     22       1   0.5852  0.0779      0.45081        0.760
 42.76     21       1   0.5573  0.0790      0.42212        0.736
 43.60     20       1   0.5295  0.0798      0.39400        0.711
```

45.51	18	1	0.5000	0.0806	0.36455	0.686
52.09	17	1	0.4706	0.0811	0.33578	0.660
54.66	16	1	0.4412	0.0812	0.30766	0.633
55.48	15	1	0.4118	0.0809	0.28019	0.605
57.32	13	1	0.3801	0.0806	0.25080	0.576
58.38	12	1	0.3484	0.0799	0.22230	0.546
75.69	9	1	0.3097	0.0799	0.18686	0.513
76.95	8	1	0.2710	0.0787	0.15339	0.479
77.40	7	1	0.2323	0.0764	0.12193	0.443
83.70	6	1	0.1936	0.0728	0.09262	0.405
93.28	4	1	0.1452	0.0688	0.05732	0.368
95.40	3	1	0.0968	0.0606	0.02840	0.330
95.79	2	1	0.0484	0.0457	0.00761	0.308
96.67	1	1	0.0000	NaN	NA	NA

factor(minor)=1

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1.80	154	1	0.994	0.00647	0.981	1.000
3.07	153	1	0.987	0.00912	0.969	1.000
3.13	152	1	0.981	0.01114	0.959	1.000
4.35	151	1	0.974	0.01282	0.949	0.999
4.86	150	1	0.968	0.01428	0.940	0.996
10.11	148	1	0.961	0.01561	0.931	0.992
10.34	147	1	0.954	0.01682	0.922	0.988
13.67	143	1	0.948	0.01798	0.913	0.984
21.87	135	1	0.941	0.01916	0.904	0.979
22.48	134	1	0.934	0.02027	0.895	0.974
24.12	132	1	0.927	0.02131	0.886	0.969
24.45	131	1	0.920	0.02229	0.877	0.964
26.56	129	1	0.912	0.02323	0.868	0.959
26.70	128	1	0.905	0.02412	0.859	0.954
28.85	125	1	0.898	0.02499	0.850	0.948
30.93	124	1	0.891	0.02582	0.842	0.943
34.37	123	1	0.884	0.02660	0.833	0.937
35.80	121	1	0.876	0.02737	0.824	0.932
36.13	119	1	0.869	0.02811	0.816	0.926
36.15	118	1	0.862	0.02882	0.807	0.920
36.66	117	1	0.854	0.02950	0.798	0.914
37.51	116	1	0.847	0.03015	0.790	0.908
38.23	115	1	0.839	0.03077	0.781	0.902

39.57	114	1	0.832 0.03137	0.773	0.896
41.51	111	1	0.825 0.03197	0.764	0.890
43.08	109	1	0.817 0.03256	0.756	0.883
43.23	108	1	0.809 0.03313	0.747	0.877
45.28	107	1	0.802 0.03367	0.739	0.871
47.88	105	1	0.794 0.03421	0.730	0.864
48.09	104	1	0.787 0.03472	0.721	0.858
48.11	103	1	0.779 0.03521	0.713	0.851
49.19	101	1	0.771 0.03570	0.704	0.845
50.69	97	1	0.763 0.03621	0.696	0.838
51.06	95	1	0.755 0.03671	0.687	0.831
51.30	94	1	0.747 0.03718	0.678	0.824
51.40	93	1	0.739 0.03764	0.669	0.817
51.53	92	1	0.731 0.03808	0.660	0.810
51.77	91	1	0.723 0.03850	0.652	0.803
52.01	90	1	0.715 0.03890	0.643	0.796
53.30	89	1	0.707 0.03929	0.634	0.788
58.49	80	1	0.698 0.03978	0.624	0.781
58.81	79	1	0.689 0.04024	0.615	0.773
59.64	77	1	0.680 0.04071	0.605	0.765
60.76	75	1	0.671 0.04116	0.595	0.757
61.55	74	1	0.662 0.04159	0.586	0.749
70.07	66	1	0.652 0.04216	0.575	0.740
71.11	63	1	0.642 0.04274	0.563	0.731
75.05	60	1	0.631 0.04335	0.552	0.722
75.78	59	1	0.621 0.04391	0.540	0.713
75.93	58	1	0.610 0.04444	0.529	0.703
77.52	56	1	0.599 0.04496	0.517	0.694
78.09	55	1	0.588 0.04544	0.505	0.684
80.36	53	1	0.577 0.04592	0.494	0.674
80.47	52	1	0.566 0.04636	0.482	0.664
81.87	51	1	0.555 0.04676	0.470	0.654
84.11	49	1	0.543 0.04715	0.458	0.644
84.82	48	1	0.532 0.04751	0.447	0.634
85.09	47	1	0.521 0.04783	0.435	0.624
89.86	41	1	0.508 0.04832	0.422	0.612
92.47	38	1	0.495 0.04886	0.408	0.600
96.46	32	1	0.479 0.04972	0.391	0.587
96.56	30	1	0.463 0.05057	0.374	0.574
97.75	28	1	0.447 0.05140	0.357	0.560

