Cox Model Building and Diagnostics

Contents

Model building

Load the data

```r
library(tidyverse)
```

```
## -- Attaching packages --------------------------------------- tidyverse 1.3.2 --
## v ggplot2 3.4.0      v purrr   0.3.5
## v tibble  3.1.8      v dplyr   1.0.10
## v tidyr   1.2.1      v stringr 1.4.1
## v readr   2.1.3      v forcats 0.5.2
## -- Conflicts ------------------------------------------ tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()    masks stats::lag()
```

```r
library(survival)
library(asaur)
library(broom)

dat <- pharmacoSmoking
```

The 4 candidate models

```r
M0 <- coxph(Surv(ttr, relapse) ~ 1, data = dat)
MA <- coxph(Surv(ttr, relapse) ~ ageGroup4, data = dat)
MB <- coxph(Surv(ttr, relapse) ~ employment, data = dat)
MC <- coxph(Surv(ttr, relapse) ~ ageGroup4 + employment, data = dat)
```

```r
summary(MA)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ ageGroup4, data = dat)
##
##   n= 125, number of events= 89
##
##                   coef exp(coef) se(coef)      z Pr(>|z|)
## ageGroup435-49  0.0293    1.0297   0.3093  0.095   0.9245
## ageGroup450-64 -0.7914    0.4532   0.3361 -2.355   0.0185 *
## ageGroup465+   -0.3173    0.7281   0.4435 -0.715   0.4744
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                exp(coef) exp(-coef) lower .95 upper .95
## ageGroup435-49    1.0297     0.9711    0.5616    1.8880
## ageGroup450-64    0.4532     2.2066    0.2345    0.8757
## ageGroup465+      0.7281     1.3734    0.3053    1.7367
##
## Concordance= 0.593  (se = 0.032 )
```

```
## Likelihood ratio test= 12.22  on 3 df,   p=0.007
## Wald test            = 11.36  on 3 df,   p=0.01
## Score (logrank) test = 11.93  on 3 df,   p=0.008
```

```
summary(MB)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ employment, data = dat)
##
##   n= 125, number of events= 89
##
##                   coef exp(coef) se(coef)     z Pr(>|z|)
## employmentother 0.1982    1.2192   0.2371 0.836    0.403
## employmentpt    0.4500    1.5683   0.3229 1.394    0.163
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## employmentother     1.219     0.8202    0.7661     1.940
## employmentpt        1.568     0.6376    0.8328     2.953
##
## Concordance= 0.541  (se = 0.028 )
## Likelihood ratio test= 2.06  on 2 df,   p=0.4
## Wald test            = 2.17  on 2 df,   p=0.3
## Score (logrank) test = 2.2  on 2 df,   p=0.3
```

```
summary(MC)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ ageGroup4 + employment,
##     data = dat)
##
##   n= 125, number of events= 89
##
##                    coef exp(coef) se(coef)      z Pr(>|z|)
## ageGroup435-49  -0.1299    0.8782   0.3213 -0.404  0.68594
## ageGroup450-64  -1.0239    0.3592   0.3585 -2.856  0.00429 **
## ageGroup465+    -0.7825    0.4573   0.5046 -1.551  0.12102
## employmentother  0.5257    1.6917   0.2748  1.913  0.05577 .
## employmentpt     0.5001    1.6489   0.3315  1.508  0.13143
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## ageGroup435-49     0.8782     1.1387    0.4678    1.6484
## ageGroup450-64     0.3592     2.7839    0.1779    0.7253
## ageGroup465+       0.4573     2.1868    0.1701    1.2295
## employmentother    1.6917     0.5911    0.9871    2.8992
## employmentpt       1.6489     0.6065    0.8610    3.1578
##
## Concordance= 0.617  (se = 0.033 )
## Likelihood ratio test= 16.79  on 5 df,   p=0.005
## Wald test            = 15.77  on 5 df,   p=0.008
## Score (logrank) test = 16.35  on 5 df,   p=0.006
```

Comparing nested models: LRT

```
anova(MA, MC)
```

```
## Analysis of Deviance Table
##  Cox model: response is  Surv(ttr, relapse)
##  Model 1: ~ ageGroup4
##  Model 2: ~ ageGroup4 + employment
##    loglik  Chisq Df Pr(>|Chi|)
## 1 -380.04
## 2 -377.76 4.5666  2     0.1019
```

Comparing non-nested models: AIC

```
fits <- list(MA = MA, MB = MB, MC = MC)
sapply(fits, AIC)
```

```
##       MA       MB       MC
## 766.0860 774.2464 765.5194
```

Model 'MC' is the best.

Automatic model selection based on AIC

```
Mfull <- coxph(Surv(ttr, relapse) ~ grp + gender + race +
                 employment + yearsSmoking + levelSmoking +
                 age + I(age^2) + priorAttempts + longestNoSmoke,
               data = dat)
```

```
MAIC <- step(Mfull)
```

```
## Start:  AIC=769.66
## Surv(ttr, relapse) ~ grp + gender + race + employment + yearsSmoking +
##     levelSmoking + age + I(age^2) + priorAttempts + longestNoSmoke
##
##                  Df    AIC
## - race            3 767.42
## - gender          1 767.68
## - priorAttempts   1 767.87
## - levelSmoking    1 767.92
## - longestNoSmoke  1 767.99
## - yearsSmoking    1 768.31
## - I(age^2)        1 769.17
## <none>              769.66
## - age             1 771.40
## - employment      2 773.89
## - grp             1 775.27
```

```
##
## Step:  AIC=767.42
## Surv(ttr, relapse) ~ grp + gender + employment + yearsSmoking +
##     levelSmoking + age + I(age^2) + priorAttempts + longestNoSmoke
##
##                  Df    AIC
## - gender          1 765.42
## - levelSmoking    1 765.43
## - priorAttempts   1 765.59
## - yearsSmoking    1 765.76
## - longestNoSmoke  1 766.28
## - I(age^2)        1 766.63
## <none>              767.42
## - age             1 768.38
## - employment      2 770.69
## - grp             1 773.24
##
## Step:  AIC=765.42
## Surv(ttr, relapse) ~ grp + employment + yearsSmoking + levelSmoking +
##     age + I(age^2) + priorAttempts + longestNoSmoke
##
##                  Df    AIC
## - levelSmoking    1 763.43
## - priorAttempts   1 763.59
## - yearsSmoking    1 763.76
## - longestNoSmoke  1 764.29
## - I(age^2)        1 764.63
## <none>              765.42
## - age             1 766.42
## - employment      2 768.88
## - grp             1 771.29
##
## Step:  AIC=763.43
## Surv(ttr, relapse) ~ grp + employment + yearsSmoking + age +
##     I(age^2) + priorAttempts + longestNoSmoke
##
##                  Df    AIC
## - priorAttempts   1 761.60
## - yearsSmoking    1 761.78
## - longestNoSmoke  1 762.29
## - I(age^2)        1 762.75
## <none>              763.43
## - age             1 764.57
## - employment      2 766.88
## - grp             1 769.31
##
## Step:  AIC=761.6
## Surv(ttr, relapse) ~ grp + employment + yearsSmoking + age +
##     I(age^2) + longestNoSmoke
##
##                  Df    AIC
## - yearsSmoking    1 759.98
## - longestNoSmoke  1 760.46
## - I(age^2)        1 760.86
```

```
## <none>              761.60
## - age             1 762.67
## - employment      2 764.95
## - grp             1 767.34
##
## Step:  AIC=759.98
## Surv(ttr, relapse) ~ grp + employment + age + I(age^2) + longestNoSmoke
##
##                  Df    AIC
## - longestNoSmoke  1 758.95
## - I(age^2)        1 759.25
## <none>              759.98
## - age             1 760.72
## - employment      2 763.30
## - grp             1 766.07
##
## Step:  AIC=758.95
## Surv(ttr, relapse) ~ grp + employment + age + I(age^2)
##
##              Df    AIC
## - I(age^2)    1 758.28
## <none>          758.95
## - age         1 759.89
## - employment  2 762.73
## - grp         1 765.15
##
## Step:  AIC=758.28
## Surv(ttr, relapse) ~ grp + employment + age
##
##              Df    AIC
## <none>          758.28
## - employment  2 762.48
## - grp         1 764.18
## - age         1 767.24
```

```
summary(MAIC)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ grp + employment + age,
##     data = dat)
##
##   n= 125, number of events= 89
##
##                     coef exp(coef) se(coef)      z Pr(>|z|)
## grppatchOnly     0.60788   1.83654  0.21837  2.784  0.00537 **
## employmentother  0.70348   2.02077  0.26929  2.612  0.00899 **
## employmentpt     0.65369   1.92262  0.32732  1.997  0.04581 *
## age             -0.03529   0.96533  0.01075 -3.282  0.00103 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## grppatchOnly       1.8365     0.5445    1.1971    2.8176
## employmentother    2.0208     0.4949    1.1920    3.4256
```

```
## employmentpt       1.9226     0.5201    1.0122    3.6518
## age                0.9653     1.0359    0.9452    0.9859
##
## Concordance= 0.638  (se = 0.03 )
## Likelihood ratio test= 22.03  on 4 df,   p=2e-04
## Wald test            = 21.91  on 4 df,   p=2e-04
## Score (logrank) test = 22.48  on 4 df,   p=2e-04
```

There's only so much we can automate: transformed variables

```
M_ageLinear <- MAIC
M_ageCat <- coxph(Surv(ttr, relapse) ~ grp + employment + ageGroup4, data = dat)
AIC(M_ageLinear)
```

```
## [1] 758.2785
```

```
AIC(M_ageCat)
```

```
## [1] 758.4157
```

