NSWPCN Predictor Training

February 3, 2015

1 Preparation

```
library(survival)

## Loading required package:  splines

library(glmulti)

## Loading required package:  rJava
## Loading required package:  methods

library(flexsurv)
library(randomForestSRC)

## Loading required package:  parallel
##
##  randomForestSRC 1.5.5
##
##  Type rfsrc.news() to see new features, changes, and bug fixes.
##

library(reshape2)
library(plyr)
library(ggplot2)

library(MASS)
library(boot)

##
## Attaching package:  'boot'
##
## The following object is masked from 'package:survival':
##
##    aml

library(timeROC)

## Loading required package:  pec
## Loading required package:  mvtnorm
## Loading required package:  timereg

source("stdca.R")

load("03_NSWPCN_subset.rda")
```

2 Cohort selection and transformation

```
x = data[,c("Patient.Sex", "History.Diagnosis.AgeAt.Cent", "Path.LocationBody", "Path.Size.Cent", "Path.
colnames(x) = c("SexM", "AgeCent", "LocBody", "SizeCent", "Ca199", "A2", "A4")
x$SexM = x$Sex == "M"
x$Ca199 = x$Ca199 > 100

y = Surv(as.numeric(data$History.Death.Date - data$History.Diagnosis.Date), data$History.DSDeath.Event)
# Note no surgery dates, though for almost all pts there were only a few days difference.

temp = NA
temp = ls()
rm(list = temp[!(temp %in% c("x", "y"))])

sel = !is.na(y[,1]) & !is.na(y[,2]) & !is.na(x$A2) & !is.na(x$A4) & !is.na(x$LocBody)
x = x[sel,]
y = y[sel,]
rm(sel)

# Remove CA-19-9 measurements as they're mostly missing
x = x[,colnames(x) != "Ca199"]

data = as.data.frame(cbind(Time = y[,1], DSD = y[,2], x))
rm(x, y)
data$DSD = data$DSD == 1
```

3 Data splitting

There's going to be an awful lot of model manipulation and black magic going on. Create a holdout validation set for final model comparison and selection.

```
set.seed(20150201)
sel.val = sample.int(nrow(data), floor(nrow(data)/5))
sel.val = 1:nrow(data) %in% sel.val
mean(sel.val)

## [1] 0.1992

data.val = data[sel.val,,drop = FALSE]
data = data[!sel.val,,drop = FALSE]
```

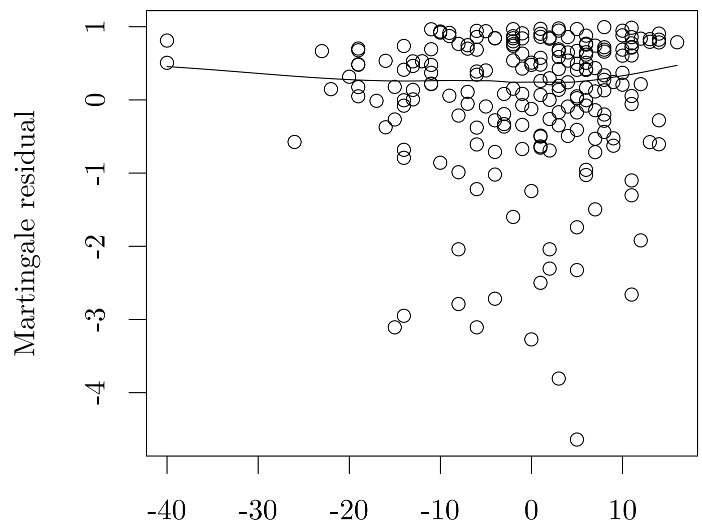
4 EDA

Use the CPH model as a convenient framework for EDA.

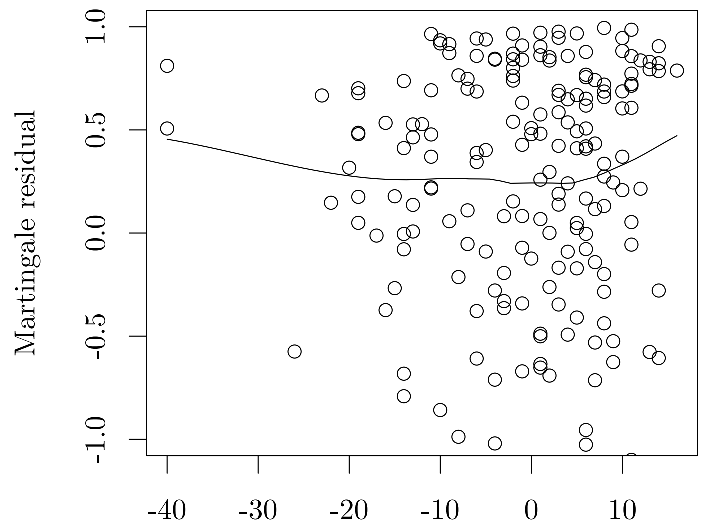
4.1 Functional form

Investigate functional form with martingale residuals.

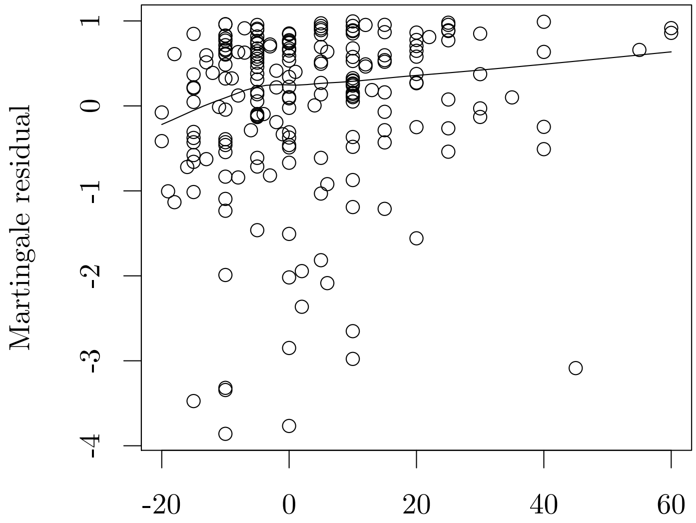
```
fit.cph.NoAge = coxph(Surv(Time, DSD) ~ SexM + LocBody + SizeCent + A2 + A4, data = data)
scatter.smooth(data$AgeCent, resid(fit.cph.NoAge, type = "martingale"), xlab = "", ylab = "Martingale re
```



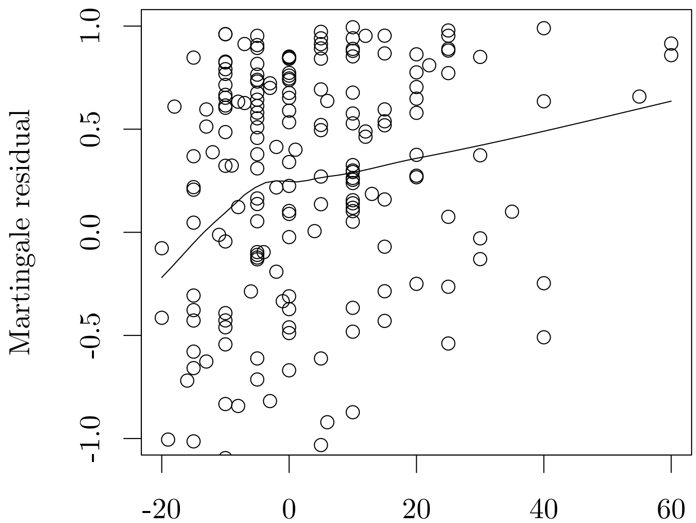

```
scatter.smooth(data$AgeCent, resid(fit.cph.NoAge, type = "martingale"), xlab = "", ylab = "Martingale re
```




```
fit.cph.NoSize = coxph(Surv(Time, DSD) ~ SexM + AgeCent + LocBody + A2 + A4, data = data)
scatter.smooth(data$SizeCent, resid(fit.cph.NoSize, type = "martingale"), xlab = "", ylab = "Martingale
```




```r
scatter.smooth(data$SizeCent, resid(fit.cph.NoSize, type = "martingale"), xlab = "", ylab = "Martingale
```



It looks like age has a minor nonlinear component, with a small uptick at advanced age. Very minor though. The size relationship appears to have a knee, close to size == 0, around which the relationship is approximately linear.

Model age as: $AgeCent + AgeCent I(AgeCent > 0) \equiv AgeCent + AgeCent_+$ Model size as: $SizeCent + SizeCent I(SizeCent > 0) \equiv SizeCent + SizeCent_+$

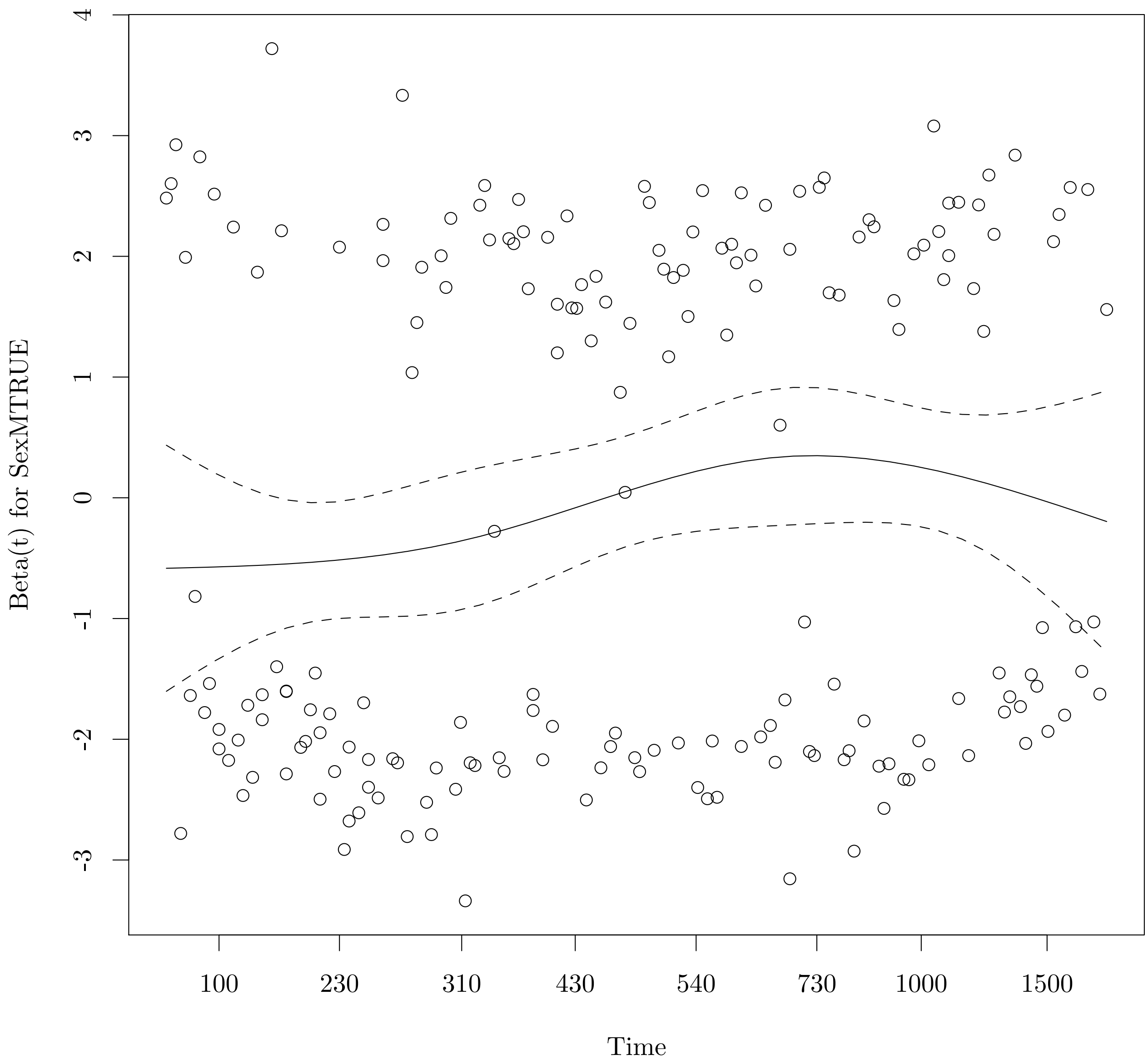
```r
data$AgePlus = pmax(data$AgeCent, 0)
data$SizePlus = pmax(data$SizeCent, 0)
```

4.2 PH assumption: full model

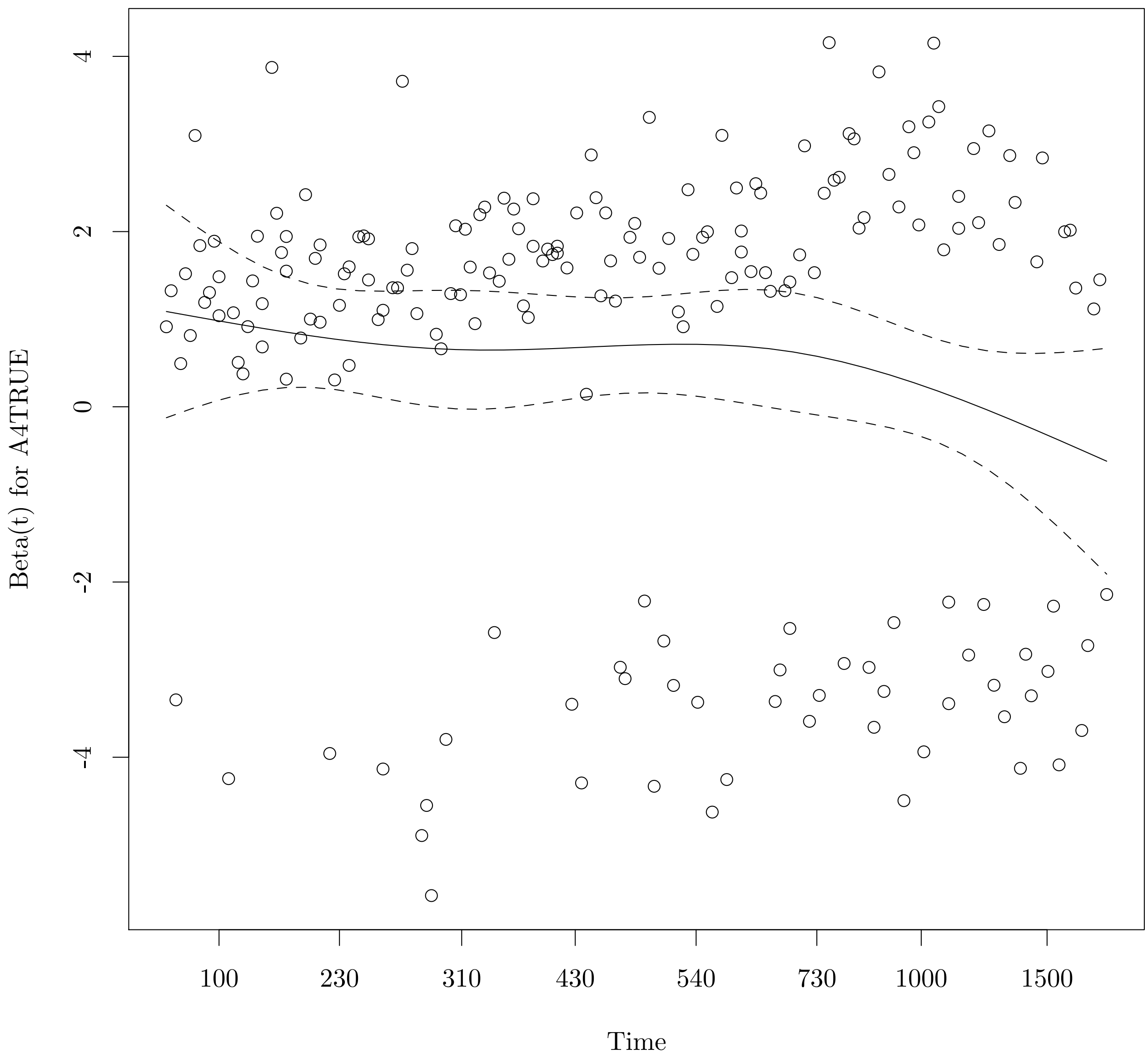
```r
fit.cph = coxph(Surv(Time, DSD) ~ SexM + AgeCent + AgePlus + LocBody + SizeCent + SizePlus + A2 + A4, da
cox.zph(fit.cph)

##                  rho   chisq      p
## SexMTRUE      0.1301  3.3440 0.0675
## AgeCent      -0.0399  0.3410 0.5592
```

```
## AgePlus       0.0270  0.1548 0.6940
## LocBodyTRUE -0.1008  1.8022 0.1794
## SizeCent    -0.0090  0.0148 0.9033
## SizePlus    -0.0128  0.0311 0.8600
## A2TRUE      -0.0203  0.0788 0.7790
## A4TRUE      -0.1354  3.3410 0.0676
## GLOBAL           NA 13.8497 0.0858
```

```
plot(cox.zph(fit.cph)[1])
```




```
plot(cox.zph(fit.cph)[8])
```



Looks OK, just weak possible effects with gender and A4.

4.3 EDA: Variable selection

```
nobs.coxph <<- function(obj, ...) sum(obj$y[,2])
set.seed(20150201)
fit.cph.as.bic = glmulti(Surv(Time, DSD) ~ SexM + AgeCent + AgePlus + LocBody + SizeCent + SizePlus + A2

## Initialization...
## TASK: Genetic algorithm in the candidate set.
## Initialization...
## Algorithm started...
##
## After 10 generations:
## Best model: Surv(Time,DSD)~1+SexM+AgePlus+LocBody+SizeCent+SizePlus+A2+AgePlus:SexM+LocBody:AgePlus+S
## Crit= 1729.11398668955
## Mean crit= 1766.92050825977
```

```
## Change in best IC: -8270.88601331045 / Change in mean IC: -8233.07949174023

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  14 ; beta may be infinite.

##
## After 20 generations:
## Best model: Surv(Time,DSD)~1+SexM+AgePlus+LocBody+SizeCent+SizePlus+A2+AgePlus:SexM+SizePlus:SexM+A2:
## Crit= 1713.89677467987
## Mean crit= 1762.03513325276
## Change in best IC: -15.2172120096811 / Change in mean IC: -4.88537500701909
##
## After 30 generations:
## Best model: Surv(Time,DSD)~1+SexM+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+AgePlus:SexM+SizePlus:SexM+
## Crit= 1713.29309640268
## Mean crit= 1757.77883565899
## Change in best IC: -0.603678277190284 / Change in mean IC: -4.25629759376807

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  4 ; beta may be infinite.

##
## After 40 generations:
## Best model: Surv(Time,DSD)~1+SexM+AgePlus+SizeCent+SizePlus+A2+A4+AgePlus:SexM+SizePlus:SexM+A2:Size(
## Crit= 1709.60872011004
## Mean crit= 1754.83822914144
## Change in best IC: -3.68437629263758 / Change in mean IC: -2.9406065175499

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  3 ; beta may be infinite.

##
## After 50 generations:
## Best model: Surv(Time,DSD)~1+SexM+SizeCent+SizePlus+A2+A4+SizePlus:SexM+A2:SizeCent+A2:SizePlus
## Crit= 1702.15368169776
## Mean crit= 1751.82996915762
## Change in best IC: -7.45503841228765 / Change in mean IC: -3.00825998381674
##
## After 60 generations:
## Best model: Surv(Time,DSD)~1+SexM+SizeCent+SizePlus+A2+A4+SizePlus:SexM+A2:SizeCent+A2:SizePlus
## Crit= 1702.15368169776
## Mean crit= 1749.23525857307
## Change in best IC: 0 / Change in mean IC: -2.59471058455279
##
## After 70 generations:
## Best model: Surv(Time,DSD)~1+SexM+SizeCent+SizePlus+A2+A4+SizePlus:SexM+A2:SizeCent+A2:SizePlus
## Crit= 1702.15368169776
## Mean crit= 1748.18423062138
## Change in best IC: 0 / Change in mean IC: -1.05102795169159
##
## After 80 generations:
## Best model: Surv(Time,DSD)~1+SexM+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus
## Crit= 1700.85916505495
## Mean crit= 1745.87214391533
## Change in best IC: -1.29451664280623 / Change in mean IC: -2.31208670604769
##
```

```
## After 90 generations:
## Best model: Surv(Time,DSD)~1+SexM+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus
## Crit= 1700.85916505495
## Mean crit= 1743.80961114713
## Change in best IC: 0 / Change in mean IC: -2.06253276820053
##
## After 100 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1741.17763508212
## Change in best IC: -13.6238075746228 / Change in mean IC: -2.63197606500398
##
## After 110 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1740.57831818846
## Change in best IC: 0 / Change in mean IC: -0.599316893664536
##
## After 120 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1738.63857426502
## Change in best IC: 0 / Change in mean IC: -1.93974392344398
##
## After 130 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1737.42400630752
## Change in best IC: 0 / Change in mean IC: -1.21456795749828
##
## After 140 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1737.12117927695
## Change in best IC: 0 / Change in mean IC: -0.302827030562639
##
## After 150 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1735.68266270197
## Change in best IC: 0 / Change in mean IC: -1.43851657498431
##
## After 160 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1735.31128667725
## Change in best IC: 0 / Change in mean IC: -0.371376024724441
##
## After 170 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1734.60899780354
## Change in best IC: 0 / Change in mean IC: -0.702288873701718
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  4 ; beta may be infinite.
```

```
##
## After 180 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1734.41964369079
## Change in best IC: 0 / Change in mean IC: -0.189354112751971
##
## After 190 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1733.36722791485
## Change in best IC: 0 / Change in mean IC: -1.05241577594325
##
## After 200 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1733.19680151486
## Change in best IC: 0 / Change in mean IC: -0.170426399986354
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  1 ; beta may be infinite.
```

```
##
## After 210 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1732.96389151369
## Change in best IC: 0 / Change in mean IC: -0.232910001176151
##
## After 220 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1732.11325171291
## Change in best IC: 0 / Change in mean IC: -0.850639800774161
##
## After 230 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1731.87559655747
## Change in best IC: 0 / Change in mean IC: -0.237655155437551
##
## After 240 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1731.61898120716
## Change in best IC: 0 / Change in mean IC: -0.256615350314632
##
## After 250 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1731.30594054392
## Change in best IC: 0 / Change in mean IC: -0.313040663238098
```

```
##
## After 260 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1730.31673935724
## Change in best IC: 0 / Change in mean IC: -0.98920118668434
##
## After 270 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1730.31673935724
## Change in best IC: 0 / Change in mean IC: 0
##
## After 280 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1730.31382715624
## Change in best IC: 0 / Change in mean IC: -0.00291220100166356
##
## After 290 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1729.85554785647
## Change in best IC: 0 / Change in mean IC: -0.458279299763944
##
## After 300 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1729.77539491139
## Change in best IC: 0 / Change in mean IC: -0.0801529450802718
##
## After 310 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1729.71168475816
## Change in best IC: 0 / Change in mean IC: -0.063710153233842
##
## After 320 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1729.09784964428
## Change in best IC: 0 / Change in mean IC: -0.613835113879759
##
## After 330 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1729.08455299787
## Change in best IC: 0 / Change in mean IC: -0.0132966464104811

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  17 ; beta may be infinite.

##
## After 340 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
```

```
## Crit= 1687.23535748033
## Mean crit= 1728.9937020156
## Change in best IC: 0 / Change in mean IC: -0.0908509822693304
##
## After 350 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1728.9381191167
## Change in best IC: 0 / Change in mean IC: -0.0555828989029123
##
## After 360 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1728.28650181196
## Change in best IC: 0 / Change in mean IC: -0.651617304730735
##
## After 370 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1728.1371550272
## Change in best IC: 0 / Change in mean IC: -0.149346784767204
##
## After 380 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1728.05668123256
## Change in best IC: 0 / Change in mean IC: -0.0804737946371006
##
## After 390 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1728.05668123256
## Change in best IC: 0 / Change in mean IC: 0
##
## After 400 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1728.05668123256
## Change in best IC: 0 / Change in mean IC: 0
##
## After 410 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1727.90861153151
## Change in best IC: 0 / Change in mean IC: -0.148069701052691
##
## After 420 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1727.65672333188
## Change in best IC: 0 / Change in mean IC: -0.251888199624773
##
## After 430 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
```

```
## Crit= 1687.23535748033
## Mean crit= 1727.42475825227
## Change in best IC: 0 / Change in mean IC: -0.23196507961643
##
## After 440 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1727.37968944642
## Change in best IC: 0 / Change in mean IC: -0.0450688058429023
##
## After 450 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1727.37968944642
## Change in best IC: 0 / Change in mean IC: 0
##
## After 460 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1727.25440946714
## Change in best IC: 0 / Change in mean IC: -0.125279979287598
##
## After 470 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1727.08037862017
## Change in best IC: 0 / Change in mean IC: -0.174030846962523
##
## After 480 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.91678585524
## Change in best IC: 0 / Change in mean IC: -0.163592764933583
##
## After 490 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.86709407315
## Change in best IC: 0 / Change in mean IC: -0.0496917820873932
##
## After 500 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.8122935298
## Change in best IC: 0 / Change in mean IC: -0.0548005433477101
##
## After 510 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.77802944676
## Change in best IC: 0 / Change in mean IC: -0.0342640830460823
##
## After 520 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
```

```
## Crit= 1687.23535748033
## Mean crit= 1726.26274628995
## Change in best IC: 0 / Change in mean IC: -0.515283156804799
##
## After 530 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.24361440849
## Change in best IC: 0 / Change in mean IC: -0.0191318814613624
##
## After 540 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.09238620418
## Change in best IC: 0 / Change in mean IC: -0.151228204315885
##
## After 550 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.09238620418
## Change in best IC: 0 / Change in mean IC: 0
##
## After 560 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.09238620418
## Change in best IC: 0 / Change in mean IC: 0
##
## After 570 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.06627923278
## Change in best IC: 0 / Change in mean IC: -0.026106971393574
##
## After 580 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.06627923278
## Change in best IC: 0 / Change in mean IC: 0
##
## After 590 generations:
## Best model: Surv(Time,DSD)~1+SizePlus+A2+A4
## Crit= 1687.23535748033
## Mean crit= 1726.06627923278
## Improvements in best and average IC have bebingo en below the specified goals.
## Algorithm is declared to have converged.
## Completed.
```

```
fit.cph.as.aicc = glmulti(Surv(Time, DSD) ~ SexM + AgeCent + AgePlus + LocBody + SizeCent + SizePlus + A
```

```
## Initialization...
## TASK: Genetic algorithm in the candidate set.
## Initialization...
## Algorithm started...
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  6 ; beta may be infinite.

##
## After 10 generations:
## Best model: Surv(Time,DSD)~1+SexM+LocBody+SizeCent+SizePlus+A2+A4+LocBody:SexM+A2:SizeCent+A2:SizePlu
## Crit= 1682.0367331261
## Mean crit= 1701.43959331731
## Change in best IC: -8317.9632668739 / Change in mean IC: -8298.56040668269
##
## After 20 generations:
## Best model: Surv(Time,DSD)~1+SexM+LocBody+SizeCent+SizePlus+A2+A4+LocBody:SexM+SizePlus:SexM+A2:SizeC
## Crit= 1680.97132981957
## Mean crit= 1698.17607519783
## Change in best IC: -1.06540330652274 / Change in mean IC: -3.2635181194878
##
## After 30 generations:
## Best model: Surv(Time,DSD)~1+SexM+SizeCent+SizePlus+A2+A4+SizeCent:SexM+A2:SizeCent+A2:SizePlus+A4:Si
## Crit= 1678.76908814612
## Mean crit= 1696.58275412683
## Change in best IC: -2.202241673456 / Change in mean IC: -1.59332107099658
##
## After 40 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1695.27966728063
## Change in best IC: -3.00658220023797 / Change in mean IC: -1.30308684619945
##
## After 50 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1694.44562102112
## Change in best IC: 0 / Change in mean IC: -0.834046259508341
##
## After 60 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1693.66057977912
## Change in best IC: 0 / Change in mean IC: -0.785041242000716
##
## After 70 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1693.30593845584
## Change in best IC: 0 / Change in mean IC: -0.354641323285932
##
## After 80 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1693.00346534139
## Change in best IC: 0 / Change in mean IC: -0.302473114443956

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  13 ; beta may be infinite.
```

```
##
## After 90 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1692.46250272724
## Change in best IC: 0 / Change in mean IC: -0.540962614148157
##
## After 100 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1692.16052441245
## Change in best IC: 0 / Change in mean IC: -0.301978314797452
##
## After 110 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1691.94450362254
## Change in best IC: 0 / Change in mean IC: -0.216020789902814
##
## After 120 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1691.71900201189
## Change in best IC: 0 / Change in mean IC: -0.225501610656238
##
## After 130 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1691.55647166699
## Change in best IC: 0 / Change in mean IC: -0.162530344895686
##
## After 140 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizeCent+A4:A2
## Crit= 1675.76250594588
## Mean crit= 1691.54947337523
## Change in best IC: 0 / Change in mean IC: -0.00699829176596722
##
## After 150 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1691.20002595634
## Change in best IC: -0.0899866655549886 / Change in mean IC: -0.349447418882619
##
## After 160 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1691.14269036956
## Change in best IC: 0 / Change in mean IC: -0.0573355867809369
##
## After 170 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1691.00186336932
## Change in best IC: 0 / Change in mean IC: -0.140827000242098
```

```
##
## After 180 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1690.73836137131
## Change in best IC: 0 / Change in mean IC: -0.263501998009588
##
## After 190 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1690.50196968902
## Change in best IC: 0 / Change in mean IC: -0.236391682293061
##
## After 200 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1690.37291838075
## Change in best IC: 0 / Change in mean IC: -0.129051308264025
##
## After 210 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1690.14564967821
## Change in best IC: 0 / Change in mean IC: -0.227268702542915
##
## After 220 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1689.89402162152
## Change in best IC: 0 / Change in mean IC: -0.251628056689697
##
## After 230 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1689.53899517239
## Change in best IC: 0 / Change in mean IC: -0.35502644913322
##
## After 240 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:A2
## Crit= 1675.67251928033
## Mean crit= 1689.40135809754
## Change in best IC: 0 / Change in mean IC: -0.137637074846907
##
## After 250 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1689.00722341922
## Change in best IC: -0.654142137557301 / Change in mean IC: -0.394134678323326
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  17 ; beta may be infinite.
```

```
##
## After 260 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
```

```
## Crit= 1675.01837714277
## Mean crit= 1688.95626024994
## Change in best IC: 0 / Change in mean IC: -0.0509631692809762
##
## After 270 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1688.95626024994
## Change in best IC: 0 / Change in mean IC: 0
##
## After 280 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1688.72623331464
## Change in best IC: 0 / Change in mean IC: -0.230026935291335
##
## After 290 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1688.5133035274
## Change in best IC: 0 / Change in mean IC: -0.212929787243411
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  4 ; beta may be infinite.
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  11 ; beta may be infinite.
```

```
##
## After 300 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1688.35219417578
## Change in best IC: 0 / Change in mean IC: -0.161109351620553
##
## After 310 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.95337990679
## Change in best IC: 0 / Change in mean IC: -0.398814268989781
##
## After 320 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.69542765853
## Change in best IC: 0 / Change in mean IC: -0.257952248265383
##
## After 330 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.64425283983
## Change in best IC: 0 / Change in mean IC: -0.0511748187000194
##
## After 340 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
```

```
## Mean crit= 1687.59517301127
## Change in best IC: 0 / Change in mean IC: -0.0490798285557048
##
## After 350 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.47004377438
## Change in best IC: 0 / Change in mean IC: -0.125129236890871
##
## After 360 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.2452591239
## Change in best IC: 0 / Change in mean IC: -0.224784650478796
##
## After 370 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.2452591239
## Change in best IC: 0 / Change in mean IC: 0
##
## After 380 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1687.06641248733
## Change in best IC: 0 / Change in mean IC: -0.178846636574235
##
## After 390 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1686.97796437564
## Change in best IC: 0 / Change in mean IC: -0.0884481116850111
##
## After 400 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1686.97796437564
## Change in best IC: 0 / Change in mean IC: 0
##
## After 410 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1686.93285703996
## Change in best IC: 0 / Change in mean IC: -0.045107335684861
##
## After 420 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1686.90184290329
## Change in best IC: 0 / Change in mean IC: -0.0310141366694552
##
## After 430 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
```

```
## Mean crit= 1686.88850429184
## Change in best IC: 0 / Change in mean IC: -0.0133386114503082
##
## After 440 generations:
## Best model: Surv(Time,DSD)~1+SizeCent+SizePlus+A2+A4+A2:SizeCent+A2:SizePlus+A4:SizePlus+A4:A2
## Crit= 1675.01837714277
## Mean crit= 1686.88850429184
## Improvements in best and average IC have bebingo en below the specified goals.
## Algorithm is declared to have converged.
## Completed.

fit.cph.as = fit.cph.as.bic
rm(nobs.coxph)
```

Also run BIC stepwise, because we can.

```
stepAIC(fit.cph, k = log(nrow(data)))

## Start:  AIC=1709
## Surv(Time, DSD) ~ SexM + AgeCent + AgePlus + LocBody + SizeCent +
##     SizePlus + A2 + A4
##
##             Df  AIC
## - SizePlus  1 1704
## - SexM      1 1704
## - LocBody   1 1704
## - SizeCent  1 1705
## - AgeCent   1 1705
## - AgePlus   1 1707
## <none>        1709
## - A2        1 1711
## - A4        1 1714
##
## Step:  AIC=1704
## Surv(Time, DSD) ~ SexM + AgeCent + AgePlus + LocBody + SizeCent +
##     A2 + A4
##
##             Df  AIC
## - SexM      1 1699
## - LocBody   1 1699
## - AgeCent   1 1700
## - AgePlus   1 1701
## <none>        1704
## - SizeCent  1 1704
## - A2        1 1706
## - A4        1 1710
##
## Step:  AIC=1699
## Surv(Time, DSD) ~ AgeCent + AgePlus + LocBody + SizeCent + A2 +
##     A4
##
##             Df  AIC
## - LocBody   1 1694
## - AgeCent   1 1695
```

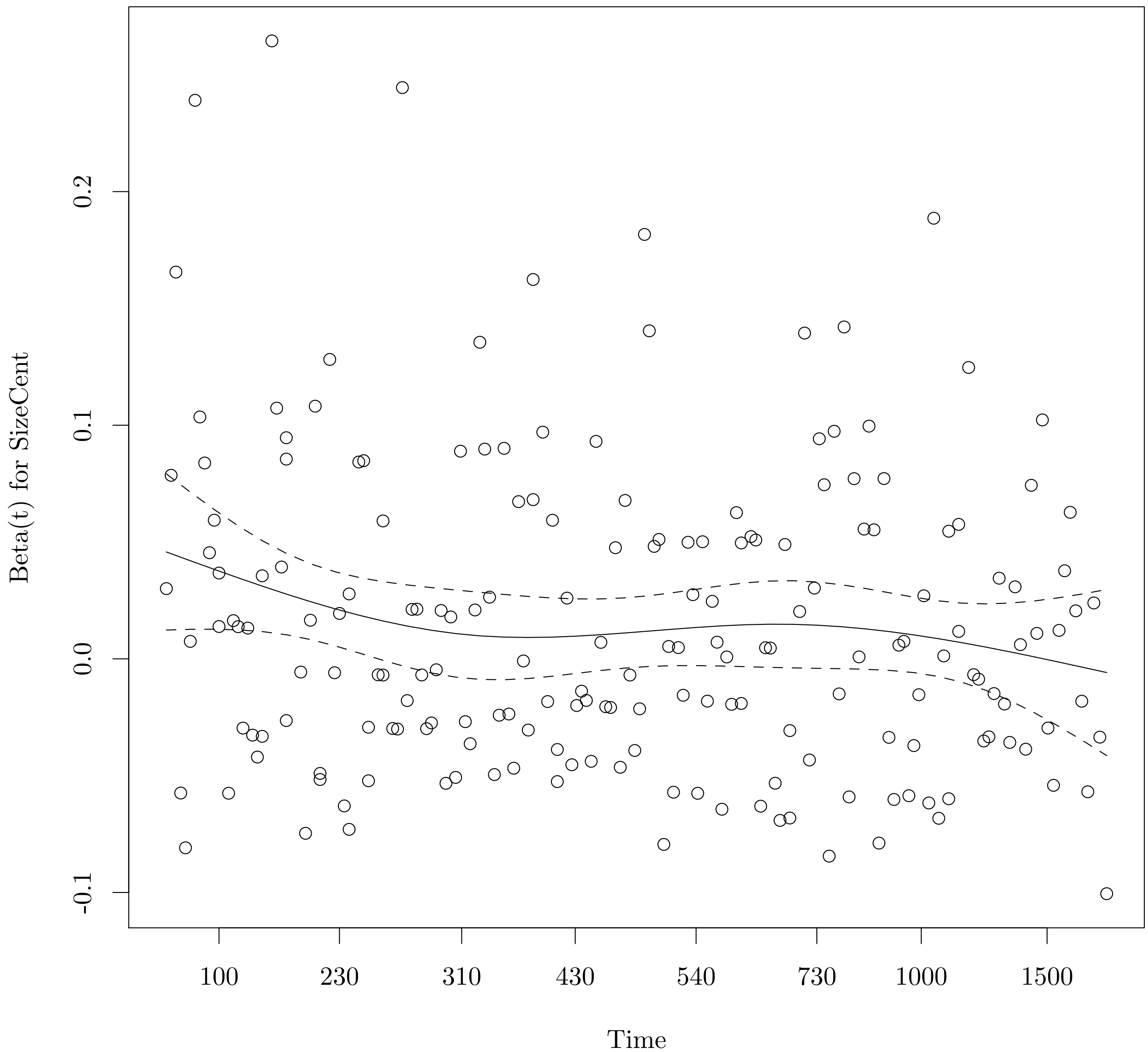
```
## - AgePlus   1 1696
## <none>        1699
## - SizeCent  1 1700
## - A2        1 1701
## - A4        1 1705
##
## Step:  AIC=1694
## Surv(Time, DSD) ~ AgeCent + AgePlus + SizeCent + A2 + A4
##
##            Df  AIC
## - AgeCent   1 1690
## - AgePlus   1 1692
## <none>        1694
## - A2        1 1696
## - SizeCent  1 1698
## - A4        1 1701
##
## Step:  AIC=1690
## Surv(Time, DSD) ~ AgePlus + SizeCent + A2 + A4
##
##            Df  AIC
## - AgePlus   1 1686
## <none>        1690
## - A2        1 1693
## - SizeCent  1 1693
## - A4        1 1696
##
## Step:  AIC=1686
## Surv(Time, DSD) ~ SizeCent + A2 + A4
##
##            Df  AIC
## <none>        1686
## - A2        1 1689
## - SizeCent  1 1689
## - A4        1 1692
## Call:
## coxph(formula = Surv(Time, DSD) ~ SizeCent + A2 + A4, data = data)
##
##
##            coef exp(coef) se(coef)    z      p
## SizeCent 0.0147      1.01   0.0049 3.00 0.0027
## A2TRUE   0.5774      1.78   0.1956 2.95 0.0032
## A4TRUE   0.5512      1.74   0.1711 3.22 0.0013
##
## Likelihood ratio test=32.1  on 3 df, p=5.09e-07  n= 205, number of events= 191
```

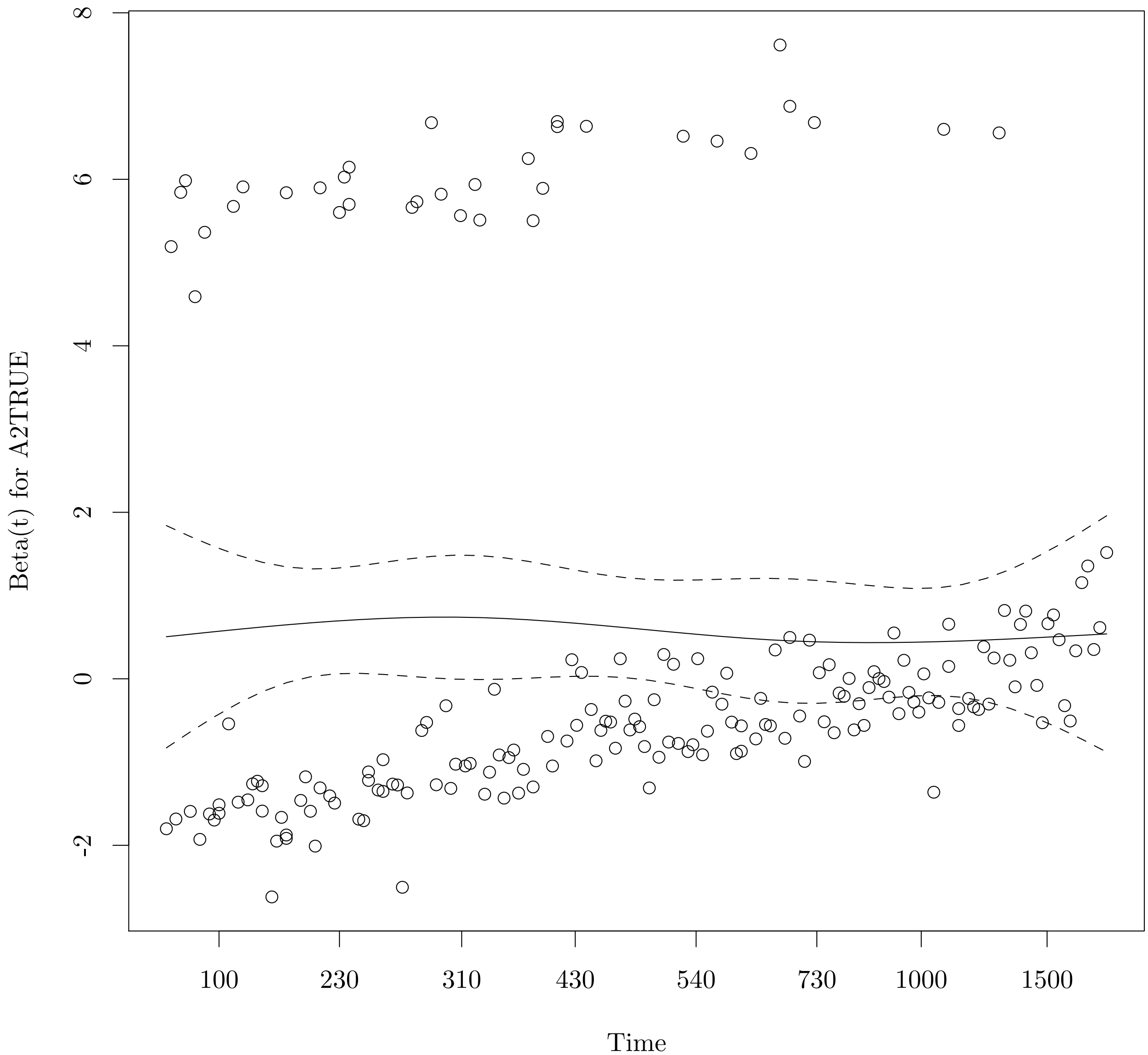
Consensus, excellent.