```
 97.76     27       1    0.430 0.05209        0.339        0.545
 99.06     24       1    0.412 0.05291        0.321        0.530
100.28     23       1    0.394 0.05356        0.302        0.515
102.84     21       1    0.376 0.05420        0.283        0.498
104.95     19       1    0.356 0.05484        0.263        0.481
105.31     18       1    0.336 0.05524        0.243        0.464
108.29     15       1    0.314 0.05591        0.221        0.445
112.26     10       1    0.282 0.05846        0.188        0.424
126.96      4       1    0.212 0.07522        0.106        0.425
```

Survfit basically calculates confidence intervals of survival at each point

1.2.6 Cox Proportional-Hazards Model

The PMM for minor should be lower than not minor. Because it is less risk.
It lets bugs survive longer.

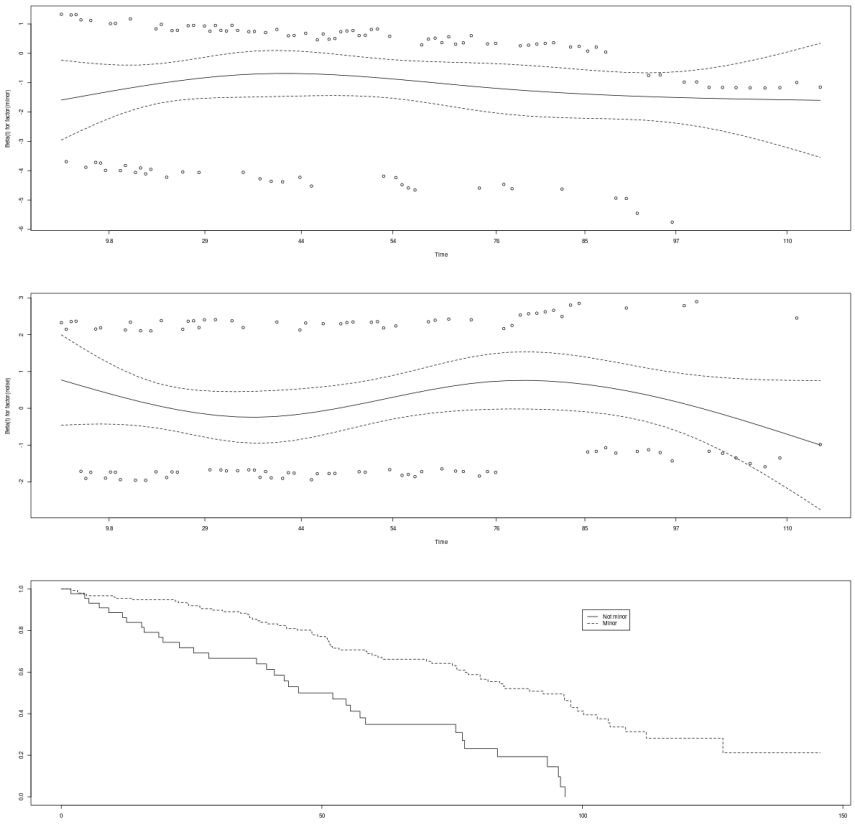
The PMM for noise should be near 1.