AIC prefers a linear term of Age. However, it might not necessarily be the best choice if the age effect is *not* actually linear, and we want to e.g. explicitly account for ethnicity:

```
M_new <- coxph(Surv(ttr, relapse) ~ grp + race +
                 employment +
                 ageGroup4,
               data = dat)
summary(M_new)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ grp + race + employment +
##     ageGroup4, data = dat)
##
##   n= 125, number of events= 89
##
##                    coef exp(coef) se(coef)      z Pr(>|z|)
## grppatchOnly     0.6497    1.9149   0.2190  2.967  0.00301 **
## racehispanic    -0.4010    0.6696   0.4984 -0.805  0.42099
## raceother       -1.1671    0.3113   1.0313 -1.132  0.25780
## racewhite       -0.2893    0.7488   0.2352 -1.230  0.21865
## employmentother  0.6914    1.9966   0.2777  2.490  0.01277 *
## employmentpt     0.5509    1.7348   0.3343  1.648  0.09943 .
## ageGroup435-49  -0.1579    0.8539   0.3273 -0.482  0.62951
## ageGroup450-64  -1.0792    0.3399   0.3623 -2.978  0.00290 **
## ageGroup465+    -0.8313    0.4355   0.5029 -1.653  0.09830 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## grppatchOnly       1.9149     0.5222   1.24664    2.9414
```

```
## racehispanic       0.6696     1.4934   0.25213    1.7785
## raceother          0.3113     3.2126   0.04124    2.3497
## racewhite          0.7488     1.3355   0.47220    1.1873
## employmentother    1.9966     0.5009   1.15857    3.4407
## employmentpt       1.7348     0.5764   0.90084    3.3407
## ageGroup435-49     0.8539     1.1711   0.44958    1.6219
## ageGroup450-64     0.3399     2.9423   0.16707    0.6914
## ageGroup465+       0.4355     2.2964   0.16252    1.1668
##
## Concordance= 0.667  (se = 0.032 )
## Likelihood ratio test= 28.78  on 9 df,   p=7e-04
## Wald test            = 27.04  on 9 df,   p=0.001
## Score (logrank) test = 27.93  on 9 df,   p=0.001
```

```
AIC(MAIC)
```

```
## [1] 758.2785
```

```
AIC(M_new)
```

```
## [1] 761.5297
```

Measuring predictions performance - C statistic

Split data into a training and a testing set

```
set.seed(1234)
i.training <- sample.int(nrow(dat), size = ceiling(nrow(dat)/2), replace = FALSE)
i.testing <- setdiff(seq_len(nrow(dat)), i.training)
d_training <- dat[i.training, ]
d_testing <- dat[i.testing, ]
```

Train 3 candidate models

```
MA <- coxph(Surv(ttr, relapse) ~ gender + age, data = d_training)
MB <- coxph(Surv(ttr, relapse) ~ gender + employment, data = d_training)
MC <- coxph(Surv(ttr, relapse) ~ gender + age + employment, data = d_training)
```

Measure predictions performance - THE WRONG WAY

WROOOOOONG! THIS WOULD BE INCORRECT:

```
models <- list(A = MA, B = MB, C = MC)
map_dbl(models, ~ summary(.)$concordance[1])
```

```
##         A         B         C
## 0.5489433 0.6315350 0.6359844
```

WROOOOOOOONG!!!!

The same dataset is used for both training and performance evaluation. This will *always* favor the model with more parameters.

Make predictions in the testing dataset

```
d_testing$lp_A <- predict(MA, newdata = d_testing, type = "lp")
d_testing$lp_B <- predict(MB, newdata = d_testing, type = "lp")
d_testing$lp_C <- predict(MC, newdata = d_testing, type = "lp")

d_testing
```

```
##      id ttr relapse         grp age gender     race employment yearsSmoking
## 1    21 182       0   patchOnly  36   Male    white         ft           26
## 7    16  14       1   patchOnly  66   Male    black         pt           54
## 10   70   0       1   patchOnly  38   Male    black         ft           23
## 11   84  12       1   patchOnly  64 Female    black      other           30
## 12   85 182       0 combination  51   Male    black         ft           35
## 13   25  21       1   patchOnly  37 Female    white         pt           23
## 15   59 170       1   patchOnly  42 Female    white         ft           30
## 18    3 182       0 combination  52 Female    white      other           19
## 19   15 140       1 combination  43   Male    white         ft           27
## 20   32  63       1 combination  34 Female    white         ft           18
## 23  110 110       1 combination  49 Female    white      other           35
## 24  127 182       0 combination  58 Female    white         ft           38
## 25  119   0       1   patchOnly  48   Male hispanic      other           33
## 27   62  15       1   patchOnly  49 Female    black         pt           35
## 29  112   4       1   patchOnly  33   Male    black         ft           12
## 30   60  56       1 combination  49 Female    black         ft           37
## 31   93   2       1 combination  46   Male    black         ft           25
## 33  130 182       0 combination  46 Female    white         pt           25
## 34   19  56       1   patchOnly  52   Male    black      other           25
## 36    4  14       1   patchOnly  48 Female    white         ft           34
## 37   20  14       1   patchOnly  48 Female    white         ft           39
## 39   26 182       0   patchOnly  58   Male    white      other           41
## 44    8 182       0 combination  70 Female    white      other           52
## 45   12  75       1 combination  62 Female    white         pt           46
## 46   13  30       1 combination  86   Male    white      other           40
## 50   36 182       0 combination  62   Male    white         ft           35
## 52   44   8       1 combination  40   Male    white         ft           27
## 53   61 140       1 combination  49   Male    white      other           14
## 55   69  63       1 combination  47 Female    white         pt           15
## 58  106  50       1 combination  29   Male    white         ft           12
## 59  114  14       1 combination  64 Female    white         pt           45
## 60  120   0       1 combination  52   Male    white         ft           38
## 61   40  84       1   patchOnly  38 Female hispanic         ft           10
## 64  123 182       0 combination  63 Female hispanic      other           45
## 65    7 182       0   patchOnly  58   Male    black         ft           40
## 68   52 182       0   patchOnly  34 Female    black         ft           20
## 69   86   0       1   patchOnly  49 Female    black         ft           36
## 73   75  12       1 combination  46 Female    black      other           30
```

```
## 75    1  49       1   patchOnly  53 Female    white         pt           18
## 76    6 182       0   patchOnly  58   Male    white         ft           46
## 77   11 182       0   patchOnly  40 Female    white         ft           25
## 81   56 182       0   patchOnly  64 Female    white      other           47
## 82   72   0       1   patchOnly  50 Female    white         ft           30
## 83   78  28       1   patchOnly  47   Male    white         ft           22
## 85   83   2       1   patchOnly  51   Male    white      other           36
## 88   95   1       1   patchOnly  22 Female    white         pt            9
## 89   99 140       1   patchOnly  34 Female    white         ft           18
## 91  115  28       1   patchOnly  30 Female    white         ft           12
## 92  116   1       1   patchOnly  31   Male    white         ft           19
## 94  126  77       1   patchOnly  56 Female    white         ft           44
## 96    2 182       0 combination  69   Male    white      other           50
## 97    5 182       0 combination  41   Male    white         ft           29
## 102  64  60       1 combination  70 Female    white      other           54
## 104  92 182       0 combination  58 Female    white         ft           36
## 106 103 182       0 combination  72   Male    white      other           55
## 109  96 182       0 combination  63 Female    other      other           52
## 110  46   2       1 combination  40 Female hispanic         pt           23
## 116 109  30       1   patchOnly  51   Male    black      other           30
## 118  45   2       1 combination  47 Female    black         ft           33
## 121  74  10       1 combination  45 Female    black         ft           32
## 124 118  15       1 combination  56 Female    black      other           39
## 125 128 182       0 combination  50 Female    black         pt           30
##     levelSmoking ageGroup2 ageGroup4 priorAttempts longestNoSmoke         lp_A
## 1          heavy     21-49     35-49             0              0 -0.109308465
## 7          heavy       50+       65+             0              0 -0.510397624
## 10         light     21-49     35-49            10             90 -0.136047742
## 11         heavy       50+     50-64            12            365 -0.216673033
## 12         heavy       50+     50-64             1              7 -0.309853044
## 13         light     21-49     35-49             5           1095  0.144307211
## 15         heavy     21-49     35-49             5            240  0.077459018
## 18         light       50+     50-64             1              7 -0.056237369
## 19         heavy     21-49     35-49             5            120 -0.202895935
## 20         heavy     21-49     21-34             8             90  0.184416127
## 23         heavy     21-49     35-49            10             60 -0.016128453
## 24         heavy       50+     50-64             1              0 -0.136455201
## 25         heavy     21-49     35-49             4            120 -0.269744128
## 27         light     21-49     35-49             4            540 -0.016128453
## 29         light     21-49     21-34             1            730 -0.069199549
## 30         heavy     21-49     35-49             3           2920 -0.016128453
## 31         light     21-49     35-49             2           1095 -0.243004851
## 33         heavy     21-49     35-49             3            365  0.023980463
## 34         light       50+     50-64            10              7 -0.323222683
## 36         heavy     21-49     35-49             6           2555 -0.002758814
## 37         heavy     21-49     35-49             1              2 -0.002758814
## 39         light       50+     50-64           100            180 -0.403440515
## 44         heavy       50+       65+             3              1 -0.296890864
## 45         heavy       50+     50-64             8           1095 -0.189933755
## 46         light       50+       65+             4           2190 -0.777790397
## 50         heavy       50+     50-64             1           2555 -0.456919069
## 52         heavy     21-49     35-49             2             90 -0.162787019
## 53         heavy     21-49     35-49             0              0 -0.283113767
## 55         heavy     21-49     35-49             1             90  0.010610824
```

```
## 58         heavy     21-49     21-34             0             0 -0.015720994
## 59         heavy       50+     50-64             4            60 -0.216673033
## 60         heavy       50+     50-64             4             7 -0.323222683
## 61         heavy     21-49     35-49             2             3  0.130937572
## 64         heavy       50+     50-64             1            28 -0.203303394
## 65         heavy       50+     50-64             0             0 -0.403440515
## 68         heavy     21-49     21-34             5            90  0.184416127
## 69         heavy     21-49     35-49             1          6205 -0.016128453
## 73         light     21-49     35-49             2            55  0.023980463
## 75         heavy       50+     50-64             6          3650 -0.069607008
## 76         heavy       50+     50-64            10            14 -0.403440515
## 77         heavy     21-49     35-49             1          2920  0.104198295
## 81         heavy       50+     50-64             4           365 -0.216673033
## 82         heavy       50+     50-64             1            90 -0.029498092
## 83         heavy     21-49     35-49             3             4 -0.256374490
## 85         heavy       50+     50-64             1             5 -0.309853044
## 88         heavy     21-49     21-34             2             3  0.344851790
## 89         light     21-49     21-34             2          2190  0.184416127
## 91         light     21-49     21-34             0             0  0.237894681
## 92         heavy     21-49     21-34            10           120 -0.042460271
## 94         heavy       50+     50-64             4          1095 -0.109715923
## 96         heavy       50+       65+             6          5475 -0.550506540
## 97         heavy     21-49     35-49            20           180 -0.176156658
## 102        heavy       50+       65+             1            90 -0.296890864
## 104        light       50+     50-64             2            90 -0.136455201
## 106        light       50+       65+            30            30 -0.590615456
## 109        heavy       50+     50-64             2           180 -0.203303394
## 110        heavy     21-49     35-49             2             3  0.104198295
## 116        heavy       50+     50-64             2            30 -0.309853044
## 118        light     21-49     35-49             4           365  0.010610824
## 121        heavy     21-49     35-49             1            75  0.037350102
## 124        heavy       50+     50-64             3             7 -0.109715923
## 125        heavy       50+     50-64             0             0 -0.029498092
##           lp_B         lp_C
## 1   -0.1527679  0.260670756
## 7    0.6226736  0.351007796
## 10  -0.1527679  0.208171444
## 11   0.6993553  0.494356461
## 12  -0.1527679 -0.133074083
## 13   0.7754415  1.161156338
## 15   0.0000000  0.152081340
## 18   0.6993553  0.809352333
## 19  -0.1527679  0.076923164
## 20   0.0000000  0.362078587
## 23   0.6993553  0.888101300
## 24   0.0000000 -0.267913155
## 25   0.5465874  0.865442437
## 27   0.7754415  0.846160467
## 29  -0.1527679  0.339419724
## 30   0.0000000 -0.031666252
## 31  -0.1527679 -0.001825803
## 33   0.7754415  0.924909435
## 34   0.5465874  0.760443813
## 36   0.0000000 -0.005416596
```

```
## 37   0.0000000 -0.005416596
## 39   0.5465874  0.602945877
## 44   0.6993553  0.336858526
## 45   0.7754415  0.504914940
## 46   0.5465874 -0.132044489
## 50  -0.1527679 -0.421820298
## 52  -0.1527679  0.155672132
## 53   0.5465874  0.839192781
## 55   0.7754415  0.898659779
## 58  -0.1527679  0.444418348
## 59   0.7754415  0.452415628
## 60  -0.1527679 -0.159323739
## 61   0.0000000  0.257079964
## 64   0.6993553  0.520606117
## 65  -0.1527679 -0.316821675
## 68   0.0000000  0.362078587
## 69   0.0000000 -0.031666252
## 73   0.6993553  0.966850268
## 75   0.7754415  0.741161843
## 76  -0.1527679 -0.316821675
## 77   0.0000000  0.204580652
## 81   0.6993553  0.494356461
## 82   0.0000000 -0.057915908
## 83  -0.1527679 -0.028075459
## 85   0.5465874  0.786693469
## 88   0.7754415  1.554901177
## 89   0.0000000  0.362078587
## 91   0.0000000  0.467077211
## 92  -0.1527679  0.391919036
## 94   0.0000000 -0.215413843
## 96   0.5465874  0.314199662
## 97  -0.1527679  0.129422476
## 102  0.6993553  0.336858526
## 104  0.0000000 -0.267913155
## 106  0.5465874  0.235450694
## 109  0.6993553  0.520606117
## 110  0.7754415  1.082407370
## 116  0.5465874  0.786693469
## 118  0.0000000  0.020833060
## 121  0.0000000  0.073332372
## 124  0.6993553  0.704353709
## 125  0.7754415  0.819910811
```