4.4 PH assumption: reduced model

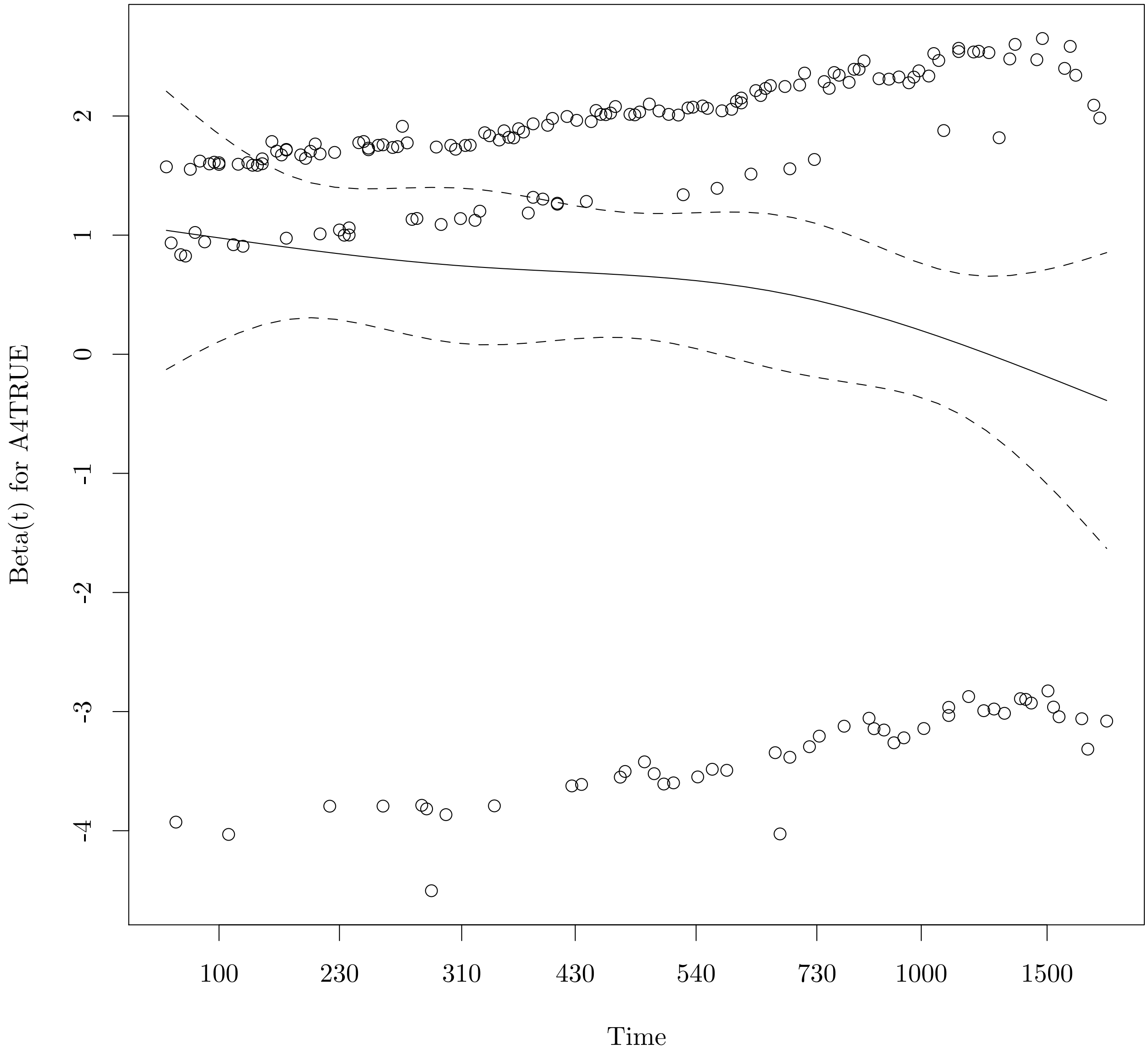
```
fit.cph = coxph(Surv(Time, DSD) ~ SizeCent + A2 + A4, data = data)
cox.zph(fit.cph)
```

```
##                rho chisq      p
## SizeCent -0.1303 3.051 0.0807
## A2TRUE   -0.0277 0.141 0.7073
## A4TRUE   -0.1468 3.839 0.0501
## GLOBAL        NA 7.386 0.0606

plot(cox.zph(fit.cph))
```





Beta(t) for A2TRUE
Time
8
6
4
2
0
-2
100
230
310
430
540
730
1000
1500

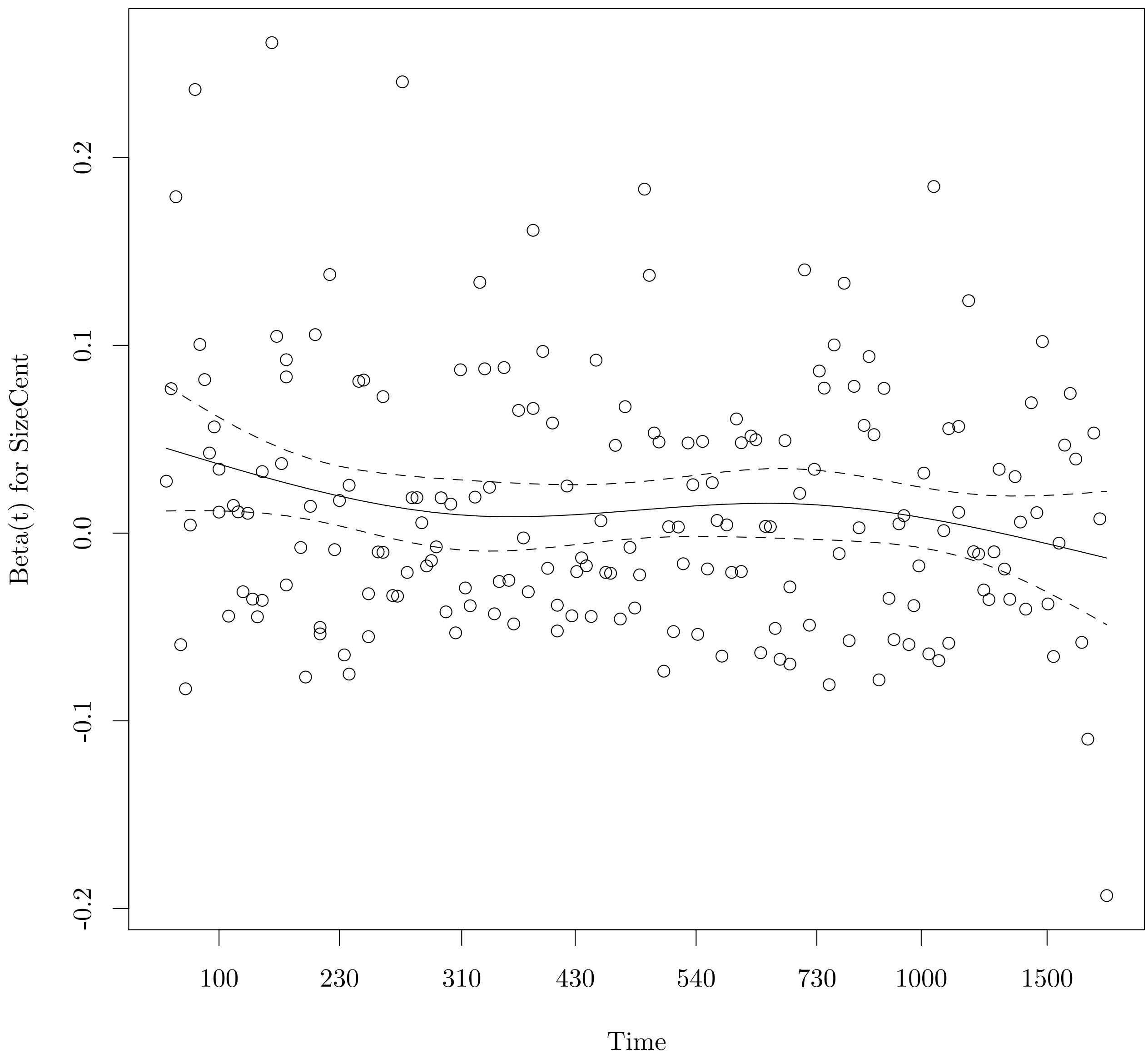


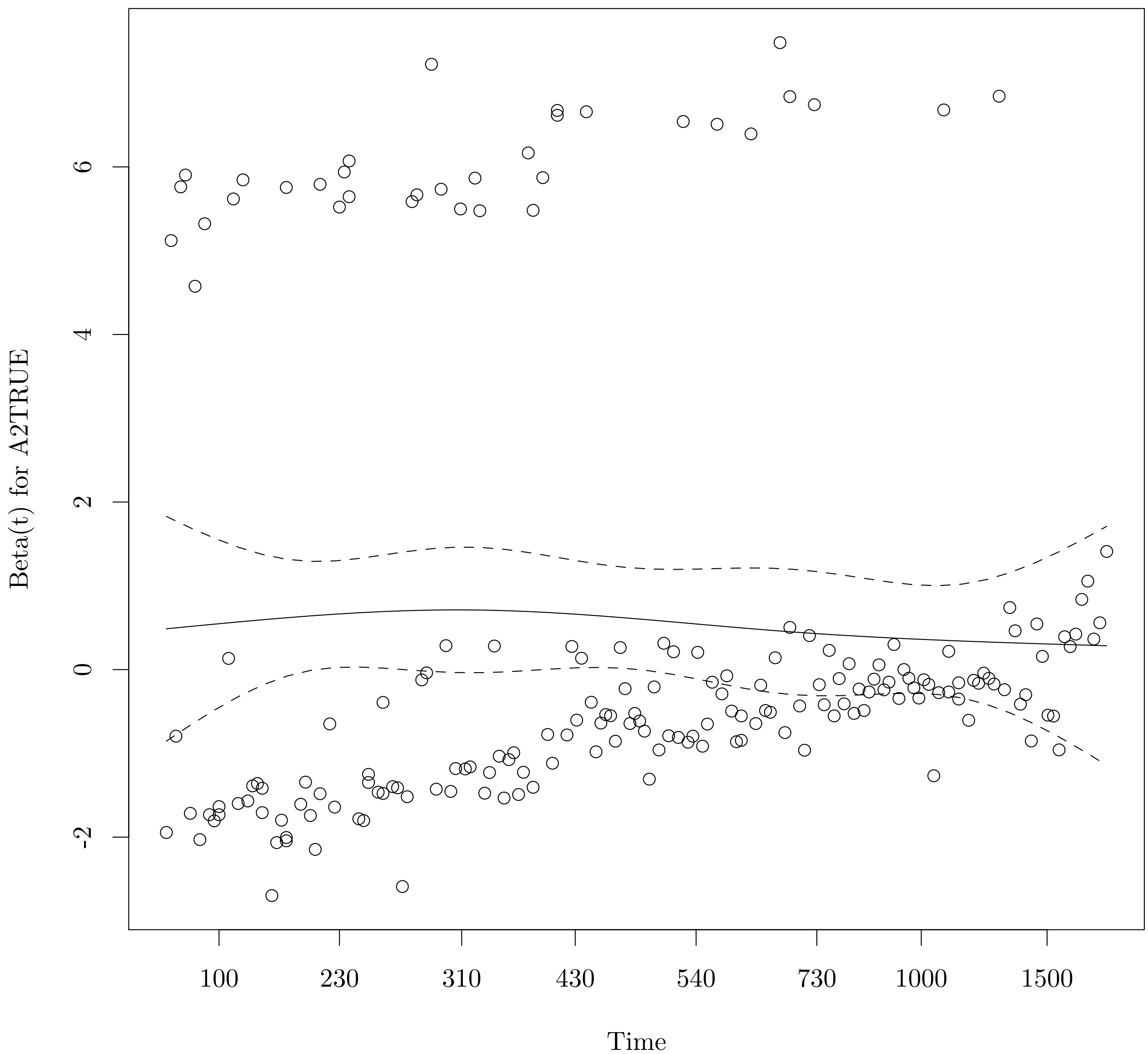
Interesting effect on A4. Betas for A4+ drop at high times. Could this suggest that high A4 is a met proxy, but *not always* – there are some A4+ pts who don't met, and thus once they've made it to 800 days or so (by which point the mets should have killed them), they're proven to have a met-free high-A4 phenotype, and consequently have good survival?

Size also has a bit of a non-PH indication, but I'm not particularly fussed as it's graphically not too worrying.

For now maybe just stratify by A4 and be done with it.

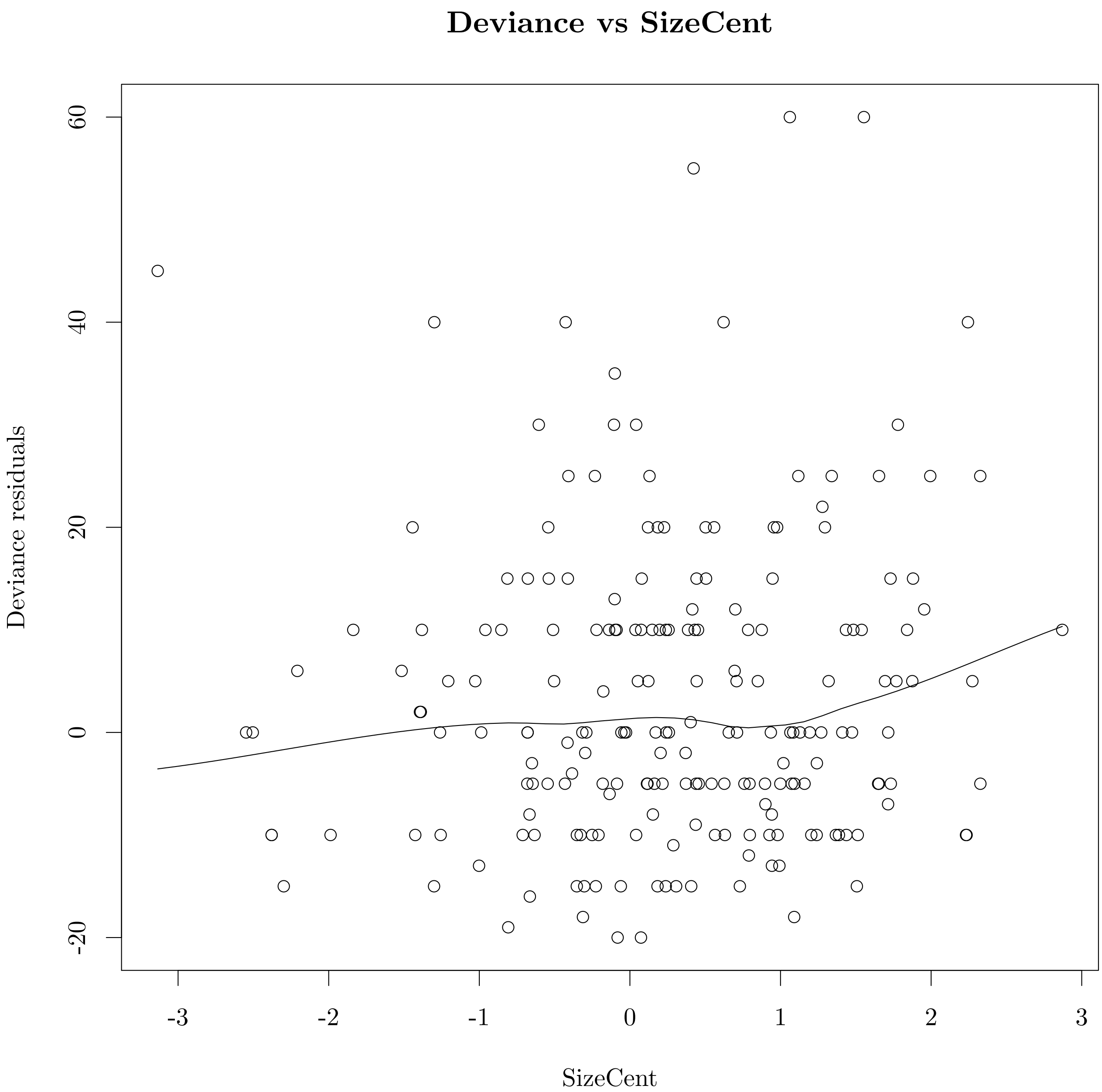
```
fit.cph = coxph(Surv(Time, DSD) ~ SizeCent + A2 + strata(A4), data = data)
cox.zph(fit.cph)

##              rho chisq      p
## SizeCent -0.1384 3.607 0.0575
## A2TRUE   -0.0415 0.318 0.5727
## GLOBAL        NA 4.198 0.1226

plot(cox.zph(fit.cph))
```


Beta(t) for SizeCent
Time
0.2
0.1
0.0
-0.1
-0.2
100
230
310
430
540
730
1000
1500

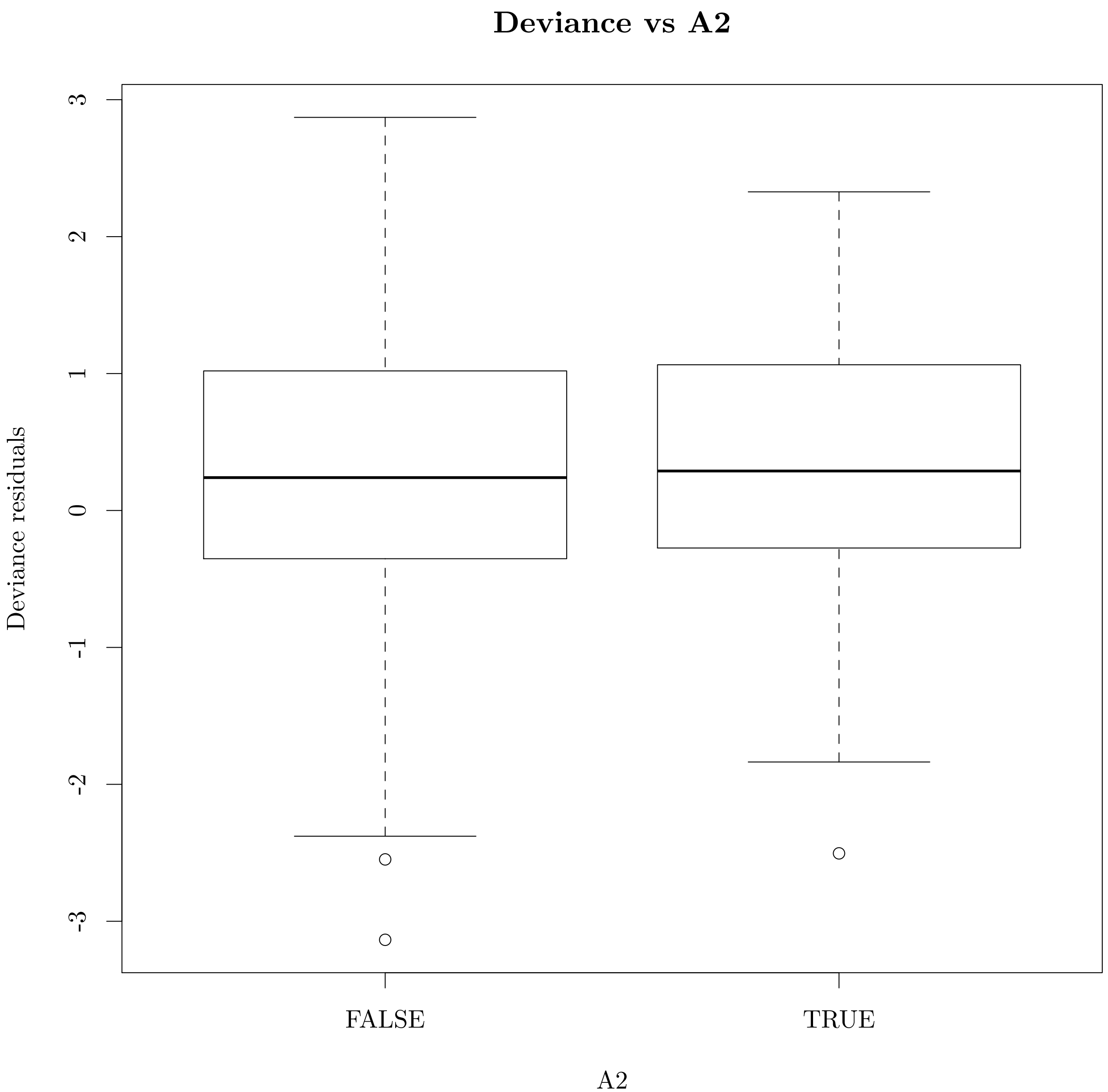


4.5 Outliers: reduced model

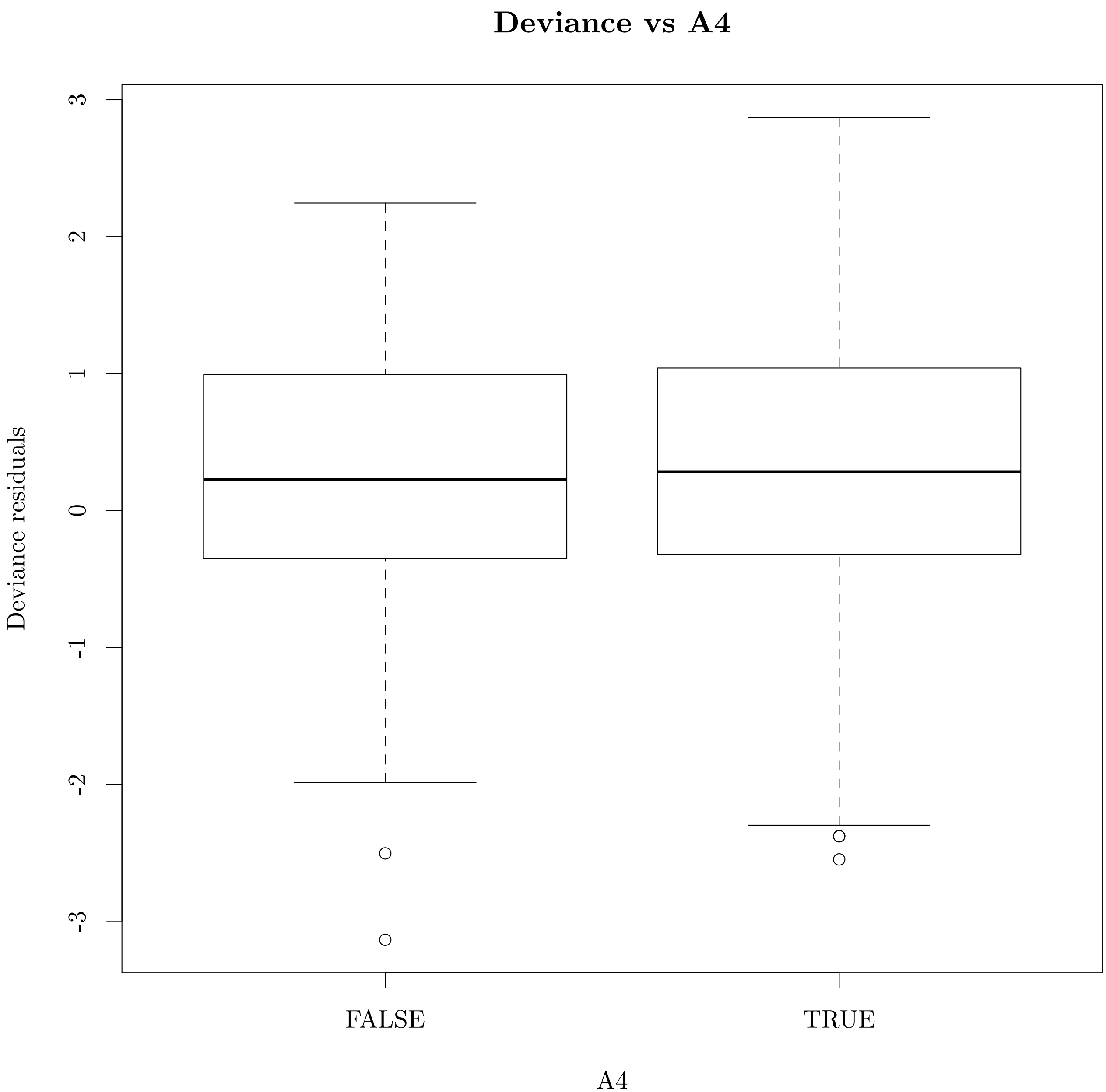
```
scatter.smooth(resid(fit.cph, type = "deviance"), data$SizeCent, xlab = "SizeCent", main = "Deviance vs
```



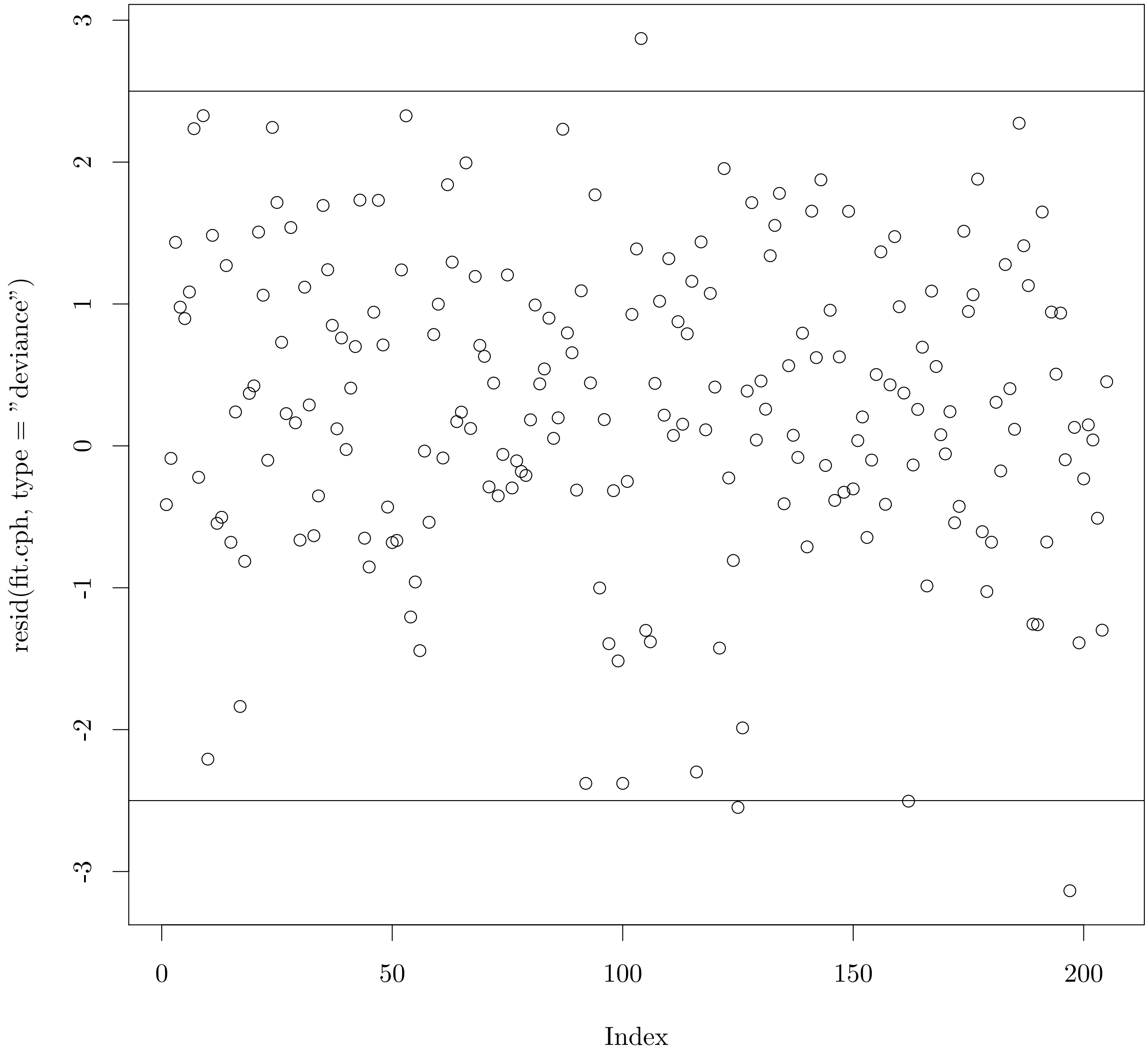

```
boxplot(resid(fit.cph, type = "deviance") ~ data$A2, main = "Deviance vs A2", xlab = "A2", ylab = "Devia
```




```
boxplot(resid(fit.cph, type = "deviance") ~ data$A4, main = "Deviance vs A4", xlab = "A4", ylab = "Devia
```



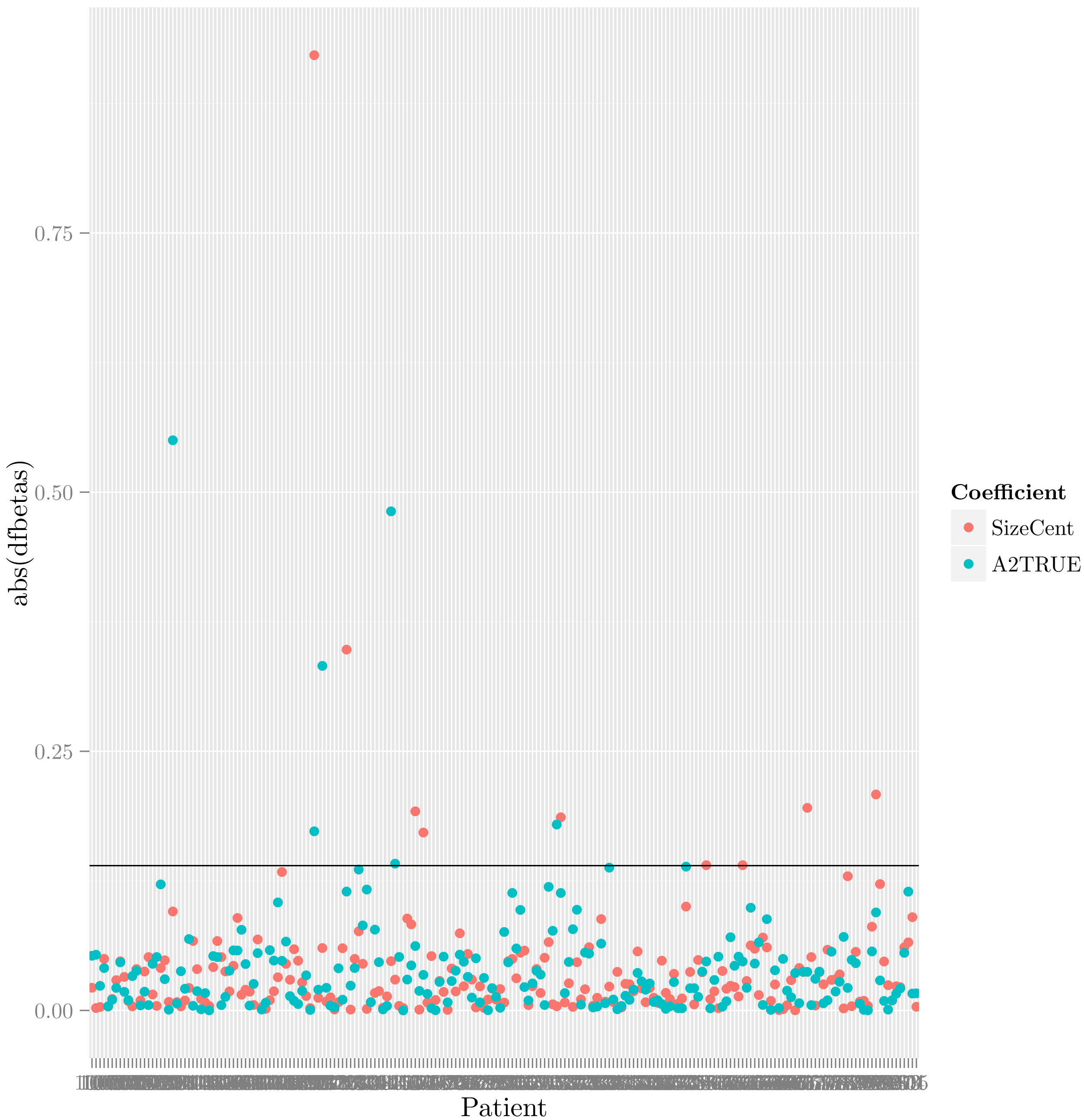

```r
plot(resid(fit.cph, type = "deviance"))
abline(h = c(-2.5, 2.5))
```




```
data$devresid = resid(fit.cph, type = "deviance")
temp = data[abs(data$devresid) >= 2.5,]
temp[order(temp$Time),]

##              Time   DSD  SexM AgeCent LocBody SizeCent    A2    A4 AgePlus
## NSWPCN_651     20  TRUE  TRUE       8    TRUE       10 FALSE  TRUE       8
## NSWPCN_1095 1836 FALSE  TRUE      -8   FALSE        0  TRUE FALSE       0
## NSWPCN_787  3287 FALSE FALSE       3   FALSE        0 FALSE  TRUE       3
## NSWPCN_1203 5063 FALSE FALSE       5    TRUE       45 FALSE FALSE       5
##              SizePlus devresid
## NSWPCN_651         10    2.871
## NSWPCN_1095         0   -2.504
## NSWPCN_787          0   -2.548
## NSWPCN_1203        45   -3.135
```