```
fit <- coxph(Surv(time,status) ~ factor(minor) + factor(noise), data = bugs)
summary(fit,rr.ci=TRUE)
yates(fit, ~ minor, predict="risk") # hazard ratio
yates(fit, ~ noise, predict="risk") # hazard ratio
```

```
Call:
coxph(formula = Surv(time, status) ~ factor(minor) + factor(noise),
    data = bugs)

  n= 200, number of events= 105

                   coef exp(coef) se(coef)      z Pr(>|z|)
factor(minor)1 -1.0992    0.3331   0.2189 -5.022 5.13e-07 ***
factor(noise)1  0.1994    1.2206   0.1973  1.010    0.312
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

               exp(coef) exp(-coef) lower .95 upper .95
factor(minor)1    0.3331     3.0018    0.2169    0.5116
factor(noise)1    1.2206     0.8193    0.8291    1.7970

Concordance= 0.613  (se = 0.03 )
Likelihood ratio test= 23.37  on 2 df,   p=8e-06
```

```
Wald test            = 26.7  on 2 df,   p=2e-06
Score (logrank) test = 29.34  on 2 df,   p=4e-07
 factor(minor)     pmm      std               test chisq df        Pr
             0 2.35565 0.426003      factor(minor) 11.41  1 0.0007322
             1 0.78475 0.041541
 factor(noise)    pmm     std               test  chisq df     Pr
             0 1.0375 0.10730      factor(noise) 0.9356  1 0.3334
             1 1.2664 0.15896
```

```
fit <- coxph(Surv(time,status) ~ factor(minor) + factor(noise), data = bugs)
par(mfrow=c(3,1))
plot(cox.zph(fit)[1]) # plot minor
plot(cox.zph(fit)[2]) # plot noise
plot(survfit(Surv(time,status) ~ factor(minor), data = bugs),lty=c(1:2))
legend(100, .9, c("Not minor", "Minor"), lty = 1:2)
```

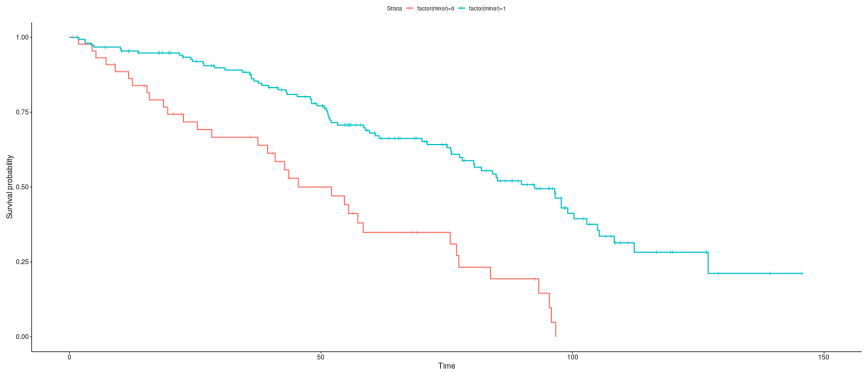


1.2.7 Pretty Plots with Survminer

A pain to install (use docker?) `https://rpkgs.datanovia.com/survminer/`

You could install devtools and run:

```
devtools::install_url("https://github.com/wilkelab/cowplot/archive/0.6.3.zip")
devtools::install_url("https://github.com/cran/mvtnorm/archive/1.0-8.zip")
devtools::install_url("https://github.com/kassambara/survminer/archive/v0.4.3.zip")
#install.packages("survminer")

library(survminer)

library(survival)
library(survminer)
fit <- survfit(Surv(time,status) ~ factor(minor), data = bugs)
ggsurvplot(fit, data = bugs)
```



1.2.8 Better

```
library(survival)
library(survminer)
fit <- survfit(Surv(time,status) ~ factor(minor), data = bugs)
ggsurvplot(
  fit,
  data = bugs,
  size = 1,                 # change line size
  palette =
    c("#E7B800", "#2E9FDF"),# custom color palettes
  conf.int = TRUE,          # Add confidence interval
  pval = TRUE,              # Add p-value
```

```
  risk.table = TRUE,        # Add risk table
  risk.table.col = "strata",# Risk table color by groups
  legend.labs =
    c("Not Minor", "Minor"),    # Change legend labels
  risk.table.height = 0.25, # Useful to change when you have multiple groups
  ggtheme = theme_bw()      # Change ggplot2 theme
)
```