Assess predictive performance

```
models <- list(
    A = coxph(Surv(ttr, relapse) ~ lp_A, data = d_testing),
    B = coxph(Surv(ttr, relapse) ~ lp_B, data = d_testing),
    C = coxph(Surv(ttr, relapse) ~ lp_C, data = d_testing)
  )

summary(models$A)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ lp_A, data = d_testing)
##
##   n= 62, number of events= 42
##
##         coef exp(coef) se(coef)     z Pr(>|z|)
## lp_A 1.3700    3.9354   0.7538 1.818   0.0691 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## lp_A     3.935     0.2541    0.8982     17.24
##
## Concordance= 0.571  (se = 0.046 )
## Likelihood ratio test= 3.44  on 1 df,   p=0.06
## Wald test            = 3.3  on 1 df,   p=0.07
## Score (logrank) test = 3.32  on 1 df,   p=0.07
```

```
summary(models$B)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ lp_B, data = d_testing)
##
##   n= 62, number of events= 42
##
##          coef exp(coef) se(coef)      z Pr(>|z|)
## lp_B -0.0540    0.9474   0.4062 -0.133    0.894
##
##      exp(coef) exp(-coef) lower .95 upper .95
## lp_B    0.9474      1.055    0.4273     2.101
##
## Concordance= 0.512  (se = 0.049 )
## Likelihood ratio test= 0.02  on 1 df,   p=0.9
## Wald test            = 0.02  on 1 df,   p=0.9
## Score (logrank) test = 0.02  on 1 df,   p=0.9
```

```
summary(models$C)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ lp_C, data = d_testing)
##
##   n= 62, number of events= 42
##
##         coef exp(coef) se(coef)     z Pr(>|z|)
## lp_C 0.6048    1.8308   0.3944 1.533    0.125
##
##      exp(coef) exp(-coef) lower .95 upper .95
## lp_C     1.831     0.5462    0.8451     3.966
##
## Concordance= 0.54  (se = 0.053 )
## Likelihood ratio test= 2.38  on 1 df,   p=0.1
## Wald test            = 2.35  on 1 df,   p=0.1
## Score (logrank) test = 2.37  on 1 df,   p=0.1
```

1. Check that the predictions go into the right direction

```
sapply(models, coef)
```

```
##      A.lp_A      B.lp_B      C.lp_C
##  1.37000089 -0.05399827  0.60475515
```

2. Extract the C-statistic from the 'summary' output

```
map_dbl(models, ~ summary(.)$concordance[1])
```

```
##         A         B         C
## 0.5710006 0.5119832 0.5401438
```

3. Flip directions as needed

```
benchmark <-
  tibble(
    model = names(models),
    sign = sapply(models, coef) |> sign(),
    C_summary = map_dbl(models, ~ summary(.)$concordance[1]),
    C = ifelse(sign > 0, C_summary, 1 - C_summary)
  )
benchmark
```

```
## # A tibble: 3 x 4
##   model  sign C_summary     C
##   <chr> <dbl>     <dbl> <dbl>
## 1 A         1     0.571 0.571
## 2 B        -1     0.512 0.488
## 3 C         1     0.540 0.540
```

```
benchmark |> select(model, C)
```

```
## # A tibble: 3 x 2
##   model     C
##   <chr> <dbl>
## 1 A     0.571
## 2 B     0.488
## 3 C     0.540
```

Measuring predictions performance - effect size

```r
d1 <- d_testing |> select(ttr, relapse, lp_A, lp_B, lp_C)
head(d1)
```

```
##    ttr relapse       lp_A       lp_B       lp_C
## 1  182       0 -0.1093085 -0.1527679  0.2606708
## 7   14       1 -0.5103976  0.6226736  0.3510078
## 10   0       1 -0.1360477 -0.1527679  0.2081714
## 11  12       1 -0.2166730  0.6993553  0.4943565
## 12 182       0 -0.3098530 -0.1527679 -0.1330741
## 13  21       1  0.1443072  0.7754415  1.1611563
```

Raw estimates

```r
A <- coxph(Surv(ttr, relapse) ~ lp_A, data = d1) |> tidy()
B <- coxph(Surv(ttr, relapse) ~ lp_B, data = d1) |> tidy()
C <- coxph(Surv(ttr, relapse) ~ lp_C, data = d1) |> tidy()
bind_rows(A, B, C)
```

```
## # A tibble: 3 x 5
##   term  estimate std.error statistic p.value
##   <chr>    <dbl>     <dbl>     <dbl>   <dbl>
## 1 lp_A    1.37       0.754     1.82   0.0691
## 2 lp_B   -0.0540     0.406    -0.133  0.894
## 3 lp_C    0.605      0.394     1.53   0.125
```