Few enough that I'm not particularly concerned. The DFBETAS will be more telling.

```
temp = resid(fit.cph, type = "dfbetas")
colnames(temp) = names(fit.cph$coefficients)
temp = melt(temp)
colnames(temp) = c("Patient", "Coefficient", "dfbetas")
temp$Patient = gsub("NSWPCN_", "", temp$Patient)
2/sqrt(nrow(data))              # The classic threshold for concern is 2/sqrt(n).

## [1] 0.1397

ggplot(temp, aes(y = abs(dfbetas), x = Patient, col = Coefficient)) + geom_point() + geom_hline(yinterce
```



```r
sort(apply(abs(resid(fit.cph, type = "dfbetas")), 1, max), decreasing = TRUE)
```

```
## NSWPCN_1203 NSWPCN_1095  NSWPCN_144 NSWPCN_1253 NSWPCN_1212  NSWPCN_799
##    0.921541    0.550030    0.481484    0.348056    0.332404    0.208381
##  NSWPCN_667  NSWPCN_154  NSWPCN_318  NSWPCN_317  NSWPCN_159  NSWPCN_145
##    0.195400    0.192054    0.186294    0.179351    0.171611    0.141562
##  NSWPCN_382  NSWPCN_645  NSWPCN_374  NSWPCN_335  NSWPCN_131 NSWPCN_1182
##    0.140095    0.140095    0.138688    0.137739    0.135884    0.133541
##  NSWPCN_788  NSWPCN_801 NSWPCN_1083  NSWPCN_315  NSWPCN_135  NSWPCN_814
##    0.129445    0.121890    0.121601    0.119204    0.116602    0.114628
##  NSWPCN_296 NSWPCN_1179  NSWPCN_647  NSWPCN_322  NSWPCN_305  NSWPCN_815
##    0.113348    0.104178    0.099055    0.097116    0.096968    0.089928
## NSWPCN_1167  NSWPCN_150  NSWPCN_333  NSWPCN_655  NSWPCN_152  NSWPCN_133
##    0.089197    0.088666    0.088096    0.088029    0.083049    0.081992
##  NSWPCN_798  NSWPCN_321  NSWPCN_138 NSWPCN_1168  NSWPCN_316  NSWPCN_284
##    0.080762    0.078351    0.077949    0.077781    0.076806    0.075677
##  NSWPCN_200  NSWPCN_787  NSWPCN_639  NSWPCN_654 NSWPCN_1143 NSWPCN_1172
##    0.074404    0.070918    0.070594    0.070312    0.068829    0.068446
## NSWPCN_1145 NSWPCN_1155 NSWPCN_1186  NSWPCN_651  NSWPCN_326  NSWPCN_813
##    0.067024    0.066960    0.066370    0.065614    0.060973    0.060895
##  NSWPCN_125  NSWPCN_304  NSWPCN_648 NSWPCN_1188  NSWPCN_777 NSWPCN_1177
##    0.060016    0.059777    0.059521    0.059040    0.058506    0.058145
## NSWPCN_1165  NSWPCN_307  NSWPCN_351  NSWPCN_779  NSWPCN_790  NSWPCN_324
##    0.057925    0.057738    0.056900    0.056653    0.056494    0.055825
##  NSWPCN_257 NSWPCN_1017   NSWPCN_10 NSWPCN_1153  NSWPCN_164  NSWPCN_182
##    0.054462    0.053716    0.052730    0.052435    0.052408    0.051863
##  NSWPCN_643  NSWPCN_445 NSWPCN_1453 NSWPCN_1082 NSWPCN_1156  NSWPCN_674
##    0.051850    0.051820    0.051576    0.051541    0.051495    0.051475
## NSWPCN_1072  NSWPCN_312  NSWPCN_268   NSWPCN_13 NSWPCN_1019  NSWPCN_661
##    0.051453    0.050800    0.050290    0.049725    0.049718    0.049690
##  NSWPCN_789  NSWPCN_377 NSWPCN_1089 NSWPCN_1178  NSWPCN_364 NSWPCN_1189
##    0.048796    0.048647    0.048333    0.048059    0.047965    0.047930
##  NSWPCN_294 NSWPCN_1023  NSWPCN_802  NSWPCN_256  NSWPCN_320  NSWPCN_141
##    0.047479    0.047408    0.047161    0.046965    0.046752    0.046576
## NSWPCN_1075 NSWPCN_1169  NSWPCN_640  NSWPCN_665 NSWPCN_1227  NSWPCN_195
##    0.044921    0.044725    0.043095    0.040923    0.040635    0.040415
##  NSWPCN_310 NSWPCN_1029 NSWPCN_1146  NSWPCN_657   NSWPCN_20 NSWPCN_1160
##    0.039997    0.039927    0.039825    0.038729    0.038275    0.038272
##  NSWPCN_636 NSWPCN_1140 NSWPCN_1157 NSWPCN_1070  NSWPCN_381  NSWPCN_770
##    0.038048    0.037796    0.037595    0.037518    0.037410    0.037408
##  NSWPCN_666  NSWPCN_341  NSWPCN_375  NSWPCN_664  NSWPCN_370  NSWPCN_784
##    0.037358    0.037181    0.037109    0.036014    0.035322    0.034775
##  NSWPCN_311 NSWPCN_1193 NSWPCN_1028 NSWPCN_1026  NSWPCN_270  NSWPCN_769
##    0.034609    0.033846    0.033099    0.032313    0.031357    0.030468
##  NSWPCN_781  NSWPCN_267 NSWPCN_1187    NSWPCN_4 NSWPCN_1022  NSWPCN_663
##    0.030153    0.029742    0.029581    0.029355    0.029211    0.029183
##   NSWPCN_17  NSWPCN_646  NSWPCN_352 NSWPCN_1190  NSWPCN_309  NSWPCN_358
##    0.028452    0.028383    0.028084    0.027072    0.026056    0.026010
##  NSWPCN_345 NSWPCN_1171  NSWPCN_348  NSWPCN_775  NSWPCN_804  NSWPCN_126
##    0.025681    0.025584    0.025263    0.025210    0.024334    0.023897
## NSWPCN_1018  NSWPCN_807  NSWPCN_269  NSWPCN_810 NSWPCN_1213  NSWPCN_273
##    0.023702    0.023320    0.023198    0.022445    0.021797    0.021516
##  NSWPCN_376  NSWPCN_638 NSWPCN_1141  NSWPCN_283  NSWPCN_350 NSWPCN_1207
##    0.021456    0.020915    0.020888    0.020617    0.020112    0.020022
```

```
##  NSWPCN_353  NSWPCN_662  NSWPCN_157 NSWPCN_1170  NSWPCN_366 NSWPCN_1150
##    0.019990    0.019073    0.018812    0.018100    0.016987    0.016706
##  NSWPCN_319    NSWPCN_9  NSWPCN_163  NSWPCN_143  NSWPCN_280 NSWPCN_1215
##    0.016695    0.016484    0.015964    0.013543    0.013043    0.012612
##  NSWPCN_360  NSWPCN_332  NSWPCN_373 NSWPCN_1148 NSWPCN_1021  NSWPCN_369
##    0.012236    0.012209    0.011551    0.011065    0.011027    0.010952
##  NSWPCN_384  NSWPCN_323  NSWPCN_272  NSWPCN_336  NSWPCN_166 NSWPCN_1027
##    0.010829    0.010679    0.010525    0.010510    0.010080    0.009928
##  NSWPCN_806  NSWPCN_363 NSWPCN_1031  NSWPCN_308  NSWPCN_796  NSWPCN_656
##    0.009815    0.009718    0.009619    0.009611    0.009246    0.009241
##  NSWPCN_793  NSWPCN_334 NSWPCN_1091 NSWPCN_1139  NSWPCN_136  NSWPCN_190
##    0.008516    0.008465    0.008244    0.007993    0.007982    0.007815
## NSWPCN_1176  NSWPCN_372  NSWPCN_330  NSWPCN_344 NSWPCN_1152  NSWPCN_797
##    0.007445    0.006494    0.004533    0.004262    0.004257    0.004255
## NSWPCN_1020 NSWPCN_1175 NSWPCN_1222  NSWPCN_142  NSWPCN_658 NSWPCN_1198
##    0.004037    0.003070    0.002912    0.002600    0.002326    0.002229
##  NSWPCN_149
##    0.002201
```

```
sum(apply(abs(resid(fit.cph, type = "dfbetas")), 1, max) > 2/sqrt(nrow(data)))
```

```
## [1] 14
```

```
data$DFBETAS_max = apply(abs(resid(fit.cph, type = "dfbetas")), 1, max)
temp = data[data$DFBETAS_max >= 2/sqrt(nrow(data)) | abs(data$devresid) >= 2.5,]
temp[order(temp$DFBETAS_max),]
```

```
##             Time   DSD  SexM AgeCent LocBody SizeCent    A2    A4 AgePlus
## NSWPCN_651    20  TRUE  TRUE       8    TRUE       10 FALSE  TRUE       8
## NSWPCN_787  3287 FALSE FALSE       3   FALSE        0 FALSE  TRUE       3
## NSWPCN_382  4915 FALSE  TRUE     -15   FALSE      -10 FALSE  TRUE       0
## NSWPCN_645  3279 FALSE  TRUE      -6   FALSE      -10 FALSE  TRUE       0
## NSWPCN_145   599  TRUE  TRUE      -6    TRUE       15  TRUE  TRUE       0
## NSWPCN_159    30  TRUE  TRUE      11    TRUE       40 FALSE FALSE      11
## NSWPCN_317   729  TRUE FALSE      11   FALSE       10  TRUE  TRUE      11
## NSWPCN_318  1464  TRUE FALSE       2   FALSE       20 FALSE  TRUE       2
## NSWPCN_154   163  TRUE  TRUE      -2    TRUE       60 FALSE  TRUE       0
## NSWPCN_667  2415 FALSE FALSE     -14   FALSE      -15 FALSE  TRUE       0
## NSWPCN_799    70  TRUE FALSE       4    TRUE       60  TRUE  TRUE       4
## NSWPCN_1212 1053  TRUE  TRUE      12   FALSE        2  TRUE  TRUE      12
## NSWPCN_1253 1044  TRUE  TRUE      -2   FALSE       40 FALSE  TRUE       0
## NSWPCN_144  1206  TRUE FALSE       0   FALSE       10  TRUE  TRUE       0
## NSWPCN_1095 1836 FALSE  TRUE      -8   FALSE        0  TRUE FALSE       0
## NSWPCN_1203 5063 FALSE FALSE       5    TRUE       45 FALSE FALSE       5
##             SizePlus devresid DFBETAS_max
## NSWPCN_651        10   2.8710     0.06561
## NSWPCN_787         0  -2.5481     0.07092
## NSWPCN_382         0  -2.3788     0.14010
## NSWPCN_645         0  -2.3788     0.14010
## NSWPCN_145        15  -0.8134     0.14156
## NSWPCN_159        40   2.2447     0.17161
## NSWPCN_317        10  -0.9593     0.17935
## NSWPCN_318        20  -1.4433     0.18629
## NSWPCN_154        60   1.0620     0.19205
## NSWPCN_667         0  -2.2984     0.19540
```

```
## NSWPCN_799         60   1.5536     0.20838
## NSWPCN_1212         2  -1.3883     0.33240
## NSWPCN_1253        40  -1.2988     0.34806
## NSWPCN_144         10  -1.8368     0.48148
## NSWPCN_1095         0  -2.5042     0.55003
## NSWPCN_1203        45  -3.1354     0.92154
```

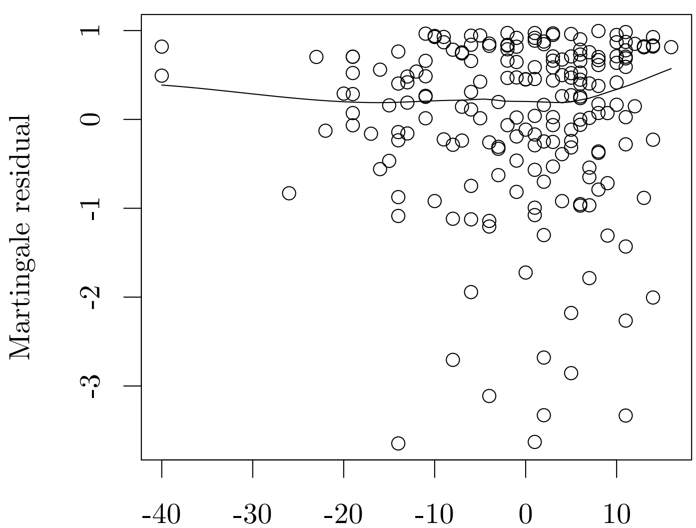
Some long survivors are causing problems. Given the data issues, it'd be prudent to remove them – it's not practical to go back to the source data and find out if they're legit or not. These guys are alive at ¿10 years, according to the data, which is near unheard-of in PDAC. I propose to remove all pts alive for 3000 days or longer, and anything with DFBETAS ¿= 0.2.

```
data = data[data$Time < 3000 & data$DFBETAS_max < 0.2,]
data.val = data.val[data.val$Time < 3000,]
```

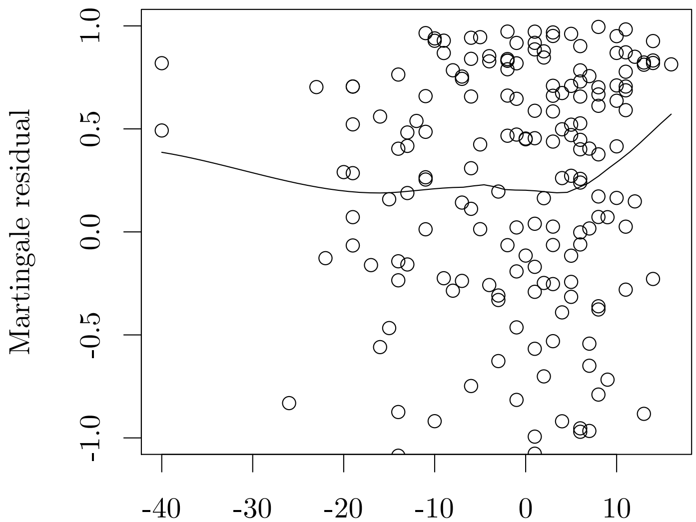
Now repeat everything...

4.6 Functional form

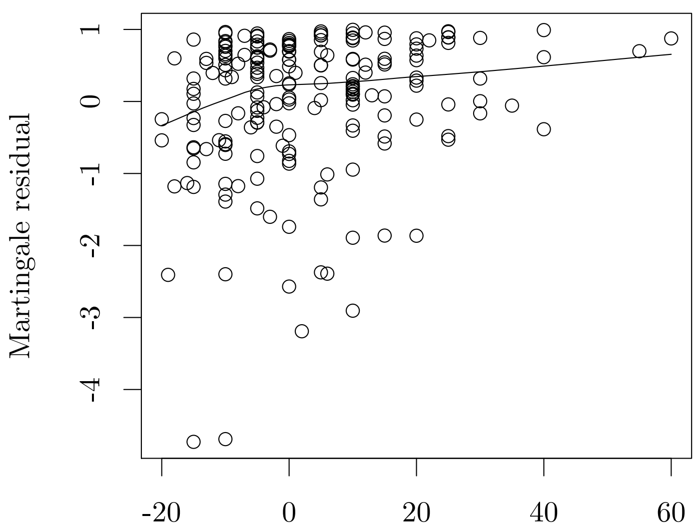
```
fit.cph.NoAge = coxph(Surv(Time, DSD) ~ SexM + LocBody + SizeCent + A2 + A4, data = data)
scatter.smooth(data$AgeCent, resid(fit.cph.NoAge, type = "martingale"), xlab = "", ylab = "Martingale re
```



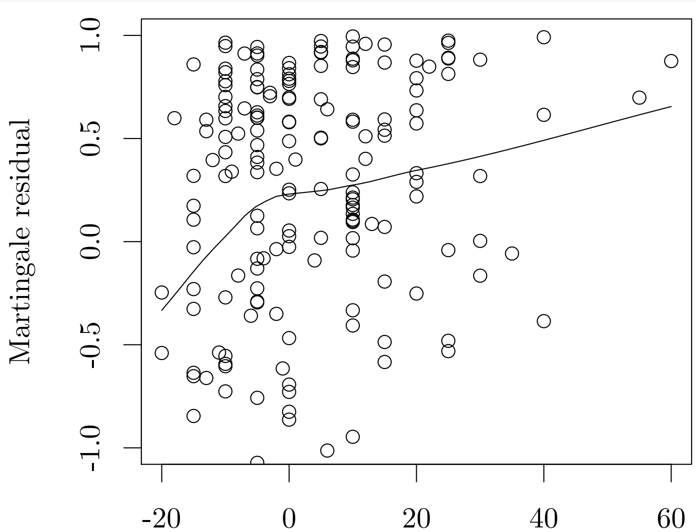

```
scatter.smooth(data$AgeCent, resid(fit.cph.NoAge, type = "martingale"), xlab = "", ylab = "Martingale re
```




```
fit.cph.NoSize = coxph(Surv(Time, DSD) ~ SexM + AgeCent + LocBody + A2 + A4, data = data)
scatter.smooth(data$SizeCent, resid(fit.cph.NoSize, type = "martingale"), xlab = "", ylab = "Martingale
```




```
scatter.smooth(data$SizeCent, resid(fit.cph.NoSize, type = "martingale"), xlab = "", ylab = "Martingale
```



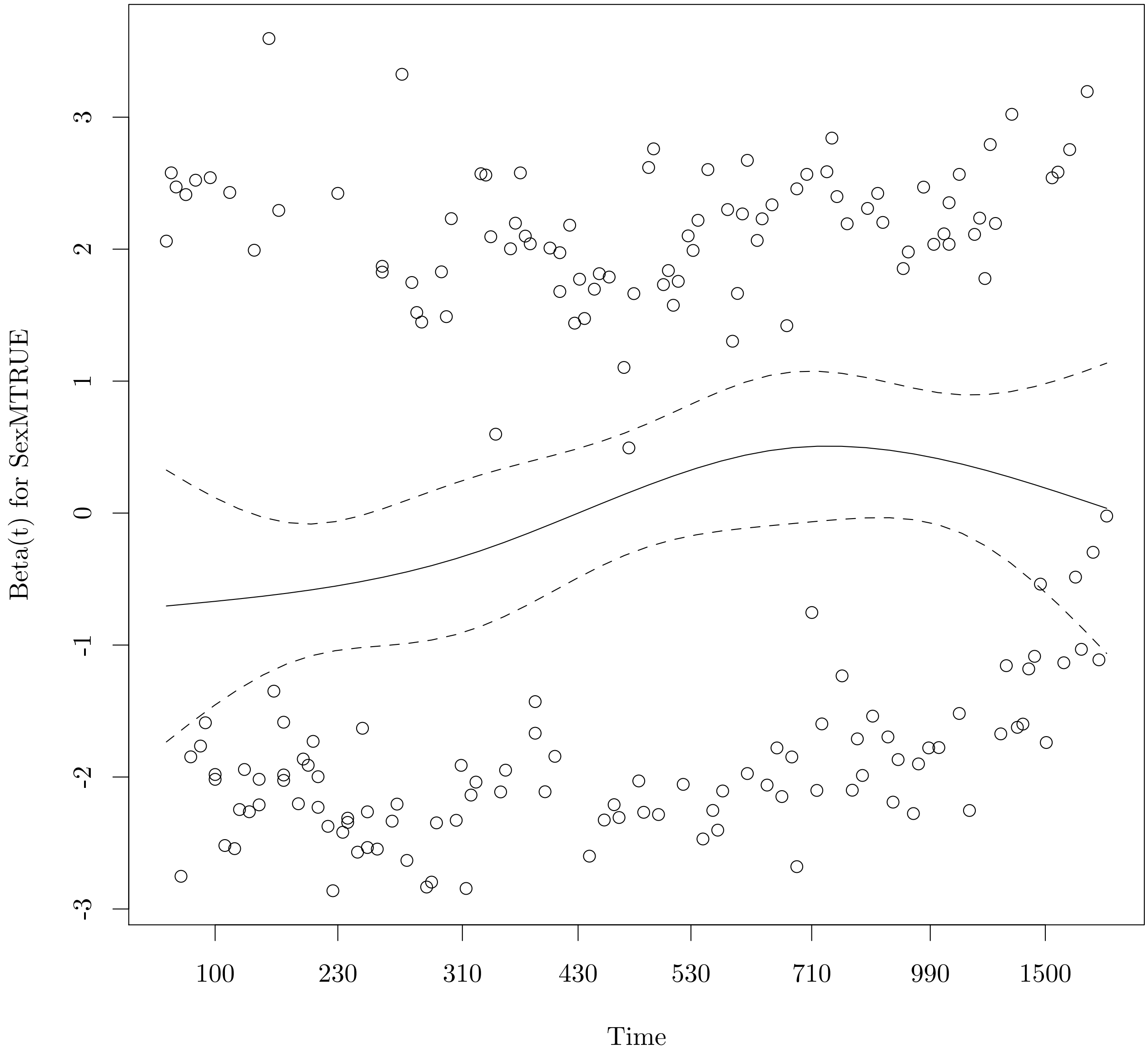
It looks like age has a minor nonlinear component, with a small uptick at advanced age. Very minor though. The size relationship appears to have a knee, close to size == 0, around which the relationship is approximately linear.

Model age as: $AgeCent + AgeCent I(AgeCent > 0) \equiv AgeCent + AgeCent_+$ Model size as: $SizeCent + SizeCent I(SizeCent > 0) \equiv SizeCent + SizeCent_+$

```
data$AgePlus = pmax(data$AgeCent, 5) - 5
data$SizePlus = pmax(data$SizeCent, 0)
```

4.7 PH assumption: full model

```
fit.cph = coxph(Surv(Time, DSD) ~ SexM + AgeCent + AgePlus + LocBody + SizeCent + SizePlus + A2 + A4, da
cox.zph(fit.cph)

##                 rho   chisq      p
## SexMTRUE     0.1781  6.1794 0.0129
## AgeCent     -0.0276  0.1590 0.6900
## AgePlus     -0.0653  0.9177 0.3381
## LocBodyTRUE -0.1213  2.5855 0.1078
## SizeCent    -0.0205  0.0798 0.7776
## SizePlus     0.0378  0.2999 0.5840
## A2TRUE       0.0973  1.9176 0.1661
## A4TRUE      -0.1033  1.9860 0.1588
## GLOBAL           NA 15.9230 0.0435

plot(cox.zph(fit.cph)[1])
```



4.8 EDA: Variable selection

```
nobs.coxph <<- function(obj, ...) sum(obj$y[,2])
set.seed(20150201)
fit.cph.as.bic = glmulti(Surv(Time, DSD) ~ strata(SexM) + AgeCent + AgePlus + LocBody + SizeCent + SizeP

## Initialization...
## TASK: Genetic algorithm in the candidate set.
## Initialization...
## Algorithm started...
##
## After 10 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgeCent+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+AgePlus:Age
## Crit= 1386.45949115679
## Mean crit= 1417.52264128484
## Change in best IC: -8613.54050884321 / Change in mean IC: -8582.47735871516
```

```
##
## After 20 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+A2+A4+A2:SizeCent+A4:LocBody+strat
## Crit= 1361.32514921699
## Mean crit= 1410.127136962
## Change in best IC: -25.1343419398004 / Change in mean IC: -7.39550432283295
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  11 ; beta may be infinite.
```

```
##
## After 30 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+LocBody+SizeCent+A2+A4+A4:LocBody+strata(SexM):SizeCent
## Crit= 1353.38950302717
## Mean crit= 1406.8093174039
## Change in best IC: -7.93564618981941 / Change in mean IC: -3.31781955810561
##
## After 40 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+LocBody+SizeCent+A2+A4+A4:LocBody
## Crit= 1352.59611072079
## Mean crit= 1403.67123867365
## Change in best IC: -0.793392306378109 / Change in mean IC: -3.13807873024439
##
## After 50 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+LocBody+SizeCent+A2+A4
## Crit= 1347.65885958051
## Mean crit= 1401.35223231976
## Change in best IC: -4.93725114028302 / Change in mean IC: -2.3190063538982
##
## After 60 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+LocBody+SizeCent+A2+A4
## Crit= 1347.65885958051
## Mean crit= 1400.20683837434
## Change in best IC: 0 / Change in mean IC: -1.1453939454118
##
## After 70 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1398.35960553043
## Change in best IC: -5.22267055702287 / Change in mean IC: -1.84723284391066
##
## After 80 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1396.84197554499
## Change in best IC: 0 / Change in mean IC: -1.51762998543973
##
## After 90 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1395.23823697744
## Change in best IC: 0 / Change in mean IC: -1.60373856754859
##
## After 100 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
```

```
## Crit= 1342.43618902348
## Mean crit= 1394.30086310397
## Change in best IC: 0 / Change in mean IC: -0.937373873473689
##
## After 110 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1394.00196516478
## Change in best IC: 0 / Change in mean IC: -0.298897939191875

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  11 ; beta may be infinite.

##
## After 120 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1393.33811464395
## Change in best IC: 0 / Change in mean IC: -0.663850520824781
##
## After 130 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1391.84719857897
## Change in best IC: 0 / Change in mean IC: -1.49091606498018
##
## After 140 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1391.02659984882
## Change in best IC: 0 / Change in mean IC: -0.820598730150095
##
## After 150 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1390.11554644204
## Change in best IC: 0 / Change in mean IC: -0.911053406781321
##
## After 160 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1389.96839555521
## Change in best IC: 0 / Change in mean IC: -0.147150886834652
##
## After 170 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1389.90514882192
## Change in best IC: 0 / Change in mean IC: -0.0632467332864053
##
## After 180 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1389.3848128011
## Change in best IC: 0 / Change in mean IC: -0.520336020818377
```

```
##
## After 190 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1389.11859422893
## Change in best IC: 0 / Change in mean IC: -0.266218572173784
##
## After 200 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1388.44051166745
## Change in best IC: 0 / Change in mean IC: -0.678082561481915
##
## After 210 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1387.34069206928
## Change in best IC: 0 / Change in mean IC: -1.09981959816264
##
## After 220 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1387.10678649674
## Change in best IC: 0 / Change in mean IC: -0.23390557254811
##
## After 230 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1386.84618495143
## Change in best IC: 0 / Change in mean IC: -0.260601545303871
##
## After 240 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1386.6750837057
## Change in best IC: 0 / Change in mean IC: -0.171101245736054
##
## After 250 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1386.50700629667
## Change in best IC: 0 / Change in mean IC: -0.168077409029138
##
## After 260 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1385.28708726569
## Change in best IC: 0 / Change in mean IC: -1.21991903097478
##
## After 270 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1385.23294237056
## Change in best IC: 0 / Change in mean IC: -0.05414489513646
```

```
##
## After 280 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1384.17099025983
## Change in best IC: 0 / Change in mean IC: -1.06195211072372
##
## After 290 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1383.61337908409
## Change in best IC: 0 / Change in mean IC: -0.557611175747297
##
## After 300 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1383.52977601147
## Change in best IC: 0 / Change in mean IC: -0.0836030726156878
##
## After 310 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1383.45204777781
## Change in best IC: 0 / Change in mean IC: -0.0777282336578082
##
## After 320 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1383.3631323826
## Change in best IC: 0 / Change in mean IC: -0.0889153952155084
##
## After 330 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1383.15810486585
## Change in best IC: 0 / Change in mean IC: -0.205027516750988
##
## After 340 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.99669514124
## Change in best IC: 0 / Change in mean IC: -0.161409724606301
##
## After 350 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.89773796153
## Change in best IC: 0 / Change in mean IC: -0.0989571797081226
##
## After 360 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.85757205316
## Change in best IC: 0 / Change in mean IC: -0.0401659083693175
```

```
##
## After 370 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.81934408111
## Change in best IC: 0 / Change in mean IC: -0.0382279720479346
##
## After 380 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.81934408111
## Change in best IC: 0 / Change in mean IC: 0
##
## After 390 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.7908363528
## Change in best IC: 0 / Change in mean IC: -0.0285077283110695
##
## After 400 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.66838336034
## Change in best IC: 0 / Change in mean IC: -0.122452992460012
##
## After 410 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.46157983736
## Change in best IC: 0 / Change in mean IC: -0.206803522980408
##
## After 420 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.38962010959
## Change in best IC: 0 / Change in mean IC: -0.071959727770718
##
## After 430 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.38962010959
## Change in best IC: 0 / Change in mean IC: 0
##
## After 440 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.35936213868
## Change in best IC: 0 / Change in mean IC: -0.0302579709082238
##
## After 450 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.31403170253
## Change in best IC: 0 / Change in mean IC: -0.0453304361485607
```

```
##
## After 460 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.31403170253
## Change in best IC: 0 / Change in mean IC: 0
##
## After 470 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1382.16954195743
## Change in best IC: 0 / Change in mean IC: -0.144489745101964
##
## After 480 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.69742567825
## Change in best IC: 0 / Change in mean IC: -0.472116279181819
##
## After 490 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.4510122746
## Change in best IC: 0 / Change in mean IC: -0.246413403652241
##
## After 500 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.32568523403
## Change in best IC: 0 / Change in mean IC: -0.125327040566845
##
## After 510 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.32568523403
## Change in best IC: 0 / Change in mean IC: 0
##
## After 520 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.16209377064
## Change in best IC: 0 / Change in mean IC: -0.163591463389821
##
## After 530 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.14638626348
## Change in best IC: 0 / Change in mean IC: -0.0157075071626878
##
## After 540 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.00300977188
## Change in best IC: 0 / Change in mean IC: -0.143376491604158
```

```
##
## After 550 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1381.00300977188
## Change in best IC: 0 / Change in mean IC: 0
##
## After 560 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.94620266906
## Change in best IC: 0 / Change in mean IC: -0.0568071028103532
##
## After 570 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.71461798994
## Change in best IC: 0 / Change in mean IC: -0.231584679125035
##
## After 580 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.71461798994
## Change in best IC: 0 / Change in mean IC: 0
##
## After 590 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.71461798994
## Change in best IC: 0 / Change in mean IC: 0
##
## After 600 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.71345104248
## Change in best IC: 0 / Change in mean IC: -0.00116694745929635
##
## After 610 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.454250208
## Change in best IC: 0 / Change in mean IC: -0.259200834477269
##
## After 620 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.42086631403
## Change in best IC: 0 / Change in mean IC: -0.0333838939732232
##
## After 630 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.42086631403
## Change in best IC: 0 / Change in mean IC: 0
```

```
##
## After 640 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.38598614413
## Change in best IC: 0 / Change in mean IC: -0.0348801699008163
##
## After 650 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.29203506725
## Change in best IC: 0 / Change in mean IC: -0.0939510768782839
##
## After 660 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.24499366374
## Change in best IC: 0 / Change in mean IC: -0.0470414035085014
##
## After 670 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.11677611251
## Change in best IC: 0 / Change in mean IC: -0.128217551231046
##
## After 680 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1380.11677611251
## Change in best IC: 0 / Change in mean IC: 0
##
## After 690 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.60358388302
## Change in best IC: 0 / Change in mean IC: -0.513192229491096
##
## After 700 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.60358388302
## Change in best IC: 0 / Change in mean IC: 0
##
## After 710 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.60358388302
## Change in best IC: 0 / Change in mean IC: 0
##
## After 720 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.60358388302
## Change in best IC: 0 / Change in mean IC: 0
```

```
##
## After 730 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.55519382004
## Change in best IC: 0 / Change in mean IC: -0.0483900629760683
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  8 ; beta may be infinite.
```

```
##
## After 740 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.38943631544
## Change in best IC: 0 / Change in mean IC: -0.165757504605381
##
## After 750 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1379.27298546878
## Change in best IC: 0 / Change in mean IC: -0.116450846662246
##
## After 760 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1378.74695480367
## Change in best IC: 0 / Change in mean IC: -0.526030665106646
##
## After 770 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1378.69726236581
## Change in best IC: 0 / Change in mean IC: -0.0496924378592212
##
## After 780 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1378.68207892706
## Change in best IC: 0 / Change in mean IC: -0.0151834387493182
##
## After 790 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1378.68207892706
## Change in best IC: 0 / Change in mean IC: 0
##
## After 800 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
## Crit= 1342.43618902348
## Mean crit= 1378.63447561721
## Change in best IC: 0 / Change in mean IC: -0.0476033098511834
##
## After 810 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+SizeCent+A2+A4
```

```
## Crit= 1342.43618902348
## Mean crit= 1378.63447561721
## Improvements in best and average IC have bebingo en below the specified goals.
## Algorithm is declared to have converged.
## Completed.

fit.cph.as.aicc = glmulti(Surv(Time, DSD) ~ strata(SexM) + AgeCent + AgePlus + LocBody + SizeCent + Size

## Initialization...
## TASK: Genetic algorithm in the candidate set.
## Initialization...
## Algorithm started...
##
## After 10 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgeCent+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:Age
## Crit= 1344.52295843843
## Mean crit= 1355.83912498052
## Change in best IC: -8655.47704156157 / Change in mean IC: -8644.16087501948
##
## After 20 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgeCent+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:Age
## Crit= 1339.18978106948
## Mean crit= 1352.60086874273
## Change in best IC: -5.33317736894764 / Change in mean IC: -3.23825623778839
##
## After 30 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+LocBody+SizeCent+SizePlus+A2+A4+SizePlus:LocBody+A2:SizeCen
## Crit= 1336.53883342693
## Mean crit= 1350.55851591467
## Change in best IC: -2.65094764254354 / Change in mean IC: -2.04235282805826
##
## After 40 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgeCent+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:Age
## Crit= 1334.61207766662
## Mean crit= 1349.1810641797
## Change in best IC: -1.9267557603182 / Change in mean IC: -1.37745173497729
##
## After 50 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgeCent+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:Age
## Crit= 1334.61207766662
## Mean crit= 1348.60649510656
## Change in best IC: 0 / Change in mean IC: -0.574569073140538
##
## After 60 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:AgePlus+Siz
## Crit= 1333.06469697369
## Mean crit= 1348.03948866998
## Change in best IC: -1.5473806929258 / Change in mean IC: -0.567006436575866
##
## After 70 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:AgePlus+Siz
## Crit= 1333.06469697369
## Mean crit= 1347.16294848992
## Change in best IC: 0 / Change in mean IC: -0.87654018006242
```

```
##
## After 80 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:AgePlus+Siz
## Crit= 1333.06469697369
## Mean crit= 1346.50703709187
## Change in best IC: 0 / Change in mean IC: -0.65591139804792
##
## After 90 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:AgePlus+Siz
## Crit= 1333.06469697369
## Mean crit= 1345.90540938663
## Change in best IC: 0 / Change in mean IC: -0.601627705236069
##
## After 100 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:AgePlus+Siz
## Crit= 1333.06469697369
## Mean crit= 1345.56481419844
## Change in best IC: 0 / Change in mean IC: -0.34059518819754
##
## After 110 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+LocBody:AgePlus+Siz
## Crit= 1333.06469697369
## Mean crit= 1345.18385131649
## Change in best IC: 0 / Change in mean IC: -0.380962881942651
##
## After 120 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1344.16814911698
## Change in best IC: -0.827551546290579 / Change in mean IC: -1.01570219951873
##
## After 130 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1343.71161625219
## Change in best IC: 0 / Change in mean IC: -0.456532864780684
##
## After 140 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1343.43013742915
## Change in best IC: 0 / Change in mean IC: -0.281478823046882
##
## After 150 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1342.99639610942
## Change in best IC: 0 / Change in mean IC: -0.433741319725186
##
## After 160 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1342.64217870369
## Change in best IC: 0 / Change in mean IC: -0.35421740573338
```

```
##
## After 170 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1342.45161681777
## Change in best IC: 0 / Change in mean IC: -0.190561885916395
##
## After 180 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1342.29832447901
## Change in best IC: 0 / Change in mean IC: -0.153292338757865
##
## After 190 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1342.09051816228
## Change in best IC: 0 / Change in mean IC: -0.207806316738925
##
## After 200 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1341.90866071186
## Change in best IC: 0 / Change in mean IC: -0.181857450420466
##
## After 210 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1341.85689820799
## Change in best IC: 0 / Change in mean IC: -0.0517625038673941

## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  8 ; beta may be infinite.

##
## After 220 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1341.68099139164
## Change in best IC: 0 / Change in mean IC: -0.175906816351471
##
## After 230 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1341.56556066349
## Change in best IC: 0 / Change in mean IC: -0.115430728148567
##
## After 240 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1341.49288101889
## Change in best IC: 0 / Change in mean IC: -0.0726796445994751
##
## After 250 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
```

```
## Crit= 1332.2371454274
## Mean crit= 1341.48192534665
## Change in best IC: 0 / Change in mean IC: -0.0109556722400157
##
## After 260 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1341.06512434637
## Change in best IC: 0 / Change in mean IC: -0.416801000276109
##
## After 270 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.8905390718
## Change in best IC: 0 / Change in mean IC: -0.174585274574383
##
## After 280 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.8728012317
## Change in best IC: 0 / Change in mean IC: -0.0177378400983343
##
## After 290 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.67467957828
## Change in best IC: 0 / Change in mean IC: -0.198121653422277
##
## After 300 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.66290570549
## Change in best IC: 0 / Change in mean IC: -0.0117738727853975
##
## After 310 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.65794972347
## Change in best IC: 0 / Change in mean IC: -0.00495598202519432
##
## After 320 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.51762265771
## Change in best IC: 0 / Change in mean IC: -0.140327065756992
##
## After 330 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1340.35497388677
## Change in best IC: 0 / Change in mean IC: -0.162648770937949
##
## After 340 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
```

```
## Crit= 1332.2371454274
## Mean crit= 1340.22610881965
## Change in best IC: 0 / Change in mean IC: -0.128865067118795
##
## After 350 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.9943454501
## Change in best IC: 0 / Change in mean IC: -0.231763369553619
##
## After 360 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.92383033082
## Change in best IC: 0 / Change in mean IC: -0.0705151192837548
##
## After 370 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.87316664227
## Change in best IC: 0 / Change in mean IC: -0.0506636885436365
##
## After 380 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.765156008
## Change in best IC: 0 / Change in mean IC: -0.108010634269931
##
## After 390 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.67855044211
## Change in best IC: 0 / Change in mean IC: -0.0866055658921141
##
## After 400 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.67855044211
## Change in best IC: 0 / Change in mean IC: 0
##
## After 410 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.58110553466
## Change in best IC: 0 / Change in mean IC: -0.0974449074453787
##
## After 420 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.47551423326
## Change in best IC: 0 / Change in mean IC: -0.105591301406776
##
## After 430 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
```

```
## Crit= 1332.2371454274
## Mean crit= 1339.47110681971
## Change in best IC: 0 / Change in mean IC: -0.00440741354600505
##
## After 440 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.47110681971
## Change in best IC: 0 / Change in mean IC: 0
##
## After 450 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.47110681971
## Change in best IC: 0 / Change in mean IC: 0
##
## After 460 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.47110681971
## Change in best IC: 0 / Change in mean IC: 0
##
## After 470 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.41262696338
## Change in best IC: 0 / Change in mean IC: -0.0584798563365894
##
## After 480 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.41129373815
## Change in best IC: 0 / Change in mean IC: -0.00133322522401613
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Loglik converged
before variable  8 ; beta may be infinite.
```

```
##
## After 490 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.3945502342
## Change in best IC: 0 / Change in mean IC: -0.0167435039495558
##
## After 500 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.3945502342
## Change in best IC: 0 / Change in mean IC: 0
##
## After 510 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.3945502342
## Change in best IC: 0 / Change in mean IC: 0
```

```
##
## After 520 generations:
## Best model: Surv(Time,DSD)~1+strata(SexM)+AgePlus+LocBody+SizeCent+SizePlus+A2+A4+SizeCent:LocBody+A2
## Crit= 1332.2371454274
## Mean crit= 1339.3945502342
## Improvements in best and average IC have bebingo en below the specified goals.
## Algorithm is declared to have converged.
## Completed.

fit.cph.as = fit.cph.as.bic
rm(nobs.coxph)
```

Also run BIC stepwise, because we can.

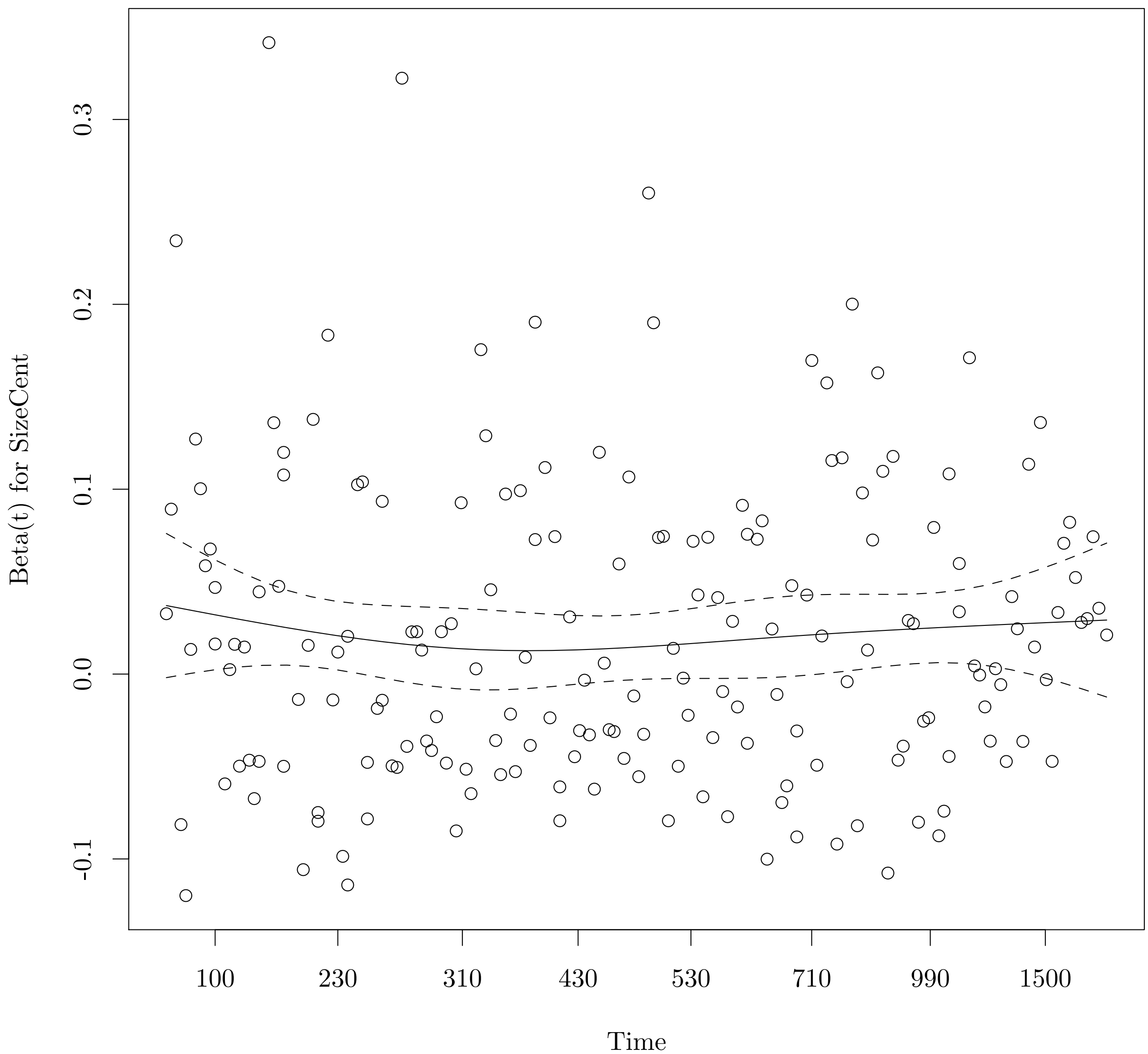
```
fit.cph = coxph(Surv(Time, DSD) ~ strata(SexM) + AgeCent + AgePlus + LocBody + SizeCent + SizePlus + A2
stepAIC(fit.cph, k = log(nrow(data)))

## Start:  AIC=1362
## Surv(Time, DSD) ~ strata(SexM) + AgeCent + AgePlus + LocBody +
##     SizeCent + SizePlus + A2 + A4
##
##            Df  AIC
## - LocBody   1 1357
## - SizePlus  1 1357
## - AgePlus   1 1358
## - AgeCent   1 1358
## - SizeCent  1 1360
## <none>        1362
## - A4        1 1365
## - A2        1 1369
##
## Step:  AIC=1357
## Surv(Time, DSD) ~ strata(SexM) + AgeCent + AgePlus + SizeCent +
##     SizePlus + A2 + A4
##
##            Df  AIC
## - SizePlus  1 1352
## - AgePlus   1 1353
## - AgeCent   1 1353
## - SizeCent  1 1355
## <none>        1357
## - A4        1 1360
## - A2        1 1364
##
## Step:  AIC=1352
## Surv(Time, DSD) ~ strata(SexM) + AgeCent + AgePlus + SizeCent +
##     A2 + A4
##
##            Df  AIC
## - AgePlus   1 1348
## - AgeCent   1 1348
## <none>        1352
## - A4        1 1356
## - A2        1 1359
```

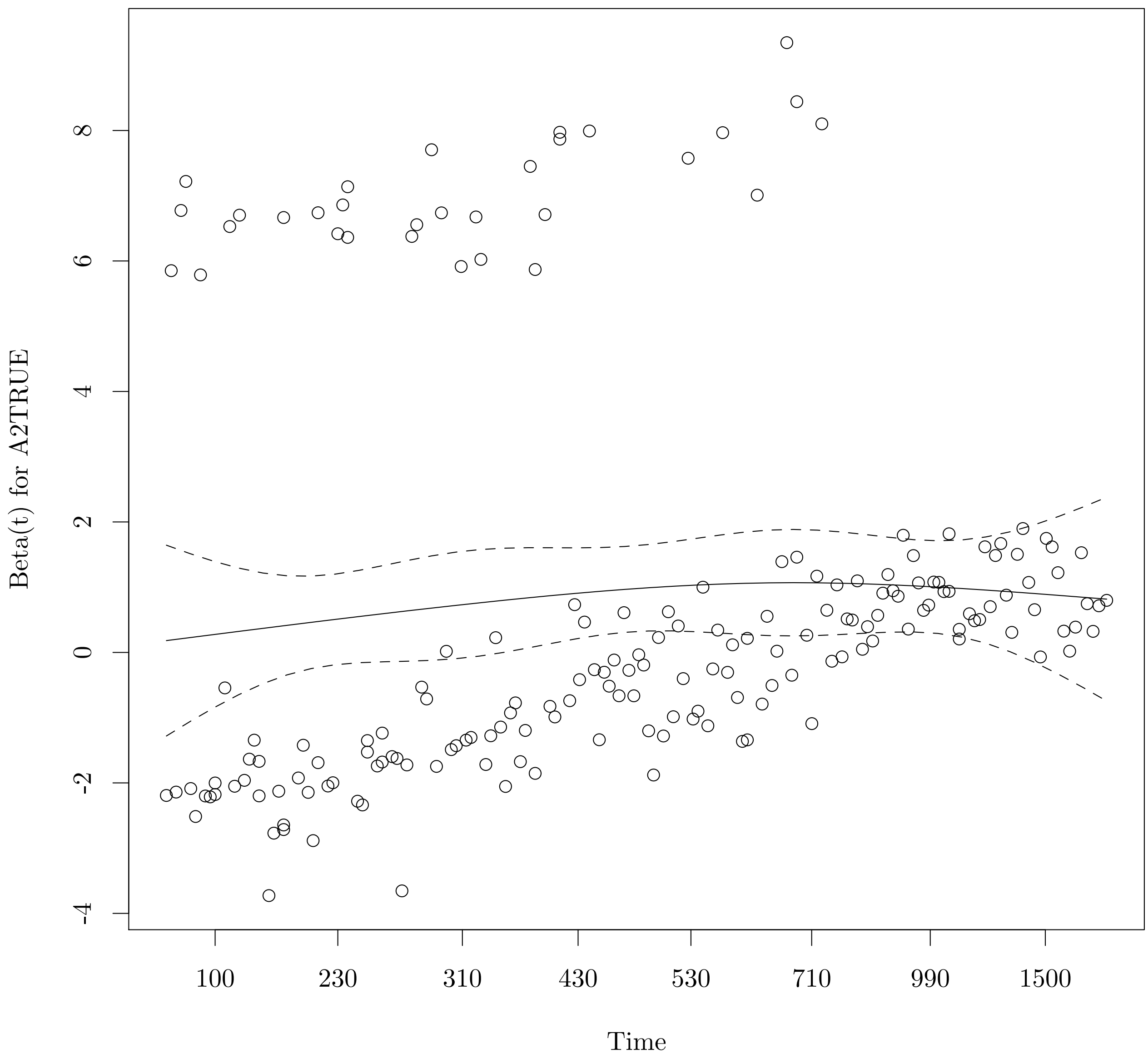
```
## - SizeCent  1 1359
##
## Step:  AIC=1348
## Surv(Time, DSD) ~ strata(SexM) + AgeCent + SizeCent + A2 + A4
##
##            Df  AIC
## - AgeCent   1 1343
## <none>        1348
## - A4        1 1351
## - A2        1 1355
## - SizeCent  1 1355
##
## Step:  AIC=1343
## Surv(Time, DSD) ~ strata(SexM) + SizeCent + A2 + A4
##
##            Df  AIC
## <none>        1343
## - A4        1 1346
## - A2        1 1349
## - SizeCent  1 1350
## Call:
## coxph(formula = Surv(Time, DSD) ~ strata(SexM) + SizeCent + A2 +
##     A4, data = data)
##
##
##            coef exp(coef) se(coef)    z       p
## SizeCent 0.0211      1.02  0.00572 3.70 0.00022
## A2TRUE   0.7983      2.22  0.21451 3.72 0.00020
## A4TRUE   0.5130      1.67  0.17824 2.88 0.00400
##
## Likelihood ratio test=44.8  on 3 df, p=1.03e-09  n= 196, number of events= 187
```

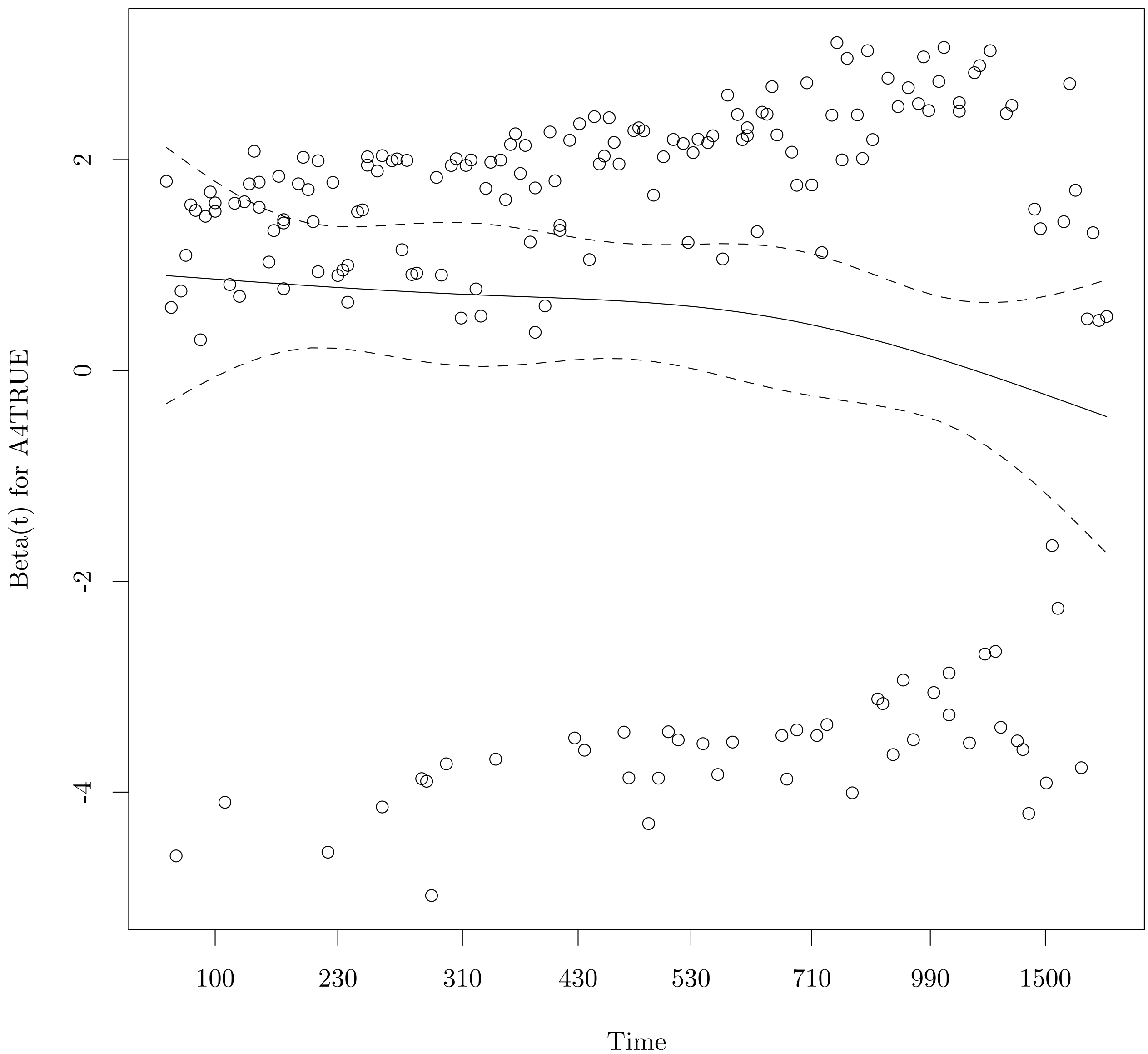
Consensus, excellent.

4.9 PH assumption: reduced model

```
fit.cph = coxph(Surv(Time, DSD) ~ strata(SexM) + SizeCent + A2 + A4, data = data)
cox.zph(fit.cph)

##               rho   chisq      p
## SizeCent  0.00381 0.00302 0.9562
## A2TRUE    0.07205 1.03357 0.3093
## A4TRUE   -0.13374 3.19494 0.0739
## GLOBAL         NA 3.80583 0.2832

plot(cox.zph(fit.cph))
```

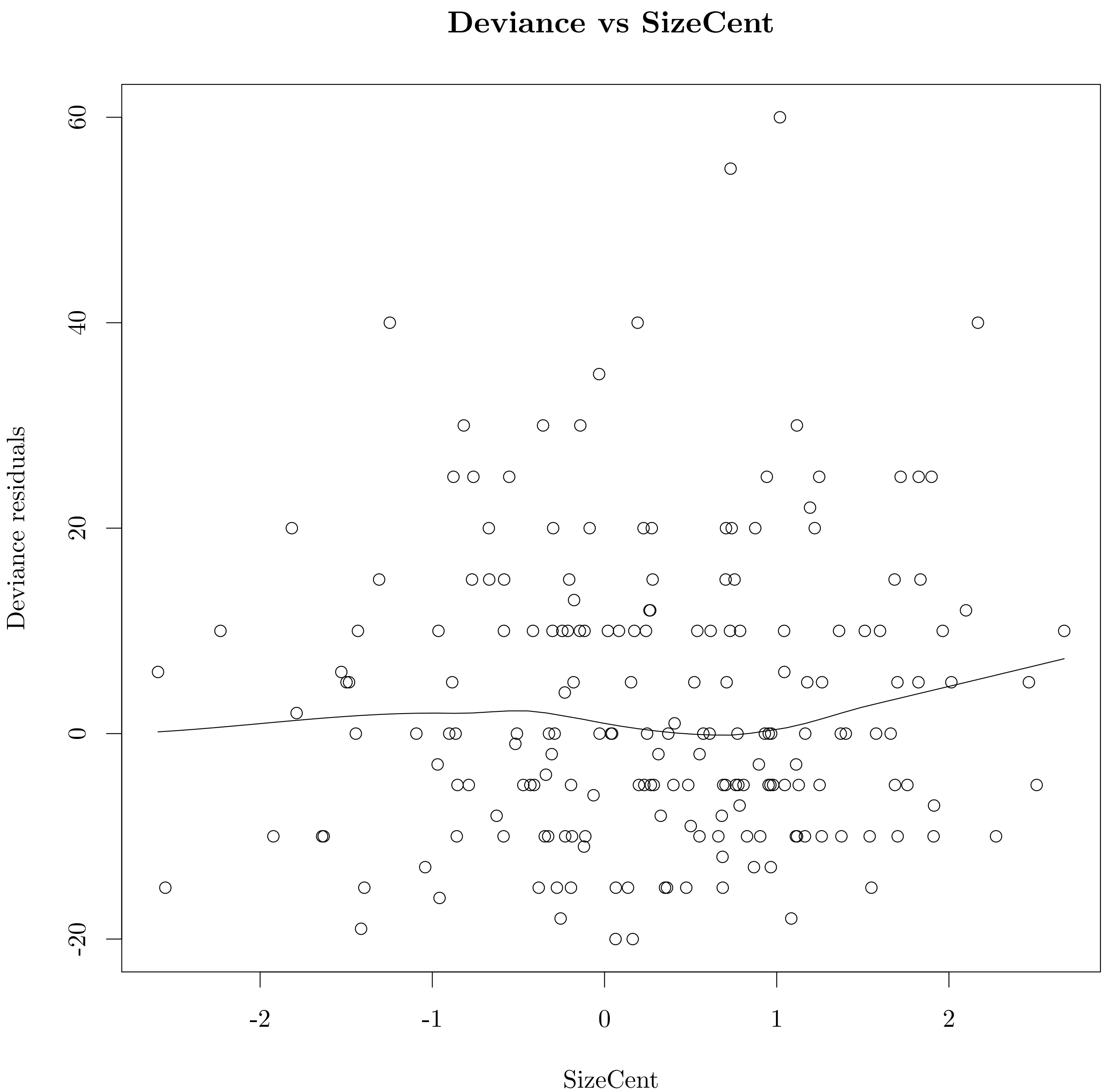

0.3
0.2
0.1
0.0
-0.1
Beta(t) for SizeCent
100
230
310
430
530
710
990
1500
Time


Beta(t) for A2TRUE
Time
-4
-2
0
2
4
6
8
100
230
310
430
530
710
990
1500

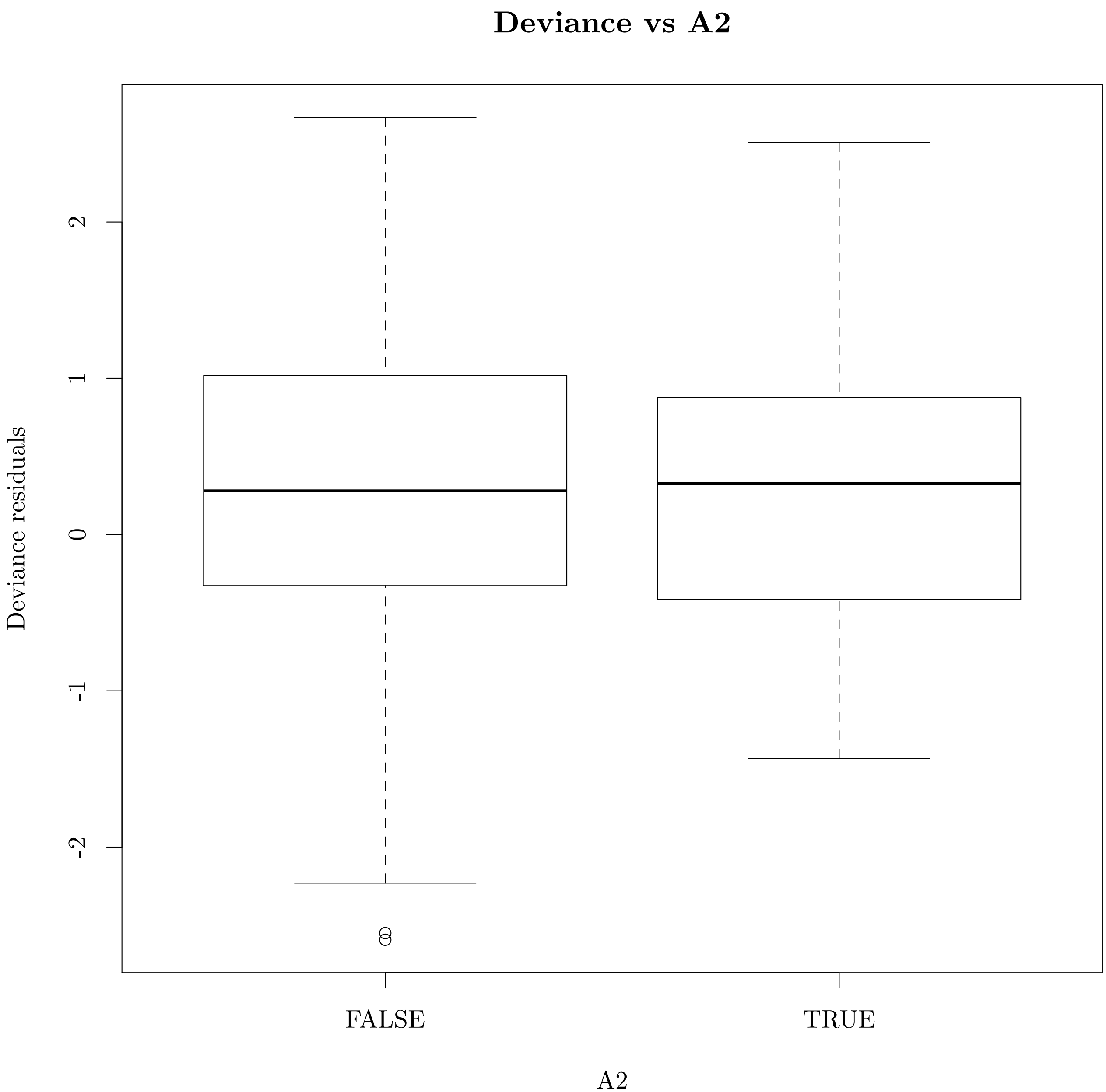


4.10 Outliers: reduced model

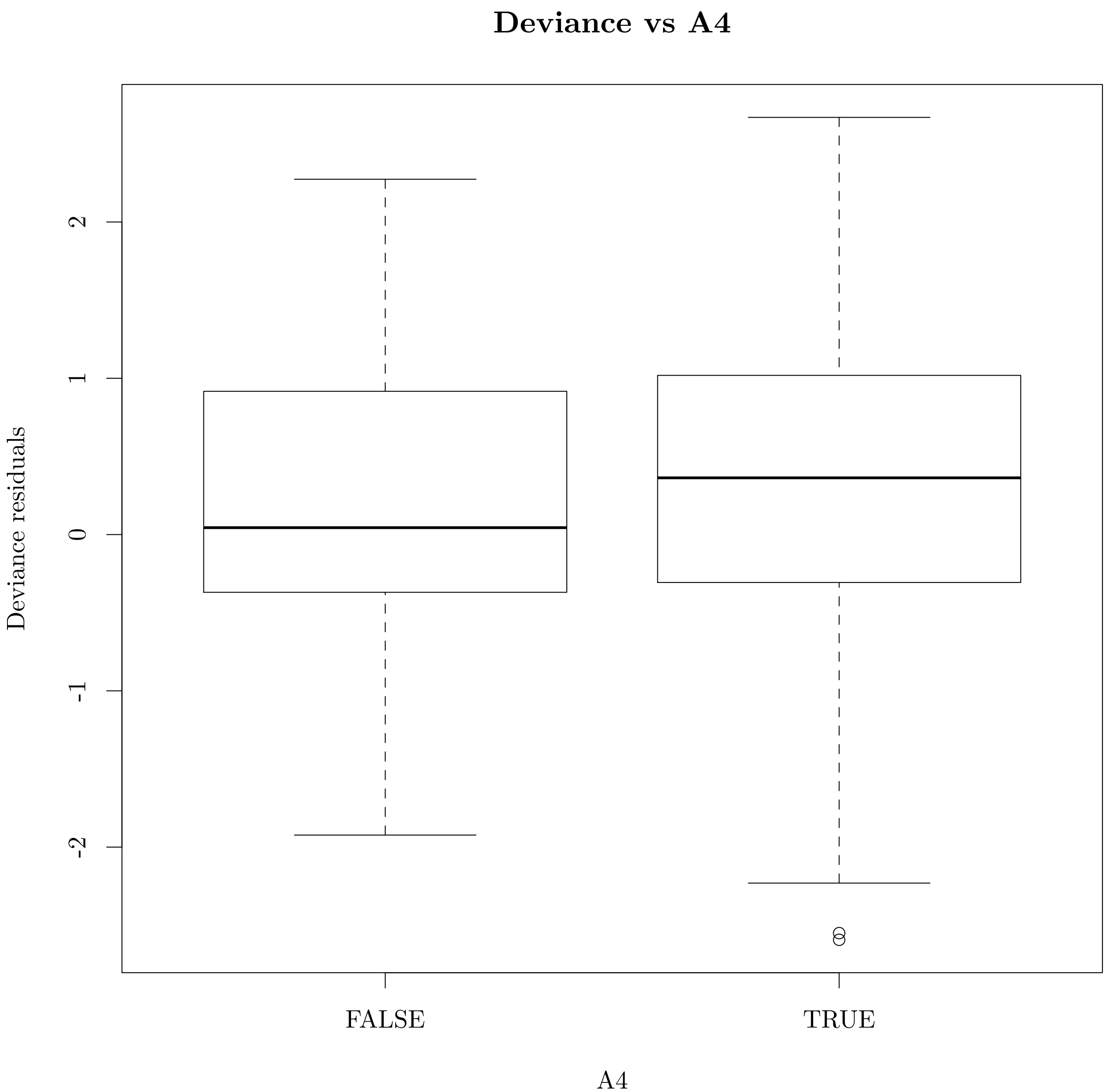
```
scatter.smooth(resid(fit.cph, type = "deviance"), data$SizeCent, xlab = "SizeCent", main = "Deviance vs
```



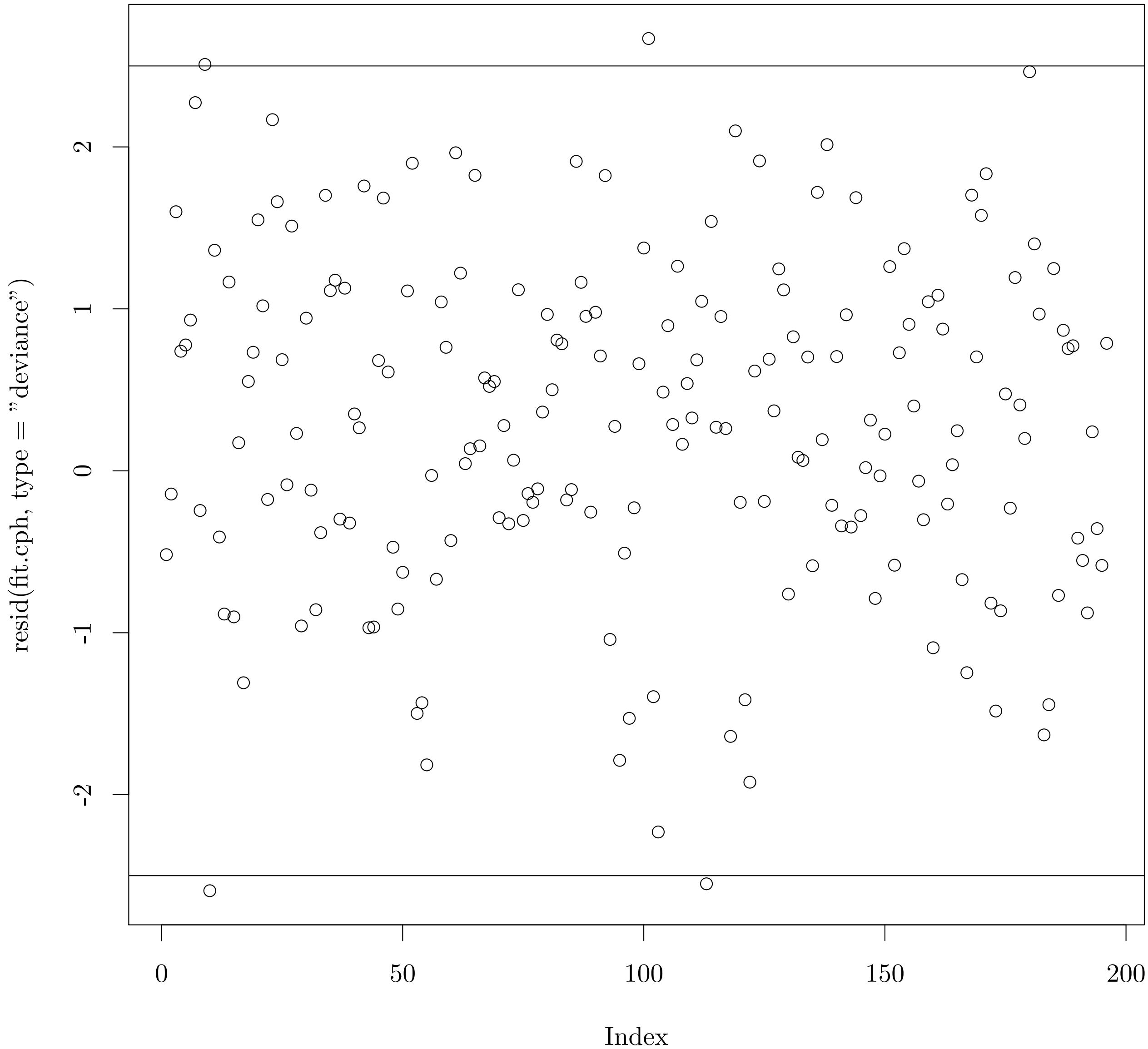

```
boxplot(resid(fit.cph, type = "deviance") ~ data$A2, main = "Deviance vs A2", xlab = "A2", ylab = "Devia
```




```
boxplot(resid(fit.cph, type = "deviance") ~ data$A4, main = "Deviance vs A4", xlab = "A4", ylab = "Devia
```




```r
plot(resid(fit.cph, type = "deviance"))
abline(h = c(-2.5, 2.5))
```

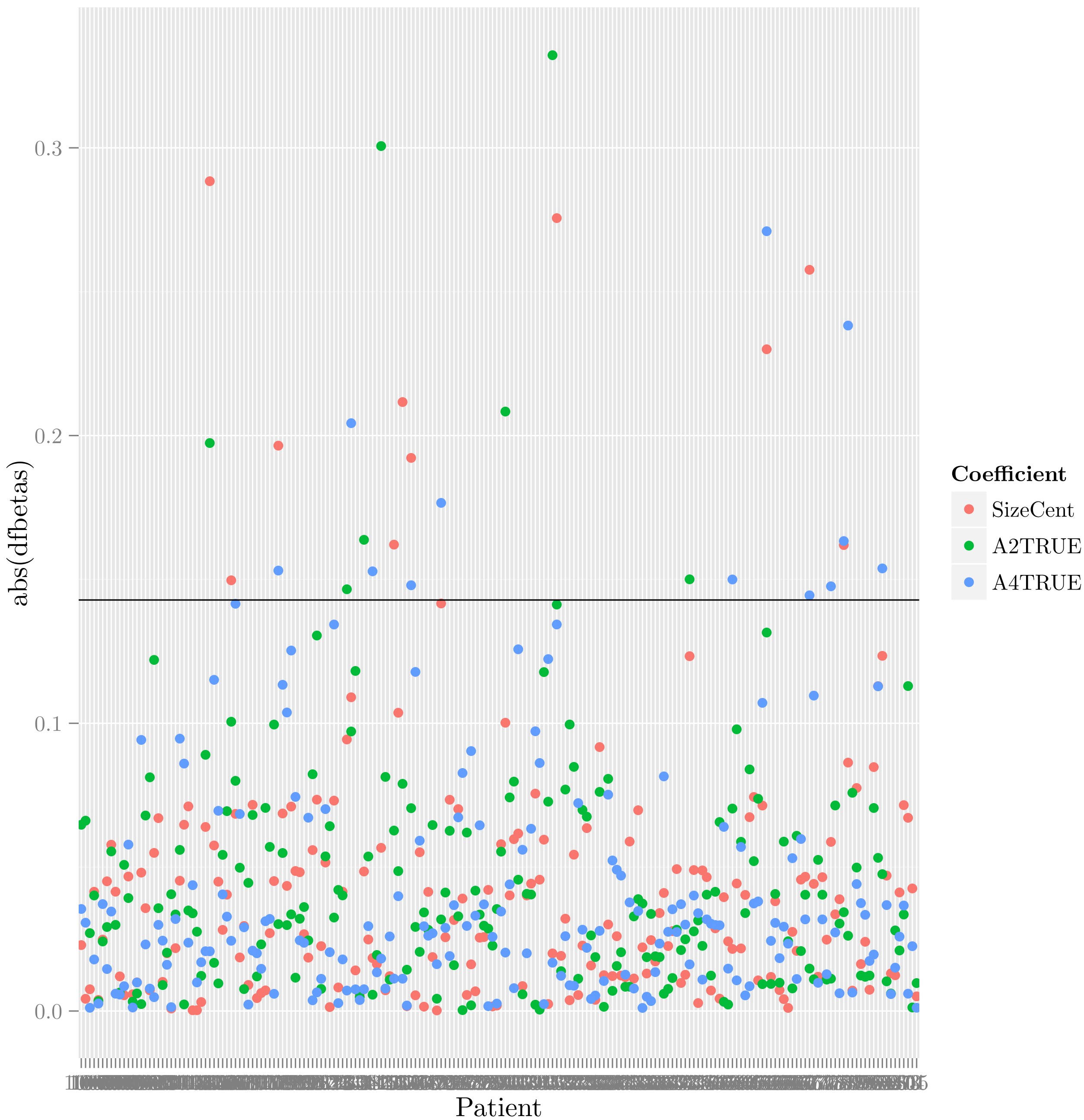



```r
data$devresid = resid(fit.cph, type = "deviance")
temp = data[abs(data$devresid) >= 2.5,]
temp[order(temp$Time),]
```

```
##             Time   DSD  SexM AgeCent LocBody SizeCent    A2   A4 AgePlus
## NSWPCN_651    20  TRUE  TRUE       8    TRUE       10 FALSE TRUE       3
## NSWPCN_131    61  TRUE FALSE     -11    TRUE       -5  TRUE TRUE       0
## NSWPCN_133 1304 FALSE  TRUE       5   FALSE        6 FALSE TRUE       0
## NSWPCN_667 2415 FALSE FALSE     -14   FALSE      -15 FALSE TRUE       0
##             SizePlus devresid DFBETAS_max
## NSWPCN_651        10    2.669     0.06561
## NSWPCN_131         0    2.510     0.13588
## NSWPCN_133         6   -2.593     0.08199
## NSWPCN_667         0   -2.550     0.19540
```

Few enough that I'm not particularly concerned. The DFBETAS will be more telling.

```
temp = resid(fit.cph, type = "dfbetas")
colnames(temp) = names(fit.cph$coefficients)
temp = melt(temp)
colnames(temp) = c("Patient", "Coefficient", "dfbetas")
temp$Patient = gsub("NSWPCN_", "", temp$Patient)
2/sqrt(nrow(data))       # The classic threshold for concern is 2/sqrt(n).

## [1] 0.1429

ggplot(temp, aes(y = abs(dfbetas), x = Patient, col = Coefficient)) + geom_point() + geom_hline(yinterce
```



```r
sort(apply(abs(resid(fit.cph, type = "dfbetas")), 1, max), decreasing = TRUE)
```

```
##  NSWPCN_317  NSWPCN_145 NSWPCN_1155  NSWPCN_318  NSWPCN_655  NSWPCN_667
##    0.332189    0.300616    0.288401    0.275569    0.271019    0.257602
##  NSWPCN_788  NSWPCN_154  NSWPCN_296  NSWPCN_133 NSWPCN_1182  NSWPCN_159
##    0.238237    0.211651    0.208340    0.204306    0.196498    0.192234
##  NSWPCN_195  NSWPCN_138  NSWPCN_784  NSWPCN_150  NSWPCN_802  NSWPCN_142
##    0.176601    0.163765    0.163336    0.162094    0.153829    0.152819
##  NSWPCN_374  NSWPCN_639 NSWPCN_1167  NSWPCN_777  NSWPCN_131 NSWPCN_1168
##    0.150036    0.149980    0.149698    0.147613    0.146578    0.141539
##  NSWPCN_125 NSWPCN_1213  NSWPCN_307 NSWPCN_1188  NSWPCN_316 NSWPCN_1083
##    0.134329    0.130502    0.125716    0.125290    0.122312    0.122024
##  NSWPCN_135  NSWPCN_163  NSWPCN_315 NSWPCN_1156 NSWPCN_1186  NSWPCN_814
##    0.118191    0.117850    0.117799    0.115109    0.113383    0.112947
##  NSWPCN_801  NSWPCN_674  NSWPCN_654 NSWPCN_1187  NSWPCN_152  NSWPCN_321
##    0.112912    0.109616    0.107101    0.103757    0.103666    0.099582
## NSWPCN_1179  NSWPCN_640  NSWPCN_311 NSWPCN_1143 NSWPCN_1072  NSWPCN_333
##    0.099561    0.097913    0.097227    0.094660    0.094222    0.091738
##  NSWPCN_269 NSWPCN_1153  NSWPCN_312 NSWPCN_1145  NSWPCN_322  NSWPCN_798
##    0.090346    0.089045    0.086195    0.085996    0.084851    0.084784
##  NSWPCN_647  NSWPCN_267 NSWPCN_1207  NSWPCN_364 NSWPCN_1453 NSWPCN_1082
##    0.083976    0.082720    0.082289    0.081549    0.081363    0.081218
##  NSWPCN_335  NSWPCN_305  NSWPCN_790  NSWPCN_320  NSWPCN_789 NSWPCN_1189
##    0.080696    0.079733    0.077517    0.076977    0.075852    0.074420
##  NSWPCN_648  NSWPCN_304  NSWPCN_651  NSWPCN_200  NSWPCN_323 NSWPCN_1172
##    0.074397    0.074231    0.073769    0.073425    0.072254    0.071668
##  NSWPCN_813  NSWPCN_779 NSWPCN_1146 NSWPCN_1177  NSWPCN_257 NSWPCN_1222
##    0.071557    0.071444    0.071121    0.070598    0.070186    0.070171
##  NSWPCN_324  NSWPCN_351 NSWPCN_1157 NSWPCN_1165 NSWPCN_1169 NSWPCN_1075
##    0.069903    0.069788    0.069587    0.069470    0.068473    0.067945
##  NSWPCN_326 NSWPCN_1198 NSWPCN_1089 NSWPCN_1017  NSWPCN_445   NSWPCN_10
##    0.067556    0.067186    0.067040    0.066158    0.065687    0.064732
##  NSWPCN_182  NSWPCN_272 NSWPCN_1227  NSWPCN_636  NSWPCN_310  NSWPCN_268
##    0.064633    0.064542    0.064241    0.063992    0.063360    0.062023
##  NSWPCN_664  NSWPCN_665  NSWPCN_164  NSWPCN_348  NSWPCN_661  NSWPCN_643
##    0.060897    0.059786    0.059209    0.058913    0.058882    0.058810
##  NSWPCN_294 NSWPCN_1029 NSWPCN_1023 NSWPCN_1178  NSWPCN_308 NSWPCN_1160
##    0.057991    0.057849    0.057788    0.057040    0.056053    0.054276
##  NSWPCN_141  NSWPCN_663  NSWPCN_769  NSWPCN_336 NSWPCN_1028  NSWPCN_370
##    0.053705    0.053123    0.052529    0.052322    0.050802    0.049322
##  NSWPCN_341  NSWPCN_375  NSWPCN_377 NSWPCN_1190  NSWPCN_344  NSWPCN_804
##    0.049121    0.048999    0.048868    0.048249    0.047066    0.047059
##  NSWPCN_666  NSWPCN_381  NSWPCN_770 NSWPCN_1022 NSWPCN_1171 NSWPCN_1148
##    0.046671    0.046532    0.046523    0.045094    0.044548    0.043732
##  NSWPCN_815  NSWPCN_280  NSWPCN_126  NSWPCN_270   NSWPCN_13 NSWPCN_1026
##    0.042601    0.042103    0.042094    0.041841    0.041485    0.041476
## NSWPCN_1019    NSWPCN_4   NSWPCN_17  NSWPCN_810   NSWPCN_20  NSWPCN_309
##    0.041459    0.041444    0.041404    0.041224    0.041183    0.040722
##  NSWPCN_657 NSWPCN_1140  NSWPCN_646  NSWPCN_781  NSWPCN_793  NSWPCN_352
##    0.040676    0.040590    0.040352    0.038840    0.037494    0.037345
## NSWPCN_1021  NSWPCN_372  NSWPCN_273  NSWPCN_256 NSWPCN_1193  NSWPCN_284
##    0.037163    0.037127    0.037070    0.036792    0.036136    0.035452
##  NSWPCN_369  NSWPCN_166  NSWPCN_363  NSWPCN_376  NSWPCN_358 NSWPCN_1141
##    0.035357    0.034278    0.034044    0.034002    0.033739    0.033556
```

```
##  NSWPCN_796  NSWPCN_350  NSWPCN_384  NSWPCN_373 NSWPCN_1170  NSWPCN_807 
##    0.033436    0.032884    0.030333    0.030047    0.029544    0.028008 
## NSWPCN_1150  NSWPCN_366 NSWPCN_1018  NSWPCN_330  NSWPCN_149  NSWPCN_283 
##    0.027565    0.027539    0.027076    0.026279    0.025914    0.025793 
##  NSWPCN_775 NSWPCN_1091  NSWPCN_656  NSWPCN_662  NSWPCN_638 NSWPCN_1176 
##    0.024801    0.024454    0.024387    0.024249    0.024214    0.023162 
## NSWPCN_1215 NSWPCN_1139 NSWPCN_1175  NSWPCN_143  NSWPCN_319  NSWPCN_360 
##    0.022560    0.020274    0.020064    0.019477    0.019173    0.019022 
##  NSWPCN_332  NSWPCN_353  NSWPCN_658  NSWPCN_797 NSWPCN_1152  NSWPCN_190 
##    0.018748    0.018719    0.018368    0.017403    0.016949    0.016279 
##  NSWPCN_157  NSWPCN_806  NSWPCN_345  NSWPCN_334 NSWPCN_1027 NSWPCN_1070 
##    0.014358    0.013072    0.012628    0.012443    0.012044    0.009948 
##    NSWPCN_9  NSWPCN_136 NSWPCN_1031 NSWPCN_1020 
##    0.009717    0.005929    0.005825    0.003856
```

```
sum(apply(abs(resid(fit.cph, type = "dfbetas")), 1, max) > 2/sqrt(nrow(data)))
```

```
## [1] 23
```

```
data$DFBETAS_max = apply(abs(resid(fit.cph, type = "dfbetas")), 1, max)
temp = data[data$DFBETAS_max >= 2/sqrt(nrow(data)) | abs(data$devresid) >= 2.5,]
temp[order(temp$DFBETAS_max),]
```

```
##             Time   DSD  SexM AgeCent LocBody SizeCent    A2    A4 AgePlus
## NSWPCN_651    20  TRUE  TRUE       8    TRUE       10 FALSE  TRUE       3
## NSWPCN_131    61  TRUE FALSE     -11    TRUE       -5  TRUE  TRUE       0
## NSWPCN_777  1197 FALSE  TRUE      -8   FALSE      -10 FALSE FALSE       0
## NSWPCN_1167  711  TRUE FALSE       1   FALSE       30 FALSE  TRUE       0
## NSWPCN_639  1990  TRUE FALSE       1   FALSE        2 FALSE  TRUE       0
## NSWPCN_374    63  TRUE  TRUE       5   FALSE      -10  TRUE  TRUE       0
## NSWPCN_142  1691  TRUE  TRUE       4   FALSE        0 FALSE FALSE       0
## NSWPCN_802  1072  TRUE FALSE     -14    TRUE       25 FALSE FALSE       0
## NSWPCN_150   270  TRUE  TRUE       6    TRUE       55 FALSE  TRUE       1
## NSWPCN_784  2701  TRUE  TRUE      14   FALSE      -19 FALSE FALSE       9
## NSWPCN_138   559  TRUE FALSE      -6   FALSE        5  TRUE  TRUE       0
## NSWPCN_195  1969  TRUE  TRUE       8   FALSE      -16 FALSE FALSE       3
## NSWPCN_159    30  TRUE  TRUE      11    TRUE       40 FALSE FALSE       6
## NSWPCN_1182 2178  TRUE FALSE      -4    TRUE      -10 FALSE  TRUE       0
## NSWPCN_133  1304 FALSE  TRUE       5   FALSE        6 FALSE  TRUE       0
## NSWPCN_296   671  TRUE  TRUE       2   FALSE       -3  TRUE  TRUE       0
## NSWPCN_154   163  TRUE  TRUE      -2    TRUE       60 FALSE  TRUE       0
## NSWPCN_788  2155 FALSE FALSE       5   FALSE      -10 FALSE FALSE       0
## NSWPCN_667  2415 FALSE FALSE     -14   FALSE      -15 FALSE  TRUE       0
## NSWPCN_655  1723  TRUE  TRUE      11    TRUE       10 FALSE  TRUE       6
## NSWPCN_318  1464  TRUE FALSE       2   FALSE       20 FALSE  TRUE       0
## NSWPCN_1155  390  TRUE FALSE       9    TRUE       40  TRUE  TRUE       4
## NSWPCN_145   599  TRUE  TRUE      -6    TRUE       15  TRUE  TRUE       0
## NSWPCN_317   729  TRUE FALSE      11   FALSE       10  TRUE  TRUE       6
##             SizePlus devresid DFBETAS_max
## NSWPCN_651        10   2.6694     0.07377
## NSWPCN_131         0   2.5095     0.14658
## NSWPCN_777         0  -1.6399     0.14761
## NSWPCN_1167       30  -0.8175     0.14970
## NSWPCN_639         2  -1.7880     0.14998
## NSWPCN_374         0   1.9109     0.15004
```

```
## NSWPCN_142          0  -0.9020     0.15282
## NSWPCN_802         25  -0.7615     0.15383
## NSWPCN_150         55   0.7320     0.16209
## NSWPCN_784          0  -1.4137     0.16334
## NSWPCN_138          5  -0.8845     0.16376
## NSWPCN_195          0  -0.9580     0.17660
## NSWPCN_159         40   2.1684     0.19223
## NSWPCN_1182         0  -1.6308     0.19650
## NSWPCN_133          6  -2.5931     0.20431
## NSWPCN_296          0  -0.9693     0.20834
## NSWPCN_154         60   1.0185     0.21165
## NSWPCN_788          0  -1.9230     0.23824
## NSWPCN_667          0  -2.5504     0.25760
## NSWPCN_655         10  -2.2303     0.27102
## NSWPCN_318         20  -1.8160     0.27557
## NSWPCN_1155        40  -1.2469     0.28840
## NSWPCN_145         15  -1.3089     0.30062
## NSWPCN_317         10  -1.4321     0.33219
```

4.11 Summary of EDA

1. On the basis of pre-operative assessability and data availability, variables were filtered down to Sex, AgeCent, LocBody, SizeCent, A2, A4.
2. Functional forms for the continuous variates AgeCent and SizeCent indicated a possible slight quadratic effect on AgeCent, and a knee on SizeCent. These were modelled by incorporating additional terms.
3. Analysis of a full model fit (with additional nonlinear terms included) indicated violation of PH for gender. This was dealt with by stratification. A slight PH violation by age was deemed unimportant.
4. Variable selection by BIC (both stepwise and genetic all-subset) settled on a final model of Surv(Time,DSD) $\sim 1 +$ strata(SexM) $+$ SizeCent $+$ A2 $+$ A4. This model was refit by coxph.
5. PH was verified on the final model. Deviance residuals showed no egregious outliers. dfBetaS indicated a number of influential observations, which require checking.