These log-HRs are not directly comparable.

```r
d_testing |> select(lp_A, lp_B, lp_C) |> sapply(sd)
```

```
##      lp_A      lp_B      lp_C
## 0.2155693 0.3863618 0.4227361
```

```r
d_testing |> select(lp_A, lp_B, lp_C) |> sapply(IQR)
```

```
##      lp_A      lp_B      lp_C
## 0.2770125 0.6993553 0.7281209
```

Standardized predictions

```r
d2 <- mutate(d1,
             ZA = lp_A / sd(lp_A),
             ZB = lp_B / sd(lp_B),
             ZC = lp_C / sd(lp_C))
head(d2)
```

```
##    ttr relapse       lp_A       lp_B       lp_C         ZA         ZB
## 1  182       0 -0.1093085 -0.1527679  0.2606708 -0.5070688 -0.3954011
## 7   14       1 -0.5103976  0.6226736  0.3510078 -2.3676733  1.6116333
## 10   0       1 -0.1360477 -0.1527679  0.2081714 -0.6311091 -0.3954011
## 11  12       1 -0.2166730  0.6993553  0.4943565 -1.0051202  1.8101045
## 12 182       0 -0.3098530 -0.1527679 -0.1330741 -1.4373710 -0.3954011
## 13  21       1  0.1443072  0.7754415  1.1611563  0.6694238  2.0070344
##            ZC
## 1   0.6166277
## 7   0.8303238
## 10  0.4924384
## 11  1.1694211
## 12 -0.3147924
## 13  2.7467644
```

```
A <- coxph(Surv(ttr, relapse) ~ ZA, data = d2) |> tidy()
B <- coxph(Surv(ttr, relapse) ~ ZB, data = d2) |> tidy()
C <- coxph(Surv(ttr, relapse) ~ ZC, data = d2) |> tidy()
bind_rows(A, B, C) |>
  transmute(term, estimate, HR = exp(estimate), p.value)
```

```
## # A tibble: 3 x 4
##   term  estimate    HR p.value
##   <chr>    <dbl> <dbl>   <dbl>
## 1 ZA      0.295  1.34   0.0691
## 2 ZB     -0.0209 0.979  0.894
## 3 ZC      0.256  1.29   0.125
```

Discretized predictions - based on quantiles

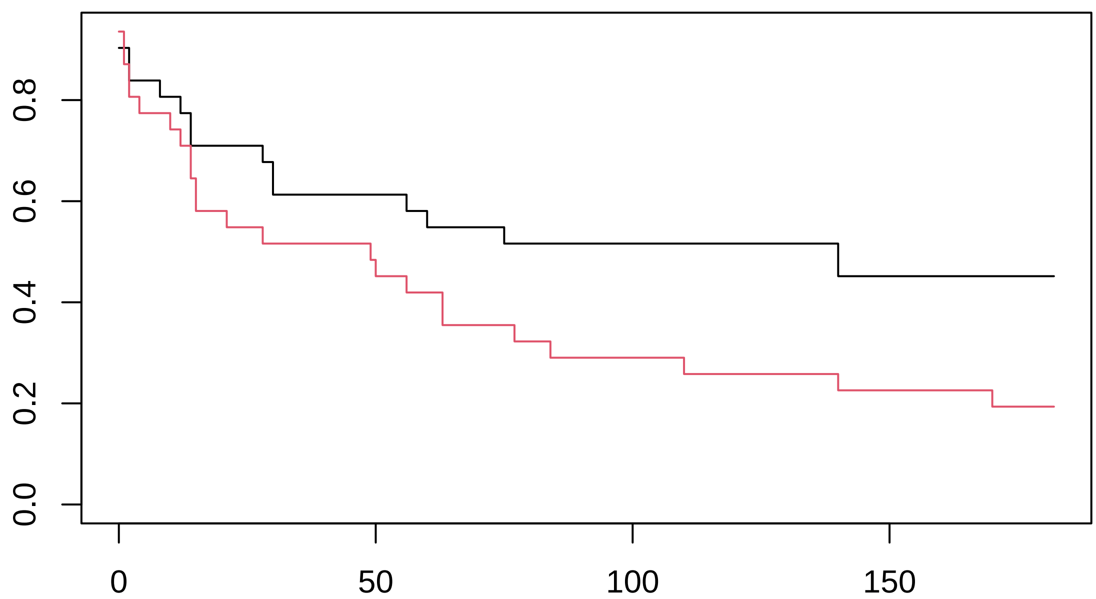
```
d3 <-
  mutate(d2,
         FA = factor((lp_A > median(lp_A)), levels = c(FALSE, TRUE), labels = c("low", "high")),
         FC = factor((lp_C > median(lp_C)), levels = c(FALSE, TRUE), labels = c("low", "high"))
         )

A <- coxph(Surv(ttr, relapse) ~ FA, data = d3) |> tidy()
C <- coxph(Surv(ttr, relapse) ~ FC, data = d3) |> tidy()
bind_rows(A, C) |>
  transmute(term, estimate, HR = exp(estimate), p.value)
```

```
## # A tibble: 2 x 4
##   term   estimate    HR p.value
##   <chr>     <dbl> <dbl>   <dbl>
## 1 FAhigh    0.599  1.82  0.0583
## 2 FChigh    0.253  1.29  0.416
```

```
fit.KM <- survfit(Surv(ttr, relapse) ~ FA, data = d3)
fit.KM
```

```
## Call: survfit(formula = Surv(ttr, relapse) ~ FA, data = d3)
##
##           n events median 0.95LCL 0.95UCL
## FA=low   31     17    140      30      NA
## FA=high  31     25     49      14     110
```

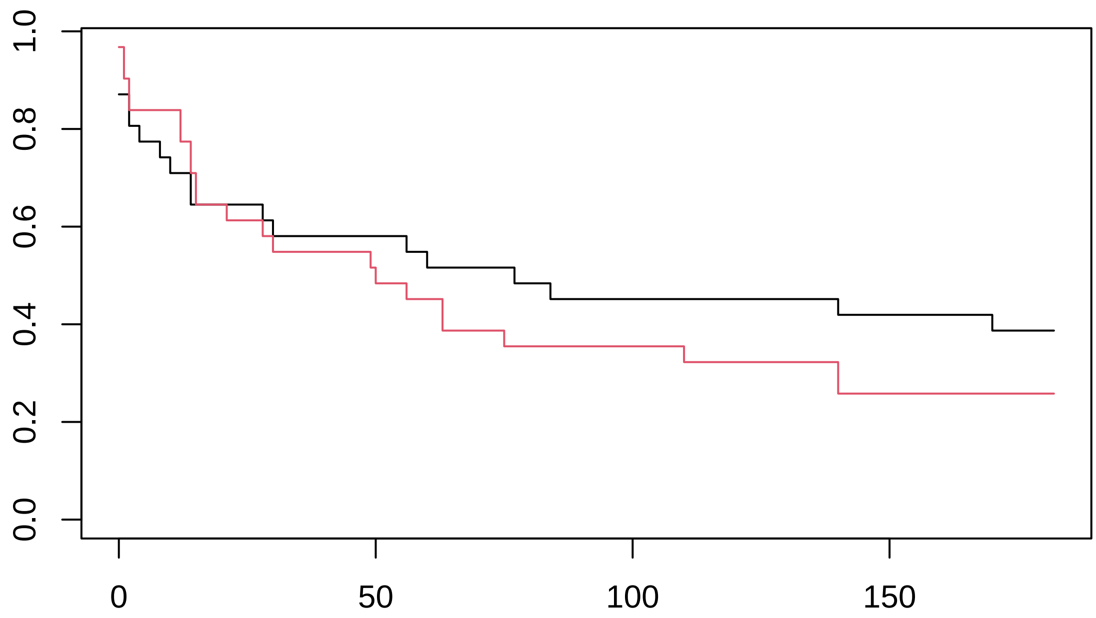
```
plot(fit.KM, col = 1:2)
```




```
fit.KM <- survfit(Surv(ttr, relapse) ~ FC, data = d3)
fit.KM
```

```
## Call: survfit(formula = Surv(ttr, relapse) ~ FC, data = d3)
##
##           n events median 0.95LCL 0.95UCL
## FC=low   31     19     77      14      NA
## FC=high  31     23     50      15     140
```

```r
plot(fit.KM, col = 1:2)
```