5 Final fits

```
fit.cph = coxph(Surv(Time, DSD) ~ strata(SexM) + SizeCent + A2 + A4, data = data)
```

```
set.seed(20150111)
fit.rsf = rfsrc(Surv(Time, DSD) ~ SexM + AgeCent + LocBody + SizeCent + A2 + A4, data = data, mtry = 1,
```

```
fit.gg = flexsurvreg(Surv(Time, DSD) ~ SexM + SizeCent + A2 + A4,
        anc = list(
                sigma = ~ SexM,
                Q = ~ SexM),
        data = data, dist = "gengamma")

fit.gf = flexsurvreg(Surv(Time, DSD) ~ SexM + SizeCent + A2 + A4,
        anc = list(
```

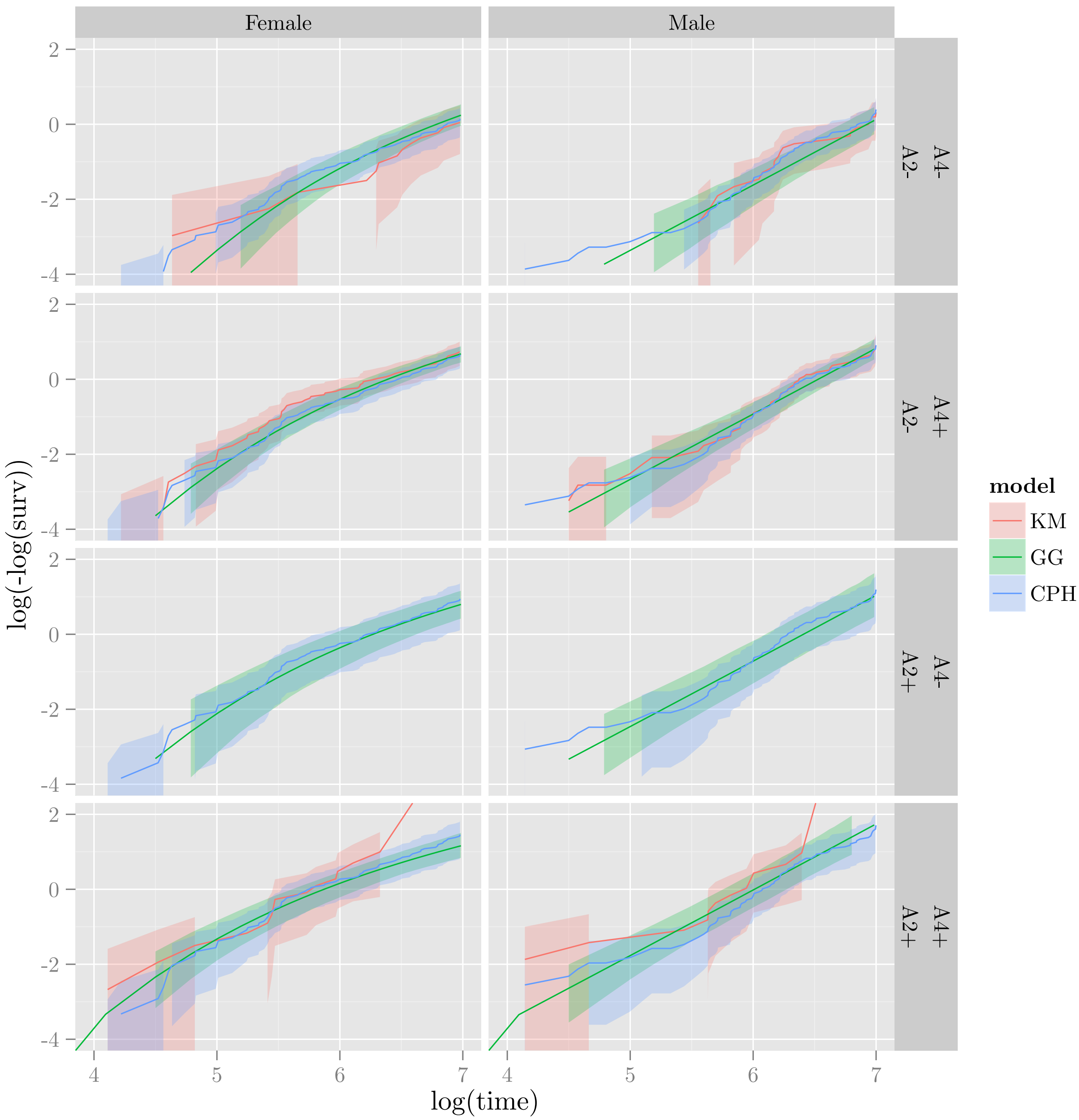
```r
                 sigma = ~ SexM,
                 Q = ~ SexM,
                 P = ~ SexM),
        data = data, dist = "genf")

fit.gg$loglik

## [1] -1355

fit.gf$loglik

## [1] -1354

pchisq(2*(fit.gf$loglik - fit.gg$loglik), 2, lower.tail = FALSE)

## [1] 0.1734

AIC(fit.gg)

## [1] 2729

AIC(fit.gf)

## [1] 2729

BIC(fit.gg)

## [1] 2758

BIC(fit.gf)

## [1] 2765

fit.gg

##
## Call:
## flexsurvreg(formula = Surv(Time, DSD) ~ SexM + SizeCent + A2 +     A4, anc = list(sigma = ~SexM, Q =
##
## Estimates:
##                  data mean  est      L95%     U95%     se       exp(est)
## mu                    NA     6.5307   6.2018   6.8597   0.1678       NA
## sigma                 NA     0.8130   0.7047   0.9380   0.0593       NA
## Q                     NA     0.0638  -0.5270   0.6546   0.3014       NA
## SexMTRUE           0.4898     0.3990   0.0642   0.7338   0.1708   1.4903
## SizeCent           2.8316    -0.0146  -0.0219  -0.0074   0.0037   0.9855
## A2TRUE             0.1582    -0.5181  -0.7854  -0.2507   0.1364   0.5957
## A4TRUE             0.7398    -0.3981  -0.6294  -0.1669   0.1180   0.6716
## sigma(SexMTRUE)    0.4898    -0.3577  -0.5946  -0.1208   0.1209   0.6993
## Q(SexMTRUE)        0.4898     0.9493   0.2087   1.6898   0.3778   2.5838
##                  L95%     U95%
## mu                    NA       NA
## sigma                 NA       NA
## Q                     NA       NA
## SexMTRUE           1.0663   2.0831
## SizeCent           0.9783   0.9926
## A2TRUE             0.4559   0.7782
```

```
## A4TRUE             0.5329   0.8463
## sigma(SexMTRUE)    0.5518   0.8862
## Q(SexMTRUE)        1.2321   5.4183
##
## N = 196,  Events: 187,  Censored: 9
## Total time at risk: 121359
## Log-likelihood = -1355, df = 9
## AIC = 2729
```

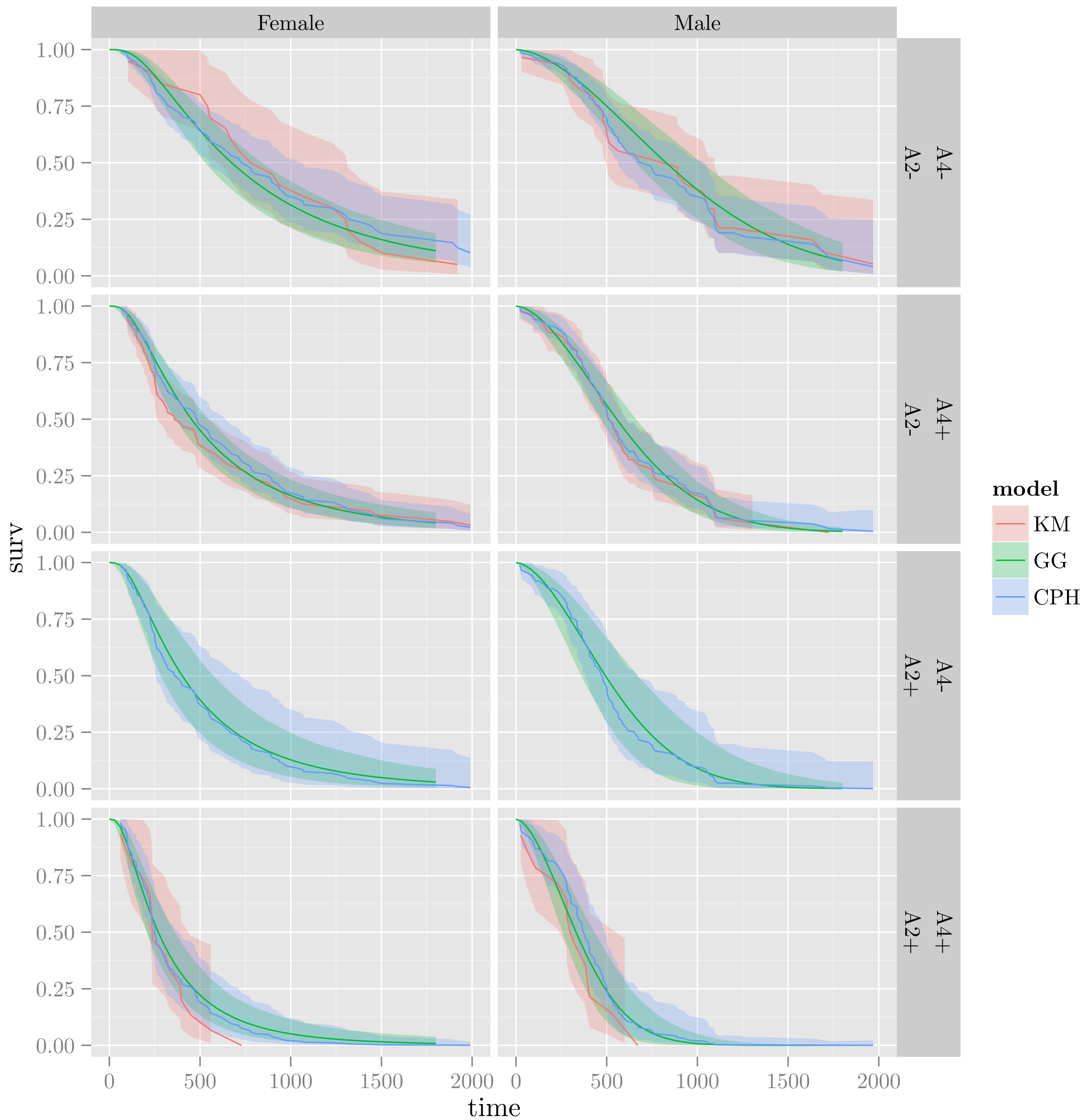
6 Fit assessment

Plot fit stratified by sex, separate curves for A2, A4 status, at median (approx.) Size.

```
temp.grid = expand.grid(A4 = c(FALSE, TRUE), A2 = c(FALSE, TRUE), SexM = c(FALSE, TRUE), SizeCent = 0)
temp.grid$ID = sprintf("SexM=%s, A2=% -5s, A4=% -5s", temp.grid$SexM, temp.grid$A2, temp.grid$A4)
temp.preds = summary(fit.gg, newdata = temp.grid, type = "survival", t = seq(0, 365*5, 30))
temp.preds2 = do.call(rbind, temp.preds)
temp.preds2$group = rep(gsub(".*ID=", "", names(temp.preds)), each = nrow(temp.preds[[1]]))
temp.preds.cox = survfit(fit.cph, newdata = temp.grid)

temp.survfit = survfit(Surv(Time, DSD) ~ SexM + A2 + A4, data)
temp.data = data.frame(time = temp.survfit$time, surv = temp.survfit$surv, upper = temp.survfit$lower, l
temp.data = rbind(temp.data, data.frame(time = temp.preds2$time, surv = temp.preds2$est, upper = temp.pr
temp.data = rbind(temp.data, data.frame(time = temp.preds.cox$time, surv = temp.preds.cox$surv, upper =

temp.data$Sex = c("Male", "Female")[grepl("SexM=FALSE", temp.data$group)+1]
temp.data$A2 = c("A2-", "A2+")[grepl("A2=TRUE", temp.data$group)+1]
temp.data$A4 = c("A4-", "A4+")[grepl("A4=TRUE", temp.data$group)+1]

ggplot(temp.data, aes(x = log(time), y = log(-log(surv)), ymin = log(-log(lower)), ymax = log(-log(upper
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() +
        xlim(4, 7) + ylim(-4, 2) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 50 rows containing missing values (geom_path).
## Warning:  Removed 45 rows containing missing values (geom_path).
## Warning:  Removed 51 rows containing missing values (geom_path).
## Warning:  Removed 43 rows containing missing values (geom_path).
## Warning:  Removed 41 rows containing missing values (geom_path).
## Warning:  Removed 38 rows containing missing values (geom_path).
## Warning:  Removed 41 rows containing missing values (geom_path).
## Warning:  Removed 39 rows containing missing values (geom_path).
```




```
ggplot(temp.data, aes(x = time, y = surv, ymin = lower, ymax = upper, colour = model, fill = model)) +
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() + xlim(0, 2000) + ylim(0, 1) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 4 rows containing missing values (geom_path).
## Warning:  Removed 2 rows containing missing values (geom_path).
## Warning:  Removed 5 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
```



Some deviation though not significant. Most concerning is the A2- A4- female group, survival of which is underestimated by the flexsurv model. To approach this in a modelling sense would require interaction terms between Sex and A2, A4. Overfitting seems likely considering the very few data available for the A2+/A4- group. Perhaps just add a single "DoubleNegFemale" term.

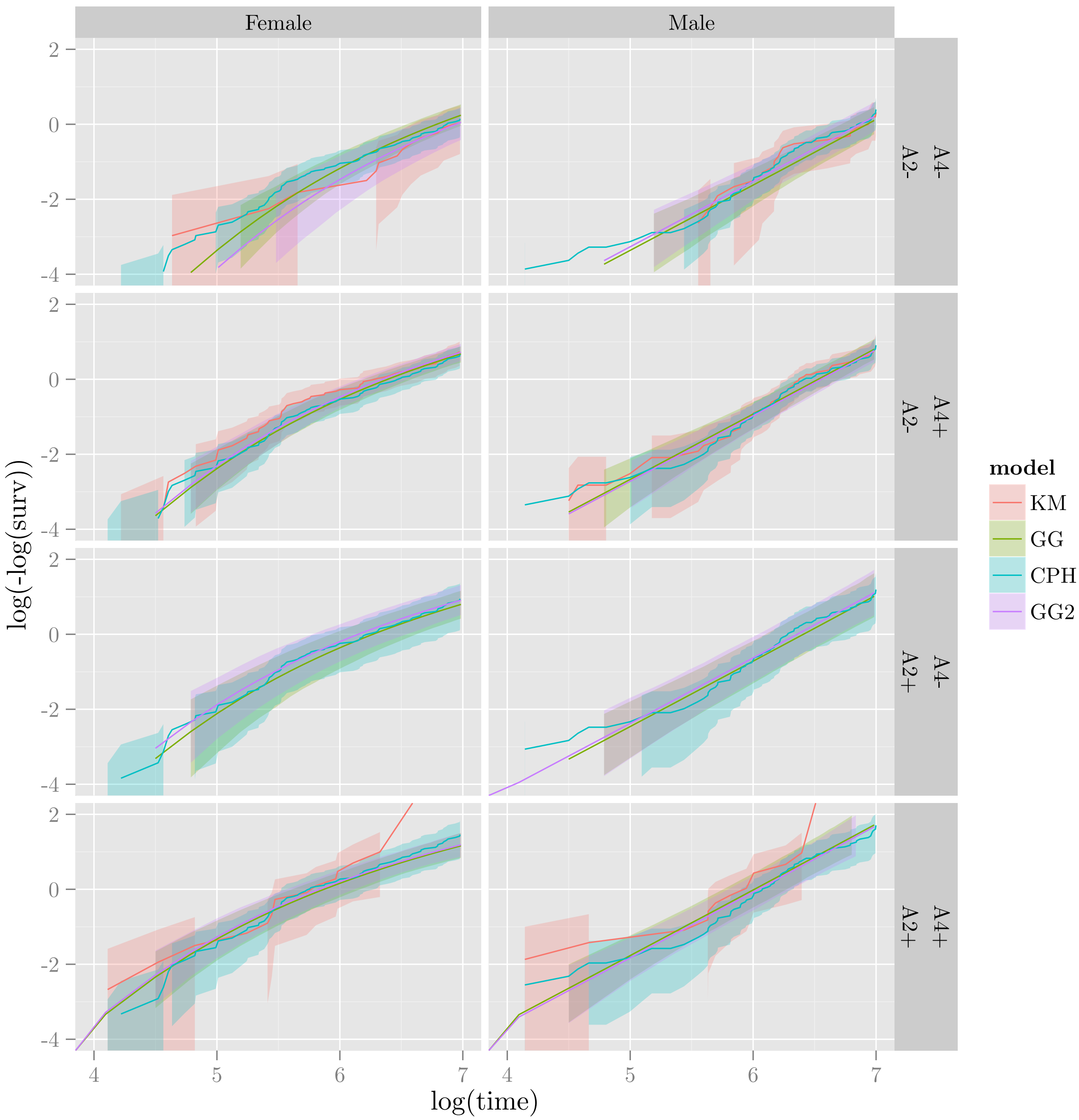
```
fit.gg2 = flexsurvreg(Surv(Time, DSD) ~ SexM + SizeCent + A2 + A4 + I(SexM == FALSE & A2 == FALSE & A4 =
        anc = list(
                sigma = ~ SexM,
                Q = ~ SexM),
        data = data, dist = "gengamma")

fit.gg2

##
```

```
## Call:
## flexsurvreg(formula = Surv(Time, DSD) ~ SexM + SizeCent + A2 +     A4 + I(SexM == FALSE & A2 == FALSE
##
## Estimates:
##                                                   data mean  est
## mu                                                      NA    6.39906
## sigma                                                   NA    0.81027
## Q                                                       NA    0.04270
## SexMTRUE                                           0.48980    0.47352
## SizeCent                                           2.83163   -0.01510
## A2TRUE                                             0.15816   -0.51111
## A4TRUE                                             0.73980   -0.31385
## I(SexM == FALSE & A2 == FALSE & A4 == FALSE)TRUE   0.10204    0.28405
## sigma(SexMTRUE)                                    0.48980   -0.35966
## Q(SexMTRUE)                                        0.48980    0.97670
##                                                   L95%      U95%
## mu                                                 6.01578   6.78235
## sigma                                              0.70295   0.93397
## Q                                                 -0.51759   0.60298
## SexMTRUE                                           0.12517   0.82188
## SizeCent                                          -0.02230  -0.00789
## A2TRUE                                            -0.78047  -0.24176
## A4TRUE                                            -0.57639  -0.05131
## I(SexM == FALSE & A2 == FALSE & A4 == FALSE)TRUE  -0.19015   0.75824
## sigma(SexMTRUE)                                   -0.59596  -0.12335
## Q(SexMTRUE)                                        0.25579   1.69761
##                                                   se        exp(est)
## mu                                                 0.19556        NA
## sigma                                              0.05874        NA
## Q                                                  0.28587        NA
## SexMTRUE                                           0.17774   1.60564
## SizeCent                                           0.00368   0.98502
## A2TRUE                                             0.13743   0.59983
## A4TRUE                                             0.13395   0.73063
## I(SexM == FALSE & A2 == FALSE & A4 == FALSE)TRUE   0.24194   1.32849
## sigma(SexMTRUE)                                    0.12057   0.69792
## Q(SexMTRUE)                                        0.36782   2.65568
##                                                   L95%      U95%
## mu                                                      NA        NA
## sigma                                                   NA        NA
## Q                                                       NA        NA
## SexMTRUE                                           1.13334   2.27477
## SizeCent                                           0.97795   0.99214
## A2TRUE                                             0.45819   0.78525
## A4TRUE                                             0.56192   0.94999
## I(SexM == FALSE & A2 == FALSE & A4 == FALSE)TRUE   0.82684   2.13452
## sigma(SexMTRUE)                                    0.55103   0.88395
## Q(SexMTRUE)                                        1.29148   5.46090
##
## N = 196,  Events: 187,  Censored: 9
## Total time at risk: 121359
## Log-likelihood = -1355, df = 10
## AIC = 2729
```

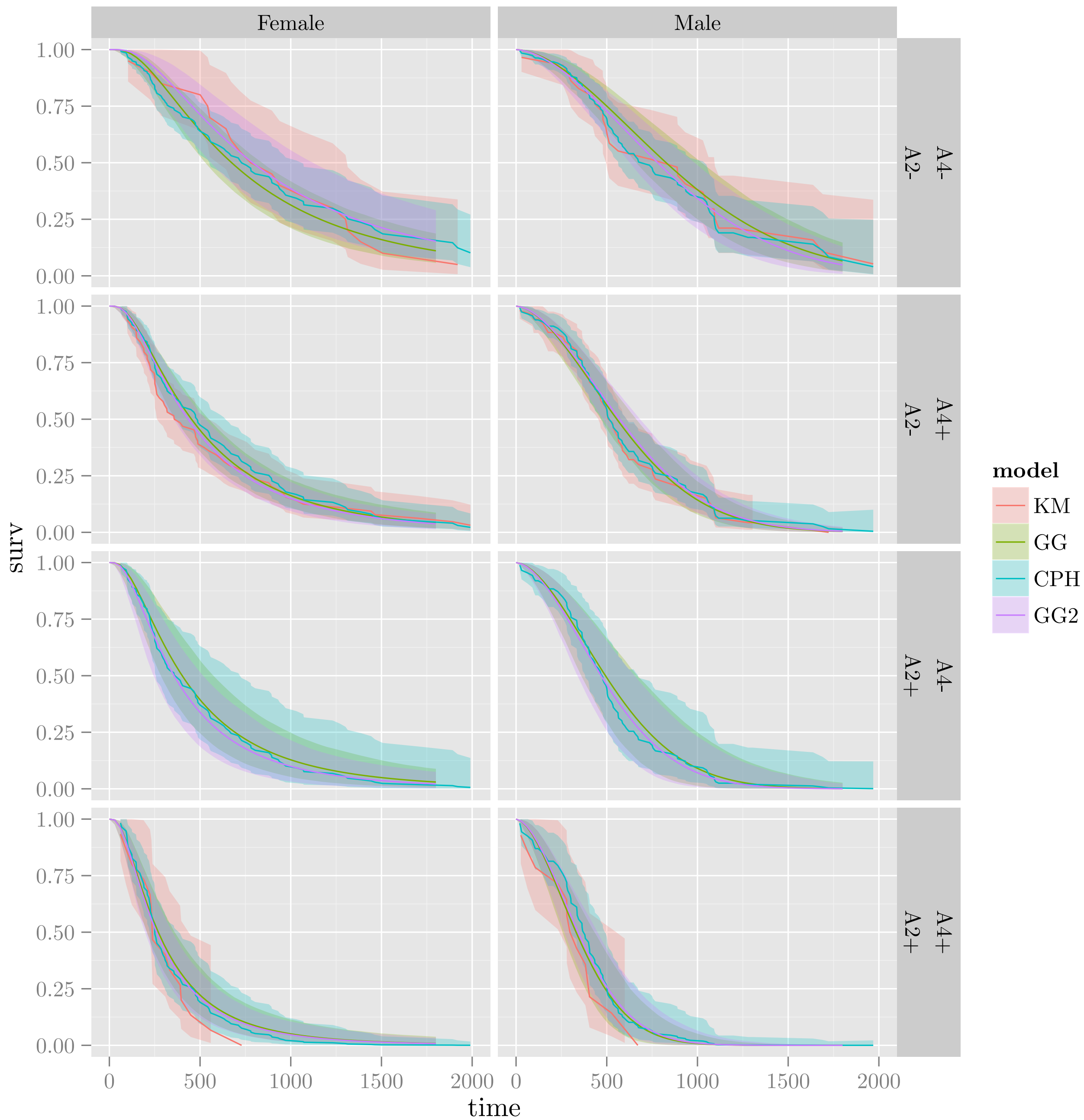
```r
AIC(fit.gg)

## [1] 2729

AIC(fit.gg2)

## [1] 2729

AIC(fit.gg) - AIC(fit.gg2)

## [1] -0.6318

# Equivocal on AIC.  BIC would favour gg then.

pchisq(-2*(fit.gg$loglik - fit.gg2$loglik), 1, lower.tail = FALSE)

## [1] 0.2421

# Not good evidence on LRT
```

See how it plots relative to the others.

```r
temp.preds = summary(fit.gg2, newdata = temp.grid, type = "survival", t = seq(0, 365*5, 30))
temp.preds2 = do.call(rbind, temp.preds)
temp.preds2$group = rep(gsub(".*ID=", "", names(temp.preds)), each = nrow(temp.preds[[1]]))
temp.data = rbind(temp.data, data.frame(time = temp.preds2$time, surv = temp.preds2$est, upper = temp.pr
temp.data$Sex = c("Male", "Female")[grepl("SexM=FALSE", temp.data$group)+1]
temp.data$A2 = c("A2-", "A2+")[grepl("A2=TRUE", temp.data$group)+1]
temp.data$A4 = c("A4-", "A4+")[grepl("A4=TRUE", temp.data$group)+1]

ggplot(temp.data, aes(x = log(time), y = log(-log(surv)), ymin = log(-log(lower)), ymax = log(-log(upper
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() +
        xlim(4, 7) + ylim(-4, 2) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 75 rows containing missing values (geom_path).
## Warning:  Removed 70 rows containing missing values (geom_path).
## Warning:  Removed 76 rows containing missing values (geom_path).
## Warning:  Removed 68 rows containing missing values (geom_path).
## Warning:  Removed 66 rows containing missing values (geom_path).
## Warning:  Removed 63 rows containing missing values (geom_path).
## Warning:  Removed 66 rows containing missing values (geom_path).
## Warning:  Removed 64 rows containing missing values (geom_path).
```



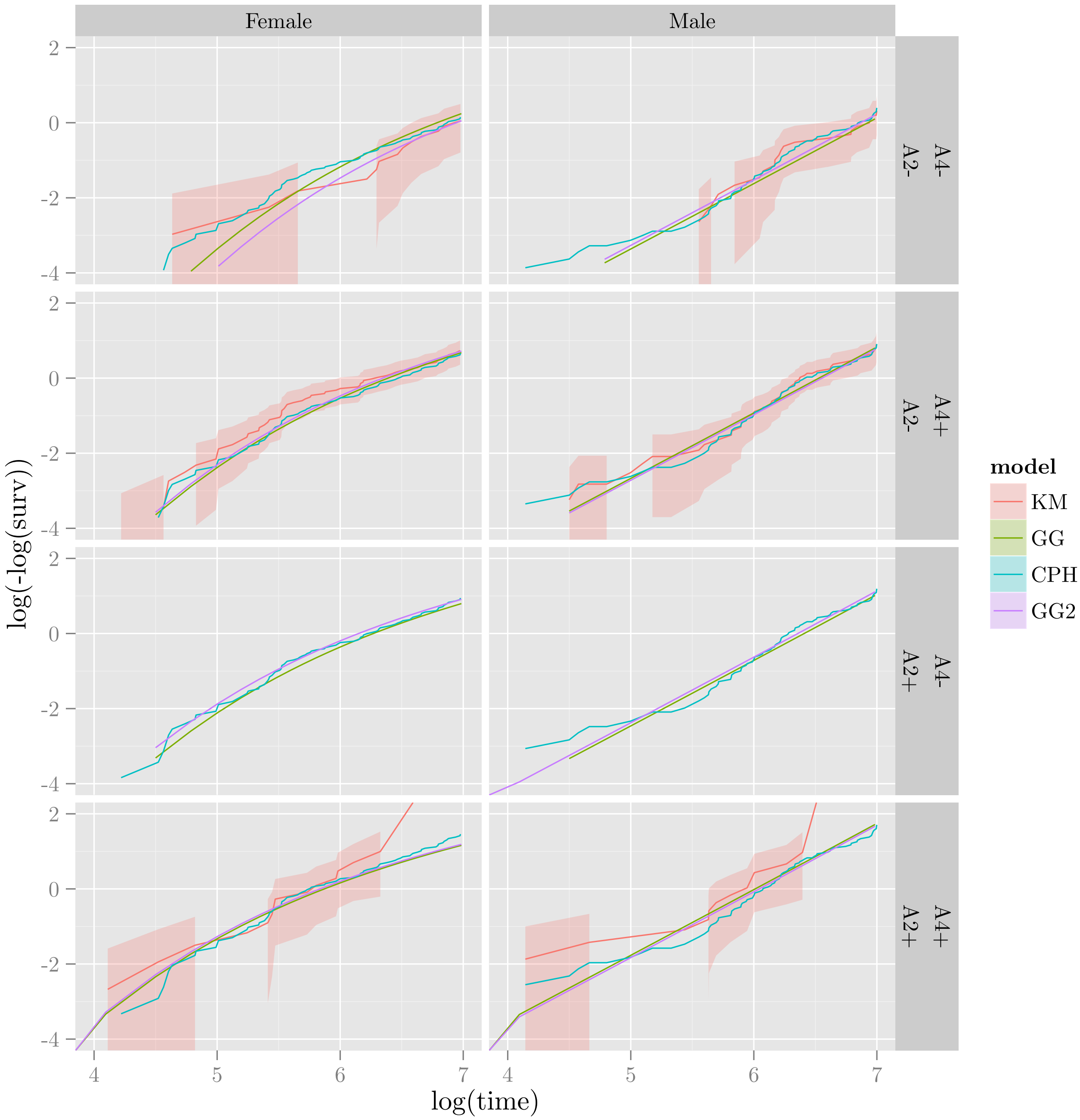

```
ggplot(temp.data, aes(x = time, y = surv, ymin = lower, ymax = upper, colour = model, fill = model)) +
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() + xlim(0, 2000) + ylim(0, 1) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 4 rows containing missing values (geom_path).
## Warning:  Removed 2 rows containing missing values (geom_path).
## Warning:  Removed 5 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
```



An alternative take, showing errors with the KMs only.

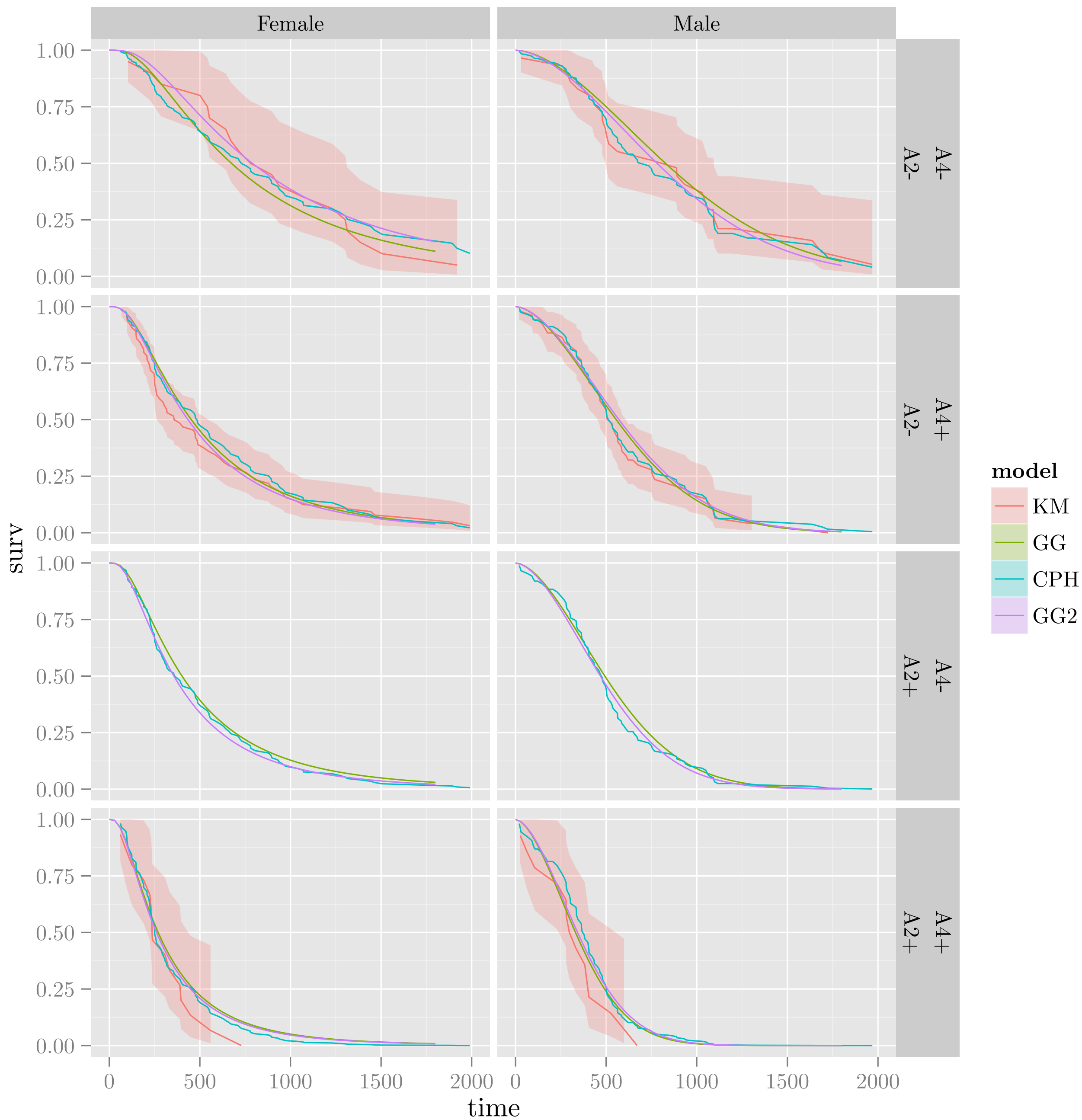
```
temp.data$lower[temp.data$model != "KM"] = NA
temp.data$upper[temp.data$model != "KM"] = NA
ggplot(temp.data, aes(x = log(time), y = log(-log(surv)), ymin = log(-log(lower)), ymax = log(-log(upper
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() +
        xlim(4, 7) + ylim(-4, 2) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 75 rows containing missing values (geom_path).
## Warning:  Removed 70 rows containing missing values (geom_path).
## Warning:  Removed 76 rows containing missing values (geom_path).
## Warning:  Removed 68 rows containing missing values (geom_path).
```

```
## Warning:  Removed 66 rows containing missing values (geom_path).
## Warning:  Removed 63 rows containing missing values (geom_path).
## Warning:  Removed 66 rows containing missing values (geom_path).
## Warning:  Removed 64 rows containing missing values (geom_path).
```



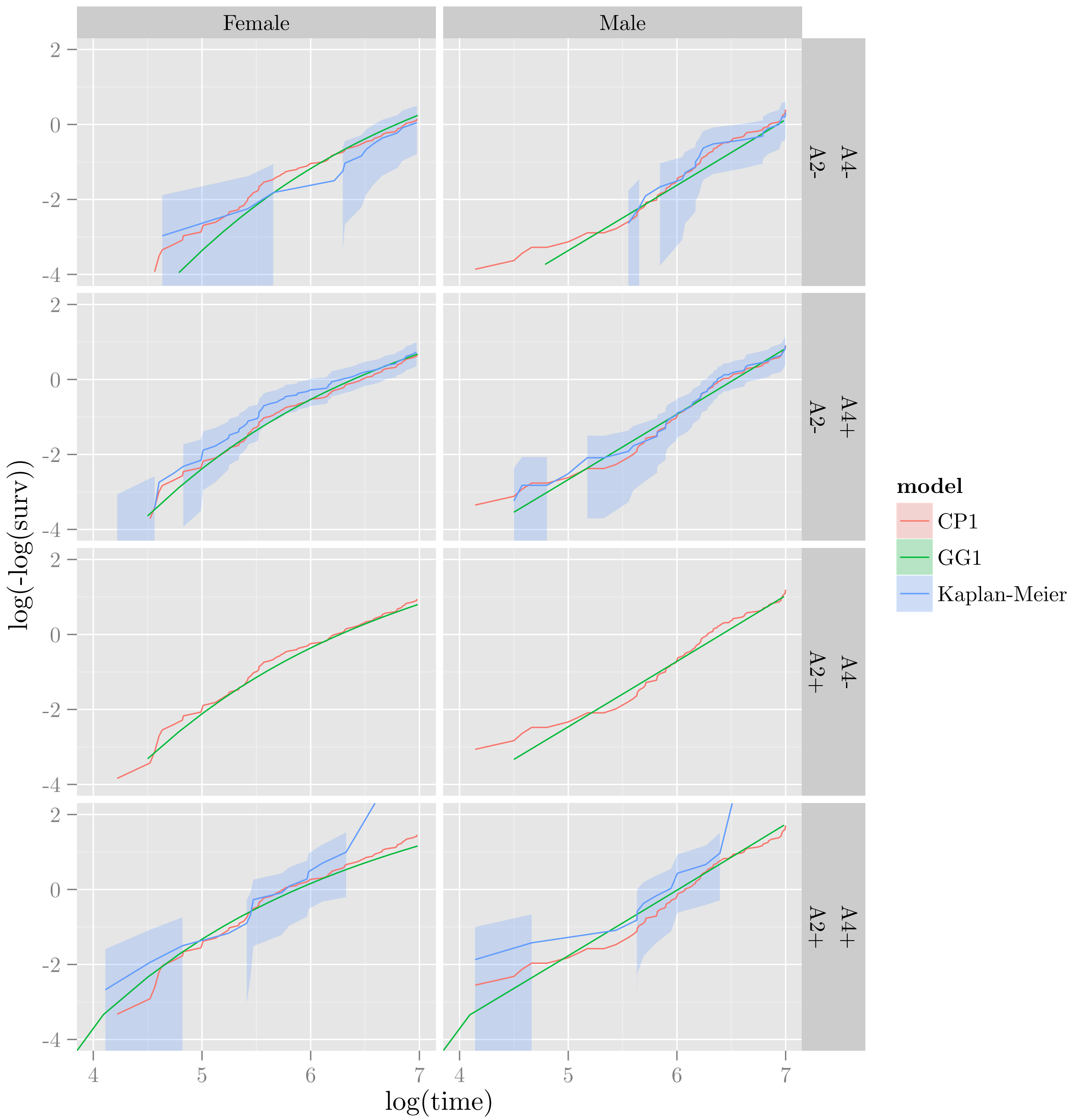

```
ggplot(temp.data, aes(x = time, y = surv, ymin = lower, ymax = upper, colour = model, fill = model)) +
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() + xlim(0, 2000) + ylim(0, 1) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 4 rows containing missing values (geom_path).
## Warning:  Removed 2 rows containing missing values (geom_path).
```

```
## Warning:  Removed 5 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
```

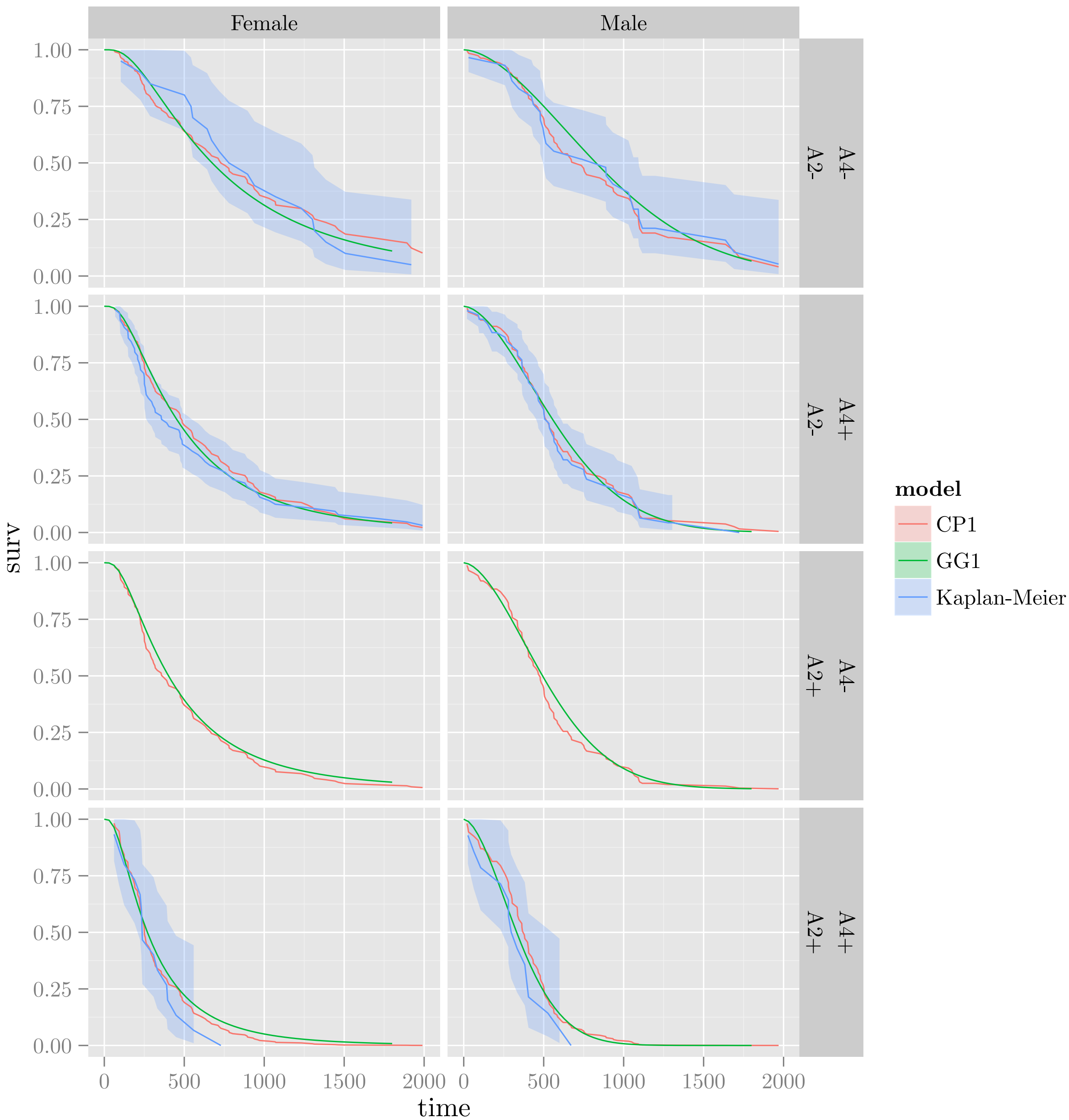



```
temp.data$lower[temp.data$model != "KM"] = NA
temp.data$upper[temp.data$model != "KM"] = NA
temp.data = temp.data[temp.data$model != "GG2",]
temp.data$model = c("KM" = "Kaplan-Meier", "GG" = "GG1", "CPH" = "CP1")[temp.data$model]
ggplot(temp.data, aes(x = log(time), y = log(-log(surv)), ymin = log(-log(lower)), ymax = log(-log(upper
        geom_ribbon(alpha = 0.25, colour = NA) +
```

```
        geom_line() +
        xlim(4, 7) + ylim(-4, 2) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 50 rows containing missing values (geom_path).
## Warning:  Removed 45 rows containing missing values (geom_path).
## Warning:  Removed 51 rows containing missing values (geom_path).
## Warning:  Removed 43 rows containing missing values (geom_path).
## Warning:  Removed 41 rows containing missing values (geom_path).
## Warning:  Removed 38 rows containing missing values (geom_path).
## Warning:  Removed 41 rows containing missing values (geom_path).
## Warning:  Removed 39 rows containing missing values (geom_path).
```



```
ggplot(temp.data, aes(x = time, y = surv, ymin = lower, ymax = upper, colour = model, fill = model)) +
        geom_ribbon(alpha = 0.25, colour = NA) +
        geom_line() + xlim(0, 2000) + ylim(0, 1) +
        facet_grid(A2 ~ A4 ~ Sex)

## Warning:  Removed 4 rows containing missing values (geom_path).
## Warning:  Removed 2 rows containing missing values (geom_path).
## Warning:  Removed 5 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
## Warning:  Removed 3 rows containing missing values (geom_path).
## Warning:  Removed 1 rows containing missing values (geom_path).
```



7 Model selection

It looks like that's as far as we can go with tweaking the fits. Time to put the different models against each other on the holdout data, and choose a winner.