Model diagnostics

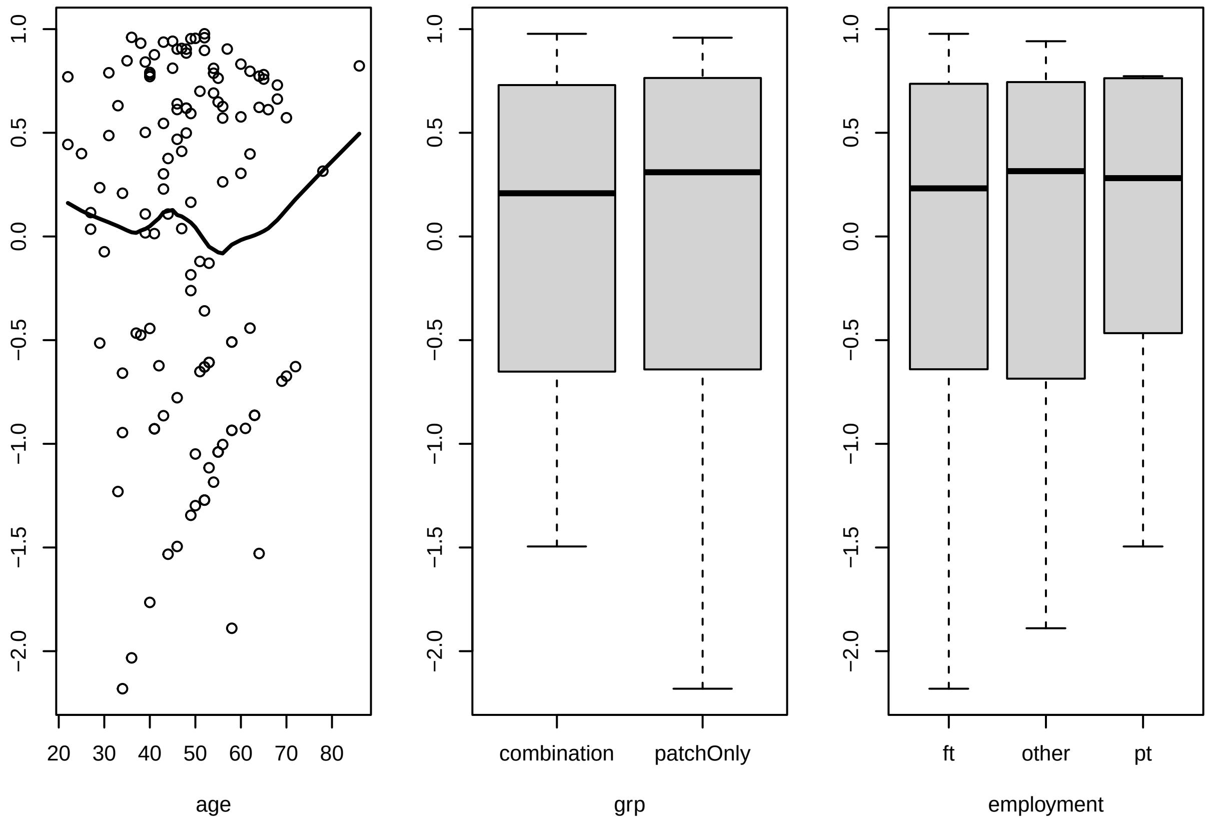
Martingale residuals

```r
library(survival)
library(asaur) ## dataset

data(pharmacoSmoking)
dat <- pharmacoSmoking
```

```r
fit <- coxph(Surv(ttr, relapse) ~ grp + age + employment, data = dat)
dat$residual <- residuals(fit, type = "martingale")
```

```r
par(mfrow = c(1, 3), mar = c(4.2, 2, 2, 2))
with(dat, {

  plot(age, residual)
  lines(lowess(age, residual), lwd = 2)

```

```
  plot(residual ~ grp)

  plot(residual ~ employment)

})
```

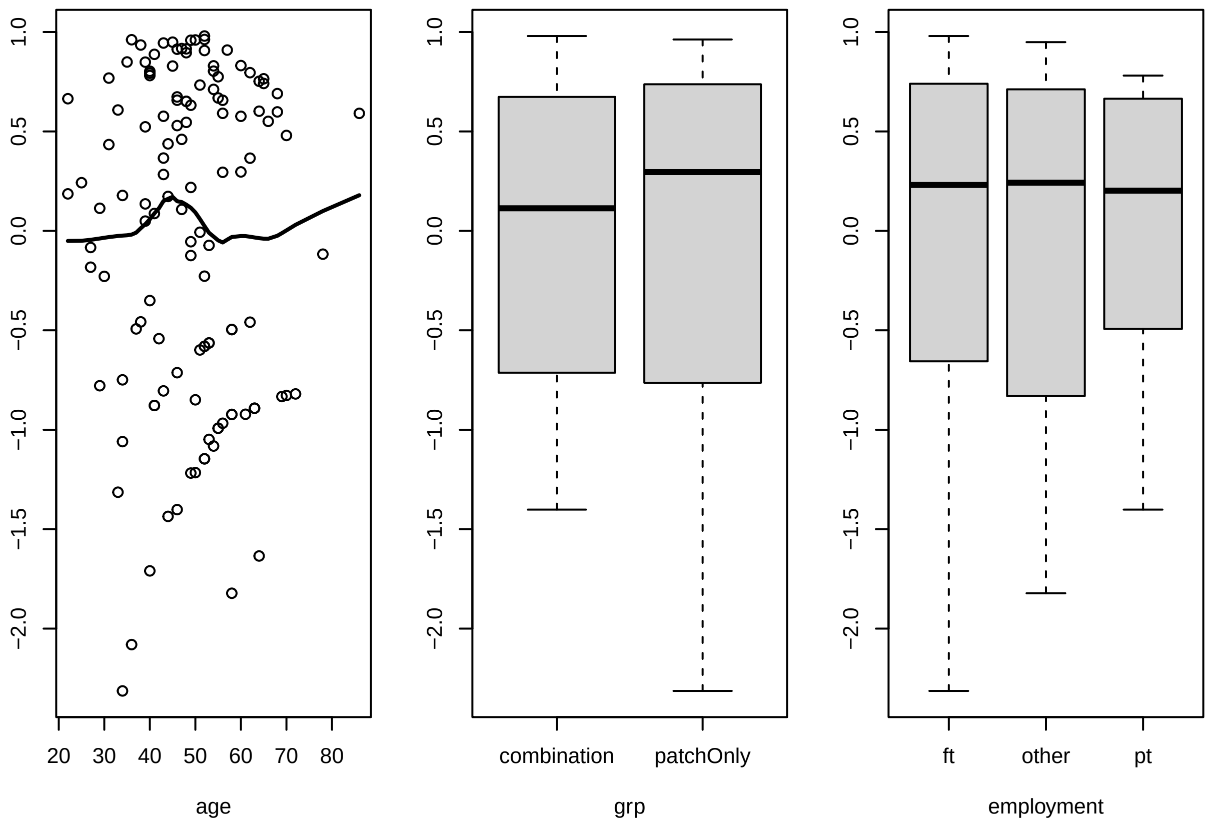



```
fit_better <- coxph(Surv(ttr, relapse) ~ grp + age + I(age^2) + employment, data = dat)
summary(fit_better)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ grp + age + I(age^2) + employment,
##     data = dat)
##
##   n= 125, number of events= 89
##
##                       coef  exp(coef)   se(coef)      z Pr(>|z|)
## grppatchOnly     0.6206075  1.8600577  0.2188288  2.836  0.00457 **
## age             -0.1001902  0.9046654  0.0549849 -1.822  0.06843 .
## I(age^2)         0.0006729  1.0006732  0.0005572  1.208  0.22713
## employmentother  0.6800741  1.9740240  0.2754600  2.469  0.01355 *
## employmentpt     0.6757762  1.9655581  0.3278821  2.061  0.03930 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                 exp(coef) exp(-coef) lower .95 upper .95
```

```
## grppatchOnly        1.8601     0.5376    1.2113     2.856
## age                 0.9047     1.1054    0.8122     1.008
## I(age^2)            1.0007     0.9993    0.9996     1.002
## employmentother     1.9740     0.5066    1.1505     3.387
## employmentpt        1.9656     0.5088    1.0337     3.737
##
## Concordance= 0.633  (se = 0.031 )
## Likelihood ratio test= 23.36  on 5 df,   p=3e-04
## Wald test            = 24.19  on 5 df,   p=2e-04
## Score (logrank) test = 24.68  on 5 df,   p=2e-04
```

```
dat$residual <- residuals(fit_better, type = "martingale")
par(mfrow = c(1, 3), mar = c(4.2, 2, 2, 2))
with(dat, {

  plot(age, residual)
  lines(lowess(age, residual), lwd = 2)

  plot(residual ~ grp)

  plot(residual ~ employment)

})
```