DIY IBS, wooo.

```
calcIBS = function(surv, pred, pred_times, max_time)
{
	stopifnot(nrow(surv) == nrow(pred) && length(pred_times) == ncol(pred))

	n = nrow(surv)
	marg_survfit = survfit(surv ~ 1)
	marg_censfit = survfit(Surv(surv[,1], !surv[,2]) ~ 1)
	marg_surv_func = approxfun(marg_survfit$time, marg_survfit$surv, method = "constant", yleft = 1,
	marg_cens_func = approxfun(marg_censfit$time, marg_censfit$surv, method = "constant", yleft = 1,

	pred_funcs = apply(pred, 1, function(pat_preds) approxfun(pred_times, pat_preds, yleft = 1, yrig

	indiv_patient_bsc = function(pat_i, tstars)
	{
		observed_time = surv[pat_i, 1]
		observed_event = surv[pat_i, 2]
		pred_func = pred_funcs[[pat_i]]
		category = 1*(observed_time <= tstars & observed_event) + 2*(observed_time > tstars) + 3
		bsc = rep(NA, length(tstars))
		bsc[category == 1] = pred_func(tstars[category == 1])^2 / marg_cens_func(observed_time)
		bsc[category == 2] = (1 - pred_func(tstars[category == 2]))^2 / marg_cens_func(tstars[ca
		bsc[category == 3] = 0
		bsc
	}

	bsc_func = function(tstars) { rowMeans(sapply(1:n, function(pat_i) indiv_patient_bsc(pat_i, tsta

	weight_func = function(tstars) { (1 - marg_surv_func(tstars)) / (1 - marg_surv_func(max_time)) }

	# Be slack and do trapezoidal int. with a fine grid.  It should be possible
	# to calulate the int. exactly but I cbfed.
	int_grid = seq(0, max_time, length.out = 1e3)
	bsc_vals = bsc_func(int_grid)
	weight_vals = weight_func(int_grid)
	int_vals = bsc_vals * weight_vals
	ibsc = (2*sum(int_vals) - int_vals[1] - int_vals[length(int_vals)]) * (diff(range(int_grid))) /

	return(list(bsc = bsc_vals, weights = weight_vals, eval_times = int_grid, ibsc = ibsc))
}
```

Calculate survival probability predictions for each of the models, on the validation data.

```
ibs_times = sort(unique(data.val$Time))
ibs_preds_gg = as.matrix(t(sapply(summary(fit.gg, newdata = data.val, type = "survival", t = ibs_times),
ibs_preds_gg2 = as.matrix(t(sapply(summary(fit.gg2, newdata = data.val, type = "survival", t = ibs_times
temp_cox_preds = survfit(fit.cph, newdata = data.val)
ibs_preds_cph = simplify2array(tapply(1:length(temp_cox_preds$time), rep(names(temp_cox_preds$strata), t
	approx(x = temp_cox_preds$time[strat_i], y = temp_cox_preds$surv[strat_i], xout = ibs_times, met
```

```
ibs_preds_cph = t(ibs_preds_cph[,rownames(data.val)])
temp_rsf_preds = predict(fit.rsf, newdata = data.val)
ibs_preds_rsf = t(apply(temp_rsf_preds$survival, 1, function(survs) approx(temp_rsf_preds$time.interest,
# Patients (from data.val) are in rows, times (from ibs_times) in columns.

# Add a no-information KM predictor
temp_km0 = survfit(Surv(Time, DSD) ~ 1, data)
ibs_preds_km0 = t(matrix(rep(approx(temp_km0$time, temp_km0$surv, xout = ibs_times, method = "constant",
ibs_preds_all = list(gg = ibs_preds_gg, gg2 = ibs_preds_gg2, cph = ibs_preds_cph, rsf = ibs_preds_rsf, k
```

```
val.prob.times = seq(0, max(data.val$Time), 1)

temp.coefs = coef(fit.gg)
val.linpred.gg = sapply(1:length(temp.coefs), function(coef_i) {
    if (names(temp.coefs)[coef_i] %in% colnames(data.val)) {
        temp.coefs[coef_i] * data.val[,names(temp.coefs)[coef_i]]
    } else if (gsub("TRUE$", "", names(temp.coefs)[coef_i]) %in% colnames(data.val)) {
        temp.coefs[coef_i] * data.val[,gsub("TRUE$", "", names(temp.coefs)[coef_i])]
    } else {
        rep(0, nrow(data.val))
    } })
val.linpred.gg = -rowSums(val.linpred.gg)   # Negate to bring into concordance with the direction of Cox
temp = summary(fit.gg, newdata = data.val, ci = FALSE)
val.prob.gg = sapply(temp, function(x) approx(x[,1], x[,2], xout = val.prob.times, yleft = 1, yright = (
colnames(val.prob.gg) = rownames(data.val)

temp.coefs = coef(fit.gg2)
val.linpred.gg2 = sapply(1:length(temp.coefs), function(coef_i) {
    if (names(temp.coefs)[coef_i] %in% colnames(data.val)) {
        temp.coefs[coef_i] * data.val[,names(temp.coefs)[coef_i]]
    } else if (gsub("TRUE$", "", names(temp.coefs)[coef_i]) %in% colnames(data.val)) {
        temp.coefs[coef_i] * data.val[,gsub("TRUE$", "", names(temp.coefs)[coef_i])]
    } else {
        rep(0, nrow(data.val))
    } })
val.linpred.gg2 = -rowSums(val.linpred.gg2)   # Negate to bring into concordance with the direction of C
temp = summary(fit.gg2, newdata = data.val, ci = FALSE)
val.prob.gg2 = sapply(temp, function(x) approx(x[,1], x[,2], xout = val.prob.times, yleft = 1, yright =
colnames(val.prob.gg2) = rownames(data.val)

val.linpred.cph = predict(fit.cph, newdata = data.val)
temp = survfit(fit.cph, newdata = data.val)
val.prob.cph = simplify2array(tapply(1:length(temp$surv), rep(names(temp$strata), temp$strata), function

temp = predict(fit.rsf, newdata = data.val)
# val.linpred.rsf = temp£predicted
# Median survival time:
val.linpred.rsf = apply(temp$survival, 1, function(s1) {
    sfunc = approxfun(temp$time.interest, s1, yleft = 1, yright = 0, rule = 2)
    med = uniroot(function(x) sfunc(x) - 0.5, lower = min(temp$time.interest), upper = max(temp$time.int
    med
})
val.linpred.rsf = -val.linpred.rsf
```

```
val.prob.rsf = apply(temp$survival, 1, function(s1) approx(temp$time.interest, s1, xout = val.prob.times
colnames(val.prob.rsf) = rownames(data.val)

summary(coxph(Surv(Time, DSD) ~ val.linpred.gg, data.val))

## Call:
## coxph(formula = Surv(Time, DSD) ~ val.linpred.gg, data = data.val)
##
##   n= 48, number of events= 46
##
##                 coef exp(coef) se(coef)   z Pr(>|z|)
## val.linpred.gg 0.160     1.173    0.397 0.4     0.69
##
##                exp(coef) exp(-coef) lower .95 upper .95
## val.linpred.gg      1.17      0.852     0.539      2.56
##
## Concordance= 0.554  (se = 0.05 )
## Rsquare= 0.003   (max possible= 0.997 )
## Likelihood ratio test= 0.16  on 1 df,   p=0.689
## Wald test            = 0.16  on 1 df,   p=0.688
## Score (logrank) test = 0.16  on 1 df,   p=0.688

summary(coxph(Surv(Time, DSD) ~ val.linpred.gg2, data.val))

## Call:
## coxph(formula = Surv(Time, DSD) ~ val.linpred.gg2, data = data.val)
##
##   n= 48, number of events= 46
##
##                  coef exp(coef) se(coef)    z Pr(>|z|)
## val.linpred.gg2 0.128     1.137    0.389 0.33     0.74
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## val.linpred.gg2      1.14       0.88      0.53      2.44
##
## Concordance= 0.551  (se = 0.05 )
## Rsquare= 0.002   (max possible= 0.997 )
## Likelihood ratio test= 0.11  on 1 df,   p=0.743
## Wald test            = 0.11  on 1 df,   p=0.742
## Score (logrank) test = 0.11  on 1 df,   p=0.742

summary(coxph(Surv(Time, DSD) ~ val.linpred.cph, data.val))

## Call:
## coxph(formula = Surv(Time, DSD) ~ val.linpred.cph, data = data.val)
##
##   n= 48, number of events= 46
##
##                  coef exp(coef) se(coef)    z Pr(>|z|)
## val.linpred.cph 0.221     1.247    0.330 0.67      0.5
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## val.linpred.cph      1.25      0.802     0.653      2.38
##
## Concordance= 0.528  (se = 0.05 )
```

```
## Rsquare= 0.009   (max possible= 0.997 )
## Likelihood ratio test= 0.45  on 1 df,   p=0.502
## Wald test            = 0.45  on 1 df,   p=0.504
## Score (logrank) test = 0.45  on 1 df,   p=0.504
```

```
summary(coxph(Surv(Time, DSD) ~ val.linpred.rsf, data.val))
```

```
## Call:
## coxph(formula = Surv(Time, DSD) ~ val.linpred.rsf, data = data.val)
##
##   n= 48, number of events= 46
##
##                    coef exp(coef) se(coef)    z Pr(>|z|)
## val.linpred.rsf 0.00195   1.00195  0.00178 1.09     0.27
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## val.linpred.rsf         1      0.998     0.998      1.01
##
## Concordance= 0.561  (se = 0.051 )
## Rsquare= 0.025   (max possible= 0.997 )
## Likelihood ratio test= 1.2  on 1 df,   p=0.272
## Wald test            = 1.19  on 1 df,   p=0.275
## Score (logrank) test = 1.19  on 1 df,   p=0.275
```

```
anova(coxph(Surv(Time, DSD) ~ offset(val.linpred.gg) + val.linpred.gg, data.val))
```

```
## Analysis of Deviance Table
##  Cox model: response is Surv(Time, DSD)
## Terms added sequentially (first to last)
##
##                loglik Chisq Df Pr(>|Chi|)
## NULL             -140
## val.linpred.gg   -137  4.57  1      0.032
```

```
anova(coxph(Surv(Time, DSD) ~ offset(val.linpred.gg2) + val.linpred.gg2, data.val))
```

```
## Analysis of Deviance Table
##  Cox model: response is Surv(Time, DSD)
## Terms added sequentially (first to last)
##
##                 loglik Chisq Df Pr(>|Chi|)
## NULL              -140
## val.linpred.gg2   -137  5.18  1      0.023
```

```
anova(coxph(Surv(Time, DSD) ~ offset(val.linpred.cph) + val.linpred.cph, data.val))
```

```
## Analysis of Deviance Table
##  Cox model: response is Surv(Time, DSD)
## Terms added sequentially (first to last)
##
##                 loglik Chisq Df Pr(>|Chi|)
## NULL              -140
## val.linpred.cph   -137  5.38  1       0.02
```

```
anova(coxph(Surv(Time, DSD) ~ offset(val.linpred.rsf) + val.linpred.rsf, data.val))
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Ran out of
iterations and did not converge
## Error in fitter(X, Y, strats, offset, init, control, weights = weights, :  NA/NaN/Inf in
foreign function call (arg 6)
```

```
summary(coxph(Surv(Time, DSD) ~ offset(val.linpred.gg) + SexM + AgeCent + LocBody + SizeCent + A2 + A4,
```

```
## Call:
## coxph(formula = Surv(Time, DSD) ~ offset(val.linpred.gg) + SexM +
##     AgeCent + LocBody + SizeCent + A2 + A4, data = data.val)
##
##   n= 48, number of events= 46
##
##                 coef exp(coef) se(coef)     z Pr(>|z|)
## SexMTRUE     0.5967    1.8161   0.3129  1.91    0.057
## AgeCent     -0.0246    0.9757   0.0185 -1.33    0.183
## LocBodyTRUE  0.3897    1.4765   0.4292  0.91    0.364
## SizeCent    -0.0209    0.9793   0.0109 -1.92    0.055
## A2TRUE       0.4593    1.5829   0.5630  0.82    0.415
## A4TRUE      -0.3345    0.7157   0.3852 -0.87    0.385
##
##             exp(coef) exp(-coef) lower .95 upper .95
## SexMTRUE        1.816      0.551     0.984      3.35
## AgeCent         0.976      1.025     0.941      1.01
## LocBodyTRUE     1.477      0.677     0.637      3.42
## SizeCent        0.979      1.021     0.959      1.00
## A2TRUE          1.583      0.632     0.525      4.77
## A4TRUE          0.716      1.397     0.336      1.52
##
## Concordance= 0.559  (se = 0.051 )
## Rsquare= 0.182   (max possible= 0.997 )
## Likelihood ratio test= 9.66  on 6 df,   p=0.14
## Wald test            = 9.65  on 6 df,   p=0.14
## Score (logrank) test = 9.97  on 6 df,   p=0.126
```

```
summary(coxph(Surv(Time, DSD) ~ offset(val.linpred.gg2) + SexM + AgeCent + LocBody + SizeCent + A2 + A4,
```

```
## Call:
## coxph(formula = Surv(Time, DSD) ~ offset(val.linpred.gg2) + SexM +
##     AgeCent + LocBody + SizeCent + A2 + A4, data = data.val)
##
##   n= 48, number of events= 46
##
##                 coef exp(coef) se(coef)     z Pr(>|z|)
## SexMTRUE     0.6712    1.9566   0.3129  2.15    0.032
## AgeCent     -0.0246    0.9757   0.0185 -1.33    0.183
## LocBodyTRUE  0.3897    1.4765   0.4292  0.91    0.364
## SizeCent    -0.0213    0.9789   0.0109 -1.96    0.050
## A2TRUE       0.4662    1.5939   0.5630  0.83    0.408
## A4TRUE      -0.2502    0.7786   0.3852 -0.65    0.516
##
##             exp(coef) exp(-coef) lower .95 upper .95
## SexMTRUE        1.957      0.511     1.060      3.61
## AgeCent         0.976      1.025     0.941      1.01
## LocBodyTRUE     1.477      0.677     0.637      3.42
```

```
## SizeCent        0.979      1.022     0.958      1.00
## A2TRUE          1.594      0.627     0.529      4.81
## A4TRUE          0.779      1.284     0.366      1.66
##
## Concordance= 0.559  (se = 0.051 )
## Rsquare= 0.193   (max possible= 0.997 )
## Likelihood ratio test= 10.3  on 6 df,   p=0.112
## Wald test            = 10.3  on 6 df,   p=0.111
## Score (logrank) test = 10.7  on 6 df,   p=0.0977
```

```
summary(coxph(Surv(Time, DSD) ~ offset(val.linpred.cph) + SexM + AgeCent + LocBody + SizeCent + A2 + A4,
```

```
## Call:
## coxph(formula = Surv(Time, DSD) ~ offset(val.linpred.cph) + SexM +
##     AgeCent + LocBody + SizeCent + A2 + A4, data = data.val)
##
##   n= 48, number of events= 46
##
##                 coef exp(coef) se(coef)     z Pr(>|z|)
## SexMTRUE     0.1500    1.1618   0.3129  0.48    0.632
## AgeCent     -0.0246    0.9757   0.0185 -1.33    0.183
## LocBodyTRUE  0.3897    1.4765   0.4292  0.91    0.364
## SizeCent    -0.0274    0.9730   0.0109 -2.51    0.012
## A2TRUE       0.1791    1.1961   0.5630  0.32    0.750
## A4TRUE      -0.4494    0.6380   0.3852 -1.17    0.243
##
##             exp(coef) exp(-coef) lower .95 upper .95
## SexMTRUE        1.162      0.861     0.629     2.145
## AgeCent         0.976      1.025     0.941     1.012
## LocBodyTRUE     1.477      0.677     0.637     3.424
## SizeCent        0.973      1.028     0.952     0.994
## A2TRUE          1.196      0.836     0.397     3.606
## A4TRUE          0.638      1.567     0.300     1.357
##
## Concordance= 0.559  (se = 0.051 )
## Rsquare= 0.191   (max possible= 0.997 )
## Likelihood ratio test= 10.2  on 6 df,   p=0.118
## Wald test            = 9.97  on 6 df,   p=0.126
## Score (logrank) test = 10.3  on 6 df,   p=0.111
```

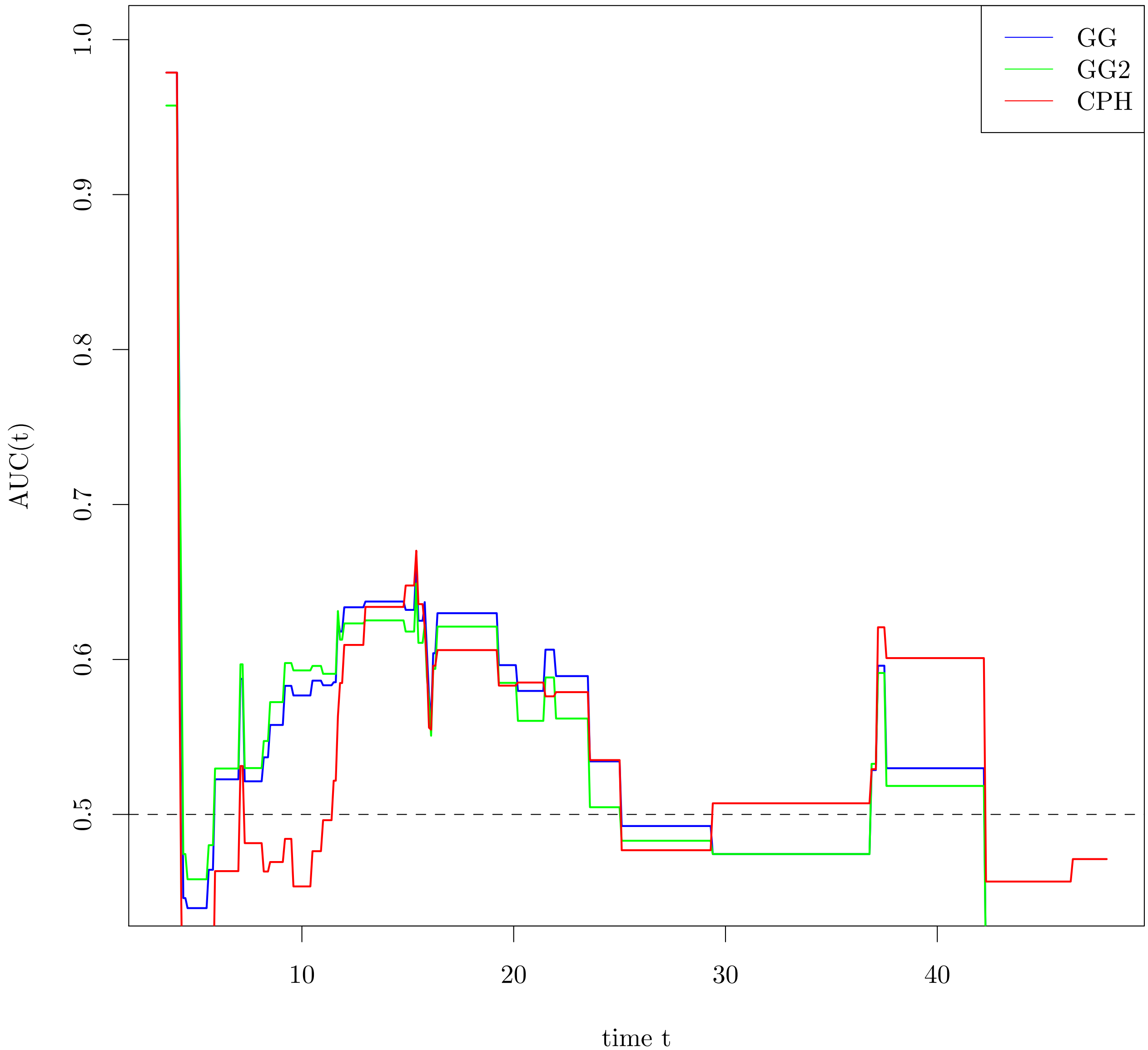
```
summary(coxph(Surv(Time, DSD) ~ offset(val.linpred.rsf) + SexM + AgeCent + LocBody + SizeCent + A2 + A4,
```

```
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, :  Ran out of
iterations and did not converge
## Error in fitter(X, Y, strats, offset, init, control, weights = weights, :  NA/NaN/Inf in
foreign function call (arg 6)
```

TD-ROC AUC

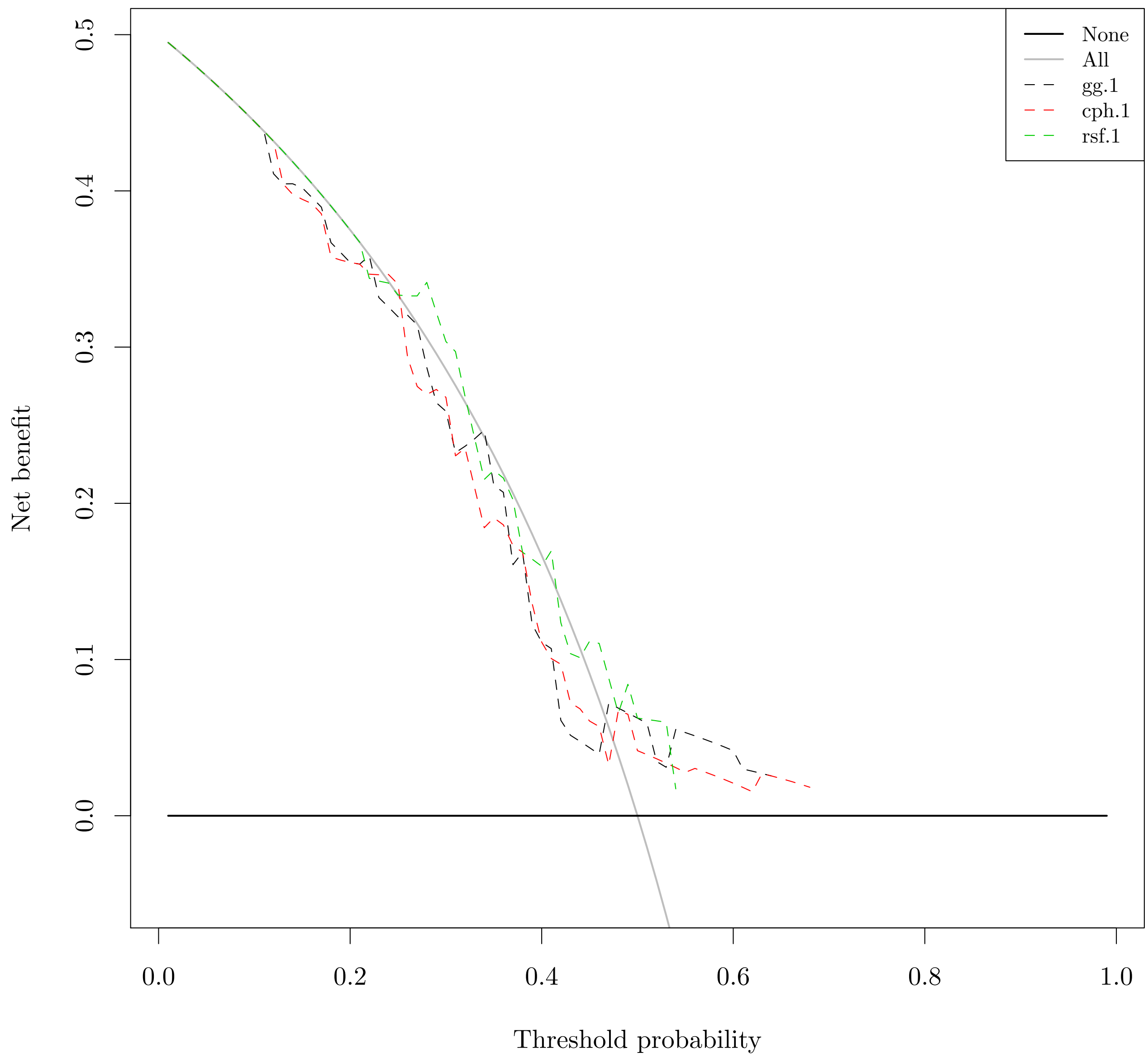
```
temp.times = seq(0.1, 48, 0.1)
temp.gg = timeROC(data.val$Time/365.25*12, data.val$DSD, val.linpred.gg, cause = 1, times = temp.times,
temp.gg2 = timeROC(data.val$Time/365.25*12, data.val$DSD, val.linpred.gg2, cause = 1, times = temp.times
temp.cph = timeROC(data.val$Time/365.25*12, data.val$DSD, val.linpred.cph, cause = 1, times = temp.times
plotAUCcurve(temp.gg, conf.int = FALSE, add = FALSE, col = "blue")
plotAUCcurve(temp.gg2, conf.int = FALSE, add = TRUE, col = "green")
```

```
plotAUCcurve(temp.cph, conf.int = FALSE, add = TRUE, col = "red")
legend("topright", legend = c("GG", "GG2", "CPH"), col = c("blue", "green", "red"), lty = "solid")
```



Decision curve analysis.

```
temp.data = data.frame(Time = data.val$Time, DSD = data.val$DSD*1,
    gg.1 = 1-val.prob.gg[val.prob.times == 365,], gg.2 = 1-val.prob.gg[val.prob.times == 365*2,], gg.3 =
    gg2.1 = 1-val.prob.gg2[val.prob.times == 365,], gg2.2 = 1-val.prob.gg2[val.prob.times == 365*2,], gg
    cph.1 = 1-val.prob.cph[val.prob.times == 365,], cph.2 = 1-val.prob.cph[val.prob.times == 365*2,], cp
    rsf.1 = 1-val.prob.rsf[val.prob.times == 365,], rsf.2 = 1-val.prob.rsf[val.prob.times == 365*2,], rs
stdca(data = temp.data, outcome = "DSD", ttoutcome = "Time", predictors = c("gg.1", "cph.1", "rsf.1"), t

## [1] "gg.1: No observations with risk greater than 65% that have followup through the timepoint select
## [2] "cph.1: No observations with risk greater than 69% that have followup through the timepoint selec
## [3] "rsf.1: No observations with risk greater than 55% that have followup through the timepoint selec
```




```
## $N
## [1] 48
##
## $predictors
##   predictor harm.applied probability
## 1      gg.1            0        TRUE
## 2     cph.1            0        TRUE
## 3     rsf.1            0        TRUE
##
## $interventions.avoided.per
## [1] 100
##
## $net.benefit
##    threshold       all none    gg.1   cph.1   rsf.1
## 1       0.01   0.49495    0 0.49495 0.49495 0.49495
## 2       0.02   0.48980    0 0.48980 0.48980 0.48980
## 3       0.03   0.48454    0 0.48454 0.48454 0.48454
```

```
## 4        0.04   0.47917    0 0.47917 0.47917 0.47917
## 5        0.05   0.47368    0 0.47368 0.47368 0.47368
## 6        0.06   0.46809    0 0.46809 0.46809 0.46809
## 7        0.07   0.46237    0 0.46237 0.46237 0.46237
## 8        0.08   0.45652    0 0.45652 0.45652 0.45652
## 9        0.09   0.45055    0 0.45055 0.45055 0.45055
## 10       0.10   0.44444    0 0.44444 0.44444 0.44444
## 11       0.11   0.43820    0 0.43820 0.43820 0.43820
## 12       0.12   0.43182    0 0.41098 0.43182 0.43182
## 13       0.13   0.42529    0 0.40445 0.40445 0.42529
## 14       0.14   0.41860    0 0.40455 0.39777 0.41860
## 15       0.15   0.41176    0 0.40196 0.39461 0.41176
## 16       0.16   0.40476    0 0.39583 0.39187 0.40476
## 17       0.17   0.39759    0 0.38956 0.38529 0.39759
## 18       0.18   0.39024    0 0.36687 0.35772 0.39024
## 19       0.19   0.38272    0 0.36060 0.35571 0.38272
## 20       0.20   0.37500    0 0.35417 0.35417 0.37500
## 21       0.21   0.36709    0 0.35311 0.35311 0.36709
## 22       0.22   0.35897    0 0.35844 0.34669 0.34402
## 23       0.23   0.35065    0 0.33171 0.34632 0.34226
## 24       0.24   0.34211    0 0.32566 0.34649 0.34101
## 25       0.25   0.33333    0 0.31944 0.34028 0.33333
## 26       0.26   0.32432    0 0.32038 0.29336 0.33277
## 27       0.27   0.31507    0 0.31421 0.27483 0.33276
## 28       0.28   0.30556    0 0.28704 0.26968 0.34144
## 29       0.29   0.29577    0 0.26438 0.27289 0.32218
## 30       0.30   0.28571    0 0.25893 0.26786 0.30357
## 31       0.31   0.27536    0 0.23249 0.23037 0.29710
## 32       0.32   0.26471    0 0.23652 0.23529 0.26838
## 33       0.33   0.25373    0 0.24129 0.20989 0.24160
## 34       0.34   0.24242    0 0.24684 0.18434 0.21528
## 35       0.35   0.23077    0 0.21154 0.19071 0.22115
## 36       0.36   0.21875    0 0.20703 0.18620 0.21615
## 37       0.37   0.20635    0 0.16071 0.17295 0.20238
## 38       0.38   0.19355    0 0.16868 0.16868 0.16868
## 39       0.39   0.18033    0 0.12261 0.13593 0.16428
## 40       0.40   0.16667    0 0.11111 0.11111 0.15972
## 41       0.41   0.15254    0 0.10699 0.10064 0.16949
## 42       0.42   0.13793    0 0.06106 0.09698 0.12356
## 43       0.43   0.12281    0 0.05154 0.07237 0.10380
## 44       0.44   0.10714    0 0.04762 0.06845 0.10119
## 45       0.45   0.09091    0 0.04356 0.06061 0.11174
## 46       0.46   0.07407    0 0.03935 0.05710 0.11034
## 47       0.47   0.05660    0 0.07193 0.03263 0.08805
## 48       0.48   0.03846    0 0.06891 0.06731 0.06571
## 49       0.49   0.01961    0 0.06577 0.06495 0.08415
## 50       0.50   0.00000    0 0.06250 0.04167 0.06250
## 51       0.51  -0.02041    0 0.05910 0.03912 0.06165
## 52       0.52  -0.04167    0 0.03472 0.03646 0.06076
## 53       0.53  -0.06383    0 0.03103 0.03369 0.05984
## 54       0.54  -0.08696    0 0.05525 0.03080 0.01721
## 55       0.55  -0.11111    0 0.05324 0.02778      NA
## 56       0.56  -0.13636    0 0.05114 0.03030      NA
## 57       0.57  -0.16279    0 0.04893 0.02810      NA
```

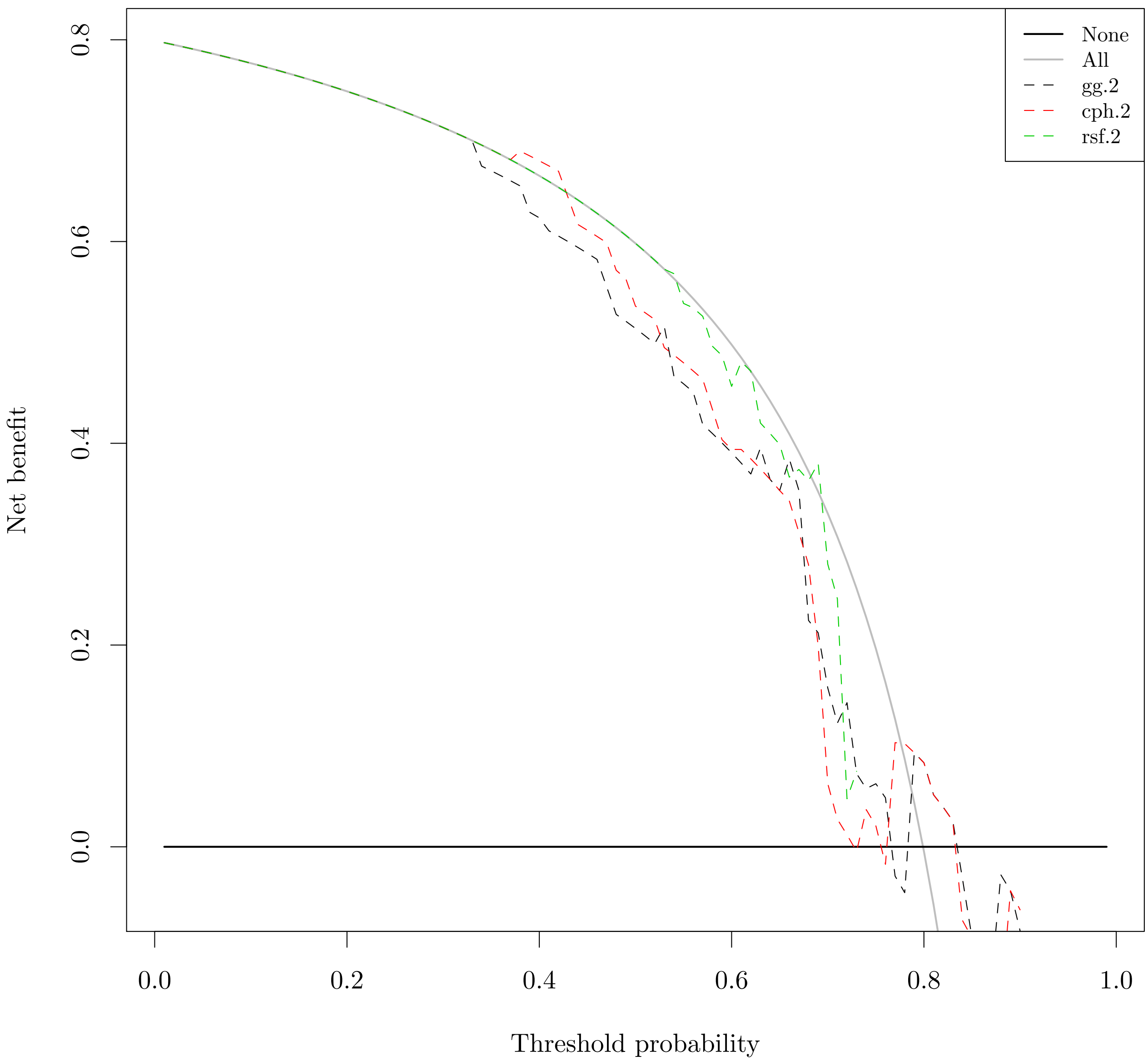
```
## 58      0.58  -0.19048    0 0.04663 0.02579      NA
## 59      0.59  -0.21951    0 0.04421 0.02337      NA
## 60      0.60  -0.25000    0 0.04167 0.02083      NA
## 61      0.61  -0.28205    0 0.02991 0.01816      NA
## 62      0.62  -0.31579    0 0.02851 0.01535      NA
## 63      0.63  -0.35135    0 0.02703 0.02703      NA
## 64      0.64  -0.38889    0 0.02546 0.02546      NA
## 65      0.65  -0.42857    0      NA 0.02381      NA
## 66      0.66  -0.47059    0      NA 0.02206      NA
## 67      0.67  -0.51515    0      NA 0.02020      NA
## 68      0.68  -0.56250    0      NA 0.01823      NA
## 69      0.69  -0.61290    0      NA      NA      NA
## 70      0.70  -0.66667    0      NA      NA      NA
## 71      0.71  -0.72414    0      NA      NA      NA
## 72      0.72  -0.78571    0      NA      NA      NA
## 73      0.73  -0.85185    0      NA      NA      NA
## 74      0.74  -0.92308    0      NA      NA      NA
## 75      0.75  -1.00000    0      NA      NA      NA
## 76      0.76  -1.08333    0      NA      NA      NA
## 77      0.77  -1.17391    0      NA      NA      NA
## 78      0.78  -1.27273    0      NA      NA      NA
## 79      0.79  -1.38095    0      NA      NA      NA
## 80      0.80  -1.50000    0      NA      NA      NA
## 81      0.81  -1.63158    0      NA      NA      NA
## 82      0.82  -1.77778    0      NA      NA      NA
## 83      0.83  -1.94118    0      NA      NA      NA
## 84      0.84  -2.12500    0      NA      NA      NA
## 85      0.85  -2.33333    0      NA      NA      NA
## 86      0.86  -2.57143    0      NA      NA      NA
## 87      0.87  -2.84615    0      NA      NA      NA
## 88      0.88  -3.16667    0      NA      NA      NA
## 89      0.89  -3.54545    0      NA      NA      NA
## 90      0.90  -4.00000    0      NA      NA      NA
## 91      0.91  -4.55556    0      NA      NA      NA
## 92      0.92  -5.25000    0      NA      NA      NA
## 93      0.93  -6.14286    0      NA      NA      NA
## 94      0.94  -7.33333    0      NA      NA      NA
## 95      0.95  -9.00000    0      NA      NA      NA
## 96      0.96 -11.50000    0      NA      NA      NA
## 97      0.97 -15.66667    0      NA      NA      NA
## 98      0.98 -24.00000    0      NA      NA      NA
## 99      0.99 -49.00000    0      NA      NA      NA
##
## $interventions.avoided
##    threshold     gg.1   cph.1      rsf.1
## 1       0.01   0.0000   0.000  0.000e+00
## 2       0.02   0.0000   0.000  0.000e+00
## 3       0.03   0.0000   0.000  0.000e+00
## 4       0.04   0.0000   0.000  0.000e+00
## 5       0.05   0.0000   0.000  0.000e+00
## 6       0.06   0.0000   0.000  0.000e+00
## 7       0.07   0.0000   0.000  0.000e+00
## 8       0.08   0.0000   0.000  0.000e+00
## 9       0.09   0.0000   0.000  0.000e+00
```

```
## 10       0.10   0.0000   0.000  0.000e+00
## 11       0.11   0.0000   0.000  0.000e+00
## 12       0.12 -15.2778   0.000  0.000e+00
## 13       0.13 -13.9423 -13.942  0.000e+00
## 14       0.14  -8.6310 -12.798  0.000e+00
## 15       0.15  -5.5556  -9.722  0.000e+00
## 16       0.16  -4.6875  -6.771  0.000e+00
## 17       0.17  -3.9216  -6.005  0.000e+00
## 18       0.18 -10.6481 -14.815  0.000e+00
## 19       0.19  -9.4298 -11.513  0.000e+00
## 20       0.20  -8.3333  -8.333  0.000e+00
## 21       0.21  -5.2579  -5.258  0.000e+00
## 22       0.22  -0.1894  -4.356 -5.303e+00
## 23       0.23  -6.3406  -1.449 -2.808e+00
## 24       0.24  -5.2083   1.389 -3.472e-01
## 25       0.25  -4.1667   2.083 -3.331e-14
## 26       0.26  -1.1218  -8.814  2.404e+00
## 27       0.27  -0.2315 -10.880  4.784e+00
## 28       0.28  -4.7619  -9.226  9.226e+00
## 29       0.29  -7.6868  -5.603  6.466e+00
## 30       0.30  -6.2500  -4.167  4.167e+00
## 31       0.31  -9.5430 -10.013  4.839e+00
## 32       0.32  -5.9896  -6.250  7.813e-01
## 33       0.33  -2.5253  -8.902 -2.462e+00
## 34       0.34   0.8578 -11.275 -5.270e+00
## 35       0.35  -3.5714  -7.440 -1.786e+00
## 36       0.36  -2.0833  -5.787 -4.630e-01
## 37       0.37  -7.7703  -5.687 -6.757e-01
## 38       0.38  -4.0570  -4.057 -4.057e+00
## 39       0.39  -9.0278  -6.944 -2.511e+00
## 40       0.40  -8.3333  -8.333 -1.042e+00
## 41       0.41  -6.5549  -7.470  2.439e+00
## 42       0.42 -10.6151  -5.655 -1.984e+00
## 43       0.43  -9.4477  -6.686 -2.519e+00
## 44       0.44  -7.5758  -4.924 -7.576e-01
## 45       0.45  -5.7870  -3.704  2.546e+00
## 46       0.46  -4.0761  -1.993  4.257e+00
## 47       0.47   1.7287  -2.704  3.546e+00
## 48       0.48   3.2986   3.125  2.951e+00
## 49       0.49   4.8044   4.719  6.718e+00
## 50       0.50   6.2500   4.167  6.250e+00
## 51       0.51   7.6389   5.719  7.884e+00
## 52       0.52   7.0513   7.212  9.455e+00
## 53       0.53   8.4119   8.648  1.097e+01
## 54       0.54  12.1142  10.031  8.873e+00
## 55       0.55  13.4470  11.364         NA
## 56       0.56  14.7321  13.095         NA
## 57       0.57  15.9722  14.401         NA
## 58       0.58  17.1695  15.661         NA
## 59       0.59  18.3263  16.879         NA
## 60       0.60  19.4444  18.056         NA
## 61       0.61  19.9454  19.194         NA
## 62       0.62  21.1022  20.296         NA
## 63       0.63  22.2222  22.222         NA
```

```
## 64      0.64  23.3073  23.307          NA
## 65      0.65       NA  24.359          NA
## 66      0.66       NA  25.379          NA
## 67      0.67       NA  26.368          NA
## 68      0.68       NA  27.328          NA
## 69      0.69       NA      NA          NA
## 70      0.70       NA      NA          NA
## 71      0.71       NA      NA          NA
## 72      0.72       NA      NA          NA
## 73      0.73       NA      NA          NA
## 74      0.74       NA      NA          NA
## 75      0.75       NA      NA          NA
## 76      0.76       NA      NA          NA
## 77      0.77       NA      NA          NA
## 78      0.78       NA      NA          NA
## 79      0.79       NA      NA          NA
## 80      0.80       NA      NA          NA
## 81      0.81       NA      NA          NA
## 82      0.82       NA      NA          NA
## 83      0.83       NA      NA          NA
## 84      0.84       NA      NA          NA
## 85      0.85       NA      NA          NA
## 86      0.86       NA      NA          NA
## 87      0.87       NA      NA          NA
## 88      0.88       NA      NA          NA
## 89      0.89       NA      NA          NA
## 90      0.90       NA      NA          NA
## 91      0.91       NA      NA          NA
## 92      0.92       NA      NA          NA
## 93      0.93       NA      NA          NA
## 94      0.94       NA      NA          NA
## 95      0.95       NA      NA          NA
## 96      0.96       NA      NA          NA
## 97      0.97       NA      NA          NA
## 98      0.98       NA      NA          NA
## 99      0.99       NA      NA          NA
```

```
stdca(data = temp.data, outcome = "DSD", ttoutcome = "Time", predictors = c("gg.2", "cph.2", "rsf.2"), t
```

```
## [1] "gg.2: No observations with risk greater than 93% that have followup through the timepoint select
## [2] "cph.2: No observations with risk greater than 91% that have followup through the timepoint selec
## [3] "rsf.2: No observations with risk greater than 74% that have followup through the timepoint selec
```




```
## $N
## [1] 48
##
## $predictors
##   predictor harm.applied probability
## 1      gg.2            0        TRUE
## 2     cph.2            0        TRUE
## 3     rsf.2            0        TRUE
##
## $interventions.avoided.per
## [1] 100
##
## $net.benefit
##    threshold        all none     gg.2    cph.2   rsf.2
## 1       0.01   0.797078    0  0.79708  0.79708 0.79708
## 2       0.02   0.795007    0  0.79501  0.79501 0.79501
## 3       0.03   0.792894    0  0.79289  0.79289 0.79289
```

```
## 4        0.04   0.790737    0  0.79074  0.79074 0.79074
## 5        0.05   0.788534    0  0.78853  0.78853 0.78853
## 6        0.06   0.786284    0  0.78628  0.78628 0.78628
## 7        0.07   0.783986    0  0.78399  0.78399 0.78399
## 8        0.08   0.781638    0  0.78164  0.78164 0.78164
## 9        0.09   0.779239    0  0.77924  0.77924 0.77924
## 10       0.10   0.776786    0  0.77679  0.77679 0.77679
## 11       0.11   0.774278    0  0.77428  0.77428 0.77428
## 12       0.12   0.771713    0  0.77171  0.77171 0.77171
## 13       0.13   0.769089    0  0.76909  0.76909 0.76909
## 14       0.14   0.766404    0  0.76640  0.76640 0.76640
## 15       0.15   0.763655    0  0.76366  0.76366 0.76366
## 16       0.16   0.760842    0  0.76084  0.76084 0.76084
## 17       0.17   0.757960    0  0.75796  0.75796 0.75796
## 18       0.18   0.755009    0  0.75501  0.75501 0.75501
## 19       0.19   0.751984    0  0.75198  0.75198 0.75198
## 20       0.20   0.748884    0  0.74888  0.74888 0.74888
## 21       0.21   0.745705    0  0.74571  0.74571 0.74571
## 22       0.22   0.742445    0  0.74245  0.74245 0.74245
## 23       0.23   0.739100    0  0.73910  0.73910 0.73910
## 24       0.24   0.735667    0  0.73567  0.73567 0.73567
## 25       0.25   0.732143    0  0.73214  0.73214 0.73214
## 26       0.26   0.728523    0  0.72852  0.72852 0.72852
## 27       0.27   0.724804    0  0.72480  0.72480 0.72480
## 28       0.28   0.720982    0  0.72098  0.72098 0.72098
## 29       0.29   0.717052    0  0.71705  0.71705 0.71705
## 30       0.30   0.713010    0  0.71301  0.71301 0.71301
## 31       0.31   0.708851    0  0.70885  0.70885 0.70885
## 32       0.32   0.704569    0  0.70457  0.70457 0.70457
## 33       0.33   0.700160    0  0.70016  0.70016 0.70016
## 34       0.34   0.695617    0  0.67478  0.69562 0.69562
## 35       0.35   0.690934    0  0.67010  0.69093 0.69093
## 36       0.36   0.686105    0  0.66527  0.68610 0.68610
## 37       0.37   0.681122    0  0.66029  0.68112 0.68112
## 38       0.38   0.675979    0  0.65515  0.68967 0.67598
## 39       0.39   0.670667    0  0.62900  0.68493 0.67067
## 40       0.40   0.665179    0  0.62351  0.68002 0.66518
## 41       0.41   0.659504    0  0.61064  0.67495 0.65950
## 42       0.42   0.653633    0  0.60536  0.66971 0.65363
## 43       0.43   0.647556    0  0.59990  0.64344 0.64756
## 44       0.44   0.641263    0  0.59425  0.61699 0.64126
## 45       0.45   0.634740    0  0.58838  0.61116 0.63474
## 46       0.46   0.627976    0  0.58230  0.60512 0.62798
## 47       0.47   0.620957    0  0.55516  0.59884 0.62096
## 48       0.48   0.613668    0  0.52778  0.57150 0.61367
## 49       0.49   0.606092    0  0.52097  0.56306 0.60609
## 50       0.50   0.598214    0  0.51389  0.53598 0.59821
## 51       0.51   0.590015    0  0.50652  0.52949 0.59001
## 52       0.52   0.581473    0  0.49884  0.52273 0.58147
## 53       0.53   0.572568    0  0.51568  0.49484 0.57257
## 54       0.54   0.563276    0  0.46665  0.48748 0.56814
## 55       0.55   0.553571    0  0.45896  0.47980 0.53864
## 56       0.56   0.543425    0  0.45093  0.47176 0.53426
## 57       0.57   0.532807    0  0.41860  0.46335 0.52585
```

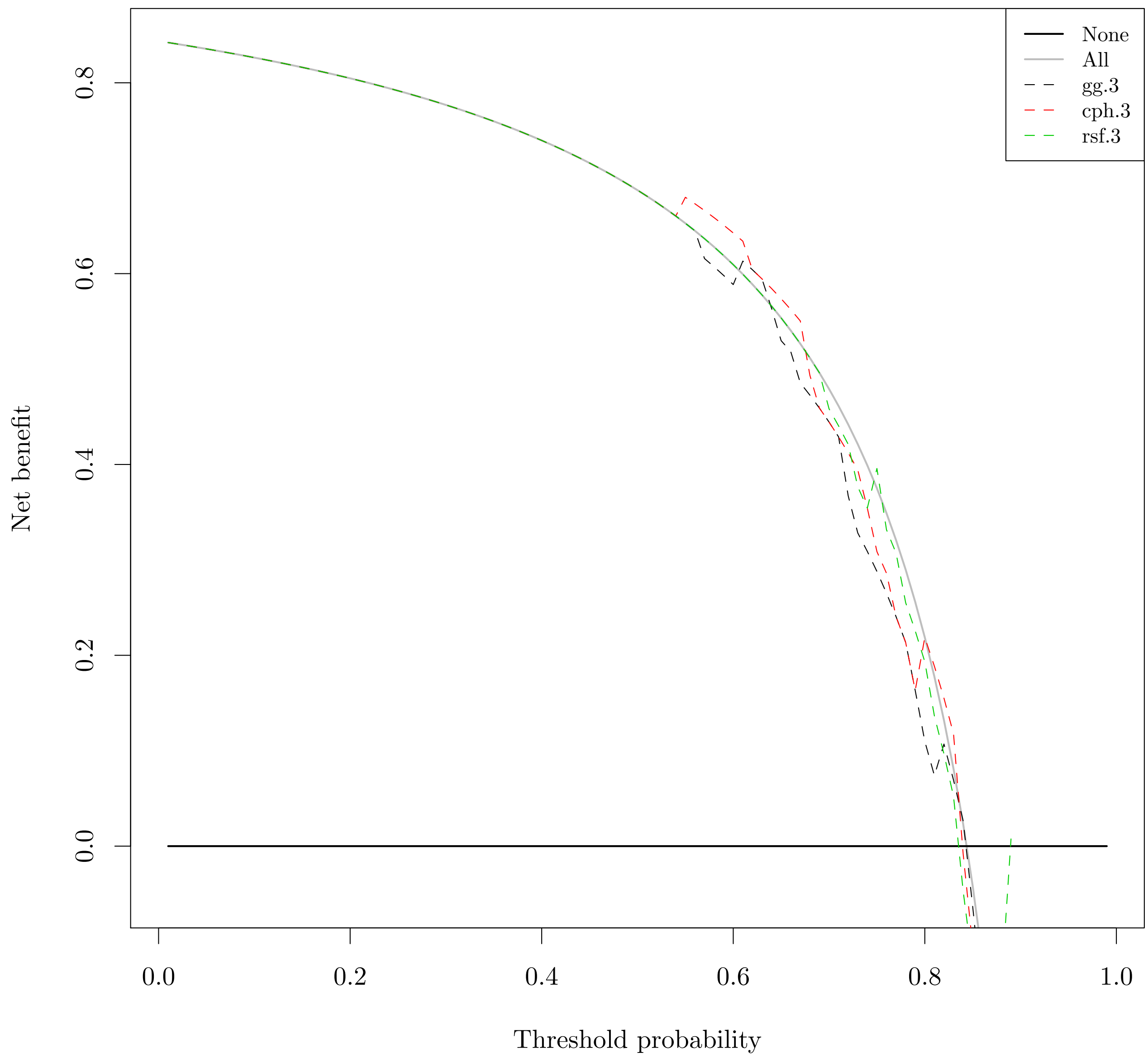
```
## 58      0.58   0.521684    0  0.40972  0.43371 0.49621
## 59      0.59   0.510017    0  0.40041  0.40364 0.48697
## 60      0.60   0.497768    0  0.39062  0.39394 0.45644
## 61      0.61   0.484890    0  0.38034  0.39387 0.48077
## 62      0.62   0.471335    0  0.36952  0.38450 0.47149
## 63      0.63   0.457046    0  0.39546  0.37462 0.42005
## 64      0.64   0.441964    0  0.36420  0.36420 0.40972
## 65      0.65   0.426020    0  0.35317  0.35317 0.39881
## 66      0.66   0.409139    0  0.38450  0.34283 0.36642
## 67      0.67   0.391234    0  0.35322  0.31155 0.37405
## 68      0.68   0.372210    0  0.22439  0.27962 0.36296
## 69      0.69   0.351959    0  0.21214  0.19931 0.38028
## 70      0.70   0.330357    0  0.15741  0.06250 0.28009
## 71      0.71   0.307266    0  0.12261  0.02730 0.24593
## 72      0.72   0.282526    0  0.14286  0.01190 0.04762
## 73      0.73   0.255952    0  0.07253 -0.00463 0.07485
## 74      0.74   0.227335    0  0.05769  0.03686      NA
## 75      0.75   0.196429    0  0.06250  0.02083      NA
## 76      0.76   0.162946    0  0.04861 -0.01736      NA
## 77      0.77   0.126553    0 -0.02899  0.10326      NA
## 78      0.78   0.086851    0 -0.04545  0.10227      NA
## 79      0.79   0.043367    0  0.09325  0.09325      NA
## 80      0.80  -0.004464    0  0.08333  0.08333      NA
## 81      0.81  -0.057331    0  0.05154  0.05154      NA
## 82      0.82  -0.116071    0  0.03935  0.03935      NA
## 83      0.83  -0.181723    0  0.02574  0.02574      NA
## 84      0.84  -0.255580    0 -0.03125 -0.07292      NA
## 85      0.85  -0.339286    0 -0.09028 -0.09028      NA
## 86      0.86  -0.434949    0 -0.11012 -0.11012      NA
## 87      0.87  -0.545330    0 -0.13301 -0.13301      NA
## 88      0.88  -0.674107    0 -0.02778 -0.15972      NA
## 89      0.89  -0.826299    0 -0.04356 -0.04356      NA
## 90      0.90  -1.008929    0 -0.08333 -0.06250      NA
## 91      0.91  -1.232143    0 -0.14815       NA      NA
## 92      0.92  -1.511161    0 -0.19792       NA      NA
## 93      0.93  -1.869898    0       NA       NA      NA
## 94      0.94  -2.348214    0       NA       NA      NA
## 95      0.95  -3.017857    0       NA       NA      NA
## 96      0.96  -4.022321    0       NA       NA      NA
## 97      0.97  -5.696429    0       NA       NA      NA
## 98      0.98  -9.044643    0       NA       NA      NA
## 99      0.99 -19.089286    0       NA       NA      NA
##
## $interventions.avoided
##    threshold   gg.2    cph.2     rsf.2
## 1       0.01  0.000   0.0000  0.000000
## 2       0.02  0.000   0.0000  0.000000
## 3       0.03  0.000   0.0000  0.000000
## 4       0.04  0.000   0.0000  0.000000
## 5       0.05  0.000   0.0000  0.000000
## 6       0.06  0.000   0.0000  0.000000
## 7       0.07  0.000   0.0000  0.000000
## 8       0.08  0.000   0.0000  0.000000
## 9       0.09  0.000   0.0000  0.000000
```

```
## 10       0.10  0.000   0.0000  0.000000
## 11       0.11  0.000   0.0000  0.000000
## 12       0.12  0.000   0.0000  0.000000
## 13       0.13  0.000   0.0000  0.000000
## 14       0.14  0.000   0.0000  0.000000
## 15       0.15  0.000   0.0000  0.000000
## 16       0.16  0.000   0.0000  0.000000
## 17       0.17  0.000   0.0000  0.000000
## 18       0.18  0.000   0.0000  0.000000
## 19       0.19  0.000   0.0000  0.000000
## 20       0.20  0.000   0.0000  0.000000
## 21       0.21  0.000   0.0000  0.000000
## 22       0.22  0.000   0.0000  0.000000
## 23       0.23  0.000   0.0000  0.000000
## 24       0.24  0.000   0.0000  0.000000
## 25       0.25  0.000   0.0000  0.000000
## 26       0.26  0.000   0.0000  0.000000
## 27       0.27  0.000   0.0000  0.000000
## 28       0.28  0.000   0.0000  0.000000
## 29       0.29  0.000   0.0000  0.000000
## 30       0.30  0.000   0.0000  0.000000
## 31       0.31  0.000   0.0000  0.000000
## 32       0.32  0.000   0.0000  0.000000
## 33       0.33  0.000   0.0000  0.000000
## 34       0.34 -4.044   0.0000  0.000000
## 35       0.35 -3.869   0.0000  0.000000
## 36       0.36 -3.704   0.0000  0.000000
## 37       0.37 -3.547   0.0000  0.000000
## 38       0.38 -3.399   2.2340  0.000000
## 39       0.39 -6.517   2.2301  0.000000
## 40       0.40 -6.250   2.2264  0.000000
## 41       0.41 -7.032   2.2229  0.000000
## 42       0.42 -6.666   2.2196  0.000000
## 43       0.43 -6.317  -0.5452  0.000000
## 44       0.44 -5.984  -3.0896  0.000000
## 45       0.45 -5.666  -2.8821  0.000000
## 46       0.46 -5.361  -2.6835  0.000000
## 47       0.47 -7.419  -2.4935  0.000000
## 48       0.48 -9.305  -4.5683  0.000000
## 49       0.49 -8.860  -4.4792  0.000000
## 50       0.50 -8.433  -6.2229  0.000000
## 51       0.51 -8.022  -5.8150  0.000000
## 52       0.52 -7.627  -5.4227  0.000000
## 53       0.53 -5.045  -6.8927  0.000000
## 54       0.54 -8.231  -6.4564  0.414632
## 55       0.55 -7.741  -6.0360 -1.221695
## 56       0.56 -7.268  -5.6306 -0.719890
## 57       0.57 -8.615  -5.2394 -0.524512
## 58       0.58 -8.108  -6.3704 -1.844492
## 59       0.59 -7.617  -7.3923 -1.601365
## 60       0.60 -7.143  -6.9219 -2.755231
## 61       0.61 -6.684  -5.8190 -0.263466
## 62       0.62 -6.240  -5.3219  0.009601
## 63       0.63 -3.617  -4.8406 -2.173091
```

```
## 64      0.64 -4.374  -4.3744 -1.813616
## 65      0.65 -3.922  -3.9225 -1.465201
## 66      0.66 -1.269  -3.4159 -2.200577
## 67      0.67 -1.872  -3.9246 -0.846215
## 68      0.68 -6.956  -4.3571 -0.435487
## 69      0.69 -6.282  -6.8582  1.272429
## 70      0.70 -7.412 -11.4796 -2.154195
## 71      0.71 -7.542 -11.4353 -2.505310
## 72      0.72 -5.432 -10.5241 -9.135251
## 73      0.73 -6.784  -9.6380 -6.698467
## 74      0.74 -5.960  -6.6924        NA
## 75      0.75 -4.464  -5.8532        NA
## 76      0.76 -3.611  -5.6939        NA
## 77      0.77 -4.646  -0.6957        NA
## 78      0.78 -3.732   0.4350        NA
## 79      0.79  1.326   1.3261        NA
## 80      0.80  2.195   2.1949        NA
## 81      0.81  2.554   2.5536        NA
## 82      0.82  3.412   3.4117        NA
## 83      0.83  4.249   4.2491        NA
## 84      0.84  4.273   3.4793        NA
## 85      0.85  4.394   4.3943        NA
## 86      0.86  5.288   5.2879        NA
## 87      0.87  6.161   6.1611        NA
## 88      0.88  8.814   7.0143        NA
## 89      0.89  9.674   9.6743        NA
## 90      0.90 10.284  10.5159        NA
## 91      0.91 10.721       NA        NA
## 92      0.92 11.420       NA        NA
## 93      0.93     NA       NA        NA
## 94      0.94     NA       NA        NA
## 95      0.95     NA       NA        NA
## 96      0.96     NA       NA        NA
## 97      0.97     NA       NA        NA
## 98      0.98     NA       NA        NA
## 99      0.99     NA       NA        NA
```

```
stdca(data = temp.data, outcome = "DSD", ttoutcome = "Time", predictors = c("gg.3", "cph.3", "rsf.3"), t
```

```
## [1] "rsf.3: No observations with risk greater than 90% that have followup through the timepoint selec
```




```
## $N
## [1] 48
##
## $predictors
##   predictor harm.applied probability
## 1      gg.3            0        TRUE
## 2     cph.3            0        TRUE
## 3     rsf.3            0        TRUE
##
## $interventions.avoided.per
## [1] 100
##
## $net.benefit
##    threshold       all none      gg.3      cph.3     rsf.3
## 1       0.01   0.84217    0   0.84217   0.842172  0.842172
## 2       0.02   0.84056    0   0.84056   0.840561  0.840561
## 3       0.03   0.83892    0   0.83892   0.838918  0.838918
```

```
## 4       0.04   0.83724    0  0.83724  0.837240  0.837240
## 5       0.05   0.83553    0  0.83553  0.835526  0.835526
## 6       0.06   0.83378    0  0.83378  0.833777  0.833777
## 7       0.07   0.83199    0  0.83199  0.831989  0.831989
## 8       0.08   0.83016    0  0.83016  0.830163  0.830163
## 9       0.09   0.82830    0  0.82830  0.828297  0.828297
## 10      0.10   0.82639    0  0.82639  0.826389  0.826389
## 11      0.11   0.82444    0  0.82444  0.824438  0.824438
## 12      0.12   0.82244    0  0.82244  0.822443  0.822443
## 13      0.13   0.82040    0  0.82040  0.820402  0.820402
## 14      0.14   0.81831    0  0.81831  0.818314  0.818314
## 15      0.15   0.81618    0  0.81618  0.816176  0.816176
## 16      0.16   0.81399    0  0.81399  0.813988  0.813988
## 17      0.17   0.81175    0  0.81175  0.811747  0.811747
## 18      0.18   0.80945    0  0.80945  0.809451  0.809451
## 19      0.19   0.80710    0  0.80710  0.807099  0.807099
## 20      0.20   0.80469    0  0.80469  0.804688  0.804688
## 21      0.21   0.80222    0  0.80222  0.802215  0.802215
## 22      0.22   0.79968    0  0.79968  0.799679  0.799679
## 23      0.23   0.79708    0  0.79708  0.797078  0.797078
## 24      0.24   0.79441    0  0.79441  0.794408  0.794408
## 25      0.25   0.79167    0  0.79167  0.791667  0.791667
## 26      0.26   0.78885    0  0.78885  0.788851  0.788851
## 27      0.27   0.78596    0  0.78596  0.785959  0.785959
## 28      0.28   0.78299    0  0.78299  0.782986  0.782986
## 29      0.29   0.77993    0  0.77993  0.779930  0.779930
## 30      0.30   0.77679    0  0.77679  0.776786  0.776786
## 31      0.31   0.77355    0  0.77355  0.773551  0.773551
## 32      0.32   0.77022    0  0.77022  0.770221  0.770221
## 33      0.33   0.76679    0  0.76679  0.766791  0.766791
## 34      0.34   0.76326    0  0.76326  0.763258  0.763258
## 35      0.35   0.75962    0  0.75962  0.759615  0.759615
## 36      0.36   0.75586    0  0.75586  0.755859  0.755859
## 37      0.37   0.75198    0  0.75198  0.751984  0.751984
## 38      0.38   0.74798    0  0.74798  0.747984  0.747984
## 39      0.39   0.74385    0  0.74385  0.743852  0.743852
## 40      0.40   0.73958    0  0.73958  0.739583  0.739583
## 41      0.41   0.73517    0  0.73517  0.735169  0.735169
## 42      0.42   0.73060    0  0.73060  0.730603  0.730603
## 43      0.43   0.72588    0  0.72588  0.725877  0.725877
## 44      0.44   0.72098    0  0.72098  0.720982  0.720982
## 45      0.45   0.71591    0  0.71591  0.715909  0.715909
## 46      0.46   0.71065    0  0.71065  0.710648  0.710648
## 47      0.47   0.70519    0  0.70519  0.705189  0.705189
## 48      0.48   0.69952    0  0.69952  0.699519  0.699519
## 49      0.49   0.69363    0  0.69363  0.693627  0.693627
## 50      0.50   0.68750    0  0.68750  0.687500  0.687500
## 51      0.51   0.68112    0  0.68112  0.681122  0.681122
## 52      0.52   0.67448    0  0.67448  0.674479  0.674479
## 53      0.53   0.66755    0  0.66755  0.667553  0.667553
## 54      0.54   0.66033    0  0.66033  0.660326  0.660326
## 55      0.55   0.65278    0  0.65278  0.680021  0.652778
## 56      0.56   0.64489    0  0.64489  0.673223  0.644886
## 57      0.57   0.63663    0  0.61579  0.666108  0.636628
```

```
## 58      0.58   0.62798    0  0.60714  0.658654  0.627976
## 59      0.59   0.61890    0  0.59807  0.650836  0.618902
## 60      0.60   0.60938    0  0.58854  0.642628  0.609375
## 61      0.61   0.59936    0  0.61317  0.633999  0.599359
## 62      0.62   0.58882    0  0.60408  0.604082  0.588816
## 63      0.63   0.57770    0  0.59451  0.594508  0.577703
## 64      0.64   0.56597    0  0.56357  0.584402  0.565972
## 65      0.65   0.55357    0  0.52976  0.573718  0.553571
## 66      0.66   0.54044    0  0.51838  0.562406  0.540441
## 67      0.67   0.52652    0  0.48548  0.550408  0.526515
## 68      0.68   0.51172    0  0.47266  0.493490  0.511719
## 69      0.69   0.49597    0  0.45901  0.459005  0.495968
## 70      0.70   0.47917    0  0.44444  0.444444  0.458333
## 71      0.71   0.46121    0  0.42888  0.428879  0.440374
## 72      0.72   0.44196    0  0.36715  0.412202  0.421131
## 73      0.73   0.42130    0  0.32828  0.394290  0.376662
## 74      0.74   0.39904    0  0.30886  0.354167  0.354290
## 75      0.75   0.37500    0  0.28788  0.308712  0.395833
## 76      0.76   0.34896    0  0.26515  0.285985  0.331597
## 77      0.77   0.32065    0  0.24045  0.240448  0.307065
## 78      0.78   0.28977    0  0.21350  0.213499  0.255165
## 79      0.79   0.25595    0  0.16315  0.163149  0.225649
## 80      0.80   0.21875    0  0.10985  0.218750  0.193182
## 81      0.81   0.17763    0  0.07396  0.188596  0.136463
## 82      0.82   0.13194    0  0.10700  0.155093  0.096591
## 83      0.83   0.08088    0  0.06917  0.117647  0.052028
## 84      0.84   0.02344    0  0.02662 -0.007813 -0.046875
## 85      0.85  -0.04167    0 -0.06327 -0.104938 -0.125000
## 86      0.86  -0.11607    0 -0.16005 -0.212054 -0.160053
## 87      0.87  -0.20192    0 -0.12843 -0.276442 -0.244480
## 88      0.88  -0.30208    0 -0.23115 -0.372396 -0.145833
## 89      0.89  -0.42045    0 -0.30330 -0.282468  0.007576
## 90      0.90  -0.56250    0 -0.56250 -0.369048        NA
## 91      0.91  -0.73611    0 -0.29861 -0.194444        NA
## 92      0.92  -0.95313    0 -0.38542 -0.385417        NA
## 93      0.93  -1.23214    0 -0.26190 -0.497024        NA
## 94      0.94  -1.60417    0 -0.38194 -0.319444        NA
## 95      0.95  -2.12500    0 -0.58333 -0.500000        NA
## 96      0.96  -2.90625    0 -0.31250 -0.791667        NA
## 97      0.97  -4.20833    0 -0.56944 -1.159722        NA
## 98      0.98  -6.81250    0 -0.97917 -0.895833        NA
## 99      0.99 -14.62500    0 -2.02083 -1.979167        NA
##
## $interventions.avoided
##    threshold       gg.3      cph.3   rsf.3
## 1       0.01  0.000e+00  0.000e+00  0.0000
## 2       0.02  0.000e+00  0.000e+00  0.0000
## 3       0.03  0.000e+00  0.000e+00  0.0000
## 4       0.04  0.000e+00  0.000e+00  0.0000
## 5       0.05  0.000e+00  0.000e+00  0.0000
## 6       0.06  0.000e+00  0.000e+00  0.0000
## 7       0.07  0.000e+00  0.000e+00  0.0000
## 8       0.08  0.000e+00  0.000e+00  0.0000
## 9       0.09  0.000e+00  0.000e+00  0.0000
```

```
## 10      0.10  0.000e+00  0.000e+00  0.0000
## 11      0.11  0.000e+00  0.000e+00  0.0000
## 12      0.12  0.000e+00  0.000e+00  0.0000
## 13      0.13  0.000e+00  0.000e+00  0.0000
## 14      0.14  0.000e+00  0.000e+00  0.0000
## 15      0.15  0.000e+00  0.000e+00  0.0000
## 16      0.16  0.000e+00  0.000e+00  0.0000
## 17      0.17  0.000e+00  0.000e+00  0.0000
## 18      0.18  0.000e+00  0.000e+00  0.0000
## 19      0.19  0.000e+00  0.000e+00  0.0000
## 20      0.20  0.000e+00  0.000e+00  0.0000
## 21      0.21  0.000e+00  0.000e+00  0.0000
## 22      0.22  0.000e+00  0.000e+00  0.0000
## 23      0.23  0.000e+00  0.000e+00  0.0000
## 24      0.24  0.000e+00  0.000e+00  0.0000
## 25      0.25  0.000e+00  0.000e+00  0.0000
## 26      0.26  0.000e+00  0.000e+00  0.0000
## 27      0.27  0.000e+00  0.000e+00  0.0000
## 28      0.28  0.000e+00  0.000e+00  0.0000
## 29      0.29  0.000e+00  0.000e+00  0.0000
## 30      0.30  0.000e+00  0.000e+00  0.0000
## 31      0.31  0.000e+00  0.000e+00  0.0000
## 32      0.32  0.000e+00  0.000e+00  0.0000
## 33      0.33  0.000e+00  0.000e+00  0.0000
## 34      0.34  0.000e+00  0.000e+00  0.0000
## 35      0.35  0.000e+00  0.000e+00  0.0000
## 36      0.36  0.000e+00  0.000e+00  0.0000
## 37      0.37  0.000e+00  0.000e+00  0.0000
## 38      0.38  0.000e+00  0.000e+00  0.0000
## 39      0.39  0.000e+00  0.000e+00  0.0000
## 40      0.40  0.000e+00  0.000e+00  0.0000
## 41      0.41  0.000e+00  0.000e+00  0.0000
## 42      0.42  0.000e+00  0.000e+00  0.0000
## 43      0.43  0.000e+00  0.000e+00  0.0000
## 44      0.44  0.000e+00  0.000e+00  0.0000
## 45      0.45  0.000e+00  0.000e+00  0.0000
## 46      0.46  0.000e+00  0.000e+00  0.0000
## 47      0.47  0.000e+00  0.000e+00  0.0000
## 48      0.48  0.000e+00  0.000e+00  0.0000
## 49      0.49  0.000e+00  0.000e+00  0.0000
## 50      0.50  0.000e+00  0.000e+00  0.0000
## 51      0.51  0.000e+00  0.000e+00  0.0000
## 52      0.52  0.000e+00  0.000e+00  0.0000
## 53      0.53  0.000e+00  0.000e+00  0.0000
## 54      0.54  0.000e+00  0.000e+00  0.0000
## 55      0.55  0.000e+00  2.229e+00  0.0000
## 56      0.56  0.000e+00  2.226e+00  0.0000
## 57      0.57 -1.572e+00  2.224e+00  0.0000
## 58      0.58 -1.509e+00  2.221e+00  0.0000
## 59      0.59 -1.448e+00  2.219e+00  0.0000
## 60      0.60 -1.389e+00  2.217e+00  0.0000
## 61      0.61  8.827e-01  2.215e+00  0.0000
## 62      0.62  9.357e-01  9.357e-01  0.0000
## 63      0.63  9.870e-01  9.870e-01  0.0000
```

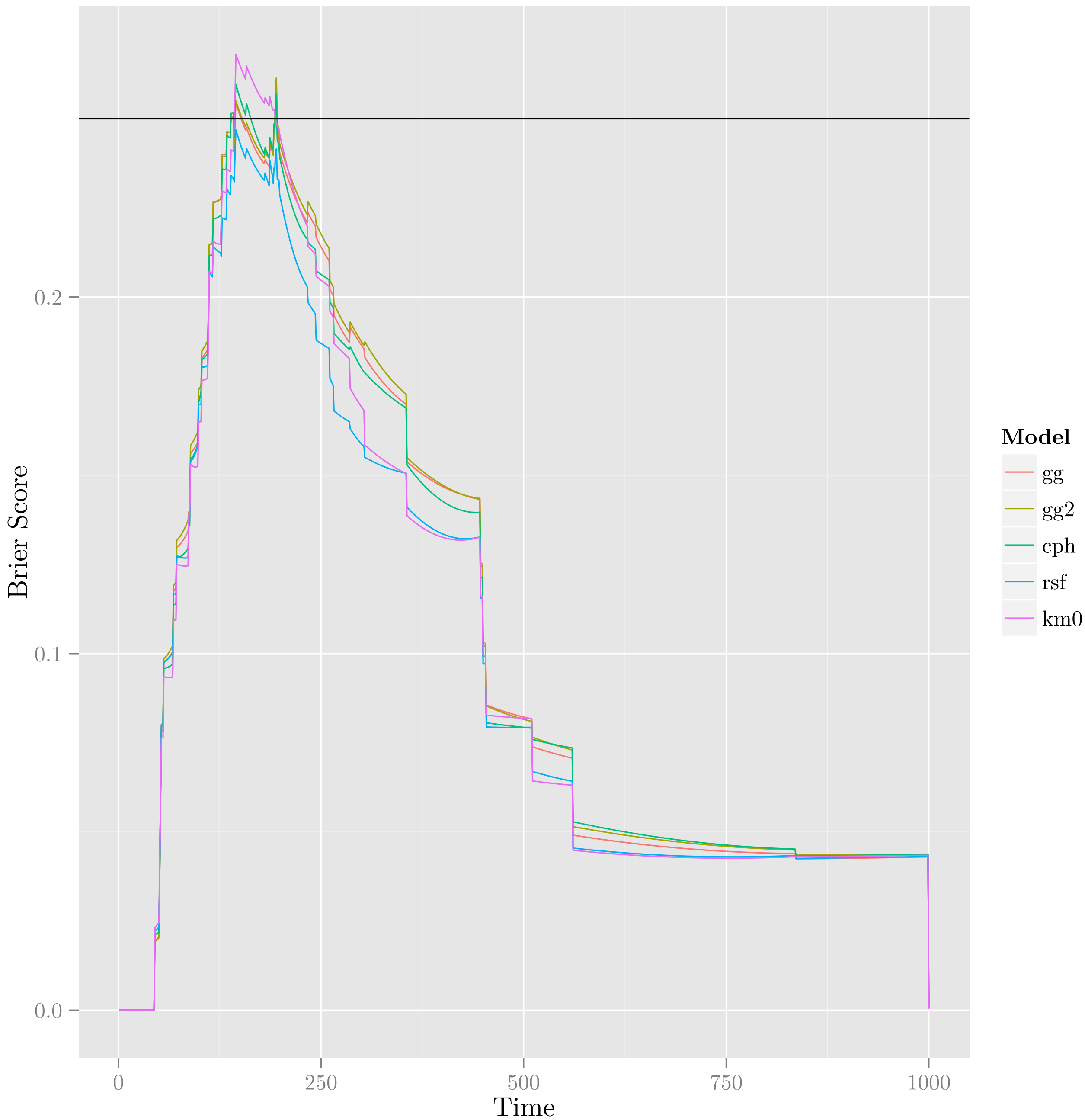
```
## 64      0.64 -1.352e-01  1.037e+00  0.0000
## 65      0.65 -1.282e+00  1.085e+00  0.0000
## 66      0.66 -1.136e+00  1.132e+00  0.0000
## 67      0.67 -2.021e+00  1.177e+00  0.0000
## 68      0.68 -1.838e+00 -8.578e-01  0.0000
## 69      0.69 -1.661e+00 -1.661e+00  0.0000
## 70      0.70 -1.488e+00 -1.488e+00 -0.8929
## 71      0.71 -1.320e+00 -1.320e+00 -0.8509
## 72      0.72 -2.909e+00 -1.157e+00 -0.8102
## 73      0.73 -3.440e+00 -9.989e-01 -1.6509
## 74      0.74 -3.169e+00 -1.577e+00 -1.5722
## 75      0.75 -2.904e+00 -2.210e+00  0.6944
## 76      0.76 -2.647e+00 -1.989e+00 -0.5482
## 77      0.77 -2.396e+00 -2.396e+00 -0.4058
## 78      0.78 -2.151e+00 -2.151e+00 -0.9761
## 79      0.79 -2.467e+00 -2.467e+00 -0.8055
## 80      0.80 -2.723e+00 -2.776e-15 -0.6392
## 81      0.81 -2.432e+00  2.572e-01 -0.9657
## 82      0.82 -5.477e-01  5.081e-01 -0.7761
## 83      0.83 -2.398e-01  7.530e-01 -0.5910
## 84      0.84  6.063e-02 -5.952e-01 -1.3393
## 85      0.85 -3.813e-01 -1.117e+00 -1.4706
## 86      0.86 -7.160e-01 -1.563e+00 -0.7160
## 87      0.87  1.098e+00 -1.114e+00 -0.6359
## 88      0.88  9.673e-01 -9.588e-01  2.1307
## 89      0.89  1.448e+00  1.705e+00  5.2903
## 90      0.90  2.467e-15  2.149e+00      NA
## 91      0.91  4.327e+00  5.357e+00      NA
## 92      0.92  4.937e+00  4.937e+00      NA
## 93      0.93  7.303e+00  5.533e+00      NA
## 94      0.94  7.801e+00  8.200e+00      NA
## 95      0.95  8.114e+00  8.553e+00      NA
## 96      0.96  1.081e+01  8.811e+00      NA
## 97      0.97  1.125e+01  9.429e+00      NA
## 98      0.98  1.190e+01  1.207e+01      NA
## 99      0.99  1.273e+01  1.277e+01      NA
```

Evaluate IBS point estimates. BS paths over time on bootstrap samples of the holdout set.