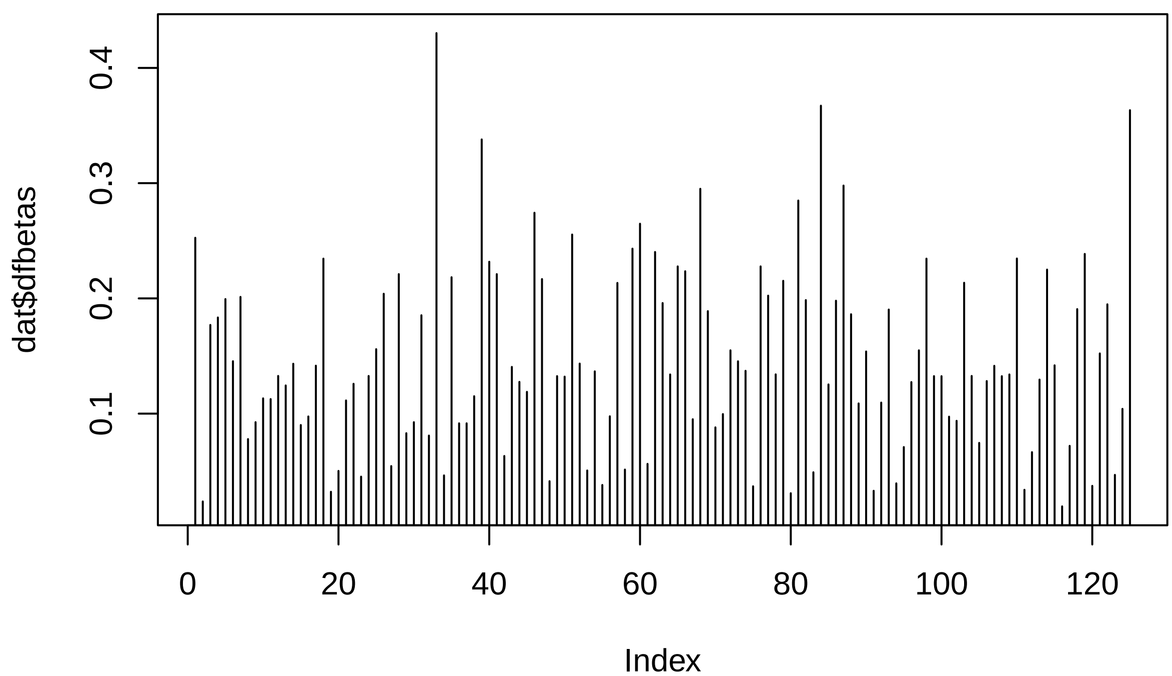


Case-deletion residuals

```r
dfbetas <- residuals(fit, type = 'dfbetas')
head(dfbetas)
```

```
##            [,1]        [,2]        [,3]         [,4]
## 1 -0.164823287  0.15809557  0.05955969  0.089952431
## 2  0.006822493 -0.01266160  0.01817193  0.005336660
## 3 -0.050525661 -0.13050951  0.10683305  0.017798812
## 4 -0.101956037  0.08958552 -0.10516817 -0.064573127
## 5 -0.126362316 -0.07386963  0.13516905 -0.008288001
## 6  0.114896122  0.01309695  0.06960045  0.054304287
```

```r
dat$dfbetas <- sqrt(rowSums(dfbetas^2))
plot(dat$dfbetas, type = 'h')
abline(h = 0)
```



Proportionality of hazards

Pancreatic cancer dataset - late vs early stage

```r
library(survival)
library(asaur) ## dataset
library(plyr)
```

```
## ------------------------------------------------------------------------------

## You have loaded plyr after dplyr - this is likely to cause problems.
## If you need functions from both plyr and dplyr, please load plyr first, then dplyr:
## library(plyr); library(dplyr)

## ------------------------------------------------------------------------------

##
## Attaching package: 'plyr'

## The following objects are masked from 'package:dplyr':
##
##     arrange, count, desc, failwith, id, mutate, rename, summarise,
##     summarize

## The following object is masked from 'package:purrr':
##
##     compact
```

```r
library(ggplot2)

fmt <- "%m/%d/%Y"
dat <- as.tibble(pancreatic) %>%
  mutate(
  onstudy = as.Date(as.character(onstudy), format = fmt),
  progression = as.Date(as.character(progression), format = fmt),
  death = as.Date(as.character(death), format = fmt),
  OS = death - onstudy,
  PFS = ifelse(is.na(progression), OS, pmin(progression - onstudy, OS))) %>%
  mutate(
  PFS = Surv(as.numeric(PFS / 30.5)),
  OS = Surv(as.numeric(OS / 30.5))
  )
```

```
## Warning: `as.tibble()` was deprecated in tibble 2.0.0.
## i Please use `as_tibble()` instead.
## i The signature and semantics have changed, see `?as_tibble`.
```

```r
dat
```

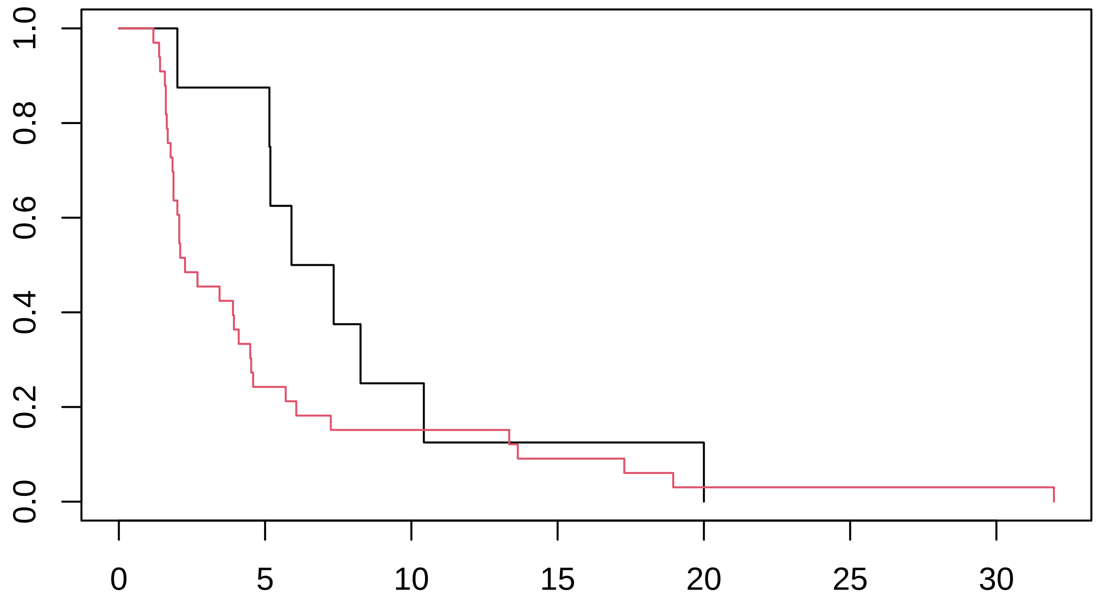
```
## # A tibble: 41 x 6
##    stage onstudy    progression death             OS       PFS
##    <fct> <date>     <date>      <date>        <Surv>    <Surv>
##  1 M     2005-12-16 2006-02-02  2006-10-19 10.065574  1.573770
##  2 M     2006-01-06 2006-02-26  2006-04-19  3.377049  1.672131
```

```
##   3 LA    2006-02-03 2006-08-02  2007-01-19 11.475410  5.901639
##   4 M     2006-03-30 NA          2006-05-11  1.377049  1.377049
##   5 LA    2006-04-27 2007-03-11  2007-05-29 13.016393 10.426230
##   6 M     2006-05-07 2006-06-25  2006-10-11  5.147541  1.606557
##   7 LA    2006-08-20 NA          2007-01-24  5.147541  5.147541
##   8 M     2007-01-22 2007-03-20  2007-04-14  2.688525  1.868852
##   9 LA    2007-03-02 NA          2008-11-01 20.000000 20.000000
##  10 M     2007-03-27 NA          2007-05-15  1.606557  1.606557
## # ... with 31 more rows
```

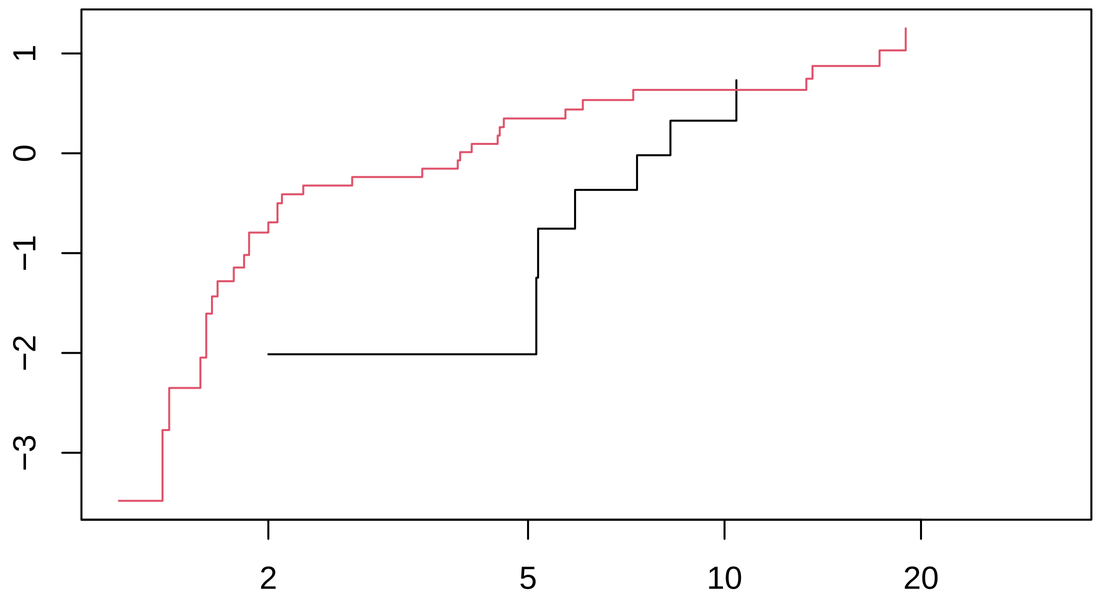
```r
fit <- coxph(PFS ~ stage, data = dat)
summary(fit)
```

```
## Call:
## coxph(formula = PFS ~ stage, data = dat)
##
##   n= 41, number of events= 41
##
##          coef exp(coef) se(coef)    z Pr(>|z|)
## stageM 0.5931    1.8095   0.4007 1.48    0.139
##
##        exp(coef) exp(-coef) lower .95 upper .95
## stageM      1.81     0.5526    0.8251     3.969
##
## Concordance= 0.589  (se = 0.033 )
## Likelihood ratio test= 2.43  on 1 df,   p=0.1
## Wald test            = 2.19  on 1 df,   p=0.1
## Score (logrank) test = 2.25  on 1 df,   p=0.1
```

```r
fit.KM <- survfit(PFS ~ stage, data = dat)
plot(fit.KM, col = 1:2)
```



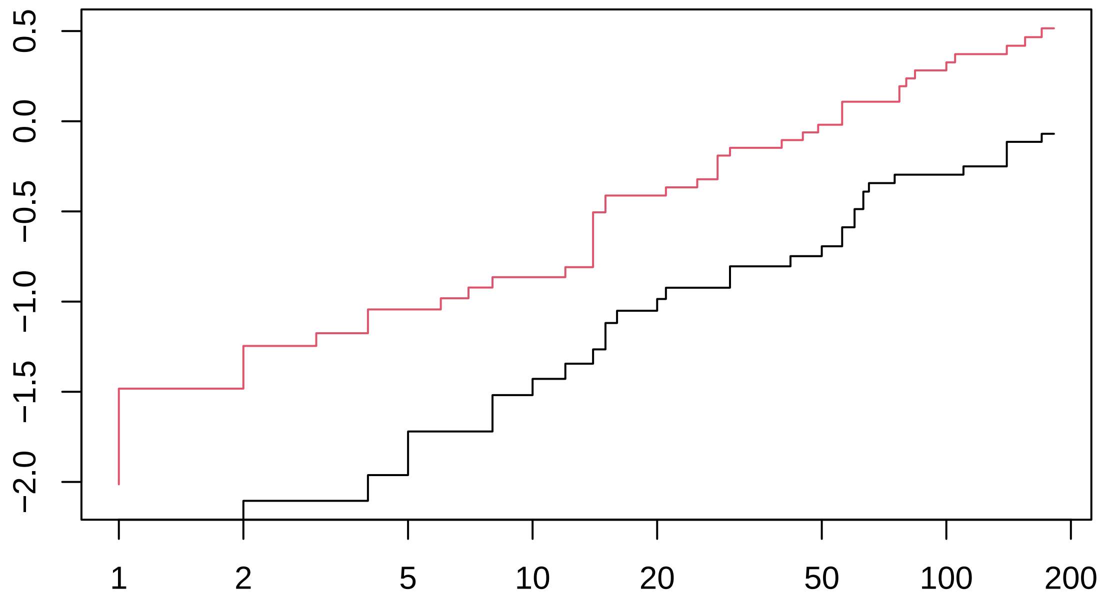

```
fit.KM <- survfit(PFS ~ stage, data = dat)
plot(fit.KM, fun= "cloglog", col = 1:2)
```



The figure indicates violation of proportionality of the hazards.

Pharmacosmoking dataset - treatment vs control

```
fit.KM <- survfit(Surv(ttr, relapse) ~ grp, data = pharmacoSmoking)

plot(fit.KM, fun = "cloglog", col = 1:2)
```



The figure indicates no violation of the assumption of proportionality of the hazards.

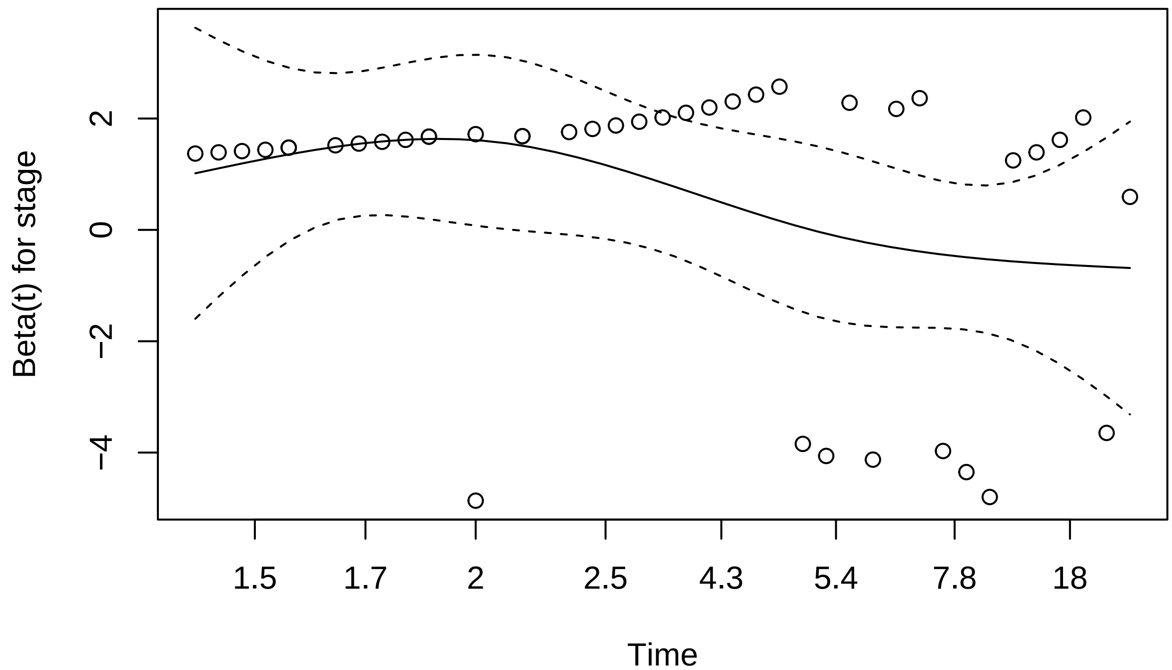
Schoenfeld residuals

```
fit <- coxph(PFS ~ stage, data = dat)
residual.sch <- cox.zph(fit)
residual.sch
```

```
##         chisq df     p
## stage   4.52  1 0.034
## GLOBAL  4.52  1 0.034
```

The null hypothesis is of constant covariates effects through time. Evidence against this hypothesis is also evidence against the assumption of proportionality of the hazards.

```
plot(residual.sch)
```



Dealing with assumptions violations

Stratification

```
library(asaur)
d <- pharmacoSmoking
d$employment <- ifelse(d$employment == "ft", "ft", "other")

table(d$employment)
```

```
##
##    ft other
##    72    53
```

Stratified Cox model:

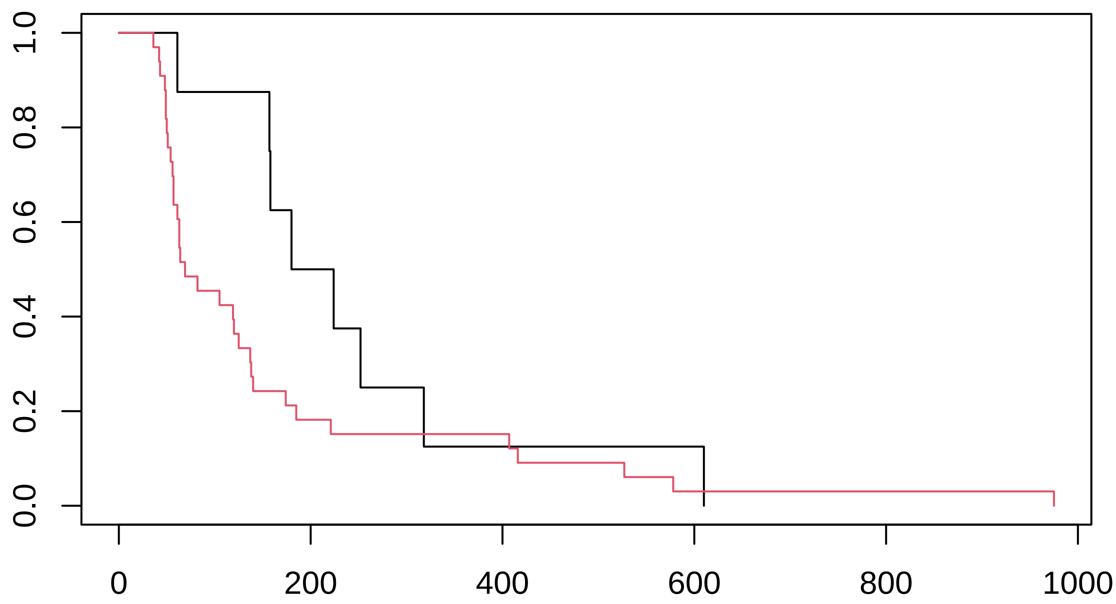
```
fit <- coxph(Surv(ttr, relapse) ~ grp + strata(employment), data = d)

summary(fit)
```

```
## Call:
## coxph(formula = Surv(ttr, relapse) ~ grp + strata(employment),
##     data = d)
##
##   n= 125, number of events= 89
##
##                coef exp(coef) se(coef)     z Pr(>|z|)
## grppatchOnly 0.6391    1.8947   0.2187 2.922  0.00348 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## grppatchOnly     1.895     0.5278     1.234     2.909
##
## Concordance= 0.577  (se = 0.029 )
## Likelihood ratio test= 8.71  on 1 df,   p=0.003
## Wald test            = 8.54  on 1 df,   p=0.003
## Score (logrank) test = 8.81  on 1 df,   p=0.003
```

Note how there is no estimate associated with 'employment'.