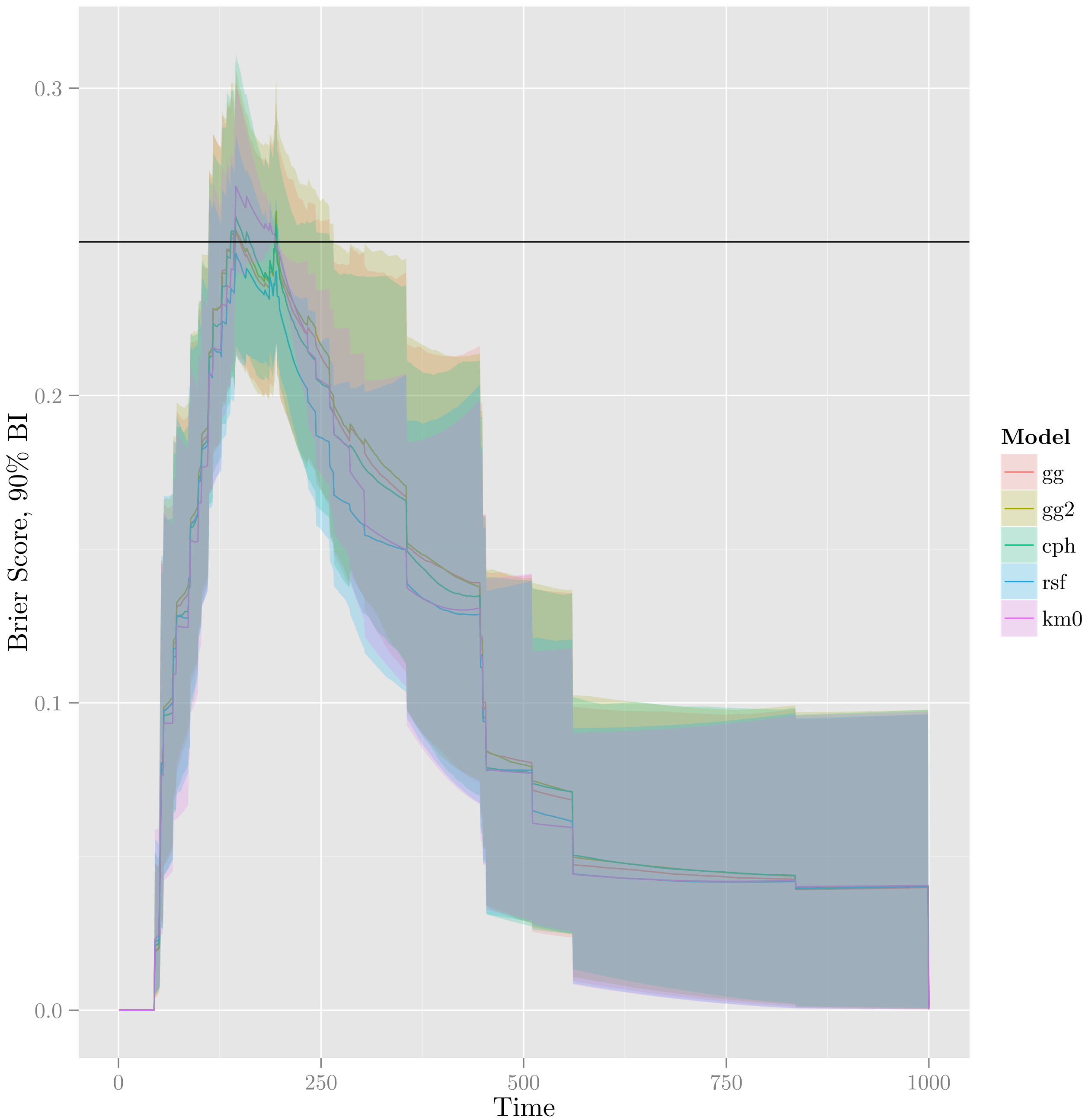
```
set.seed(20150111)
ibs_eval_times = calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_gg, ibs_times, max(data.val$Time))
# bsc_boot2 = lapply(ibs_preds_all, function(preds) boot(data.val, statistic = function(d, i) calcIBS(Su
# bsc_boot2ci = lapply(bsc_boot2, function(single_boot) t(sapply(1:length(ibs_eval_times), function(time
#  temp = try(boot.ci(single_boot, index = time_index, type = "bca")£bca, silent = TRUE)
#  if (class(temp) == "try-error" || is.null(temp)) { temp = rep(NA, 5) }
#  temp })))
bsc_boots = laply(1:500, function(i) {
        if (i %% 50 == 0)       { message(i) }
        boot_samp = sample.int(nrow(data.val), replace = TRUE)
        gg = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_gg[boot_samp,], ibs_times,
        gg2 = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_gg2[boot_samp,], ibs_time
        cph = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_cph[boot_samp,], ibs_time
        rsf = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_rsf[boot_samp,], ibs_time
        km0 = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_km0[boot_samp,], ibs_time
```

```
        rbind(gg, gg2, cph, rsf, km0)
})

## 50
## 100
## 150
## 200
## 250
## 300
## 350
## 400
## 450
## 500
```

```
temp = sapply(list(gg = ibs_preds_gg, gg2 = ibs_preds_gg2, cph = ibs_preds_cph, rsf = ibs_preds_rsf, km(
temp = melt(temp)
colnames(temp) = c("Time", "Model", "BS")
ggplot(temp, aes(x = Time, y = BS, colour = Model)) + geom_line() + ylab("Brier Score") + geom_hline(yir
```

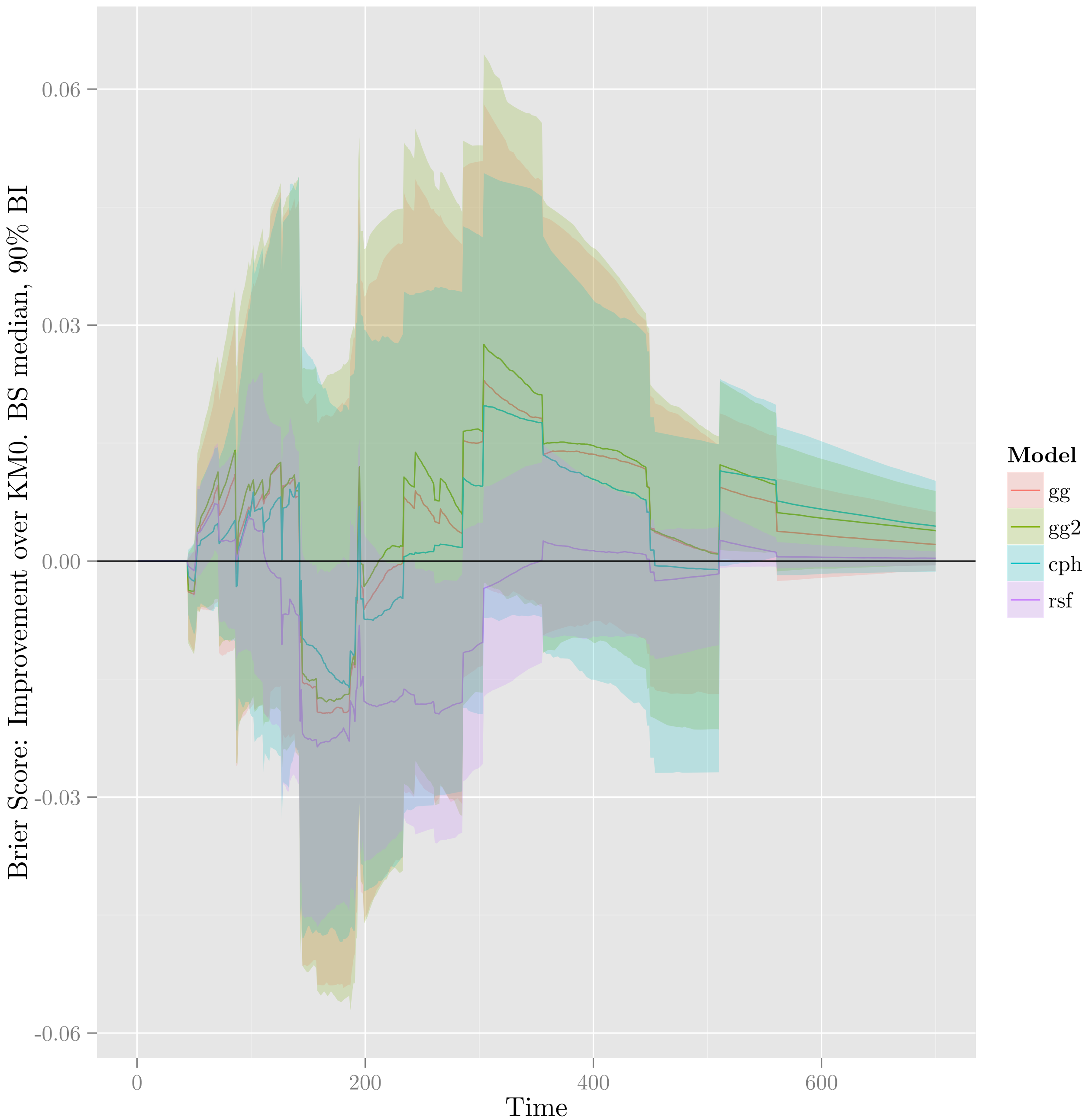



```
temp = melt(aaply(bsc_boots, 2:3, quantile, probs = c(0.05, 0.5, 0.95)))
colnames(temp) = c("Model", "Time", "Quantile", "Value")
temp$Quantile = paste("Q", gsub("%", "", temp$Quantile), sep = "")
temp = dcast(temp, Model + Time ~ Quantile, value.var = "Value")
ggplot(temp, aes(x = Time, y = Q50, ymin = Q5, ymax = Q95, colour = Model, fill = Model)) + geom_line()
```

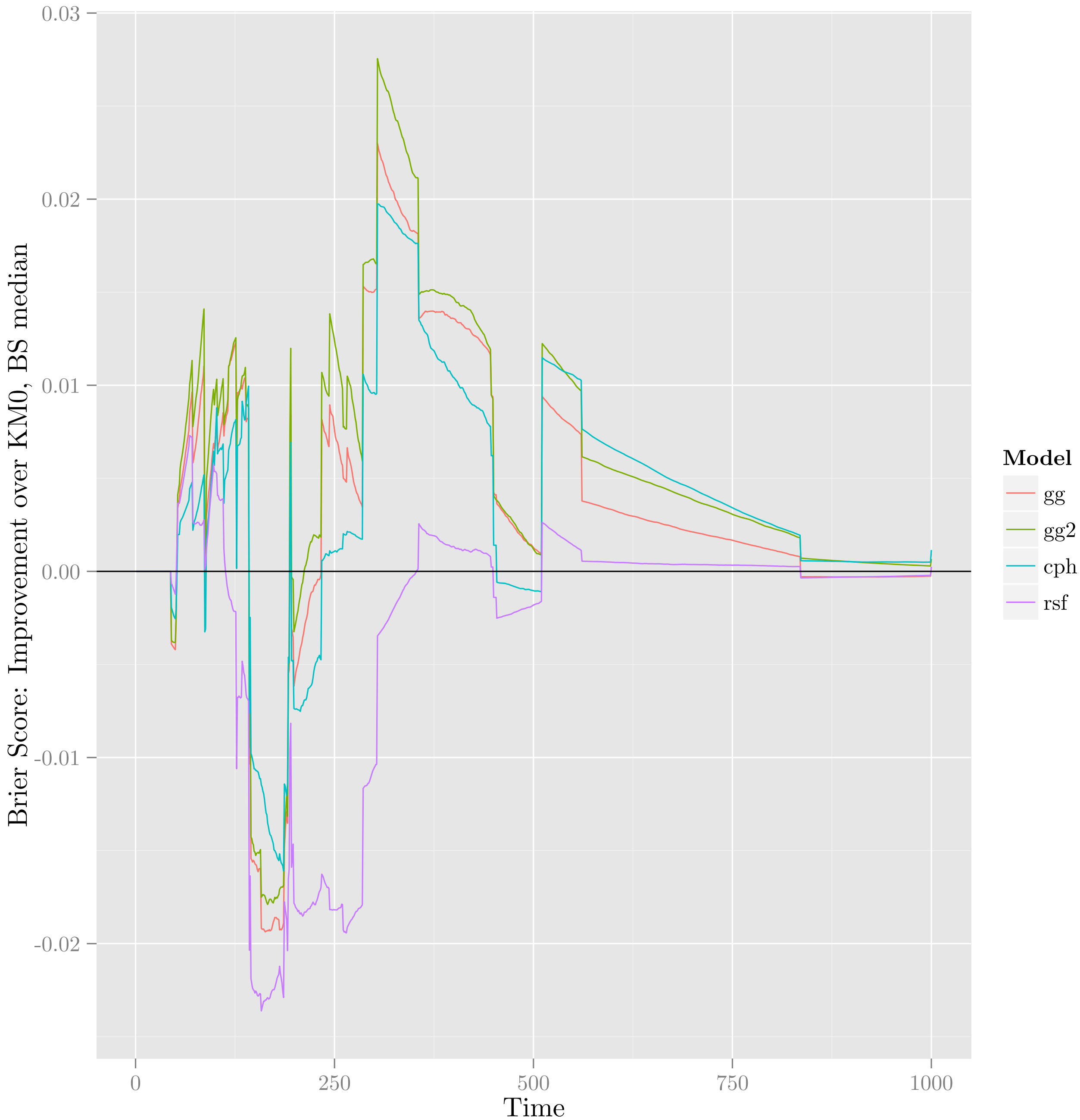



```
bsc_boots_diff = aaply(bsc_boots, 2, function(x) x - bsc_boots[,5,])[1:4,,]
temp = melt(aaply(bsc_boots_diff, c(1,3), quantile, probs = c(0.05, 0.5, 0.95)))
colnames(temp) = c("Model", "Time", "Quantile", "Value")
temp$Quantile = paste("Q", gsub("%", "", temp$Quantile), sep = "")
temp = dcast(temp, Model + Time ~ Quantile, value.var = "Value")
ggplot(temp, aes(x = Time, y = Q50, ymin = Q5, ymax = Q95, colour = Model, fill = Model)) + geom_line()
```

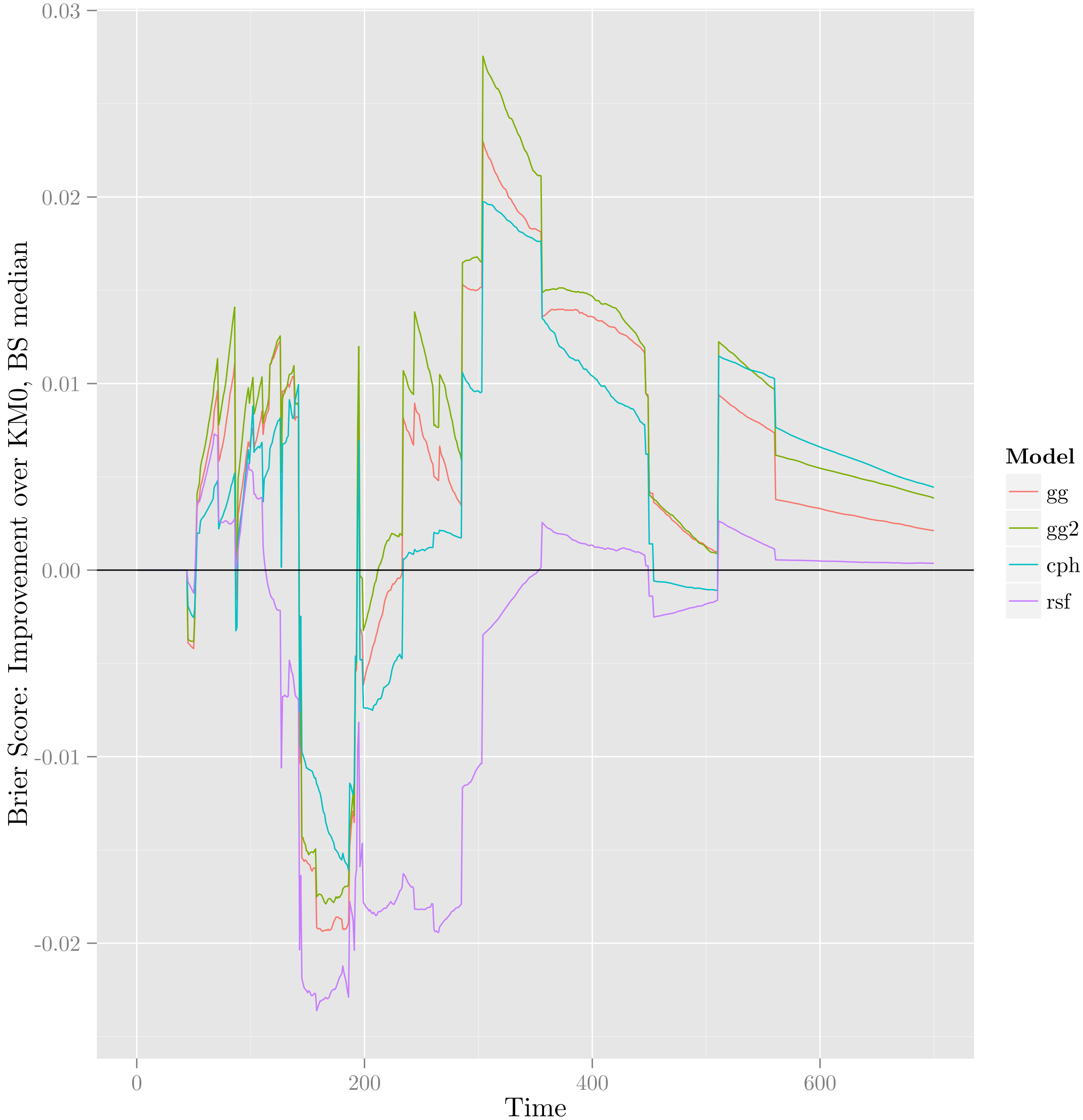

```
ggplot(temp, aes(x = Time, y = Q50, ymin = Q5, ymax = Q95, colour = Model, fill = Model)) + geom_line()

## Warning:  Removed 1200 rows containing missing values (geom_path).
```




```
ggplot(temp, aes(x = Time, y = Q50, colour = Model)) + geom_line() + ylab("Brier Score: Improvement over
```




```
ggplot(temp, aes(x = Time, y = Q50, colour = Model)) + geom_line() + ylab("Brier Score: Improvement over

## Warning:  Removed 1200 rows containing missing values (geom_path).
```

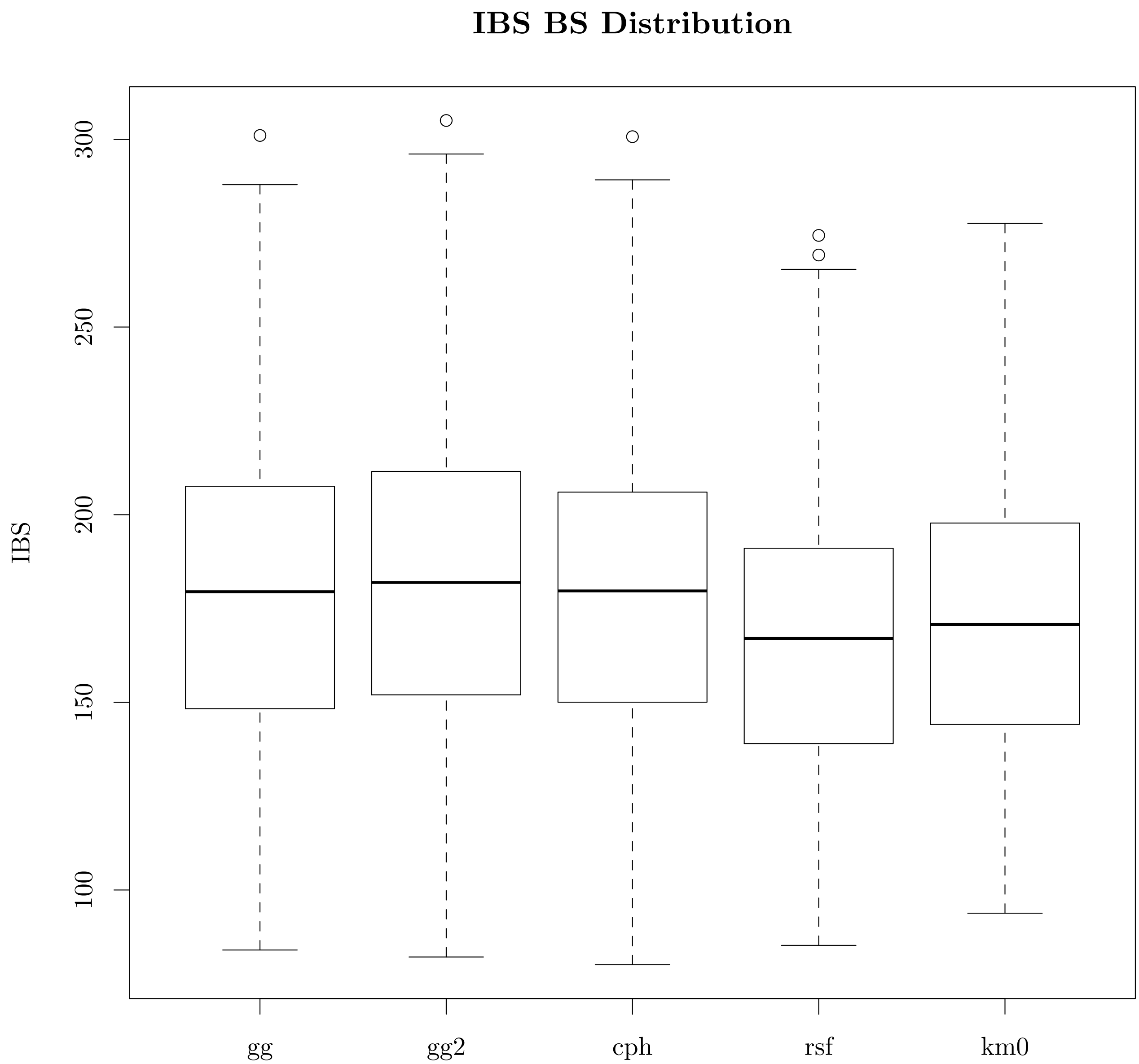


IBS comparisons.

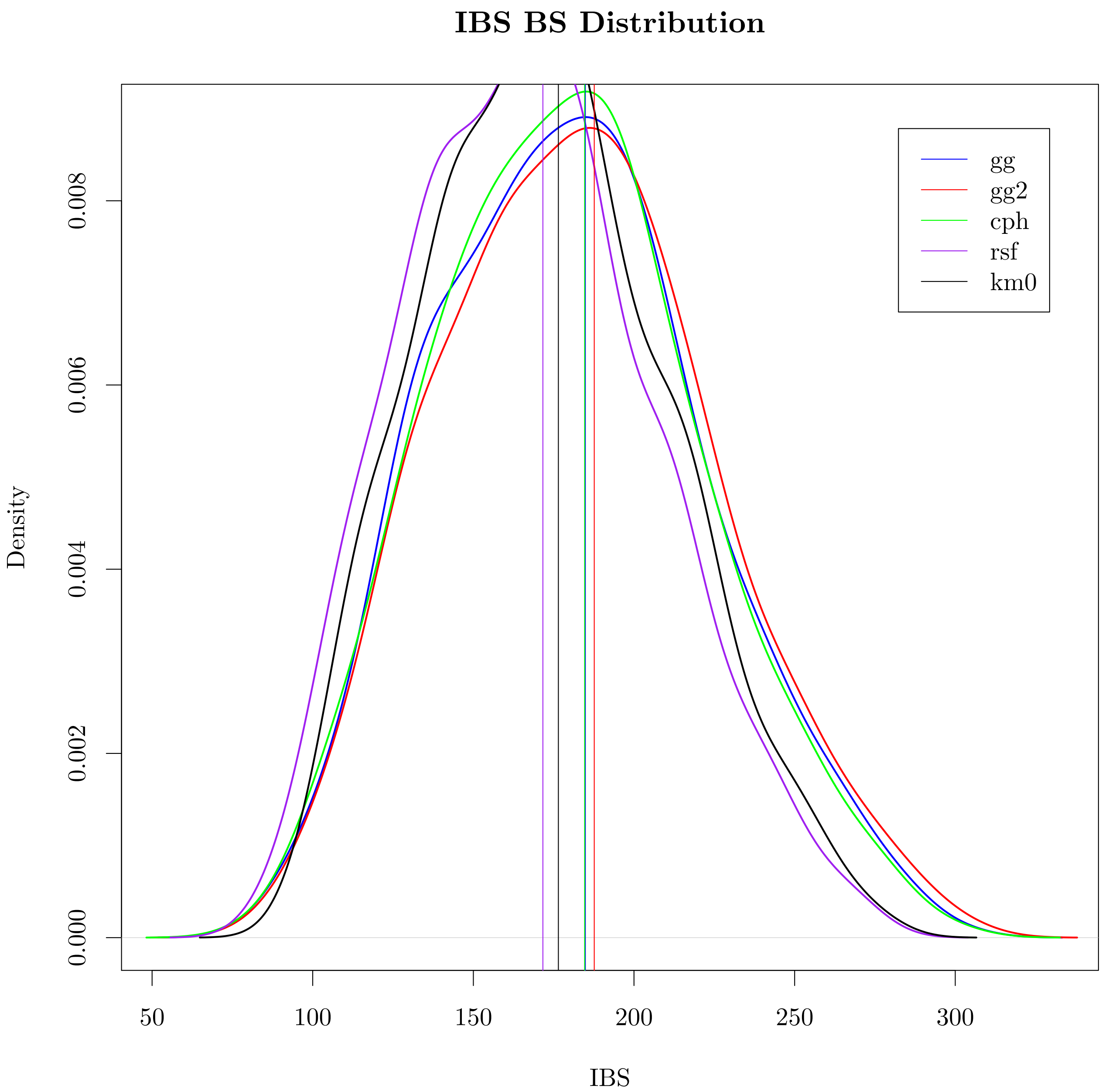
```
set.seed(20150111)
ibsc_boots = t(sapply(1:5e2, function(i) {
        if (i %% 5e1 == 0)      { message(i) }
        boot_samp = sample.int(nrow(data.val), replace = TRUE)
        gg = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_gg[boot_samp,], ibs_times,
        gg2 = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_gg2[boot_samp,], ibs_time
        cph = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_cph[boot_samp,], ibs_time
        rsf = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_rsf[boot_samp,], ibs_time
        km0 = calcIBS(Surv(data.val$Time, data.val$DSD)[boot_samp,], ibs_preds_km0[boot_samp,], ibs_time
        c(gg, gg2, cph, rsf, km0)
}))
```

```
## 50
## 100
## 150
## 200
## 250
## 300
## 350
## 400
## 450
## 500
colnames(ibsc_boots) = c("gg", "gg2", "cph", "rsf", "km0")
```

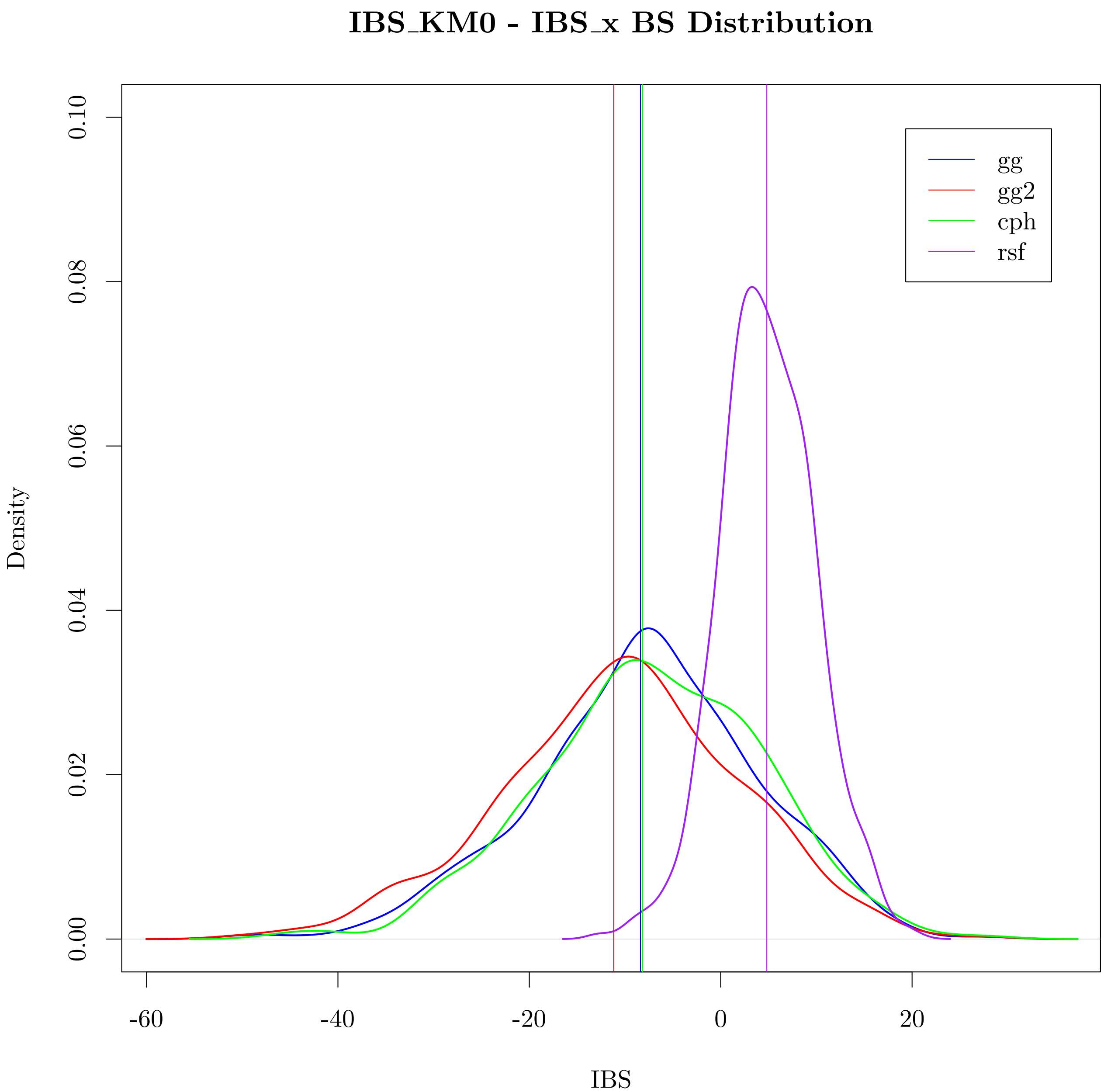
```
calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_gg, ibs_times, max(data.val$Time))$ibs
## [1] 184.8
calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_gg2, ibs_times, max(data.val$Time))$ibs
## [1] 187.6
calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_cph, ibs_times, max(data.val$Time))$ibs
## [1] 184.6
calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_rsf, ibs_times, max(data.val$Time))$ibs
## [1] 171.6
calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_km0, ibs_times, max(data.val$Time))$ibs
## [1] 176.5
boxplot(ibsc_boots, main = "IBS BS Distribution", ylab = "IBS")
```




```
plot(density(ibsc_boots[,1]), col = "blue", lwd = 2, main = "IBS BS Distribution", xlab = "IBS")
lines(density(ibsc_boots[,2]), col = "red", lwd = 2)
lines(density(ibsc_boots[,3]), col = "green", lwd = 2)
lines(density(ibsc_boots[,4]), col = "purple", lwd = 2)
lines(density(ibsc_boots[,5]), col = "black", lwd = 2)
abline(v = calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_gg, ibs_times, max(data.val$Time))$ibs,
abline(v = calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_gg2, ibs_times, max(data.val$Time))$ibs,
abline(v = calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_cph, ibs_times, max(data.val$Time))$ibs,
abline(v = calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_rsf, ibs_times, max(data.val$Time))$ibs,
abline(v = calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_km0, ibs_times, max(data.val$Time))$ibs,
legend("topright", legend = c("gg", "gg2", "cph", "rsf", "km0"), col = c("blue", "red", "green", "purple
```




```
plot(density(ibsc_boots[,5] - ibsc_boots[,1]), col = "blue", lwd = 2, main = "IBS\\_KM0 - IBS\\_x BS Dis
lines(density(ibsc_boots[,5] - ibsc_boots[,2]), col = "red", lwd = 2)
lines(density(ibsc_boots[,5] - ibsc_boots[,3]), col = "green", lwd = 2)
lines(density(ibsc_boots[,5] - ibsc_boots[,4]), col = "purple", lwd = 2)
abline(v = (calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_km0, ibs_times, max(data.val$Time))$ibs
abline(v = (calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_km0, ibs_times, max(data.val$Time))$ibs
abline(v = (calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_km0, ibs_times, max(data.val$Time))$ibs
abline(v = (calcIBS(Surv(data.val$Time, data.val$DSD), ibs_preds_km0, ibs_times, max(data.val$Time))$ibs
legend("topright", legend = c("gg", "gg2", "cph", "rsf"), col = c("blue", "red", "green", "purple"), lty
```



Do some proper BCA bootstrapping on the differences, just as a double-check test.

```
set.seed(20150111)
ibsc_boots2 = boot(data.val, statistic = function(d, i) {
        gg = calcIBS(Surv(d$Time, d$DSD)[i,], ibs_preds_gg[i,], ibs_times, max(d$Time[i]))$ibs
        gg2 = calcIBS(Surv(d$Time, d$DSD)[i,], ibs_preds_gg2[i,], ibs_times, max(d$Time[i]))$ibs
        cph = calcIBS(Surv(d$Time, d$DSD)[i,], ibs_preds_cph[i,], ibs_times, max(d$Time[i]))$ibs
        rsf = calcIBS(Surv(d$Time, d$DSD)[i,], ibs_preds_rsf[i,], ibs_times, max(d$Time[i]))$ibs
        km0 = calcIBS(Surv(d$Time, d$DSD)[i,], ibs_preds_km0[i,], ibs_times, max(d$Time[i]))$ibs
        c(gg - km0, gg2 - km0, cph - km0, rsf - km0, gg - rsf, gg2 - rsf, cph - rsf, gg - cph, gg2 - cph
}, R = 500)
ibsc_boots2_ci = t(sapply(1:length(ibsc_boots2$t0), function(i) boot.ci(ibsc_boots2, index = i, type = '
rownames(ibsc_boots2_ci) = c("gg-km0", "gg2-km0", "cph-km0", "rsf-km0", "gg-rsf", "gg2-rsf", "cph-rsf",
colnames(ibsc_boots2_ci) = c("level", "orderi1", "orderi2", "lci", "uci")
ibsc_boots2
```

```
##
## ORDINARY NONPARAMETRIC BOOTSTRAP
##
##
## Call:
## boot(data = data.val, statistic = function(d, i) {
##     gg = calcIBS(Surv(d$Time, d$DSD)[i, ], ibs_preds_gg[i, ],
##         ibs_times, max(d$Time[i]))$ibs
##     gg2 = calcIBS(Surv(d$Time, d$DSD)[i, ], ibs_preds_gg2[i,
##         ], ibs_times, max(d$Time[i]))$ibs
##     cph = calcIBS(Surv(d$Time, d$DSD)[i, ], ibs_preds_cph[i,
##         ], ibs_times, max(d$Time[i]))$ibs
##     rsf = calcIBS(Surv(d$Time, d$DSD)[i, ], ibs_preds_rsf[i,
##         ], ibs_times, max(d$Time[i]))$ibs
##     km0 = calcIBS(Surv(d$Time, d$DSD)[i, ], ibs_preds_km0[i,
##         ], ibs_times, max(d$Time[i]))$ibs
##     c(gg - km0, gg2 - km0, cph - km0, rsf - km0, gg - rsf, gg2 -
##         rsf, cph - rsf, gg - cph, gg2 - cph, gg - gg2)
## }, R = 500)
##
##
## Bootstrap Statistics :
##      original   bias    std. error
## t1*    8.3816 -0.39581      11.215
## t2*   11.1692 -0.62946      12.042
## t3*    8.1730 -0.81447      11.557
## t4*   -4.8194 -0.07519       4.942
## t5*   13.2010 -0.32062       7.411
## t6*   15.9885 -0.55427       7.973
## t7*   12.9923 -0.73928       7.861
## t8*    0.2086  0.41866       3.439
## t9*    2.9962  0.18501       3.412
## t10*  -2.7876  0.23365       2.616
```

```
ibsc_boots2_ci
```

```
##         level orderi1 orderi2      lci    uci
## gg-km0   0.95   19.84   493.8 -10.8484 33.776
## gg2-km0  0.95   17.42   492.4 -11.3453 35.196
## cph-km0  0.95   21.22   494.3 -13.2424 34.133
## rsf-km0  0.95   14.58   490.2 -14.1529  4.356
## gg-rsf   0.95   26.87   496.7   2.0387 31.854
## gg2-rsf  0.95   21.71   494.9   2.2010 33.379
## cph-rsf  0.95   28.75   497.0   0.3927 34.086
## gg-cph   0.95    9.08   483.6  -5.9993  6.931
## gg2-cph  0.95   22.70   495.2  -2.2832 11.342
## gg-gg2   0.95    4.05   472.6  -9.2566  1.352
```

All models perform equivalently on the validation set. Select the simplest: gg.

Final model fitting:

```
data.all = rbind(data[colnames(data.val)], data.val)
head(data.all)
```

```
##           Time  DSD  SexM AgeCent LocBody SizeCent    A2   A4
```

```
## NSWPCN_4   937 TRUE  TRUE     -16   FALSE       -1 FALSE TRUE
## NSWPCN_9   587 TRUE  TRUE       5   FALSE       10 FALSE TRUE
## NSWPCN_10  177 TRUE  TRUE      -9   FALSE       10 FALSE TRUE
## NSWPCN_13  247 TRUE FALSE     -19    TRUE       20 FALSE TRUE
## NSWPCN_17  316 TRUE FALSE     -23   FALSE       -5 FALSE TRUE
## NSWPCN_20  256 TRUE FALSE      -8   FALSE        0 FALSE TRUE

fit.final.gg = flexsurvreg(Surv(Time, DSD) ~ SexM + SizeCent + A2 + A4,
        anc = list(
                sigma = ~ SexM,
                Q = ~ SexM),
        data = data.all, dist = "gengamma")
fit.final.gg2 = flexsurvreg(Surv(Time, DSD) ~ SexM + SizeCent + A2 + A4 + I(SexM == FALSE & A2 == FALSE
    anc = list(
        sigma = ~ SexM,
        Q = ~ SexM),
    data = data.all, dist = "gengamma")
fit.final.cph = coxph(Surv(Time, DSD) ~ strata(SexM) + SizeCent + A2 + A4, data = data.all, x = TRUE, y
set.seed(20150111)
fit.final.rsf = rfsrc(Surv(Time, DSD) ~ SexM + AgeCent + LocBody + SizeCent + A2 + A4, data = data.all,
fit.final.km0 = survfit(Surv(Time, DSD) ~ 1, data.all)
saveRDS(list(gg = fit.final.gg, km0 = fit.final.km0, gg2 = fit.final.gg2, cph = fit.final.cph, rsf = fit
```

```
save.image("05_train_NSWPCN_2.rda")
```

8 Session information

```
sessionInfo()

## R version 3.1.1 (2014-07-10)
## Platform: x86_64-unknown-linux-gnu (64-bit)
##
## locale:
##  [1] LC_CTYPE=en_AU.UTF-8          LC_NUMERIC=C
##  [3] LC_TIME=en_AU.UTF-8           LC_COLLATE=en_AU.UTF-8
##  [5] LC_MONETARY=en_AU.UTF-8       LC_MESSAGES=en_AU.UTF-8
##  [7] LC_PAPER=en_AU.UTF-8          LC_NAME=en_AU.UTF-8
##  [9] LC_ADDRESS=en_AU.UTF-8        LC_TELEPHONE=en_AU.UTF-8
## [11] LC_MEASUREMENT=en_AU.UTF-8    LC_IDENTIFICATION=en_AU.UTF-8
##
## attached base packages:
## [1] parallel  methods   splines   stats     graphics  grDevices utils
## [8] datasets  base
##
## other attached packages:
##  [1] timeROC_0.2           timereg_1.8.6         mvtnorm_1.0-1
##  [4] pec_2.4.4             boot_1.3-13           MASS_7.3-35
##  [7] ggplot2_1.0.0         plyr_1.8.1            reshape2_1.4
## [10] randomForestSRC_1.5.5 flexsurv_0.5          glmulti_1.0.7
## [13] rJava_0.9-6           survival_2.37-7       tikzDevice_0.8.1
## [16] knitr_1.8
```

```
##
## loaded via a namespace (and not attached):
##  [1] codetools_0.2-9  colorspace_1.2-4 deSolve_1.11     digest_0.6.4
##  [5] evaluate_0.5.5   filehash_2.2-2   foreach_1.4.2    formatR_1.0
##  [9] grid_3.1.1       gtable_0.1.2     highr_0.4        iterators_1.0.7
## [13] labeling_0.3     lava_1.3         muhaz_1.2.6      munsell_0.4.2
## [17] prodlim_1.5.1    proto_0.3-10     Rcpp_0.11.3      scales_0.2.4
## [21] stringr_0.6.2    tools_3.1.1
```