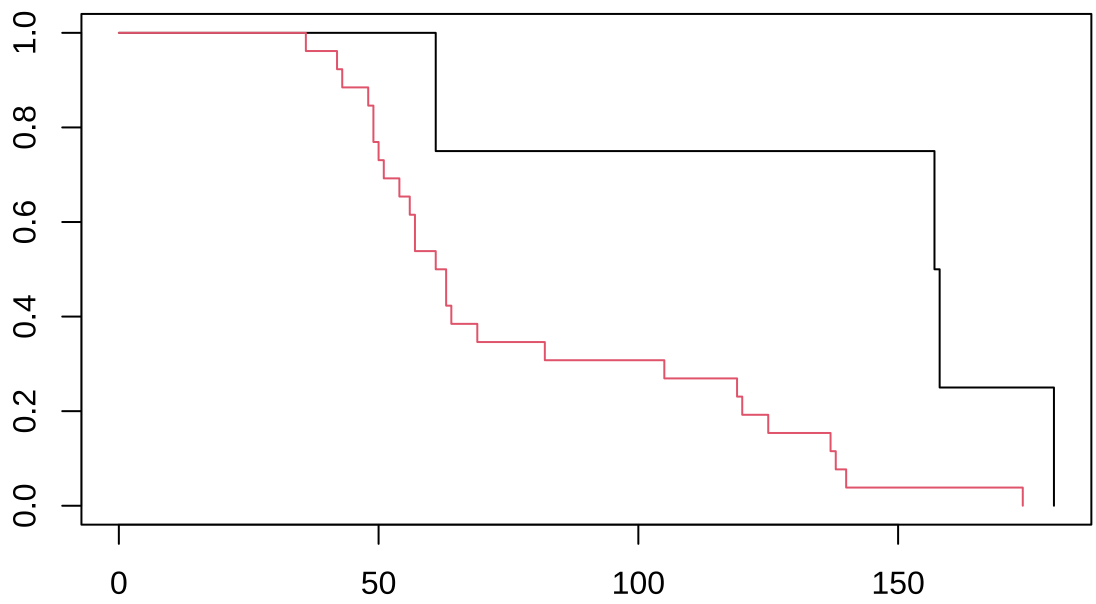
Truncation

```
library(asaur)
library(survival)
d <- pancreatic2

plot(survfit(Surv(pfs, status) ~ stage, data = d), col = 1:2)
```



THIS IS *NOT* HOW IT IS DONE:

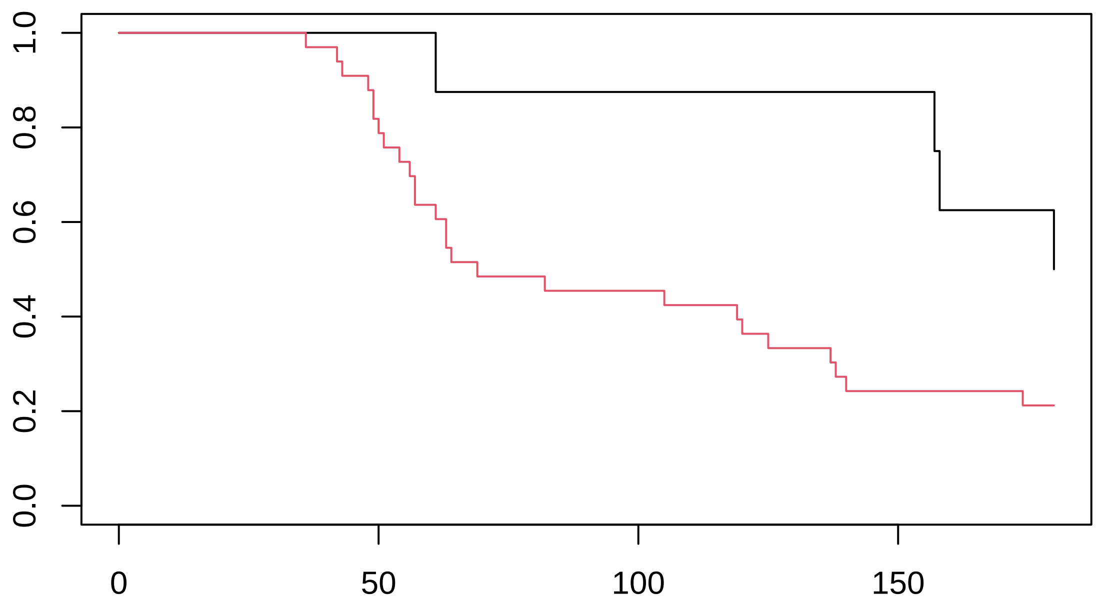
```
d_WRONG <- subset(d, pfs <= 180)

plot(survfit(Surv(pfs, status) ~ stage, data = d_WRONG), col = 1:2)
```



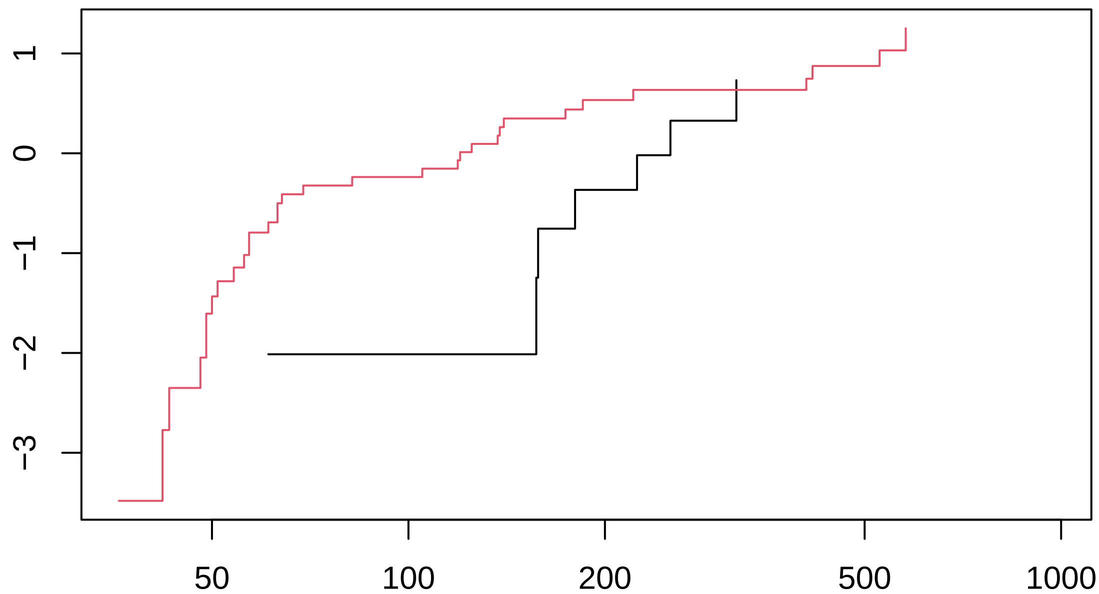
Here is how you do it:

```
d_RIGHT <- within(d, {
  status_truncated <- ifelse(pfs > 180, 0, status)
  pfs_truncated <- ifelse(pfs > 180, 180, pfs)
})
```

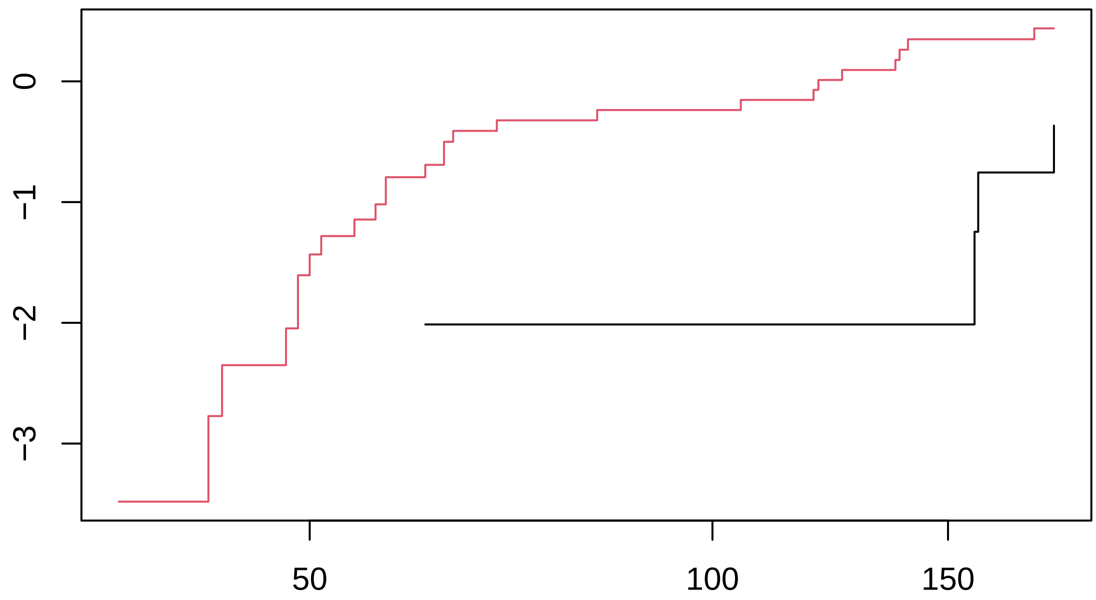
```
plot(survfit(Surv(pfs_truncated, status_truncated) ~ stage, data = d_RIGHT),
     col = 1:2)
```




```r
plot(survfit(Surv(pfs, status) ~ stage, data = d_RIGHT),
     fun = "cloglog",
     col = 1:2)
```




```
plot(survfit(Surv(pfs_truncated, status_truncated) ~ stage, data = d_RIGHT),
     fun = "cloglog",
     col = 1:2)
```




```
summary(coxph(Surv(pfs_truncated, status_truncated) ~ stage, data = d_RIGHT))
```

```
## Call:
## coxph(formula = Surv(pfs_truncated, status_truncated) ~ stage,
##     data = d_RIGHT)
##
##   n= 41, number of events= 30
##
##          coef exp(coef) se(coef)     z Pr(>|z|)
## stageM 1.0466    2.8479   0.5418 1.932   0.0534 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##        exp(coef) exp(-coef) lower .95 upper .95
## stageM     2.848     0.3511    0.9848     8.236
##
## Concordance= 0.598  (se = 0.035 )
## Likelihood ratio test= 4.71  on 1 df,   p=0.03
## Wald test            = 3.73  on 1 df,   p=0.05
## Score (logrank) test = 4.07  on 1 df,   p=0.04
```